September 25th, 2023

Non-confidential comments for Annex XV restriction report: Derogated PFAS subgroups

Dear Madame or Sir,

We welcome the opportunity to provide input on the restriction proposal regarding per- and polyfluoroalkyl substances (PFAS). This submission was prepared by Dr. Juliane Glüge (ETH Zürich) with input of members of the Global PFAS Science Panel (GPSP). The GPSP is a collaborative partnership among academic researchers, regulatory scientists and policy analysts dedicated to enhancing understanding of PFAS and to protecting human and environmental health from potentially adverse effects associated with PFAS through better informed decision-making. The scientific work of the GPSP in the last five years has considerably advanced the understanding of PFAS and the GPSP would like to take the opportunity to also give input to the PFAS restriction proposal.

We see the restriction proposal as a very important initiative and good way forward to counteract the ongoing emissions of PFAS in Europe (and in part even worldwide). Our submissions should therefore be seen as a support of the restriction proposal to make it even stronger and more fully complete. The current submission is on the derogated PFAS subgroups.

In the following we present information that show that some of the derogated substances that include aromatic rings do not readily biodegrade and that it is very likely that it is the CF_3-O group attached to the aromatic ring that hinders the biodegradation in these ready-biodegradation tests. We also comment on the submitted comment 4418 and the points raised there.

1) Substances registered under REACH that are not ready-biodegradable

In the PFAS restriction proposal, PFAS are defined as substances that contain at least one fully fluorinated methyl (CF_3-) or methylene (-CF_2-) carbon atom, without any H/Cl/Br/I attached to it. Excluded are substances with CF_3-X or X-CF_2-X', where X = -OR or -NRR' and X' = methyl (-CH_3), methylene (-CH_2-), an aromatic group, a carbonyl group (-C(O)-), -OR'', -SR'' or –NR''R'''; and where R/R'/R''/R''' is a hydrogen (-H), methyl (-CH_3), methylene (-CH_2-), an aromatic group or a carbonyl group (-C(O)-).

The reasoning according to the dossier is that the excluded substances are expected to be fully degradable and that they cannot form persistent PFAS arrowheads. For aromatic compounds, e.g., Annex B of the restriction proposal describes some interim results of a study that tested the degradation of 4-(trifluoromethoxy)benzoic acid in soil. According to the study, 57% to 58% mineralization occurred after 14 days in soil. We question the results of this study here, as the data available in the REACH registration dossiers are not in line with these data.

We have shown in our recent publication (Rudin et al. 2023) that there are 26 substances that are registered under REACH either with a full registration, as NONS or as intermediates that fulfill the OECD definition for PFAS (OECD 2021) but are excluded from the PFAS restriction proposal. The substances are shown in the Supporting Information of Rudin et al. (2023) and are listed here in Table 1. Interestingly, all CF_3-O or CF_2-O groups that are included in these molecules are attached to aromatic rings.

Table 1: Substances that are PFAS according to the OECD definition but that are excluded from the scope of the Broad PFAS Restriction Proposal

EC number	SMILES	Ready-biodegradation	Conclusion in Rudin et al. (2023)
Full registrations			
695-906-1	CCCC[C@H]1CO[C@@H](OC1)C1=CC(F)=C(C=C1)C1=CC(F)=C(C(F)=C1)C(F)(F)OC1=CC(F)=C(F)C(F)=C1	0% degrad.	vPvB
616-651-4	CCC1CCC(OC1)C1=CC=C(C=C1)C1=CC(F)=C(C(F)=C1)C(F)(F)OC1=CC(F)=C(F)C(F)=C1	0% degrad.	vPvB
606-647-0	CCC[C@H]1CC[C@@H](CC1)[C@H]1CC[C@@H](CC1)C(F)(F)OC1=CC(F)=C(F)C(F)=C1	no data available	vPvB
603-782-7	CCC[C@H]1CC[C@@H](CC1)[C@H]1CC[C@@H](CC1)C1=CC=C(OC(F)(F)F)C=C1	0% degrad.	vPvB
610-847-3	CCC[C@H]1CC[C@@H](CC1)C1=CC=C(C=C1)C1=CC=C(C(F)=C1)C1=CC(F)=C(OC(F)(F)F)C(F)=C1	0% degrad.	vPvB
918-322-3	CCC[C@H]1CC[C@@H](CC1)C1CCC(=CC1)C1=CC=C(OC(F)(F)F)C=C1	7% degrad.	vPvB
608-462-0	CCCC1=CC=C(C=C1)C1=CC(F)=C(C(F)=C1)C(F)(F)OC1=CC(F)=C(F)C(F)=C1	0% degrad.	vPvB
619-490-8	CCCC1=CC=C(C=C1)C1=CC=C(C(F)=C1)C1=CC(F)=C(C(F)=C1)C(F)(F)OC1=CC(F)=C(F)C(F)=C1	no data available	vPvB

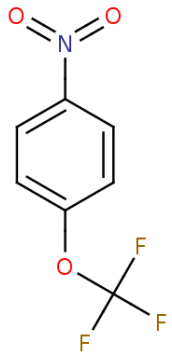
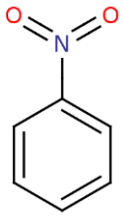
605-263-0	FC1=C(OC(F)(F)F)OC(F)(F)O1	no data available	not PBT
610-623-5	FC1=CC(OC(F)(F)C2=C(F)C=C(Br)C=C2F)=CC(F)=C1F	0% degrad.	vPvB
942-738-4	FC1=CC(OC(F)(F)C2=C(F)C=C(C=O)C=C2F)=CC(F)=C1F	0% degrad.	screening hazard
935-976-5	CCCCC1=CC=C(C=C1)C2=CC(=C(C=C2)C3=CC(=C(C(=C3)F)C(OC4=CC(=C(C(=C4)F)F)F)(F)F)F)F	no data available	vPvB
935-977-0	CCCCCC1=CC=C(C=C1)C2=CC(=C(C=C2)C3=CC(=C(C(=C3)F)C(OC4=CC(=C(C(=C4)F)F)F)(F)F)F)F	no data available	
NONS			
440-080-8	[H][C@]1(CC)CC[C@@]([H])(CC1)C1=CC=C(C(=O)OC2=CC=C(OC(F)(F)F)C=C2)C(F)=C1	0% degrad.	not assessed
439-400-9	FC(F)(F)OC1=CC=C(C=C1)N(=O)=O	0% degrad.	not assessed
448-450-0	NS(=O)(=O)C1=CC=CC=C1OC(F)(F)F	0% degrad.	not assessed
430-850-1	FC1=C(OC(F)(F)F)C=CC(Br)=C1	13% degrad.	not assessed
Intermediates			
601-363-3	FC1=CC(Br)=CC(F)=C1OC(F)(F)F	no data available	not assessed
800-308-2	CC1=CC=C(NC(=O)C2(CC2)C2=CC3=C(OC(F)(F)O3)C=C2)N=C1C1=CC=CC(=C1)C(=O)OC(C)(C)C	no data available	not assessed
700-476-6	FC1(F)OC2=CC=CC(C=O)=C2O1	0-1% degrad.	not assessed
216-431-4	FC1(F)OC2=C(O1)C=CC=C2	1% degrad.	not assessed
252-328-0	FC(F)(F)OC1=CC=C(C=C1)N=C=O	0% degrad.	not assessed
206-979-2	FC(F)(F)OC1=CC=C(Br)C=C1	no data available	not assessed
207-317-5	NC1=CC=C(OC(F)(F)F)C=C1	0% degrad.	not assessed
616-458-5	COC(=O)C1=CC2=C(OC(F)(F)O2)C=C1	no data available	not assessed
700-526-7	COC(=O)C(=C\C1=CC=CC2=C1OC(F)(F)O2)\C#N	14-30% degrad.	not assessed

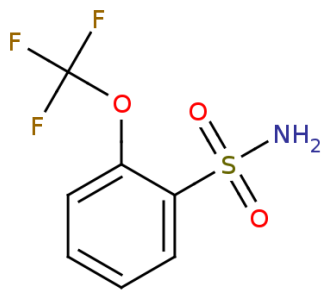
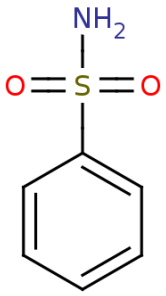
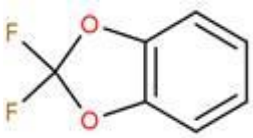
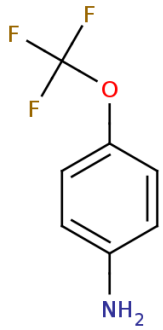
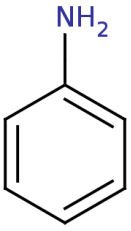
For 17 of these 26 substances, data on ready biodegradation are available in the REACH registration dossiers and the data show that none of the substances with available data are readily biodegradable. This might be in part due to the non-fluorinated functional groups in the molecules. However, there are also some cases where the other functional groups in the molecules are expected to be biodegradable. Table 2 list in the first column four of those substances and shows that they are not readily biodegradable under the applied conditions of EU Method C.4-D (Determination of the "Ready" Biodegradability - Manometric Respirometry Test). On the other hand, we found two substances with

registrations under REACH that are very similar to the fluorinated substances in Table 2, but do not contain fluorinated moieties (second column in Table 2). These two substances (EC no. 202-716-0 and EC no. 200-539-3) degrade to a much larger extent in the ready-biodegradation tests than their fluorinated analogues, showing that it is very likely the fluorinated moiety that is preventing biodegradation in the 28 days ready-biodegradation test.

We also searched for structures that were similar to the substances in Table 2 but had a non-fluorinated methyl group at the ether bond. The corresponding substances would be CAS RN 2109-72-0 (SMILES O=N(=O)C1=CC=C(OC(C)(C)C)C=C1), CAS RN 2520350-06-3 (SMILES O=S(=O)(N)C=1C=CC=CC1OC(C)(C)C), CAS RN 14005-14-2 (SMILES O1C=2C=CC=CC2OC1(C)C) and CAS RN 57120-36-2 (O(C1=CC=C(N)C=C1)C(C)(C)C). Unfortunately, none of these substances have a REACH registration, hampering a comparison with more structural similar homologues.

Table 2: Fluorinated and non-fluorinated substances and their ready-biodegradation test results

Fluorinated substance	Non-fluorinated substance
EC no.: 439-400-9 SMILES: FC(F)(F)OC1=CC=C(C=C1)N(=O)=O 0% degradation in ready-biodegradation test after 28 days Link: https://echa.europa.eu/de/registration-dossier/-/registered-dossier/3915/5/3/2 	EC no.: 202-716-0 SMILES: O=N(=O)C1=CC=CC=C1 Key study: 50-60% degradation in ready-biodegradation test after 28 days Link: https://echa.europa.eu/de/registration-dossier/-/registered-dossier/14701/5/3/2/?documentUUID=2c06d164-b27d-4952-b1a4-dc21aa03d1e6 
EC no.: 448-450-0 SMILES: NS(=O)(=O)C1=CC=CC=C1OC(F)(F)F 0% degradation in ready-biodegradation test after 28 days Link: https://echa.europa.eu/de/registration-dossier/-/registered-dossier/3430/5/3/2	EC no.: 202-637-1 SMILES: S(=O)(=O)C1=CC=CC=C1

	Registered as intermediate, no information on biodegradation 
EC no.: 216-431-4 SMILES: FC1(F)OC2=C(O1)C=CC=C2 1% degradation in ready-biodegradation test after 28 days Link: https://echa.europa.eu/de/registration-dossier/-/registered-dossier/11884/5/3/2 	No similar substance registered under REACH
EC no.: 207-317-5 SMILES: NC1=CC=C(OC(F)(F)F)C=C1 0% degradation in ready-biodegradation test after 28 days Link: https://echa.europa.eu/de/registration-dossier/-/registered-dossier/11758/5/3/2/?documentUUID=1f6aa8ca-7b9b-4dde-b079-28c343648f35 	EC no.: 200-539-3 SMILES: NC1=CC=CC=C1 ca. 90% biodegradation in ready-biodegradation test after 30 days Link: https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15333/5/3/2/?documentUUID=b5ad66fd-7e72-48be-9a8d-c253171ef20d 

On the other hand, there is evidence that *Pseudomonas putida F1* can defluorinate 2,2-difluoro-1,3-benzodioxole (EC no.: 216-431-4) (Bygd et al. 2021). This information is included in Annex B of the

restriction proposal along with information that Fludioxonil can be defluorinated by microbial consortia. It seems therefore that at least CF_2-O groups on aromatic rings can be defluorinated if sufficient time and the right microbial consortia are available.

From our point of view, this is still unclear for CF_3-O groups on aromatic rings. It would be important to clarify, if the substances exceed the half-life of 180 days in soil or sediment (using biodegradation simulation tests) which would classify them as very persistent substances under REACH (ECHA 2017). The interim results of the study mentioned in Annex B of the PFAS restriction proposal that report a mineralization of 57% to 58% after 14 days in soil seem, however, questionable. Biodegradation is normally expected to occur slower in soil than in sludge and having such a high mineralization rate after 14 days in soil for a substance that is very similar to the substances listed in Table 2 seems counterintuitive.

2) New literature study

The study of Licul-Kucera et al. (2023) investigated the biotransformation of two trifluoromethoxy-substituted surfactants that are also shown in Figure 1.

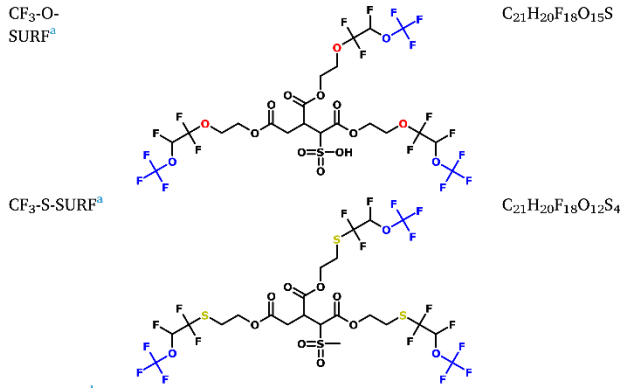


Figure 1: Trifluoromethoxy-substituted surfactants investigated in Licul-Kurcera et al. (2023).

Long-term microbial transformation studies under aerobic conditions in activated sludge- wastewater medium were performed for 126 days. Licul-Kucera et al. (2023) summarize their results as: 'Significant decrease in the concentration of the surfactants was observed over the incubation period. The main detected transformation products were short-chained carboxylic acids (CAs), including a CA with two fluorinated carbon atoms representing the last product prior to mineralization. High stability of these CAs and lack in the formation of inorganic fluoride over the incubation time was however observed. Consequently, unequivocal final mineralization of the investigated surfactants could not be confirmed.'

The observation that no mineralization occurred was 'likely due to the –CFH–CF2- linkage which ensures higher fluorination degree and therefore, better technical performance'.

The study therefore supports the inclusion of substances with CF_3-$OCFHCF_2$ groups in the PFAS restriction proposal.

3) Comment 4418 submitted to ECHA by Reiner Friedrich from Merck Electronics KGaA

The comment with ID 4418 was submitted by Reiner Friedrich from Merck Electronics KGaA and will in the following be referred to as 'comment by Merck'.

In their comment, Merck request that:

1. PMVE (Perfluoro methyl vinyl ether; CAS-No.: 1187-93-5; EC/List No.: 214-703-7) and its low-molecular-weight reactions products made from alcohols and mercaptans, and
2. PMMVE (Perfluoro methoxy methyl vinyl ether; CAS-No.: 700874-87-9; EC/List No.: 615-064-0) and its low-molecular-weight reactions products made from alcohols and mercaptans; and
3. PPVE (Perfluoro propyl methyl vinyl ether; CAS-No.: 1623-05-8; EC/List No.: 216-600-2) and its low-molecular-weight reactions products made from alcohols and mercaptans

are to be added under Annex B.4.1.4 (which is the subsection on fully degradable PFASs).

<u>On substance 3 – PPVE</u>

Merck show in their comment in Figure 8 that one of the terminal degradation products of PPVE is perfluoropropanoic acid (PFPrA), which itself is a PFAS (and persistent). Also, other similar substances with a $CF_3CF_2CF_2$-O group (see Figures 13 and 18 in the comment) give PFPrA as one of the final degradation products.

From our point of view, PPVE should therefore not be considered as a fully degradable PFAS.

Merck themselves note in the comment, 'Three studies concerning environmental fate and degradation of a modified PPVE version were conducted by independent research institutes. They concluded, that FESOH has a significantly lower persistence in the environment than standard PFAS. Degradation is triggered by the special design of the molecule, which involves intermediates that can be degraded further to PFPA as the terminal product.' With PFPA, Merck mean most probably PFPrA, FESOH is a reaction product made from PPVE and mercapto ethanol (Figure 12 in the comment).

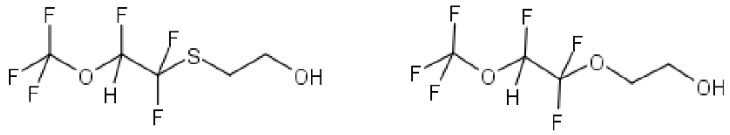
Merck further state in their comment 'Short chain perfluorinated carboxylic acids like PFPA are not regarded to be bioaccumulate in humans or other organisms like fish and mammals) and therefore impose a minor threat to the environment[21].'

We do not agree with the statement by Merck. Ultra-short-chain PFAS such as trifluoroacetic acid and PFPrA are persistent and mobile in the environment and are therefore a threat to the environment. Data for TFA in rain and snow in Switzerland (Berg et al. 2000), Japan (Taniyasu et al. 2008), China (Wang et al. 2014), the US (Kazil et al. 2014; Wujcik et al. 1998), Poland (von Sydow et al. 2000), the Netherlands (Sadia et al. 2023) and Germany (Scheurer et al. 2017) show concentrations up to the µg/L-range. Some of these measured concentrations are close to the revised groundwater/drinking water health guidance value of 60 µg/L TFA set by Germany in 2020 (Scheurer et al. 2017; UBA 2020). The drinking water health guidance value is based on the life-long tolerable daily intake of TFA, at which no harm to human health

is to be expected, and was established because of concerns about build-ups of TFA over time. Having concentrations close to Germany's health guidance value for TFA in so many places of the world is an alarming signal and shows that emissions need to be stopped.

On substance 1 – PMVE

Merck state in their comment that PMVE can be converted to functional alcohols which are suitable candidates for fully degradable PFAS. Therefore, the thioether compound MeFESOH and the diether alcohol MeFdiEOH were synthesized (Figure 2).



MeFESOH MeFdiEOH

Figure 2: Thioglycole and glycole based PMVE derivates as representatives for a Methylpolyfluoroetherthioether alcohol (MeFESOH) and a Methylpolyfluorodiether alcohol (MeFdiEOH) – given by Merck in their comment 4418.

The final active compound made out of MeFESOH by Merck is CF_3-O-SURF (see Figure 1), the final active compound made out of MeFdiEOH is CF_3-S-SURF (Figure 1).

Merck refers to the study described in Section 2 (Licul-Kucera et al. (2023)) and states 'After 126 days only a small amount of 2H-1:2 PFECA (~4%) which is created by the first mineralization step (MeFESCA -> 2H-1:2 PFECA). Although no significant further degradation of 2H-1:2 PFECA could not be detected in the studies, they conclude that "based on fundamental chemical knowledge, it should completely degrade at some point, even if it takes a long time."However, the statement "based on fundamental chemical knowledge, it should completely degrade at some point, even if it takes a long time." is **not** included in Licul-Kucera et al. (2023). Rather, Licul-Kucera et al. (2023) conclude that 'As complete degradation was not experienced over the 126-days incubation time, possible concerns are carried by the short-chained carboxylic acids which remained in the aqueous phase after 126 days. Hence, the transformation products could probably be classified as persistent substances although official classification is not possible as REACH regulation did not include persistence requirements in activated sludge-wastewater matrix.' The statement added by Merck, "based on fundamental chemical knowledge, it should completely degrade at some point, even if it takes a long time" is therefore unsubstantiated and misleading.

Another line of evidence by Merck is the atmospheric degradation. According to Merck, the atmospheric degradation of MeFESOH yields $O=CF_2$ and O=HCF. However, the publication with these data is not yet available and the results therefore cannot be verified. Also, Merck gives only few details on the study, which makes it difficult to understand the individual degradation steps.

Merck shows also data of a force degradation experiment. These are experiments that are conducted under harsh conditions (a small amount of fluorinated alcohol (0.05 g) was dissolved in ethanol (0.2 g), added to 30% aqueous KOH (0.6 g) and was kept at 80°C for several hours). According to Merck, these experiments allow to investigate the overall stability of compounds. Merck conducted such an experiment for MeFESOH and measured the 19F NMR spectra at the beginning of the experiment and after 18 hours. Merck states 'A comparison of both spectra show clearly that the MeFESOH is decomposed under the give condition to yield 2H-1:2PFECA and fluoride (Signal G in Figure 24). Since the fluorine mass balance does not change during reaction, the molecular ration of the compounds can be calculated indicating that after 15 h at 80°C 37% of MeFESOS is still present, 7% converted to 2H-1:2 PFECA and 56% mineralized. It is worth mentioning that 2H-1:2PFECA is again not the terminal product but decomposes further under full mineralization.'

However, there is no proof for the last part of the sentence. The spectra in Figure 24 are no proof of full mineralization or degradation of 2H-1:2PFECA, since this would give a spectrum with only a peak G (fluoride) in it. We conclude therefore that the evidence presented is **not sufficient** to classify PMVE or PPVE as fully degradable. No evidence has been presented for PMMVE and given that the evidence for the other two substances was not sufficient, we can also not conclude for PMMVE that it is fully degradable.

4) Bibliography

Berg M, Müller SR, Mühlemann J, Wiedmer A, Schwarzenbach RP. 2000. Concentrations and Mass Fluxes of Chloroacetic Acids and Trifluoroacetic Acid in Rain and Natural Waters in Switzerland. Environ Sci Technol 34:2675–2683; doi:10.1021/es990855f.

Bygd MD, Aukema KG, Richman JE, Wackett LP. 2021. Unexpected Mechanism of Biodegradation and Defluorination of 2,2-Difluoro-1,3-Benzodioxole by Pseudomonas putida F1. C.S. Harwood, ed MBio 12:1–15; doi:10.1128/mBio.03001-21.

ECHA. 2017. Guidance on Information Requirements and Chemical Safety Assessment - Chapter R.11: PBT/vPvB assessment.

Kazil J, McKeen S, Kim SW, Ahmadov R, Grell GA, Talukdar RK, et al. 2014. Deposition and rainwater concentrations of trifluoroacetic acid in the united states from the use of hfo-1234yf. J Geophys Res 119:14,059-14,079; doi:10.1002/2014JD022058.

Licul-Kucera V, Frömel T, Kruså M, van Wezel AP, Knepper TP. 2023. Finding a way out? Comprehensive biotransformation study of novel fluorinated surfactants. Chemosphere 339:139563; doi:10.1016/j.chemosphere.2023.139563.

OECD. 2021. Reconciling Terminology of the Universe of Per- and Polyfluoroalkyl Substances: Recommendations and Practical Guidance. Series on Risk Management No. 61.

Rudin E, Glüge J, Scheringer M. 2023. Per- and polyfluoroalkyl substances (PFASs) registered under REACH—What can we learn from the submitted data and how important will mobility be in PFASs hazard assessment? Sci Total Environ 877:162618; doi:10.1016/j.scitotenv.2023.162618.

Sadia M, Nollen I, Helmus R, Ter Laak TL, Béen F, Praetorius A, et al. 2023. Occurrence, Fate, and Related Health Risks of PFAS in Raw and Produced Drinking Water. Environ Sci Technol 57:3062–3074; doi:10.1021/acs.est.2c06015.

Scheurer M, Nödler K, Freeling F, Janda J, Happel O, Riegel M, et al. 2017. Small, mobile, persistent: Trifluoroacetate in the water cycle – Overlooked sources, pathways, and consequences for drinking water supply. Water Res 126:460–471; doi:10.1016/j.watres.2017.09.045.

Taniyasu S, Kannan K, Yeung LWY, Kwok KY, Lam PKS, Yamashita N. 2008. Analysis of trifluoroacetic acid and other short-chain perfluorinated acids (C2–C4) in precipitation by liquid chromatography–tandem mass spectrometry: Comparison to patterns of long-chain perfluorinated acids (C5–C18). Anal Chim Acta 619:221–230; doi:10.1016/j.aca.2008.04.064.

UBA. 2020. Trifluoressigsäure (TFA) – Gewässerschutz im Spannungsfeld von toxikologischem Leitwert, Trinkwasserhygiene und Eintragsminimierung.

von Sydow LM, Grimvall AB, Borén HB, Laniewski K, Nielsen AT. 2000. Natural Background Levels of Trifluoroacetate in Rain and Snow. Environ Sci Technol 34:3115–3118; doi:10.1021/es9913683.

Wang Q, Wang X, Ding X. 2014. Rainwater trifluoroacetic acid (TFA) in Guangzhou, South China: Levels, wet deposition fluxes and source implication. Sci Total Environ 468–469:272–279; doi:10.1016/j.scitotenv.2013.08.055.

Wujcik CE, Zehavi D, Seiber JN. 1998. Trifluoroacetic acid levels in 1994–1996 fog, rain, snow and surface waters from California and Nevada. Chemosphere 36:1233–1245; doi:10.1016/S0045-6535(97)10044-3.