Electronic Supplementary Material (ESI) for Environmental Science: Processes & Impacts.

The determination of two emerging perfluoroalkyl substances and related halogenated sulfonic acids and their significance for the drinking water supply chain

D Vughs[1], KA Baken[1,1], MML Dingemans[1], P de Voogt[1,2,*]
[1]KWR Watercycle Research Institute, Groningenhaven 7, 3430 BB Nieuwegein, The Netherlands
[2] IBED-FAME, University of Amsterdam, Science Park 904, Amsterdam, The Netherlands
*Corresponding author, pim.de.voogt@kwrwater.nl

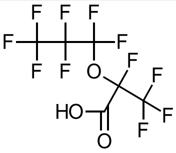
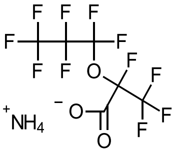
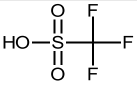
Supplementary information

Table of contents

---

[1] Current address: VITO N.V., Boeretang 200,2400 Mol, Belgium

Table SI-1. Technical names, structures, CAS numbers and full molecular names of emerging fluorinated compounds used in this study

Technical name	Structure	Mol weight	CAS	Full names	Note	Estimated Log D (ACD)	pKa
HFPO-DA		330	13252-13-6	2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoic acid / heptafluoropropoxypropanoic acid / perfluoro-2-(n-propoxy)propanoic acid	synonym: FRD-903; precursor of FRD-902; H-28307	1.34[a]	2.84 [c,e]
FRD-902		347	62037-80-3	ammonium 2,3,3,3-tetrafluoro-2-heptafluoropropoxy)propanoate	H-28308	2.58[b]	3.87[d,e] -0.77[f,e]
F_3-MSA		150	1493-13-6	trifluoromethanesulfonic acid; triflic acid		-3.88[a]	-3.43[a]

[a] Chemspider, estimated properties/ACD, log D at pH = 7.4

[b] ECHA dossier https://echa.europa.eu/registration-dossier/-/registered-dossier/2679/4/8 accessed 20-05-2019

[c] Murrell BS, Nixon WB (2008) Determination of the dissociation constant and uv-vis absorption spectra of H-28307. Easton, Maryland, USA: Wildlife International, Ltd

[d] Nixon WB, Lezotte FJ (2008) Determination of the dissociation constant of H-28308. Easton, Maryland, USA: Wildlife International, Ltd

[e] According to the ECHA (dossier HFPO-DA: SVHC support document - HFPO-DA and its salts/acyl halides. ECHA, Helsinki 2019), the reliability of these two pKa values cannot be sufficiently assigned.

[f] With the QSAR program MarvinSketch v16.10.24, a pKa value of -0.77 is estimated for this compound (taken from ECHA dossier HFPO-DA: SVHC support document - HFPO-DA and its salts/acyl halides. ECHA, Helsinki 2019)

Materials and methods

Chemicals

All solvents used were of analytical grade quality. Methanol (ultra gradient HPLC grade) and Ammonium hydroxide were obtained from Avantor Performance Materials B.V. (Deventer, the Netherlands). Formic acid (HPLC quality) and hydrochloric acid 30% suprapur were purchased from Sigma-Aldrich (Steinheim, Germany) and Merck (Darmstadt, Germany), respectively. The internal standards HFPO-DA-$^{13}C_3$ and PFBA-$^{13}C_3$ were obtained from Greyhound Chromatography and Allied Chemicals (Birkenhead, United Kingdom). The reference standards HFPO-DA and trifluoromethanesulfonic acid (F_3-MSA) were obtained from SynQuest Laboratories (Alachua, FL, USA) and Toronto Research Chemicals (Toronto, Canada), respectively. Ultrapure water was obtained by purifying demineralized water in an Elga Purelab Chorus ultrapure water system. (High Wycombe, United Kingdom). Stock solutions of reference and internal standards were prepared in methanol at a concentration of 100 and 5 mg/L, respectively. Stock solutions were stored at -25 ^{o}C.

For FOSA[2] the internal standard $^{13}C_8$-FOSA was obtained from Wellington laboratories (Ontario, Canada).

Sample pre-treatment F_3-MSA and HFPO-DA

All materials used for sample storage and handling were from high quality plastics such as polypropylene, and no PTFE materials were used. Aliquots of 500 mL were acidified to pH 4 using hydrochloric acid, to which 50 ng/L of HFPO-DA-$^{13}C_3$ internal standard was added. Then the samples were loaded onto a SPE cartridge (OASIS WAX, 150 mg, 6 cc) obtained from Waters (Etten-Leur, Netherlands) and subsequently washed with 5 mL ultrapure water (pH 4). The SPE cartridge was dried for 1 hour by air and elution was performed with 10 mL of methanol containing 0.25% ammonium hydroxide. The eluate was evaporated using a Barkey optocontrol (Leopoldshöhe, Germany) with a gentle nitrogen stream at circa 75 °C (block temperature at 300 °C) until a volume of 250 µL was reached. Then 750 µL ultrapure water was added to the extract, containing PFBA-$^{13}C_3$ internal standard at a concentration of 16.67 µg/L. The extracted was filtered using a 0.2 µm Phenomenex Phenex regenerated cellulose filter (Utrecht, Netherlands) and was transferred to a 1.8 mL autosampler vial for LC-Orbitrap-MS analysis.

Sample pre-treatment for FOSA

Aliquots of 200 ml of sample material were taken by weight and spiked with internal standard and, if necessary, with FOSA (e.g. validation and control samples) and centrifuged (2000 RPM) for at least 20 minutes. Samples were then loaded on a solid phase extraction (SPE) cartridge containing 60 mg Oasis WAX sorbent (Waters Chromatography B.V., Etten-Leur, the Netherlands). The cartridge was subsequently washed with 25 mM ammonium acetate buffer (pH 4) and eluted with 2x 550 µL methanol containing 0.1% ammonium hydroxide. Extracts were filtered (0.20 µm, polypropylene, Filter-Bio, Jiangsu, China), stored at -20 °C, and prior to analysis, diluted twice with an aqueous solution of 0.1% acetic acid.

Liquid chromatography and mass spectrometry conditions F_3-MSA

Settings UHPLC, autosampler and column oven (Vanquish; Thermo Fisher Scientific, Bremen):

- Column: Obelisc N, 2.1 x 150 mm, 5 µm (SIELC Technologies, IL, USA)
- Mobile phase A: ultrapure water +10 mM ammonium acetate + 0.05% formic acid
- Mobile phase B: Methanol + 10 mM ammonium acetate + 0.05% formic acid
- Gradient: linear from 20% to 90% B in 7 min. Held at 90% B for 7 min. Then returned to initial conditions in 1min and held for 6 min.
- Flow: 300 µL/min
- Injection volume: 10 µL
- Column oven: 25 °C

Settings mass spectrometer (Orbitrap Fusion; Thermo Fisher Scientific, Bremen):

- Resolution MS1: 120 000 FWHM

---

[2] FOSA was included as a target analyte in the sample campaign. None of the water samples was found to contain FOSA at levels above the LOQ. The analytical methodology used for FOSA was based on a method developed by Eschauzier et al. Environ. Sci. Technol., 2012, 46, 1708-1715.

- Mass range full scan: 120-500 m/z
- Mass accuracy < 2 ppm
- Source: electrospray (ESI)
- Ionisation: negative mode
- Vaporizer: 350 °C
- Ion transfer tube: 300 °C
- Spray voltage: 2500 volt
- Sheat gas: 45 arbitrary units
- Auxiliary gas: 5 arbitrary units
- Sweep gas: 5 arbitrary units
- RF lens: 50%
- Resolution MS2: 15 000 FWHM
- Massrange MS2 scan: 50-160 m/z
- Precursor MS2: 148.95
- HCD: 50%
- Data dependent scans per cycle: 8
- Mass range data dependent MS2 scan: 120-500 m/z
- HCD data dependent scan: 35%

Liquid chromatography and mass spectrometry conditions HFPO-DA

Settings UHPLC , autosampler and column oven (Vanquish; Thermo Fisher Scientific, Bremen):
- Column: Xbridge BEH C18 XP 2.1 x 150 mm, 2.5 µm (Waters, Etten-Leur, Netherlands)
- Mobile phase A: ultrapure water +5 mM ammonium acetate
- Mobile phase B: Methanol + 5 mM ammonium acetate
- Gradient: linear from 25% to 100% B in 10 min. Held at 100% B for 4 min. Then returned to initial conditions in 0.5 min and held for 3.5min.
- Flow: 250 µL/min
- Injection volume: 50 µL
- Column oven: 25 °C

Settings mass spectrometer (Orbitrap Fusion; Thermo Fisher Scientific, Bremen):
- Resolution MS1: 120 000 FWHM
- Mass range full scan: 150-500 m/z
- Mass accuracy < 2 ppm
- Source: electrospray (ESI)
- Ionisation: negative mode
- Vaporizer: 250 °C
- Ion transfer tube: 200°C
- Spray voltage: 2500 volt
- Sheat gas: 50 arbitrary units
- Auxiliary gas: 10 arbitrary units
- Sweep gas: 5 arbitrary units
- RF lens: 30%
- Resolution MS2: 15 000 FWHM
- Massrange MS2 scan: 100-300 m/z

- Precursor MS2: 284.97
- HCD: 30%

Liquid chromatography and mass spectrometry conditions FOSA

Quantitative analysis was performed with liquid chromatography (Prominence XR, Shimadzu, Den Bosch, the Netherlands) coupled to a tandem mass spectrometer (4000 Q-TRAP, AB-Sciex (Applied Biosystems, Toronto, Canada).

HPLC settings:

- Column: Kinetex C18 Evo column (100 mm x 2.1 mm ID; 2.6 µm) with C18 Evo guard column (Phenomenex, Utrecht, the Netherlands)
- Eluent A: 2 mM ammonium acetate in ultrapure water
- Eluent B: 2 mM ammonium acetate in methanol
- Gradient: linear from 20% to 65% B in 2 min, then increased to 100% B in 7min. Held at 100% B for 1 min. Then returned to initial conditions in 1 min and was held for 5 min.
- Flow: 300 µL/min
- Injection volume: 20 µL (standards) or 50 µL (samples)
- Retention time 3.4

Mass spectrometry settings:

- Source: Electrospray Ionisation (ESI)
- MS polarity: Negative
- MRM time window: 60 sec
- Total dwell time: 0.5 sec
- Transition* (FOSA): 498 -> 78
- Transition* ($^{13}C_8$ FOSA): 498 -> 78

** A second transition was also detected for both analytes (498 -> 169 and 506 ->172), but found inadequate due to low sensitivity.*

Table SI-2. Sample description sampling campaign

Sample description and origin	**Matrix**	**Sampling date**
Keizersveer	Surface water	12-09-2017
Biesboschbekkens	Surface water	12-09-2017
Purified water Kralingen	Drinking water	11-09-2017
Raw groundwater Jeugddorp (Dordrecht)	Groundwater	11-09-2017
Purified groundwater Baanhoek	Drinking water	11-09-2017
Purified water Baanhoek	Drinking water	11-09-2017
Heel, Intake Lateraalkanaal	Surface water	12-09-2017

Sample description and origin	Matrix	Sampling date
Heel, Reservoir De lange Vlieter	Surface water	13-09-2017
Heel, raw water Galgenberg	River bank filtrate	12-09-2017
Heel, raw water De Reut en Langven	River bank filtrate	12-09-2017
Heel, purified water Helden	Drinking water	12-09-2017
Vessem raw water	Groundwater	12-09-2017
Vessem purified water	Drinking water	12-09-2017
Waalwijk raw water	Groundwater	12-09-2017
Waalwijk purified water (Vlijmen)	Drinking water	12-09-2017
Intake Brakel	Surface water	11-09-2017
Dune filtrate Meijendell	Dune filtrate	12-09-2017
Dune filtrate Berkheide	Dune filtrate	12-09-2017
Tap water Scheveningen	Drinking water	12-09-2017
Lake Ijsselmeer water	Surface water	11-09-2017
Effluent WPJ	Surface water	12-09-2017
Influent UV/H_2O_2-AKF	Surface water	12-09-2017
Influent dune (effluent UV/H_2O_2)	Surface water	12-09-2017
Effluent dunes	Dune filtrate	11-09-2017
Tap water Bergen	Drinking water	11-09-2017
Grondwater Laren	Groundwater	11-09-2017
Raw water intake WCB (Lekkanaal)	Surface water	11-09-2017
Raw water Bethunepolder	Surface water	12-09-2017
Raw water (dune filtrate)	Surface water	11-09-2017
Purified water Leiduin	Drinking water	11-09-2017
Purified water Weesperkarspel	Drinking water	11-09-2017
Vechterweerd raw water	River bank filtrate	14-09-2017
Vechterweerd purified water	Drinking water	14-09-2017
Engelse Werk purified water	Drinking water	13-09-2017
Buren purified	Drinking water	12-09-2017
Doorn purified	Drinking water	13-09-2017
Soestduinen purified	Drinking water	14-09-2017
Edese Bos purified	Drinking water	14-09-2017
Dinxperlo purified	Drinking water	13-09-2017
Lekkerkerk-Tiendweg raw water	River bank filtrate	14-09-2017
Lekkerkerk-Tiendweg purified water	Drinking water	14-09-2017
RO Feed	River bank filtrate	14-09-2017
RO Permeate	River bank filtrate	14-09-2017
RO Concentrate	River bank filtrate	15-09-2017
Drentse Aa	Surface water	11-09-2017
WMD Purified water	Drinking water	11-09-2017
Noordbargeres raw water	Groundwater	11-09-2017
Noordbargeres purified water	Drinking water	11-09-2017
Blankaart raw water	Surface water	13-09-2017
Blankaart purified water	Drinking water	13-09-2017
WPC Zele raw water	Surface water	12-09-2017
WPC Zele purified water	Drinking water	12-09-2017

Sample description and origin	**Matrix**	**Sampling date**
Lobith (river Rhine)	Surface water	14-09-2017

Quality assurance

Absolute recovery

The absolute recovery was determined for F_3-MSA (50 ng/L; n=2) and HFPO-DA (20 ng/L; n=2), in spiked surface water, yielding a recovery of 93.5% and 89.16% respectively. No major loss of analytes was observed, showing that the sample pre-treatment method developed is satisfactory. Subsequently the matrix effects in surface water were determined. No matrix effects were observed for HFPO-DA, but moderate ion suppression (circa 25%) was observed for F_3-MSA in surface water. Because no isotope labeled internal standard is available for F_3-MSA, for which now the surrogate standard PFBA-$^{13}C_3$ is used, it is currently not possible to correct the results obtained for the observed ion suppression.

Sample storage stability

Perfluorinated compounds are known to be persistent, therefore it is unlikely that degradation would occur during the storage time study. However, it is also known that PFAS can adsorb to surfaces including sample bottle walls. In order to determine if adsorption really is an issue for F_3-MSA and HFPO-DA, a stability study was performed for drinking- and surface water in polypropylene sample bottles. After spiking the samples with 200 ng/L of HFPO-DA and 1 µg/L of F_3-MSA, the samples were stored at 1-5^{o}C for 21 d. A number of blank samples were also prepared, in order to demonstrate that the sample bottles do not contain any PFAS. After 21 d new drinking- and surface water samples were prepared containing 200 ng/L of HFPO-DA and 1 µg/L of F_3-MSA. The stability was determined by analysing the "0 day" and "21 day" samples. The results of the stability study are shown in table S-3.

Table SI-3. Stability study results for F_3-MSA and HFPO-DA in drinking and surface water after 21 days (N=7)

	Drinking water					**Surface water**				
	0 days		**21 days**		**difference**	**0 days**		**21 days**		**difference**
	conc (µg/L)	**RSD (%)**	**conc (µg/L)**	**RSD (%)**	**(%)**	**conc (µg/L)**	**RSD (%)**	**conc (µg/L)**	**RSD (%)**	**(%)**
F_3-MSA	1.12	3.5	1.16	2.0	3.2	0.967	4.1	0.978	4.3	1.2
HFPO-DA	0.189	3.6	0.190	2.7	0.7	0.187	2.6	0.190	2.1	1.1

No degradation or adsorption was observed for F_3-MSA and HFPO-DA, neither in drinking water nor in surface water after 21 d. It can be concluded that the samples can be safely stored for 21 d at 1-5^{o}C prior to sample analysis. Furthermore, no PFAS were detected in the blank samples, showing that the polypropylene sample bottles are applicable for the sampling campaign.

Method validation

The two methods developed for F_3-MSA and HFPO-DA were validated for drinking and surface water. First the instrumental repeatability was determined using a reference standard of 20 ng/L of HPFO-DA and 50 ng/L F_3-MSA, for which an instrumental repeatability (n=8) was found of 0.4% and 2.0%, respectively. The limit of detection (LOD), limit of quantification (LOQ), repeatability (RSD) and SPE recovery were determined in drinking and surface water. The validation results are shown in tables S-4 and S-5 for F_3-MSA and HFPO-DA, respectively.

Table SI-4. Validation results of F_3-MSA in drinking- and surface water (n=8)

Matrix	**LOD ng/L**	**LOQ ng/L**	**Repeatability (%)**		**SPE recovery (10 ng/L) (%)**
			1 ng/L	**50 ng/L**	
Drinking water	0.242	1.0	6.0	7.1	118.4
Surface water	*	1.0	4.8**	6.9	75.8

** = Because there was no surface water available in which low concentration of F_3-MSA (< 2 ng/L) were present, it was not possible to determine the LOD in surface water. The LOD of drinking water is therefore used as reference*
*** = Determined at 10 ng/L.*

Table SI-5. Validation results of HFPO-Da in drinking- and surface water (n=8)

Matrix	**LOD ng/L**	**LOQ ng/L**	**Repeatability (%)**		**SPE Recovery (0.2 ng/L) (%)**
			0.2 ng/L	**20 ng/L**	
Drinking water	0.011	0.20	1.8	1.9	102.6
Surface water	0.049	0.20	6.5	1.0	99.2

Satisfactory LOD and LOQ results were obtained for F_3-MSA and HFPO-DA in drinking- and surface water. In surface water, for F_3-MSA it was not possible to determine a proper LOD, due to the presence of low concentrations of this compound in every surface water sample that was tested. Therefore the LOD of drinking water was used as a reference and to calculate a LOQ. A practical quantification limit was used, which was calculated by multiplying the LOD by 3.3x and rounding the results upwards, in order to obtain the same LOQ for drinking and surface water. The LOQ was determined at 1.0 and 0.2 ng/L for F_3-MSA and HFPO-DA, respectively. Recoveries in drinking- and surface water are between 75 and 120%. The obtained recovery of 75.8% for F_3-MSA is not due to the loss of analyte, rather a result of matrix effects. The repeatability for both compounds is ≤7.1%.

Table SI-6. Results sampling campaign: concentrations of F_3-MSA AND HFPO-DA

Sample description	**Matrix**	**Concentration**	
		F_3-MSA ng/L	HFPO-DA ng/L
Evides			
Keizersveer	Surface water	28	5.8
Afgeleverd water Biesboschbekkens	Surface water	24	10
Reinwater Kralingen	Drinking water	21	8.9
Ruw grondwater Jeugddorp (Dordrecht)	Groundwater	< 1.0	< 0.20
Reinwater grondwaterzuivering Baanhoek	Drinking water	22	10
Reinwater Baanhoek (dw uit ow en gw)	Drinking water	22	9.8
WML			
Heel, Innamewerk Lateraalkanaal	Surface water	32	0.60
Heel, Spaarbekken De lange Vlieter	Surface water	150	0.84
Heel, Gezamenlijk ruwwater Galgenberg	River bank filtrate	135	0.40
Heel, Gezamenlijk ruwwater De Reut en Langven	River bank filtrate	230	0.22
Heel, Reinwaterlevering Helden	Drinking water	165	0.34
Brabant Water			
Vessem ruwwater	Groundwater	< 1.0	< 0.20
Vessem reinwater	Drinking water	< 1.0	< 0.20
Waalwijk ruwwater	Groundwater	< 1.0	< 0.20
Waalwijk reinwater (vlijmen)	Drinking water	< 1.0	< 0.20
Dunea			
Inname Lagedrukpompstation Brakel	Surface water	29	9.7
Duinfiltraat Meijendell	Dune filtrate	24	6.7
Duinfiltraat Berkheide	Dune filtrate	45	5.0
reinwater Scheveningen	Drinking water	43	4.6
PWN			
IJsselmeerwater	Surface water	49	0.28
Effluent WPJ	Surface water	46	0.30
Toevoer UV/H2O2-AKF	Surface water	39	0.22
Toevoer duin (na passage UV/H2O2)	Surface water	39	0.22
Na duinpassage	Dune filtrate	45	0.22
Drinkwater Bergen	Drinking water	27	0.20
Grondwater secundair Zuid in Laren	Groundwater	< 1.0	< 0.20
Waternet			
Ruw water inlaat WCB (Lekkanaal)	Surface water	35	< 0.20
Bethunepolder	Surface water	8.5	0.53
Ruwwater (duinfiltraat)	Surface water	52	0.20
Reinwater Leiduin	Drinking water	50	0.28
Reinwater Weesperkarspel	Drinking water	10	0.28
Vitens			
Vechterweerd ruw	River bank filtrate	7.4	< 0.20
Vechterweerd rein	Drinking water	4.9	< 0.20
Pb. Engelse Werk rein	Drinking water	21	< 0.20
Pb. Buren rein	Drinking water	< 1.0	< 0.20
Pb. Doorn rein	Drinking water	< 1.0	< 0.20
Pb. Soestduinen rein	Drinking water	< 1.0	< 0.20
Pb. Edese Bos rein	Drinking water	< 1.0	< 0.20
Pb. Dinxperlo rein	Drinking water	20	< 0.20
Oasen			
Lekkerkerk-Tiendweg ruw	River bank filtrate	62	59

Sample description	**Matrix**	**Concentration**	
		F_3-MSA	HFPO-DA
		ng/L	ng/L
Lekkerkerk-Tiendweg rein	Drinking water	32	28
RO Feed	River bank filtrate	59	5.3
RO Permeaat	River bank filtrate	< 1.0	< 0.20
RO Concentraat	River bank filtrate	165	28
Waterbedrijf Groningen			
Drentse Aa	Surface water	1.5	0.28
reinwater	Drinking water	1.1	< 0.20
WMD			
Noordbargeres ruw	Groundwater	< 1.0	< 0.20
Noordbargeres rein	Drinking water	< 1.0	< 0.20
De Watergroep			
WPC Blankaart ruwwater	Surface water	82	0.20
WPC Blankaart reinwater	Drinking water	85	0.23
WPC Zele ruwwater	Surface water	4.4	< 0.20
WPC Zele reinwater	Drinking water	4.5	< 0.20
Overige			
Lobith	Surface water	49	< 0.20

Table SI-7. Halogenated MSAs selected for suspect screening

Name	**Abbreviation**	**Formula**	**Accurate mass [M-H]**
Chloromethane sulfonic acid	Cl-MSA	CH_3ClSO_3	128.9419
Dichloromethane sulfonic acid	Cl_2-MSA	$CH_2Cl_2SO_3$	162.9029
Trichloromethane sulfonic acid	Cl_3-MSA	$CHCl_3SO_3$	196.8639
Bromomethane sulfonic acid	Br-MSA	CH_3BrSO_3	172.8914
Dibromomethane sulfonic acid	Br_2-MSA	$CH_2Br_2SO_3$	250.8019
Bromochloromethane sulfonic acid	BrCl-MSA	$CH_2BrClSO_3$	206.8524

Table SI-8. Results suspect screening of Cl-MSA, Cl_2-MSA, Cl_3-MSA, Br-MSA, Br_2-MSA and BrCl-MSA

Sample description	**Matrix**	**n**	**Cl-MSA** (ng/L)*	**Cl_2-MSA** (ng/L)*	**Cl_3-MSA** (ng/L)*	**Br-MSA** (ng/L)*	**Br_2-MSA** (ng/L)*	**BrCl-MSA** (ng/L)*
Reinwater Kralingen	DW	1	n.d.	5.2	1.4	n.d.	n.d.	n.d.
Reinwater grondwaterzuivering Baanhoek	DW	2	n.d.	11	1.4	n.d.	n.d.	1.0
Reinwater Baanhoek (dw uit ow en gw)	DW	3	n.d.	13	1.5	n.d.	n.d.	1.2
Heel, Reinwaterlevering Helden	DW	4	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Vessem reinwater	DW	5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Waalwijk reinwater (vlijmen)	DW	6	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Reinwater Scheveningen	DW	7	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Drinkwater Bergen	DW	8	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Reinwater Leiduin	DW	9	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Reinwater Weesperkarspel	DW	10	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Vechterweerd rein	DW	11	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Pb. Engelse Werk rein	DW	12	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Pb. Buren rein	DW	13	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Pb. Doorn rein	DW	14	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Pb. Soestduinen rein	DW	15	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Pb. Edese Bos rein	DW	16	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Pb. Dinxperlo rein	DW	17	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Lekkerkerk-Tiendweg rein	DW	18	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Reinwater (WBG)	DW	19	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

Sample description	**Matrix**	**n**	**Cl-MSA** (ng/L)*	**Cl_2-MSA** (ng/L)*	**Cl_3-MSA** (ng/L)*	**Br-MSA** (ng/L)*	**Br_2-MSA** (ng/L)*	**BrCl-MSA** (ng/L)*
Noordbargeres rein	DW	20	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
WPC Blankaart reinwater	DW	21	n.d.	75	4.0	n.d.	65	108
WPC Zele reinwater	DW	22	n.d.	148	n.d.	n.d.	3.7	52
ruw grondwater Jeugddorp (Dordrecht)	GW	1	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Vessem ruwwater	GW	2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Waalwijk ruwwater	GW	3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Grondwater secundair Zuid in Laren	GW	4	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Noordbargeres ruw	GW	5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Keizersveer	SW	1	n.d.	12	3.1	n.d.	1.2	n.d.
Afgeleverd water Biesboschbekkens	SW	2	n.d.	33	1.8	1.1	11	17
Heel, Innamewerk Lateraalkanaal	SW	3	n.d.	10	1.6	n.d.	n.d.	n.d.
Heel, Spaarbekken De lange Vlieter	SW	4	n.d.	3.4	n.d.	n.d.	n.d.	n.d.
Inname Lagedrukpompstation Brakel	SW	5	n.d.	7.5	2.2	n.d.	2.1	n.d.
IJsselmeerwater	SW	6	n.d.	1.4	n.d.	n.d.	1.3	n.d.
Ruw water inlaat WCB (Lekkanaal)	SW	7	n.d.	3.3	1.2	n.d.	n.d.	n.d.
Bethunepolder	SW	8	n.d.	0.9	n.d.	n.d.	n.d.	n.d.
ruwwater (duinfiltraat)	SW	9	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Drentse Aa	SW	10	n.d.	1.7	n.d.	n.d.	n.d.	n.d.
WPC Blankaart ruwwater	SW	11	n.d.	32	3.7	n.d.	10	19
WPC Zele ruwwater	SW	12	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Lobith	SW	13	n.d.	3.8	1.0	n.d.	n.d.	n.d.
Heel, gezamenlijk ruwwater Galgenberg	RBF/DF	1	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Heel, gezamenlijk ruwwater De Reut en Langven	RBF/DF	2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Vechterweerd ruw	RBF/DF	3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Lekkerkerk-Tiendweg ruw	RBF/DF	4	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Duinfiltraat Meijendell	RBF/DF	5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Duinfiltraat Berkheide	RBF/DF	6	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Na duinpassage	RBF/DF	7	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
RO Feed	PW	1	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
RO Permeaat	PW	2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
RO Concentraat	PW	3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Effluent WPJ	PW	4	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Toevoer UV/H2O2-AKF	PW	5	n.d.	1.9	n.d.	n.d.	n.d.	n.d.
Toevoer duin (na passage UV/H2O2)	PW	6	n.d.	1.2	n.d.	n.d.	1.1	n.d.

** = F_3-MSA equivalents*

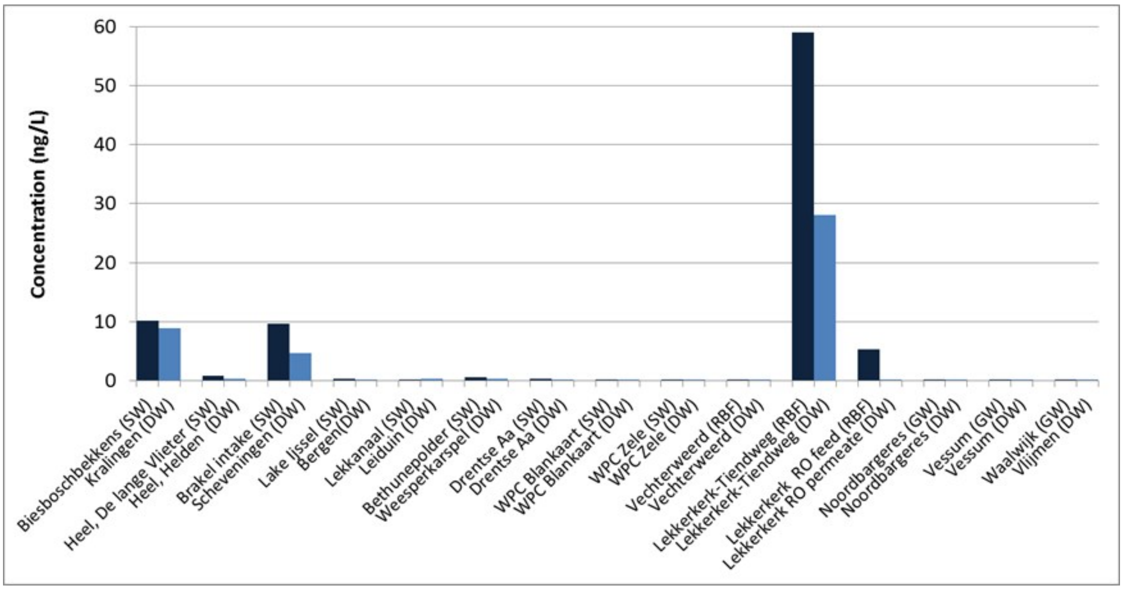


Figure SI-1: Concentrations of HFPO-DA detected in raw water and the corresponding drinking water from several locations. Side-to-side bars reflect corresponding water works (i.e. water from same source before and after treatment). Raw water is dark blue, drinking water light blue. SW, surface water; DW, drinking water; RBF, river bank filtrate; GW, groundwater; RO, reverse osmosis

Toxicological evaluation

HFPO-DA

A provisional oral Tolerable Daily Intake (TDI) level for FRD-902 was derived by RIVM[1] from the No Observed Adverse Effect Level (NOAEL) observed in a chronic rat study (submitted by REACH registration applicant): 0.1 mg/kg body weight/day based on an increase in albumin and the albumin/globulin ratio (which indicates possible immunotoxic effects) at higher doses. Using an extrapolation factor for interspecies differences in kinetics (standard value of 4), an additional factor for potential differences in kinetics (a worst-case value of 66 due to lack of data), a factor for differences between species (1.8) and a factor for differences between humans (standard value of 10), a TDI of 21 ng/kg/day was calculated. Additional information on the bioaccumulation of FRD-902 in humans would allow derivation of an improved exposure limit[2]. In addition, potential carcinogenic effects have not been incorporated in this TDI level.

The provisional TDI of 21 ng/kg bw/day was converted to a drinking water guideline value by assuming the WHO default of 20% allocation of the total exposure to drinking-water, an adult body weight of 70 kg and a standard drinking-water consumption of 2L per day. This resulted in a provisional drinking water guideline value for FRD-902 of 0.15 µg/L. This value also applies to HFPO-DA and the anion, and to the sum of the three substances.

During the fluoropolymer production process, HFPO-DA, and possibly some FRD-902, is released to air and HFPO-DA and FRD-902 are emitted to wastewater. The estimated concentration of HFPO-DA in air is 20 ng/m^3 for the nearest populated areas of the fluoropolymer manufacturing site in The Netherlands[2]. At a default adult inhalation volume of 20 m^3/day, the inhalatory exposure to HFPO-DA would amount to 400 ng/day (5.7 ng/kg bw/day) in this region.

Concentrations of HFPO-DA up to 0.02 µg/L have been reported in drinking water produced from surface water downstream from the plant. Since both substances will be present in water in the anion form, this concentration reflects the emission of both HFPO-DA and FRD-902 to surface water. The summed exposure through drinking water will thus be 40 ng/day (0.6 ng/kg bw/day). No information is currently available regarding levels of HFPO-DA and FRD-902 in food[2]. Exposure of consumers to HFPO-DA via food contact materials, for which quantitative information has not been identified, is expected to be negligible[3]. However, since these substances are persistent, it is likely that they also end up in the food chain. The allocation factor of 20% applied to derive the provisional drinking water guideline value thus seems appropriate.

F_3-MSA

No toxicity studies and health risk assessments for F_3-MSA were retrieved from the consulted authorities and databases. Three negative study results for genotoxicity (Ames mutagenicity test, *in vitro* chromosome aberration, and mammalian gene mutation assay) and no structural alerts for genotoxicity are reported in the OECD QSAR Toolbox. F_3-MSA was inactive in >50 ToxCast *in vitro* assays on various cellular processes[4] and 145 *in vitro* bioassays tests reported by the U.S. EPA Chemistry Dashboard. Literature search did not yield additional toxicological information on F_3-MSA. The derived pGLV is based on a short term repeated dose oral exposure study in rats (OECD TG-407) that is reported in the REACH registration dossier for F_3-MSA (NOAEL: 1000 mg/kg bw)[5]. Effects observed at lower doses in the study described in the REACH dossier for F_3-MSA (see Toxicological information, Repeated dose toxicity) are local effects in the rat forestomach, in which food is stored for hours before emptying into the stomach for further digestion. These effects are not transposable to humans as there is no forestomach in human physiology.

Exposure information on F_3-MSA was not found in the consulted information sources and literature. Although the substance has been predicted not to be a PBT chemical[6,7], its widespread detection in the aquatic environment[8] suggests human exposure through other routes than drinking water as well.

Table SI-9 Structural alerts and Cramer classification indicated by OECD QSAR Toolbox (V3.4.0.17) profiling

Technical name	CAS	Structural alerts	Cramer class
HPFO-DA	13252-13-6	DNA Binding by OASIS v.1.4: AN2 >> Schiff base formation by aldehyde formed after metabolic activation >> Geminal Polyhaloalkane Derivatives Radical >> Radical mechanism via ROS formation (indirect) >> Geminal Polyhaloalkane Derivatives SN1 >> Carbenium ion formation >> Alpha-Haloethers SN2 >> Acylation involving a leaving group after metabolic activation >> Geminal Polyhaloalkane Derivatives SN2 >> Nucleophilic substitution at sp3 carbon atom after thiol (glutathione) conjugation >> Geminal Polyhaloalkane Derivatives SN2 >> SN2 at sp3-carbon atom >> Alpha-Haloethers In vivo mutagenicity (Micronucleus) alerts by ISS: H-acceptor-path3-H-acceptor	High (Class III)
FRD-902	62037-80-3	DNA Binding by OASIS v.1.4: AN2 >> Schiff base formation by aldehyde formed after metabolic activation >> Geminal Polyhaloalkane Derivatives Radical >> Radical mechanism via ROS formation (indirect) >> Geminal Polyhaloalkane Derivatives SN1 >> Carbenium ion formation >> Alpha-Haloethers SN2 >> Acylation involving a leaving group after metabolic activation >> Geminal Polyhaloalkane Derivatives SN2 >> Nucleophilic substitution at sp3 carbon atom after thiol (glutathione) conjugation >> Geminal Polyhaloalkane Derivatives SN2 >> SN2 at sp3-carbon atom >> Alpha-Haloethers In vivo mutagenicity (Micronucleus) alerts by ISS: H-acceptor-path3-H-acceptor	High (Class III)
F_3-MSA	1493-13-6	No structural alerts	High (Class III)

References

---

[1] Janssen P (2016) Derivation of a lifetime drinking-water guideline value for 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoic acid (FRD-902). Advice of 17 November 2016 to Ministry of Infrastructure and Environment. Project M/300007/16/PF. Bilthoven, RIVM.

[2] Beekman M, Zweers P, Muller A, de Vries W, Janssen P, Zeilmaker M (2016) Evaluation of substances used in the GenX technology by Chemours, Dordrecht. RIVM Report 2016-0174, Bilthoven.

---

[3] EFSA (2009) Scientific Opinion of the Panel on food contact materials, enzymes, flavourings and processing aids (CEF) on 24th list of substances for food contact materials. The EFSA Journal, 2009: p. 1157-116

[4] *ToxCast database* 2017; Available from: https://actor.epa.gov/dashboard/

[5] *ECHA (2017) Trifluoromethanesulphonic acid Registration Dossier*. Available from: https://echa.europa.eu/registration-dossier/-/registered-dossier/5311/1.

[6] *Categorization Results from the Canadian Domestic Substance List*. 2017; Available from: http://webnet.oecd.org/ccrweb/ChemicalDetails.aspx?ChemicalID=4F8DF918-8830-4839-8A04-96CF211AEBDF.

[7] Rayne S, Forest K (2016) Estimated pKa values for the environmentally relevant C1 through C8 perfluorinated sulfonic acid isomers. J. Environ, Sci. Health, Part A, 51, 1018-1023. https://doi.org/10.1080/10934529.2016.1198191

[8] D Zahn, T Froemel, TP Knepper (2016) Halogenated methanesulfonic acids: A new class of organic micropollutants in the water cycle, Water Res. 101, 292-299.