

Annex to the
ANNEX XV RESTRICTION REPORT

PROPOSAL FOR A RESTRICTION

SUBSTANCE NAME(S): Per- and polyfluoroalkyl substances (PFASs)

IUPAC NAME(S): n.a.

EC NUMBER(S): n.a.

CAS NUMBER(S): n.a.

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TABLE OF CONTENTS

Annex B	Information on hazard and risk.....	1
B.1.	Identity of the substance(s) and physical and chemical properties	1
B.1.1.	Name and other identifiers of the substance(s).....	1
B.1.2.	Physicochemical properties.....	2
B.1.3.	Justification for grouping	3
B.2.	Manufacture and uses (summary)	7
B.3.	Classification and labelling.....	8
B.3.1.	Classification and labelling in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation)	8
B.3.2.	Classification and labelling in classification and labelling inventory/ Industry's self-classification(s) and labelling ¹	11
B.4.	Environmental fate properties.....	17
B.4.1.	Degradation.....	17
B.4.2.	Environmental distribution	70
B.4.3.	Persistence compensating low bioaccumulation potential for mobile substances	130
B.4.4.	Accumulation in plants	132
B.4.5.	Removal from the environment, decontamination and purification	136
B.5.	Human health hazard assessment	141
B.5.1.	Toxicokinetics/ADME (absorption, metabolism, distribution and elimination)	149
B.5.2.	Evidence from experimental animal data.....	156
B.5.3.	Evidence from epidemiological data.....	170
B.5.4.	Human data on oligomeric/polymeric PFASs	188
B.5.5.	Combined toxicity.....	189
B.5.6.	Derivation of DNEL(s)/DMEL(s)	191
B.6.	Human health hazard assessment of physicochemical properties	192
B.7.	Environmental hazard assessment.....	193

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

B.7.1. Ecotoxicity	193
B.7.2. Effects on wildlife	204
B.7.3. Atmospheric compartment – global warming potential.....	208
B.7.4. Microbiological activity in sewage treatment systems	212
B.7.5. Endocrine activity and endocrine disruption.....	213
B.7.6. Hazard and occurrence of fluoropolymers.....	219
B.8. PBT and vPvB assessment.....	223
B.9. Exposure assessment.....	224
B.9.1. Introduction to hazard and risk	226
B.9.2. PFASs manufacturing	227
B.9.3. Textiles, upholstery, leather, apparel and carpets	232
B.9.4. Food contact materials and packaging	241
B.9.5. Metal plating and manufacturing of metal products	253
B.9.6. Consumer mixtures	256
B.9.7. Cosmetics.....	257
B.9.8. Ski wax	260
B.9.9. Applications of fluorinated gases	265
B.9.10. Medical devices	272
B.9.11. Transport.....	275
B.9.12. Electronics and semiconductors.....	277
B.9.13. Energy	280
B.9.14. Construction products	283
B.9.15. Lubricants.....	288
B.9.16. Petroleum and mining	292
B.9.17. Active substances in Plant Protection Products (PPP), Biocidal Products (BP) and Medicinal Products (MP).....	298
B.9.18. Waste.....	299
B.9.19. Other sources (for example natural sources, unintentional releases)	320
B.9.20. Overall environmental exposure assessment.....	321
B.9.21. Human exposure	324
B.9.22. Combined human exposure assessment.....	330
Appendices to Annex B.....	345

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Appendix B.1.2. Physicochemical Properties	345
Appendix B.4.1.2. Key arrowhead subgroups.....	389
Appendix B.4.1.3.1. Degradation of PFCA precursors.....	392
Appendix B.4.2.1.3. Mobility in water	398
Appendix B.4.2.3. Soil	419
Appendix B.4.2.6.1. EOF/AOF	422
Appendix B.4.2.7. Monitoring of specific PFASs in environmental samples	429
Appendix B.4.2.9. Bioaccumulation	442
Appendix B.4.4. Accumulation in plants	444
Appendix B.5.1.1.2. Distribution	460
Appendix B.7.5. Endocrine activity and endocrine disruption	503
Appendix B.9.3. Textiles, upholstery, leather, apparel and carpets	527
Appendix B.9.4. Food contact materials and packaging.....	534
Appendix B.9.8. Ski wax	536
Appendix B.9.11. Transport.....	539
Appendix B.9.12. Electronics and semiconductors	540
Appendix B.9.13. Energy.....	542
Appendix B.9.14. Construction products	544
Appendix B.9.15. Lubricants	545
Appendix B.9.16. Petroleum and mining	546
Appendix B.9.21. Human exposure	551
References	571

TABLES

Table B.1. PFAS applications and researched uses.	7
Table B.2. 43 PFASs with harmonised classification.....	8
Table B.3. PFASs (subdivided into PFAS categories)	11
Table B.4. Details on available classification information for the endpoints of concern	15
Table B.5. List of substances selected for QSAR modelling of degradation.....	18
Table B.6. Properties of compared substances.	67
Table B.7. Log K _{OC} for PFAAs.....	74
Table B.8. Log K _{OC} for PFCs	76
Table B.9. Log K _{OC} for perfluoroalkylamines and perfluoroethers.....	77
Table B.10. Estimated characteristic travel distances of fluorotelomeric alcohols.....	110
Table B.11. Estimated characteristic travel distances of selected PFCAs.....	110
Table B.12. Overview on bioconcentration factors (BCFs) and bioaccumulation factors ...	121

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.13. Non-exhaustive list of PFASs.....	141
Table B.14. Ecotoxicological threshold values for different PFASs.....	197
Table B.15. GWP-values (GWP- 100) collected from the IPCC fourth Assessment Report..	208
Table B.16. GWP-values (GWP- 100) for selected fluranes.....	209
Table B.17. Overview over EA/ED of different PFASs.	214
Table B.18. Methodology used to estimate emissions per sector.	225
Table B.19. Average emission factors to environmental compartments.....	228
Table B.20 Estimated annual EEA emissions.....	228
Table B.21. Comparison of past, current, and expected future emissions	230
Table B.22. Assigning major use applications to release groupings.....	234
Table B.23. Market splits for situations where more than one release grouping exists. ...	235
Table B.24. Estimated annual EEA emissions.....	236
Table B.25. Assumed TULAC usage rates for PFASs 1990 – 2020.....	239
Table B.26. Emissions of PFASs and methods used in the manufacturing stage.	243
Table B.27. Quantities of PTFE in Industrial Cookware re-coating.....	247
Table B.28. Emissions of PFASs and methods used. Service life stage	249
Table B.29. Estimated annual EEA emissions in the FCM and packaging sector.....	250
Table B.30. Estimated annual EEA emission in the metal plating subsector.....	254
Table B.31. Estimated annual EEA emissions in the manufacturing of metal products.....	254
Table B.32. Estimated annual EEA emissions in the consumer mixtures sector	256
Table B.33. Total emissions of PFAS from use of cosmetic products/year.....	258
Table B.34. Estimates for total emissions for the different cosmetic product categories ..	258
Table B.35. Estimated annual EEA emission in the ski wax sector.....	262
Table B.36. Estimates of total emissions of fluorinated gases.....	268
Table B.37. Estimated total emissions of HFCs and PFCs	270
Table B.38. Estimated annual EEA emissions in the medical devices sector	273
Table B.39. Estimated annual EEA emissions in transportation products and articles.....	276
Table B.40. Estimated annual EEA emissions in electronics and semiconductor sectors...	278
Table B.41. Estimated annual EEA emissions in the energy sector.....	281
Table B.42. Estimated annual EEA emissions in the construction sector	285
Table B.43. Estimated annual EEA emissions in the lubricants sector	289
Table B.44. Content of monomeric PFASs in fluoropolymers "high" scenario.	293
Table B.45. Estimated annual EEA emissions in the petroleum and mining industry	294
Table B.46. Concentrations of monomeric PFAS in fluoropolymer (high scenario)	296
Table B.47. Concentrations of non-polymeric PFASs in fluoropolymer (low scenario).....	296
Table B.48. Groups of PFASs used in the various sectors	302
Table B.49. Calculated total PFAS annual loads.....	304
Table B.50. End products of the thermal degradation of reported PFAS compounds.	306
Table B.51. Calculated mean and median concentrations in incineration bottom ash.....	307
Table B.52. Amount of bottom ash (rounded).....	307
Table B.53. Calculated total PFAS amounts in incinerator bottom and fly ash.....	308
Table B.54. Calculated mean and median concentrations in the influent/effluent water...	310
Table B.55. Reported influent, effluent and sludge data from Eurostat for 2016.....	310
Table B.56. Calculated total yearly PFAS load for selected EU-Member States.....	310
Table B.57. PFAS emissions (rounded) in EEA for three main waste treatment methods .	311
Table B.58. ECHA ERCs for the waste stage (ECHA, 2012a).....	315
Table B.59. Waste stage emissions based on ECHA ERCs.....	316
Table B.60. Summary of EEA yearly emissions of PFASs per use sector	322
Table B.61. Biomonitoring studies of extractable organofluorine (EOF).....	331
Table B.62. Median levels (ng/mL) of restricted (or proposed for restriction) PFAAs.....	333
Table B.63. Detection frequencies of PFAAs	335
Table B.64. Findings of 6:2 Cl-PFESA, ADONA, HFPO-DA and PFECHS in serum.....	339
Table B.65. Serum levels (ng/mL) of PFAEs	342
Table B.66. Basic substance information and physical chemical properties of PFCAs	345
Table B.67. Basic substance information and physical chemical properties of PFSAAs	353
Table B.68. Basic substance information and physical chemical properties of PFCs	366
Table B.69. Basic substance information and physical chemical properties of PFAEs.....	372
Table B.70. Basic substance information and physical chemical properties of PFPAs.....	376

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.71. Perfluoroalkylamines. Basic substance information	382
Table B.72. Basic substance information and physical chemical properties of FTOHs	385
Table B.73. Presence (YES) or absence (NO) of fragments for different BIOWIN models .	389
Table B.74. Maximum number of instances of each fragment in the training set	391
Table B.75. Summary of formed PFCAs during degradation of n:2 FTOHs	392
Table B.76. Summary of formed PFCAs during degradation of n:2 fluorotelomer.....	394
Table B.77. Concentrations of PFASs in ground water described by detection frequency .	398
Table B.78. Concentrations of PFASs in surface water described by detection frequency .	399
Table B.79. Concentrations of PFASs in drinking water described by detection frequency	411
Table B.80. Concentrations of PFASs in precipitation described by detection frequency...	416
Table B.81. Concentrations of PFASs in sediment and soil.....	419
Table B.82. Studies of EOF, AOF and/or TF in abiotic environmental samples.....	422
Table B.83. Studies of EOF and/or TF in biota.....	427
Table B.84. Concentrations of PFASs in air described by detection frequency	429
Table B.85. Concentrations of PFASs in WWTP influent and effluent.....	430
Table B.86. Concentrations of PFASs in WWTP sludge.....	431
Table B.87. Concentrations of PFASs in biota described by detection frequency	432
Table B.88. Concentrations of PFASs in plants described by detection frequency.....	441
Table B.89. Summary of bioaccumulation studies in fish according to OECD 305	442
Table B.90. Uptake of PFASs in plants.	444
Table B.91. Serum (S), plasma (P) or whole blood (WB) concentrations (ng/mL) of PFAAs	460
Table B.92. Serum (S), plasma (P) or whole blood (WB) concentrations (ng/mL) of PFAEs	486
Table B.93. Breast milk concentrations (ng/mL) of PFASs.....	493
Table B.94. Concentrations of PFAAs in urine, follicular fluid, semen.....	495
Table B.95. Concentrations of precursors, PFAEs and PFECs in urine	500
Table B.96. Studies investigating the EA / ED of PFAS.	503
Table B.97. TULAC – emission estimates (ERC assumptions).	527
Table B.98. Assumptions for backward facing usage rates.....	530
Table B.99. Default ERFs for ERCs 10a and 11a.	535
Table B.100. Emission factors for “Other uses” during service life.	535
Table B.101. Summary of assumptions and factors applied to (emission) data.	536
Table B.102. Annual emissions to air, water and soil	539
Table B.103. Selected Environmental Release Categories (ERC).	540
Table B.104. Calculated one compartment based on default release factors (%) per ERC.	540
Table B.105. Emission factors (%) to the environment.....	540
Table B.106. Selected Environmental Release Categories (ERC).	542
Table B.107. Calculated one compartment based on default release factors (%) per ERC.	542
Table B.108. Emission factors (%) to the environment.....	543
Table B.109. ERC for the total release to the environment.	544
Table B.110. ERC for the total release to the environment.	545
Table B.111. Concentration of PFAS in indoor air (pg/m ³)	551
Table B.112. Concentrations (ng/g) of PFASs in indoor dust	555

FIGURES

Figure B.1. Extract of Figure 1 of Wang et al. (2021c)	2
Figure B.2. Relative frequency of hazard classes regarding health effects	14
Figure B.3. Self-classifications on hazardous to the aquatic environment and ozone layer. .	16
Figure B.4. Predicted biodegradability of the analysed PFAS categories and molecules	20
Figure B.5. Example structure: perfluorohexane.....	21
Figure B.6. Example structure: chloropentafluoroethane.....	21
Figure B.7. Example structure: 1,1,2,2-tetrafluoro-1,2-bis(trifluoromethoxy) ethane.	22
Figure B.8. Example structure: Perfluorobutanoic acid (PFBA).....	23
Figure B.9. Example structure: Perfluorobutane sulfonic acid (PFBS).	25
Figure B.10. Example structure: Perfluorohexyl phosphonic acid.....	26
Figure B.11. Example structure: Perfluamine (=perfluoro(tripropyl)amine).....	27

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Figure B.12. Examples of substances with a combination of structural elements.	29
Figure B.13. Examples of fluoropolymers.....	30
Figure B.14. Example of an n:2 fluorotelomer alcohol: 4:2 FTOH.....	32
Figure B.15. Proposed 6:2 FTOH biotransformation pathways in aerobic sediment system.....	33
Figure B.16. Aerobic degradation pathways of 8:2 FTOH in soil and activated sludge	34
Figure B.17. Example of an n:2 fluorotelomer iodide: 4:2 FTI.....	35
Figure B.18. Example of an ester of an n:2 FTOH	35
Figure B.19. Example of an n:2 monoPAP/diPAP.....	36
Figure B.20. Example of an n:2 fluorotelomer urethane monomer	36
Figure B.21. Example of an n:2 fluorotelomer sulfonic acid	36
Figure B.22. Example of an n:2 fluorotelomer thioether amido sulfonate	37
Figure B.23. Example of an n:2 fluorotelomer silane	37
Figure B.24. Example of an n:2 fluorotelomer olefin	38
Figure B.25. Proposed atmospheric degradation pathway for n:2 fluorotelomer olefins	38
Figure B.26. Example of an n:2 fluorotelomer-based side-chain fluorinated polymer.....	38
Figure B.27. Example of an amide of a perfluoroalkyl carboxylic acid.....	39
Figure B.28. Example of a n:1 fluorotelomer alcohol	39
Figure B.29. Example of a perfluoroalkyl alcohol	40
Figure B.30. Example of a perfluoroalkyl iodide.....	40
Figure B.31. Example of a perfluorinated olefin	40
Figure B.32. Mechanism for the atmospheric oxidation of perfluorobut-2-ene	41
Figure B.33. Example of a side-chain fluorinated aromatic: (Heptafluoropropyl)benzene... ..	41
Figure B.34. Structural formula of flutramone.....	42
Figure B.35 Structural formula of saflufenacil.	42
Figure B.36 Structural formula of fluazinam.	43
Figure B.37 Structural formulas of fluometuron (a); trifloxystrobin (b); cyflumetofen (c). .	43
Figure B.38. Pharmaceutical active substances	44
Figure B.39. Degradation pathways for fluoxetine based on the predicted intermediates... ..	46
Figure B.40. Photolysis degradation pathways of TFM	47
Figure B.41. Degradation routes of some key intermediates from fluorinated gases.....	49
Figure B.42. Degradation scheme of a selection of PFSA precursors	53
Figure B.43. Oxidation processes from sulphides/thiols to the corresponding PFASs.....	54
Figure B.44. Generic structures of PFSA precursors.....	55
Figure B.45. Degradation pathway of 6:6 perfluoroalkyl phosphinic acid (6:6 PFPIA).....	55
Figure B.46. Inherently unstable key fluorinated compounds.	57
Figure B.47. Degradation pathway of trifluoromethanol.....	58
Figure B.48. Degradation pathway of trifluoromethylamine	58
Figure B.49. Postulated hydrolysis via difluoromethanediol	58
Figure B.50. Degradation pathways of 10-(trifluoromethoxy)decane-1-sulfonate	60
Figure B.51. Degradation pathways of TFMHxOH.....	61
Figure B.52. Degradation pathways of TFMPROH.....	62
Figure B.53. CYP-mediated degradation of OSI-930.	62
Figure B.54. Degradation pathways of 4-(¹⁴ C-trifluoromethoxy)benzoic acid.....	63
Figure B.55. Representative examples of trifluoromethylamino-derivatives	64
Figure B.56. Biodegradation pathways of 2,2-difluoro-1,3-benzodioxole (DFBD)	65
Figure B.57. Fludioxonil.	65
Figure B.58. Implications of high persistence.....	68
Figure B.59. EOF (ng F/g) detected in different matrices	88
Figure B.60. Time trends (percent per year) in suspended particulate matter	101
Figure B.61. Five-year moving average deposition fluxes of TFA, PFPrA, and PFBA	102
Figure B.62. Time trends of trifluoroacetic acid (TFA) in leaves (µg/g dry weight)	103
Figure B.63. Time trend of HFC-134a (+5.19 ppt per year) in air.....	104
Figure B.64. Measured BCFs and BAFs.....	125
Figure B.65. Reproduction of model for biota concentration development.....	130
Figure B.66. Affected areas in contamination cases.	136
Figure B.67. Estimated annual emissions of PFCA	230
Figure B.68. Indicative PFAS tonnage flows (t/y) for paper & board packaging	246
Figure B.69. Indicative PFAS (Fluoropolymers) tonnage flows (t/y)	248

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Figure B.70. Loss of PFAS coating during use.	251
Figure B.71. Concentration PFAS found in rinsate of packaging containers (ppb).....	252
Figure B.72. Material flow diagram for PFASs (all species) in ski-waxes	261
Figure B.73. Emissions of fluorinated gases from stocks 2018. Source EEA (2022).	266
Figure B.74. Quantity of projected demand and emissions of sum HFCs/HCFs	267
Figure B.75. EU imports of fluorinated-gases within air-conditioning equipment.....	269
Figure B.76. Overview waste stage emissions.....	300
Figure B.77. Schematic overview of PFAS emissions with waste treatment facilities.....	301
Figure B.78. PFAS mass imbalance landfill. Source: SANBORN (2019).....	305
Figure B.79. PFAS exposure pathways to humans from Oliaei et al. (2013).	325
Figure B.80. Default worst-case release factors.....	529
Figure B.81. Source flow diagram for estimated emissions from tracer products.	547
Figure B.82. Source flow diagram for estimated emissions from anti-foaming agents.....	548
Figure B.83. Source flow diagram for estimated emissions (low scenario) from FP.....	549
Figure B.84. Source flow diagram for estimates emissions (high scenario) from FP.....	550

Annex B Information on hazard and risk

B.1. Identity of the substance(s) and physical and chemical properties

Please, refer to section 1.1.1. in the main report for the main definitions. In the following subsections only additional information is provided.

B.1.1. Name and other identifiers of the substance(s)

Per- and polyfluoroalkyl substances (PFASs) are a class of synthetic compounds that have attracted much public attention since the late 1990s, when the hazards and ubiquitous occurrence in the environment of two PFASs, perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS), started to be reported and recognized. Early communications used many different terminologies for what nowadays are called PFASs (e.g. per- and polyfluorinated chemicals, perfluorinated organics, perfluorochemical surfactants, highly fluorinated compounds).

It is noted that the definition of PFASs historically encompasses both per- and polyfluoroalkyl substances, however the polyfluoroalkyl substances belong to the scope of the PFASs only when containing also at least one perfluorinated alkyl moiety (one fully fluorinated methyl or methylene group) and hence can also be called perfluoroalkyl substances. Polyfluoroalkyl substances which only contain partially fluorinated carbon atoms are not within the scope of the restriction proposal. OECD (2021) provides example molecular structures of included and excluded substances (see also Figure B.1 below).

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

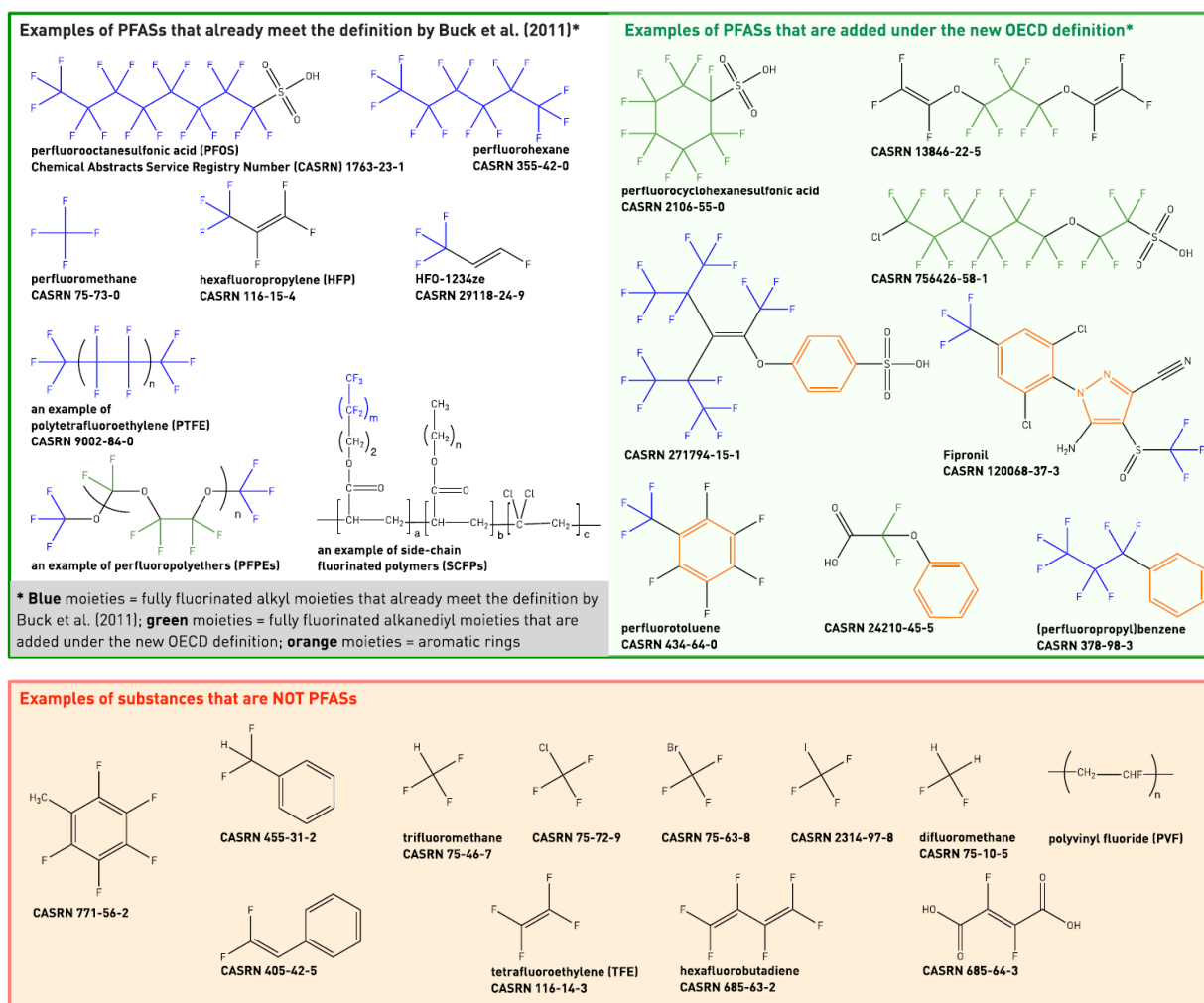


Figure B.1. Extract of Figure 1 of Wang et al. (2021c) illustrating examples of substances, which belong or do not belong to the scope of the PFASs. (Remark: The substance identified by CAS No. 24210-45-5 is a PFAS under the new OECD definition but out of scope for this restriction proposal by derogation.)

The new OECD definition also mentioned in the Figure B.1 above and given in section 1.1.1. in the main report reads as: "PFASs are defined as fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon atom (without any H/Cl/Br/I atom attached to it), i.e. with a few noted exceptions, any chemical with at least a perfluorinated methyl group ($-\text{CF}_3$) or a perfluorinated methylene group ($-\text{CF}_2-$) is a PFAS." (OECD, 2021).

B.1.2. Physicochemical properties

Certain trends in the physicochemical properties within smaller, limited and structurally similar subgroups can be found. For some PFAS subgroups (e.g. Perfluoroalkylcarboxylic acids (PFCAs), Perfluoroalkane sulfonic acids (PFSAs), Perfluoroalkanes, Perfluoroalkylphosphonic acids (PFPA) and Perfluoroalkylamines) the physicochemical properties of several corresponding molecules have been compiled (see Appendix B.1.2.).

Within the individual subgroups (e.g. the PFCAs or the PFSAs), an increase in the log K_{ow} and the boiling point can be observed with increasing chain length (equivalent to an increasing number of F atoms). In addition, a decrease in water solubility and vapour pressure of the substances can be observed with increasing chain length within the

homologous series of the subgroups.

However, due to the wide scope of the proposed restriction entry and the large number of substances covered by this restriction proposal, general conclusions on the physicochemical properties of all PFASs are complicated or even impossible.

See Table B.66 to Table B.72 in Appendix B.1.2. for the basic substance information and physical chemical properties of PFCAs, PFSA, Perfluoroalkanes, Haloperfluoroalkanes and Perfluoroalkylethers, PFPAs and Perfluoroalkylamines.

B.1.3. Justification for grouping

Generally, due to the perfluoroalkyl moieties, PFASs are either very persistent themselves or degrade to form (over a short or long timescale) terminal degradation products which still contain one or several perfluoroalkyl moieties (rendering them very persistent). Hence, all members of the PFAS group share a common hazard and risk (described in sections 1.1.4. and 1.1.6. of the main report).

For analogy, according to ECHA guidance R.11 (ECHA, 2017b), if transformation/degradation products with PBT/vPvB properties are generated, the substances themselves must be regarded as PBT/vPvB substances and should be treated like PBT/vPvB substances with regard to emission estimation and exposure control.

If there are specific PFASs for which sufficient evidence is provided that the perfluorinated moiety is fully degraded at a rate which indicates them to be not persistent, resulting in a substance/substances which is/are not a PFAS, then those substances/groups should be considered excluded from the scope.

The terminal PFAS degradation products are often referred to as **arrowhead substances**, while the parent substances degrading to the arrowheads are referred to as **precursors** (e.g. 6:2 FTOH is a precursor of PFHxA). The term **related substance(s)** is used interchangeably with the term precursor. Over sufficient time horizons all precursor substances will contribute to environmental stocks of their corresponding arrowhead substances (see section 1.1.4. of the main report for further details).

PFASs have so far been subjected to regulatory risk management on a subgroup-by-subgroup basis (see section B.4.1). For the following PFASs the Committee for risk assessment (RAC) and the Committee for Socio-economic analysis (SEAC) adopted the suggested restrictions as appropriate on reducing the risk to human health and/or the environment due to the PBT/vPvB properties of the terminal PFAS degradation products: PFOA, its salts and PFOA-related substances (ECHA, 2015b); PFNA, PFDA, PFUnDA, PFDoDA, PFTTrDA, PFTeDA including their salts and precursors (ECHA, 2018a); PFHxS including its salts and related substances (ECHA, 2019b); PFHxA, its salts and related substances (ECHA, 2019c). All of the above substances were also identified as SVHC (ECHA, 2012b; ECHA, 2012c; ECHA, 2012d; ECHA, 2012e; ECHA, 2013; ECHA, 2015b; ECHA, 2016b; ECHA, 2017c). Additionally, PFBS and HFPO-DA have been identified as SVHC (ECHA, 2019d; ECHA, 2019e).

Due to the high number of PFAS subgroups (see section 1.1.1. of the main report) on the global market, it would take a significant amount of time to submit and process restriction proposals on all PFASs on a subgroup-by-subgroup basis, whereas the environmental stock of the very persistent PFASs would simultaneously continue to increase. Ban of single PFAS substances or subgroups may also lead to the substitution by other PFASs as the number of substances in this group is very high, so-called regrettable substitution. For some applications, production volumes may be low for specific PFASs (or even zero currently). Also, novel unregulated PFASs could theoretically be developed for these or other uses in the future. The precise identities of the PFASs currently used are oftentimes largely unknown due to manufacturer confidentiality. It is noted that the overall PFAS volume

across all uses is assumed to be significant (EC, 2020b). Consequently, the European Commission's Chemicals Strategy for Sustainability (CSS) reiterates the concern for the class of PFAS substances and suggests a group approach under relevant regulations in order to address PFASs. They state their aim as phasing out persistent substances such as per- and polyfluoroalkyl substances (PFASs), unless their use is proven essential for society (EC, 2020a).

Based on the above considerations, managing all PFASs together as a group is a clear benefit to environment and humans.

A class-based approach has been chosen for the current restriction proposal in order to prevent the possibility for regrettable substitution. This dossier has put some weight on the link between the physicochemical properties of PFASs (persistence) and their environmental and toxicological effects. This is in line with the findings from the examination of strategies for grouping of PFASs by Cousins et al. (2020a), although these authors went one step further and recommended to regulate PFASs solely on the basis of persistence ("the P-sufficient approach"). The selected grouping approach in this dossier is based on the persistence of PFASs as its *main concern*. However, there are supporting properties triggering additional concerns in combination with persistence that add to the overall assessment. Those are other environmental or toxicological concerns like bioaccumulation, aqueous mobility, long-range transport, effects on humans or the environment, and high global warming potential.

Cousins et al. (2022) compiled information about PFAS in rainwater and compared the concentrations found with various regulatory limit values. They found that, for PFOA and PFOS, levels in rainwater often greatly exceed Lifetime Drinking Water Health Advisory levels from the US Environmental Protection Agency (EPA) and concluded that for these substances the planetary boundary for chemical pollution has been exceeded. In a follow-up paper, the authors discussed the property of persistence in relation to the study on PFAS in rainwater (Scheringer et al., 2022). The authors argue that there is no need to consider chemical partitioning for persistent substances such as PFAS as the substances anyway cover virtually the entire partitioning space. The continuous release of PFAS will lead to their accumulation somewhere in the environment until some known or unknown effect threshold is exceeded. Again, regulation of chemicals on the basis of persistence alone is the recommended approach.

It is noted that the first example of regulation of PFASs as a chemical class according to the P-sufficient approach has been introduced in California. Here a regulation of PFASs as a class is in place for certain consumer products under the California Safer Consumer Products Program (Balan et al., 2021).

In a review paper, Cousins et al. (2016) looked at the precautionary principle and chemicals management in relation to PFAA contamination of groundwater. The authors argue that all PFASs entering groundwater, irrespective of their perfluoroalkyl chain length and bioaccumulation potential, will result in poorly reversible exposures and risks, as well as further clean-up costs for society. In order to protect groundwater resources for future generations, the authors call for a precautionary approach and prevention of use and release of highly persistent and mobile chemicals such as PFASs. For most of the investigated PFASs at least one of the mentioned additional hazardous properties applies. For the majority of PFASs, data is still lacking, but the current restriction dossier justifies that the probability for harmful effects for the less-studied PFASs, in addition to the intrinsic persistence, is sufficient for a preventive approach and a class-based restriction. A preventive approach of not using highly persistent synthetic organic substances is more protective and also overall less costly for society, both in terms of fewer tests and reduction in externalized societal costs including the expected costs of health care, loss of biodiversity, loss of ecosystem services, loss of property value and remediation (Cousins et al., 2020b).

The proposed scope definition is in line with previous PFAS restriction proposals with an analogue approach to, e.g. PFOA, PFHxS and PFHxA with a scope definition based on a molecular structure formula. The inclusion of perfluorinated alkyl moieties as short as one perfluorinated carbon atom is in agreement with the definition of PFASs according to the UNEP/OECD Global PFC Group. Trifluoromethyl fragments are also linked via degradation to trifluoroacetic acid (TFA) which has been demonstrated to be a persistent substance with harmful properties in a comparable way as other PFASs with longer fluorinated alkyl chains. Support for the outlined justification for grouping may be found in the scientific literature, and in particular in the key papers of Cousins et al. (2020a); Kwiatkowski et al. (2020); Wang et al. (2017b).

In summary, the grouping is based on structural similarity (common perfluoroalkyl moieties) that triggers equivalent hazards and risks among the substances covered, primarily related to the very persistent property of the substances. However, the grouping is also justified by the desire to avoid regrettable substitution and prevention of future exposures of those PFASs which are not currently in use.

B.1.3.1. Naturally occurring organofluorine substances

In a review article on fluorine-containing natural products from 1999, O'Hagan and Harper explain that although ca. 3000 secondary metabolites containing the halogens chlorine, bromine and iodine have been reported, only 13 secondary metabolites containing fluorine have been discovered. This is in contrast to fluorine being the most abundant halogen in the earth's crust (O'Hagan and Harper, 1999). The majority of the natural fluorine-containing substances are fatty acids with a single fluorine atom at the end of the carbon chain. None of the reported substances were per- or polyfluorinated. On several of the major continents, plants have been found that biosynthesise the highly toxic monofluoroacetate, presumably for the purpose of defence.

In a study of the concentrations of trifluoroacetate (TFA) in ocean waters, Frank et al. (2002) concluded that TFA in oceans have mostly a natural origin, while in the atmosphere, precipitate, freshwaters and needles of conifers, TFA most likely stems from anthropogenic sources. The authors stated that the total amount of trifluoroacetate (TFA) present in the global environment greatly exceeds what may be expected to be contributed from various industrial sources.

Scott et al. (2005) further investigated whether TFA concentrations in the marine environment could have natural sources by determining a series of depth profiles of TFA in the Arctic, North and South Atlantic, and Pacific Oceans. They concluded that underwater vents could contribute to the TFA concentrations in the oceans. It was indicated that the heterogeneous distribution of TFA can only be partially explained by recent anthropogenic sources, while the total inventory of TFA in the oceans cannot be explained entirely by human activities. TFA in freshwaters is thought to have solely anthropogenic sources, while TFA found in oceans may be of both natural and anthropogenic origin (Fleet D et al., 2017).

Solomon et al. (2016) investigated the sources, fates, toxicity, and risks of TFA and its salts. They concluded that TFA is both produced naturally and synthetically and that it could be a breakdown product of more than 1 million chemicals, including refrigerants, pharmaceuticals, pesticides and polymers. The study indicates an annual input of 6 T from natural sources, while the total cumulative contribution of TFA to the environment from HFCs/HFOs (refrigerants) from 1990 to 2050 was estimated at more than 20 million tonnes. However, in a classical risk assessment the authors concluded that it is not likely that the environmental concentrations of TFA will exceed the effect levels as TFA has only a low to moderate toxicity.

The evidence for natural TFA was carefully examined by Joudan et al. (2021), and they came to a different conclusion with regards to the origin of TFA in the oceans. Their methods included: (i) critical evaluation of measurements of TFA in pre-industrial samples;

(ii) examination of the likelihood of TFA formation by hypothesized mechanisms; (iii) exploration of other potential TFA sources to the deep ocean; and (iv) examination of global budgets of TFA. The authors concluded that the presence of TFA in the deep ocean and lack of closed TFA budget is not sufficient evidence that TFA occurs naturally, especially without a reasonable mechanism of formation.

Zhai et al. (2015) measured the concentrations of TFA in urban landscape waters, tap water and snow in Beijing, China. A comparison between 2002- and 2012-values demonstrated a 17-fold increase from 23–98 ng/L to 345–828 ng/L in urban landscape waters. In the same period an increase of TFA from not detected to 155 ng/L occurred in tap water.

TFA in precipitation was measured by Freeling et al. (2020) in samples collected in Germany over one year. The article points to anthropogenic sources, and in particular formation of TFA in the atmosphere by photodegradation of certain hydrofluorocarbons (HFCs), hydrochlorofluorocarbons (HCFCs), and unsaturated hydrofluorocarbons (hydrofluoroolefins, HFOs) as sources of atmospheric TFA. Their findings indicate a considerable increase in the atmospheric deposition of TFA in Germany over the last two decades. Substitution of HFCs and HFOs by halogen-free gases was suggested as an effective measure to reduce the TFA load in precipitation, as HFCs and HFOs are considered as rising sources.

In summary, the number of naturally occurring organic fluorine-containing substances is low compared to other halogenated substances. TFA has been indicated to have natural sources in oceans (underwater vents) but evidence for the existence of natural trifluoroacetic acid is considered insufficient. Oceans are considered the final environmental sink of the substance. However, natural sources for TFA in the oceans have been questioned. TFA in the atmosphere, precipitate, freshwaters and needles of conifers most likely stems from anthropogenic sources. Concentrations of TFA in urban waters and tap water have been increasing over the last decades.

B.2. Manufacture and uses (summary)

PFASs consist of substances with very variable characteristics (gaseous, liquids and solids) and thus are applied in a wide variety of applications as can be seen in Table B.1.

Especially PFAS polymers have a very broad application in hundreds if not thousands of sub-applications. In Table B.1 detailed researched PFAS applications (including PFAS manufacturing and waste stage) as well as less researched PFAS applications are presented. A detailed description can be found in Annex A.

Table B.1. PFAS applications and researched uses.

PFAS applications			
PFAS manufacturing	Textile, upholstery, leather apparel and carpets	Food contact materials and packaging	Metal plating and manufacturing of metal products
Consumer mixtures	Cosmetics	Ski wax	Applications of fluorinated gases
Medical devices	Transport	Electronics and semiconductors	Energy
Construction products	Lubricants	Petroleum and mining	Waste stage PFAS applications
Laboratory equipment & filtration	Plant protection products and biocides	Chemical industry	Firefighting foam
Medicinal products	Plastics (other than packaging) and rubber/elastomer production (including flame retardants)	Pyrotechnics	Personal care products other than cosmetics
Fracking (currently hardly applicable in EEA)	Immersion cooling (currently not a use in the EEA)	Defence industry	Printing inks
Cement industry	Professional cleaning and polishing	Other niche applications	Uses (yet) unknown

- Green uses are researched in detail
- Blue uses are researched in general
- Orange uses not researched in detail
- Purple use: Separate restriction proposal

B.3. Classification and labelling

B.3.1. Classification and labelling in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation)

Harmonised classifications on human health hazards:

In a screening of Annex VI of CLP for PFASs with harmonised classifications, human health endpoints carcinogenicity (Carc.), mutagenicity (Muta.), reproductive toxicity (Repr.) including effects on or via lactation (Lact.), and specific target organ toxicity following repeated exposure (STOT RE) were considered of most concern following long-term exposure. In total, 41 PFASs were identified at the time of screening (Q4 2020) as having such a classification for one or more of these five endpoints. Since the time of screening, the Committee for Risk Assessment (RAC) has evaluated classification proposals for additional PFASs. PFHpA is listed as Repr. 1B and STOT RE since February 2022 and 6:2 FTOH is included in Table B.2 indicated as "CLH proposal agreed", because so far (June 2022) it has not been officially inserted in Annex VI of CLP. Only 6:2 FTOH was considered in the assessment for Table B.3 and Table B.4 and Figure B.2, below (since it was included already in ECHA dataset from 2020). Thus, 43 PFASs in sum are listed in Table B.2, having a classification for one or more of the above mentioned five endpoints. Please note that most of these substances have additional harmonised classifications for other endpoints (human health, environment and/or physicochemical properties) as well; these are however not listed in Table B.2, which is limited to Carc., Muta., Repr., Lact. and STOT RE classifications. Of further note, a number of the harmonised classifications were based on read-across and not on actual data on the substance. The list contains a number of PFASs known to be used as active substances in plant protection products and biocides that are further known to be TFA precursors.

Table B.2. 43 PFASs with harmonised classification for carcinogenicity (Carc.), mutagenicity (Muta.), reproductive toxicity (Repr.), effects on or via lactation (Lact.) and/or specific target organ toxicity following repeated exposure (STOT RE). PFASs known as active substances in plant protection products (PPP) and biocidal products (BP) are listed in the second part of the table.

EC Number	CAS number	Substance name/abbr.	Harmonised classification for Carc./Muta./Repr./Lact. and/or STOT RE
206-397-9	335-67-1	PFOA	Carc. 2; H351 / Repr. 1B; H360D / Lact.; H362 / STOT RE 1; H372 [liver]
206-400-3	335-76-2	PFDA	Carc. 2; H351 / Repr. 1B; H360Df / Lact.; H362
206-801-3	375-95-1	PFNA	Carc. 2; H351 / Repr. 1B; H360Df / Lact.; H362 / STOT RE 1; H372 [liver; thymus; spleen]
217-179-8	1763-23-1	PFOS	Carc. 2; H351 / Repr. 1B; H360D / Lact.; H362 / STOT RE 1; H372
220-527-1	2795-39-3	PFOS-Potassium salt	Carc. 2; H351 / Repr. 1B; H360D / Lact.; H362 / STOT RE 1; H372
223-320-4	3825-26-1	APFO (PFOA Ammonium salt)	Carc. 2; H351 / Repr. 1B; H360D / Lact.; H362 / STOT RE 1; H372 [liver]
249-415-0	29081-56-9	PFOS Ammonium salt	Carc. 2; H351 / Repr. 1B;

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

EC Number	CAS number	Substance name/abbr.	Harmonised classification for Carc./Muta./Repr./Lact. and/or STOT RE
			H360D / Lact.; H362 / STOT RE 1; H372
249-644-6	29457-72-5	PFOS Lithium salt	Carc. 2; H351 / Repr. 1B; H360D / Lact.; H362 / STOT RE 1; H372
274-460-8	70225-14-8	PFOS Diethanolamine	Carc. 2; H351 / Repr. 1B; H360D / Lact.; H362 / STOT RE 1; H372
402-190-4	113674-95-6	4-(2-chloro-4-trifluoromethyl)phenoxy-2-fluoroaniline hydrochloride	STOT RE 2; H373 / STOT RE 1; H372
406-740-4	1939-27-1	3'-trifluoromethylisobutyrilide	STOT RE 2; H373
407-810-7	-	(PFAS mixture)	STOT RE 2; H373
413-640-4	-	(PFAS mixture)	STOT RE 2; H373
415-300-0	90076-65-6	lithium bis(trifluoromethylsulfonyl)imide	STOT RE 2; H373
415-500-8	145963-84-4	2-amino-4-dimethylamino-6-trifluoroethoxy-1,3,5-triazine	STOT RE 2; H373
421-080-7	161462-35-7	1-cyclopropyl-3-(2-methylthio-4-trifluoromethylphenyl)-1,3-propanedione	STOT RE 2; H373
422-500-1	-	(PFAS reaction mass)	STOT RE 2; H373
423-180-6	-	(PFAS mixture)	STOT RE 2; H373
424-520-6	65753-47-1	2-chloro-3-trifluoromethylpyridine	STOT RE 1; H372
427-880-2	90357-53-2	N-[4-cyano-3-trifluoromethylphenyl]methacrylamide	STOT RE 2; H373
429-560-8	4274-38-8	2-amino-4-(trifluoromethyl)benzenethiol hydrochloride	STOT RE 2; H373
432-190-1	182176-52-9	(PFAS reaction mass)	STOT RE 2; H373
433-580-2	214353-17-0	1-(2-amino-5-chlorophenyl)-2,2,2-trifluoro-1,1-ethanediol, hydrochloride [containing ≥0.1% 4-chloroaniline (EC No 203-401-0)]	Carc. 1B; H350
-	21049-39-8	PFNA Sodium salt	Carc. 2; H351 / Repr. 1B; H360Df / Lact.; H362 / STOT RE 1; H372 [liver; thymus; spleen]
221-470-5	3108-42-7	PFDA Ammonium salt	Carc. 2; H351 / Repr. 1B; H360Df / Lact.; H362
-	3830-45-3	PFDA Sodium salt	Carc. 2; H351 / Repr. 1B; H360Df / Lact.; H362
-	4149-60-4	PFNA Ammonium salt	Carc. 2; H351 / Repr. 1B; H360Df / Lact.; H362 / STOT RE 1; H372 [liver; thymus; spleen]
PFASs with harmonised classification agreed after Q4 2020:			

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

EC Number	CAS number	Substance name/abbr.	Harmonised classification for Carc./Muta./Repr./Lact. and/or STOT RE
206-798-9	375-85-9	PFHpA	Repr. 1B, H360D / STOT RE1 [liver]
211-477-1	647-42-7	6:2 FTOH	CLH proposal agreed (STOT RE 2; H373 [teeth, bone])
PFASs known as active substances in plant protection products a./o. biocidal products (approved or not approved)			
216-428-8	1582-09-8	Trifluralin (containing <0.5 ppm NPDA)*	Carc. 2; H351
274-125-6	69806-50-4	Fluazifop-butyl*	Repr. 1B; H360D
405-090-9	67485-29-4	Hydramethylnon*	STOT RE 1; H372
417-680-3	101463-69-8	Flufenoxuron**	Lact.; H362
421-960-0	90035-08-8	Flocoumafen**	Repr. 1B; H360D / STOT RE 1; H372 [blood]
424-610-5	120068-37-3	Fipronil**	STOT RE 1; H372
603-146-9	126535-15-7	Trisulfuron-methyl*	Carc. 2; H351
604-222-4	141112-29-0	Isoxaflutole*	Repr. 2; H361d
604-290-5	142459-58-3	Flufenacet*	STOT RE 2; H373
608-879-8	335104-84-2	Tembotrione*	Repr. 2; H361d / STOT RE 2; H373 [eyes; kidneys; liver]
614-708-8	68694-11-1	Triflumizole*	Repr. 1B; H360D / STOT RE 2; H373 [liver]
616-669-2	79241-46-6	Fluazifop-P-butyl*	Repr. 2; H361d
616-712-5	79622-59-6	Fluazinam*	Repr. 2; H361d
617-373-6	82657-04-3	Bifenthrin*/**	Carc. 2; H351 / STOT RE 1; H372 [nervous system]

* = PPP; ** = BP

B.3.2. Classification and labelling in classification and labelling inventory/ Industry's self-classification(s) and labelling¹

Self-classifications on human health hazards:

Of the approximately 6 800 PFASs listed in the ECHA database, around 6 600 PFASs have a (self-)classification indicated in the registrations or notifications for at least one environmental, human health and/or physicochemical endpoint at the time of screening (Q4 2020). Among these, 316 substances (additional to the 41 (PFHpA and 6:2 FTOH not included) already identified in B.3.1) have a self-classification for one or more of the five human health endpoints considered of most concern following long term exposure of humans to PFASs (Carc., Muta., Repr., Lact., STOT RE). Table B.3 presents the total of 357 PFASs classified for Carc., Muta., Repr., Lact. and/or STOT RE (mostly self-classifications), subdivided at screening into PFAS categories and subsequently re-arranged into 'arrowheads' and 'possible PFAA precursors', as per Figure 1 in section 1.1.1. of the main report. Around 200 PFASs from ECHA's database have no classification indicated for ecotoxicological, toxicological and/or physicochemical properties in either the registrations or notifications. This might be because of absence of data and not because of data showing that classification is not required.

Table B.3. PFASs (subdivided into PFAS categories) with harmonised or self-classification (ECHA database status: Q4 2020) for carcinogenicity (Carc.), mutagenicity (Muta.), reproductive toxicity (Repr.), effects on or via lactation (Lact.) and/or specific target organ toxicity following repeated exposure (STOT RE), re-arranged into 'arrowheads' and 'possible PFAA precursors'. PFASs can be classified for multiple endpoints of concern; thus, the sum of percentages of total PFASs classifications can exceed 100%.

EC-no. Counts	ECHA categories	Carc.	Muta.	Repr.	STOT RE	Lact.
Possible PFAA precursors						
13	CnF2n*	3	5	9	9	0
5	Complex**	3	0	1	1	0
5	Fluorotelomer alcohol	1	0	2	4	0
2	Fluorotelomer epoxides	2	2	0	0	0
1	Fluorotelomer methacrylates (other)	0	0	0	1	0
4	Hydrofluoroethers	2	0	1	2	0
2	Hydrofluoroolefins	0	2	0	1	0
4	n:1 Fluorotelomer alcohols (FTOHs)	1	0	2	2	0
27	n:1 Fluorotelomer-based non-polymers	4	2	15	13	1
1	n:1 FT (meth)acrylate	1	0	0	0	0
1	n:2 Fluorotelomer acrylates	0	0	0	1	0
1	n:2 Fluorotelomer alcohols	0	0	1	1	0

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

EC-no. Counts	ECHA categories	Carc.	Muta.	Repr.	STOT RE	Lact.
1	n:2 Fluorotelomer ethoxylates	0	1	1	0	0
1	n:2 Fluorotelomer methacrylates	0	0	0	1	0
4	n:2 Fluorotelomer olefins	0	0	1	4	0
1	n:2 Fluorotelomer phosphate esters	0	0	0	1	0
2	n:2 Fluorotelomer silanes	0	0	1	2	0
6	n:2 Fluorotelomer sulfonic acids	0	0	0	6	0
1	n:2 Fluorotelomer sulfonyl based compounds	0	0	0	1	0
5	n:2 Fluorotelomer-based non-polymers	0	0	0	5	0
1	n:2 Fluorotelomer-thiol derivatives	0	0	1	1	0
4	Other carbonyl-based non-polymers	3	0	0	2	0
20	Other fluorotelomer-based non-polymers	2	0	16	9	8
9	Other per- and polyfluoroalkyl ether based substances	0	0	2	7	1
4	Pther sulfonyl-based non-polymers	0	0	0	4	0
2	Perfluoroalkenes	1	0	0	2	0
5	Perfluoroalkyl carbonyl amides	3	1	3	1	0
2	Perfluoroalkyl carbonyl halides	0	0	0	2	0
2	Perfluoroalkyl carboxylic acids (PFCA) esters	0	1	1	0	1
1	Perfluoroalkyl epoxides	0	0	0	1	0
4	Perfluoroalkyl iodides	0	0	2	3	0
2	Perfluoroalkyl ketones	0	0	2	1	0
5	Perfluoroalkane sulfonamides	0	0	2	4	0
2	Perfluoroalkane sulfonamidoethanols	0	0	1	2	0
1	Per- and polyfluoroether carboxylic acids (PFECAs) halides	0	0	0	1	0

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

EC-no. Counts	ECHA categories	Carc.	Muta.	Repr.	STOT RE	Lact.
1	Perfluoroalkane sulfonyl halides	0	0	1	1	0
7	Perfluoroalkane sulfonic acids (PFSA) esters	2	2	2	2	2
154	Side-chain fluorinated aromatics	25	14	81	89	14
2	Perfluoroalkyl phosphate esters (PAPs)	0	0	0	2	0
315	Possible PFAA precursors	53	30	148	189	27
88%	Of total PFAS (n=357)	17%	10%	46%	60%	9%
Arrowheads (PFAAs)						
4	No ECHA category, OECD category: perfluoroalkyl carboxylic acids (PFCAs) + salts	4	0	4	2	4
5	Per- and polyfluoroether carboxylic acids (PFECAs)	0	0	1	4	0
8	Perfluoroalkyl carboxylic acids (PFCAs) + salts	5	0	7	4	4
10	Perfluoroalkane sulfonic acids (PFSAs) + salts	8	0	7	8	6
27	Arrowheads (PFAAs)	17	0	19	18	14
8%	Of total PFAS (n=357)	63%	0%	70%	67%	52%
Not assignable to a category (currently)						
10	No ECHA category, no OECD category, entry in ECHA list	3	0	3	7	0
5	Other PFAS	0	2	2	3	0
15	Not assignable to a category	3	2	5	10	0
4%	Of total PFAS (n=357)	20%	13%	33%	67%	0%

* The PFAS category 'CnF2n' refers to PFASs containing a -CF₂- moiety. These substances fulfil the PFAS definition in section 1.1.1. of the main report.

** The PFAS category 'complex' refers to metal complexes.

The 357 substances fall into 43 PFAS categories in total. The listed PFASs are most often classified for STOT RE (217), followed by Repr. (172), Carc. (73), Lact. (41), and Muta. (32) (Table B.3 and Figure B.2).

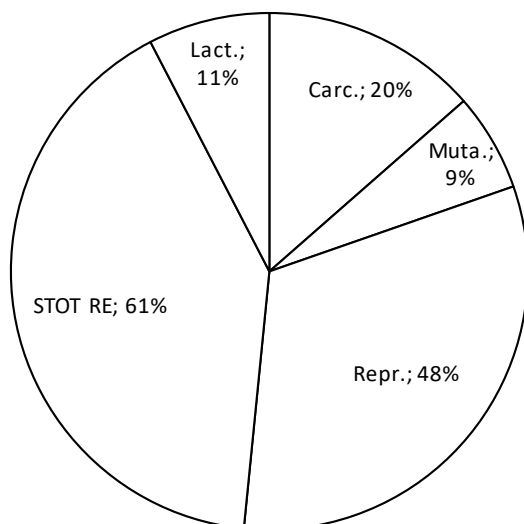


Figure B.2. Relative frequency of hazard classes regarding health effects of 357 PFASs on the five endpoints of concern (Carc. = Carcinogenicity, Muta. = Mutagenicity, Repr. = Reproductive toxicity, Lact. = effects on or via lactation, STOT RE = specific target organ toxicity following repeated exposure).

The fact that several thousands of PFASs do not bear (self-)classifications for the endpoints of most concern (Carc., Muta., Repr., Lact. and/or STOT RE) does not mean that these PFASs do not have these properties, but most likely that study data are lacking for the majority of them to base classification on. Hence, the fact that the current list of PFASs with (self-)classifications already includes so many different PFAS categories suggests that PFASs currently without (self-)classifications may exhibit one or more similar properties of concern.

From Table B.3, it can be seen that the majority (88%) of the 357 substances classified for Carc., Muta., Repr., Lact. and/or STOT RE are possible PFAA precursors (such as fluorotelomers, perfluoroalkyl carbonyl amides, hydrofluoroethers, etc.) including potential TFA precursors. Moreover, these PFASs are not only PFAA precursors, because the groups are very diverse and degradation pathways are complex/uncertain.

Repeated exposure to the classified PFASs affected various organs, such as liver, kidney, thymus, endocrine system, immune system, nervous system, respiratory system, spleen, blood, heart and cardiovascular system, brain, bone marrow, skin, lymph nodes, testicles, uterus, and gastrointestinal tract. Target effects of reproductive and developmental toxicity are reported as adverse effects on e.g. fertility, pup survival, offspring viability and on the foetal skeleton. Carcinogenicity and mutagenicity in categories 1 and 2 are reported as well as effects on or via lactation. Further details are listed in Table B.4.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.4. Details on available classification information for the endpoints of concern for classified PFASs in two main PFAS classes, and for not assignable PFASs. PFASs can be classified for multiple endpoints of concern; thus, the sum of percentages of total PFASs classifications can exceed 100%. Further details are listed in Table B.3.

PFAS class	Number (percentage) of 357 classified PFASs	Carc.	Muta.	Repr.	Lact.	STOT RE	STOT RE affected organs:
Possible PFAA precursors incl. TFA precursors (incl. telomers, epoxides, halides, fluorinated gases, olefins, esters, side-chain aromatics, etc.)	315 (88%)	15%	8%	41%	8%	53%	Damage to multiple tissues and organs, for example: liver, hepatobiliary system, kidneys, adrenal glands, lower urinary tract, blood, nervous system, heart, respiratory system, reproductive organs, thyroid, immune system, thyroid muscle, spleen, endocrine system, bones, eyes, gastrointestinal tract, teeth.
Arrowheads (incl. carboxylic, sulfonic acids and salts)	27 (8%)	63%	0%	70%	52%	67%	Damage to organs; liver, kidneys, blood, lung, central nervous system, cardiovascular system.
Not assignable PFASs	15 (4%)	20%	13%	33%	0%	67%	Liver, kidneys, adrenals, renal system, ovary, testes, gastrointestinal tract, nervous system, hematopoietic system, immune system, respiratory system.

Carc. = carcinogenicity, Muta. = mutagenicity, Repr. = reproductive toxicity, Lact. = effects on or via lactation, STOT RE = specific target organ toxicity – repeated exposure

Self- classifications on environmental hazards:

1 129 PFASs of the 6 800 PFASs listed in the ECHA database on registration and C&L notification have a self-classification on hazardous to the aquatic environment (Aquatic Acute and/or Aquatic Chronic) or hazardous to the ozone layer. Further 4 substances have self-classifications on hazardous to the aquatic environment (Aquatic Chronic 2 and 3) as well as to the ozone layer. The PFASs are most often classified for Aquatic Chronic 4 (444) followed by Aquatic Acute 1 + Aquatic Chronic 1 (322), Aquatic Chronic 2 (135) and Aquatic Chronic 3 (110). Further self-classifications are shown in Figure B.3. For information on the evaluation of the database: If for one substance different self-classifications on long-term aquatic hazard (different categories on Aquatic Chronic) were listed, the classification with the most entries were chosen. If the number was the same, the more stringent was selected.

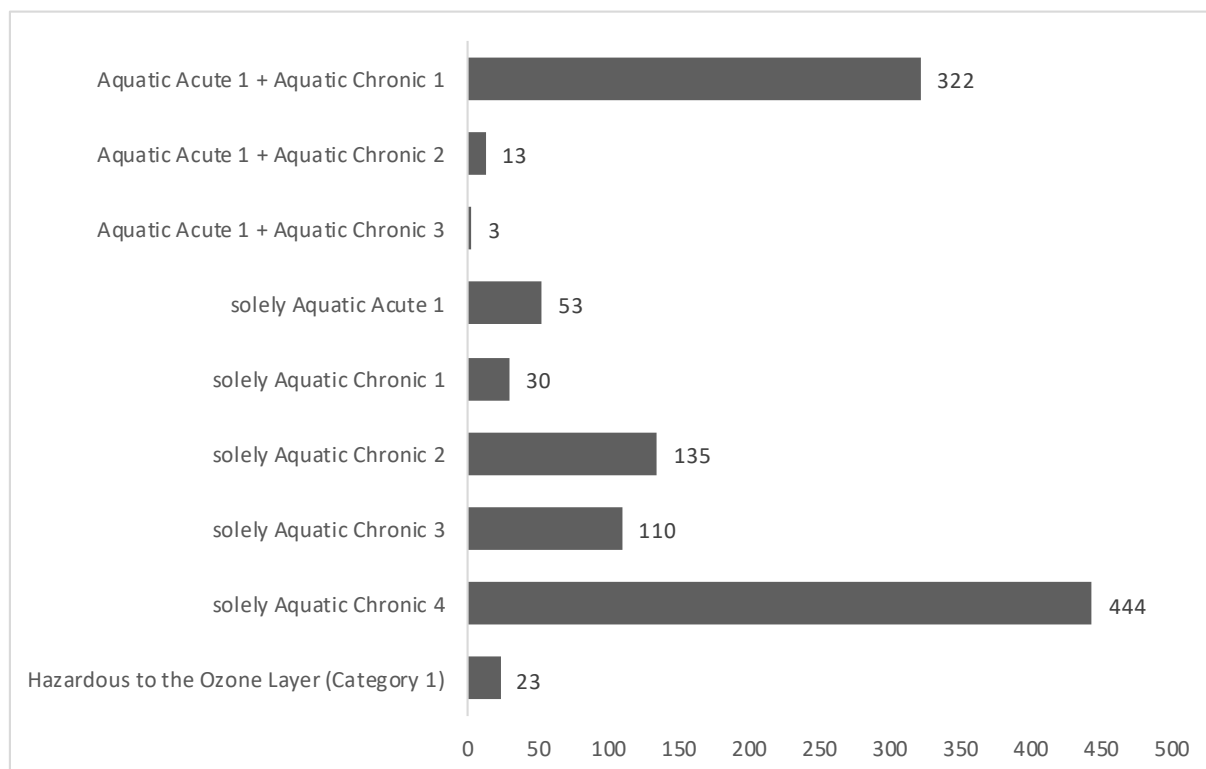


Figure B.3. Self-classifications on hazardous to the aquatic environment and ozone layer.

B.4. Environmental fate properties

B.4.1. Degradation

B.4.1.1. Degradation - general

There is a broad diversity in the chemical and physical properties of PFASs. However, despite this high diversity, members of the PFAS group have in common that they contain perfluoroalkyl moieties that are extremely resistant to environmental and metabolic degradation. There are a few exceptions to this general rule, see section B.4.1.4. The resistance to degradation of the perfluoroalkyl moiety is primarily due to the high electronegativity and low polarisability of fluorine, which results in the strongest covalent bond known in organic chemistry: the C-F bond (Kissa, 2001). The C-F bond is resistant to acids, bases, oxidation and reduction, and even high temperatures. Multiple C-F bonds on the same geminal carbon lead to additional strengthening of the C-F bond. The strong electron-withdrawing effect of the fluorine atoms in perfluoroalkyl moieties also strengthens the skeletal bonds in the carbon chain (Cousins et al., 2020b). It is not expected that the length of the perfluoroalkyl chain has any major impact on the inherent stability of PFASs.

As illustrated in Figure 1 in section 1.1.1. in the main report, many PFASs have non-fluorinated moieties attached to the perfluorinated moiety. During degradation processes non-fluorinated moieties of molecules are transformed and oxidative processes often lead to a gradual conversion of non-fluorinated carbon atoms to CO₂, which is emitted to the atmosphere while the degrading substance structure is gradually getting smaller. In the end, most of the non-fluorinated parts are fully degraded while the perfluoroalkyl part remains, often attached to a functional group at its highest oxidation state (e.g. carboxylic acid). For additional details, see section B.4.1.3.

Cousins et al. (2020a) considered that PFASs in general are, or ultimately transform into, stable substances, often PFAAs. Wang et al. (2017b) explained that perfluoroalkyl (C_nF_{2n+1}-) and perfluoroether (C_nF_{2n+1}-O-C_mF_{2m+1}-) moieties are very persistent under natural conditions. Even though some PFASs may partially degrade in abiotic and biotic degradation processes, they will all ultimately transform into highly stable end products, which are usually the very persistent perfluoroalkyl or perfluoroalkyl(poly)ether acids (here collectively termed "PFAAs"), for example, PFCAs, PFSAs, PFECAs, and PFESAs.

In laboratory photochemical experiments it has been possible to achieve degradation of PFCAs (for C1 to C4 PFCAs) in reaction with OH radicals. However, this transformation was found to be a minor pathway in the environment, while the main atmospheric removal mechanism is via wet and dry deposition which occurs in a timescale of the order of 10 days (Hurley et al., 2004a). Liou et al. (2010) investigated the biodegradability of PFOA and found the substance to be microbiologically inert and environmentally persistent. If PFAAs degrade, they do it so slowly that it is not observable and their half-lives could be in the order of decades, centuries or even greater (Parsons et al., 2008).

Parsons et al. (2008) reviewed the biodegradation of perfluorinated compounds. The authors pointed out that the most theoretically plausible degradation pathway for PFASs is via reductive defluorination, which could occur under anaerobic conditions. The same authors reported for PFOS that no biodegradation was observed under aerobic conditions, while there were some observations of degradation of PFOS under anaerobic conditions though no metabolites were measured in these studies. In principle, it cannot be ruled out that some degradation of other PFASs under anaerobic conditions can occur (e.g. in hypoxic groundwater, marine water or sediments), or will occur in the future if bacteria adapt to utilise the energy present in the PFAS substrates. Indications for such bacterial behaviour were found when a PFOA-degrading bacterial strain was isolated from soil near a PFAS production plant (Yi et al., 2016). The PFOA-degradation has been demonstrated at lab conditions with a low degradation efficiency only, and have yet to be observed at significant rates in the

environment (Arp and Slinde, 2018).

B.4.1.2. Key arrowhead subgroups

In the present section lack of degradation of selected PFAS subgroups is considered in more detail. The subgroups have been selected on the basis of their expected stability in the environment, and they are representing **arrowhead substances** or **arrowhead subgroups**, i.e. final degradation products that do not undergo any further degradation in the environment. The arrowhead approach may be defined as a risk management approach when a representative PFAS is managed together with its salts and precursors. The approach has been recognized by scientists (e.g. (Cousins et al., 2020a)) and represents the dominant current approach to grouping PFASs for risk assessment and risk management globally.

It is noted that the information presented below covers PFASs where the perfluoroalkyl moieties constitute the largest part of the substance. However, there are many PFASs in which the perfluoroalkyl moiety contributes to a relatively small part of the substance compared to the non-fluorinated parts. For these substances it can generally be expected that the primary degradation will target the non-fluorinated part, see section B.4.1.3.

B.4.1.2.1. QSAR modelling of degradation

The persistence of selected subgroups was investigated with QSAR modelling of abiotic/biotic degradation of three representative members of the different subgroups (apart from haloperfluoroalkanes). The QSAR models used in this study were selected according to their capacity and competence of predicting abiotic and biotic degradation of the selected PFASs. For the purpose of this study, capacity means that the substance or similar substances are part of the training set of the model, while competence refers to the applicability domain (AD) for the endpoint to be predicted. For additional details on the training sets for the QSAR models and their reliability, see Appendix B.4.1.2.

A complete list of substances selected for QSAR modelling is found in Table B.5.

Table B.5. List of substances selected for QSAR modelling of degradation.

PFAS category	PFAS name	CAS number
Perfluoroalkyl carboxylic acids (PFCAs)	PFOA	335-67-1
	PFHxA	307-24-4
	PFBA	375-22-4
Perfluoroalkane sulfonic acids (PFSAAs)	PFOS	1763-23-1
	PFHxS	355-46-4
	PFBS	375-73-5
Perfluoroalkyl phosphonic acids (PFPAs)	Perfluorooctyl phosphonic acid (PFOPA)	40143-78-0
	Perfluorohexyl phosphonic acid (PFHxPA)	40143-76-8
	Perfluorobutyl phosphonic acid (PFBPA)	52299-24-8
Perfluoroalkanes	Perfluorohexane	355-42-0
	Perfluorooctane	307-34-6
	Perfluorodecaline (perflunafene)	306-94-5
Perfluoroalkylamines	Perfluamine	338-83-0
	Perfluoromethyldiethylamine	758-48-5
	Perfluorotrihexylamine	432-08-6

PFAS category	PFAS name	CAS number
Perfluoroalkyl ethers (PFAEs)	Perfluorodiethylether, CF ₃ CF ₂ -O-CF ₂ CF ₃	358-21-4
	CF ₃ -O-CF ₂ -CF ₂ -O-CF ₃	378-11-0
	2,2,3,3,4,4,5-heptafluorotetrahydro-5-(nonafluorobutyl)furan	335-36-4

B.4.1.2.2. Abiotic degradation

For abiotic degradation, the modelling suites used were AOPWIN and HYDROWIN from EPI Suite, which predict the atmospheric and water degradation, respectively; OPERA, which predicts the hydroxylation rate; and VEGA, which predicts persistence in air, water, sediment, and soil in seven (7) different models.

Abiotic degradation predictions were of low reliability for all analysed PFASs in water, sediment and soil. The abiotic degradation models have a very low coverage of perfluorinated compounds in their training sets, and overall, the models were found unsuitable to reliably predict photodegradation of PFASs. Hence, the Dossier Submitters do not recommend the use of any of the models investigated to estimate abiotic degradation of PFASs, as the currently available versions of the QSARs are not adapted to accurately model perfluoroalkyl compounds.

B.4.1.2.3. Biotic degradation

For biodegradation, the modelling suites used were BIOWIN v4.11 of EpiSuite, which incorporates seven (7) different models to predict different endpoints related to biodegradability; OPERA, which predicts biodegradation and ready biodegradability; and VEGA, which predicts ready biodegradability.

BIOWIN1 (linear probability model) and BIOWIN2 (non-linear probability model) are intended to convey a general indication of biodegradability under aerobic conditions. BIOWIN3 (expert survey ultimate biodegradation model) and BIOWIN4 (expert survey primary biodegradation model) rate the ultimate and primary biodegradation of each compound on a semi-quantitative scale of 1 (longer than months) to 5 (hours). Primary biodegradation is the transformation of a parent compound to an initial metabolite. Ultimate biodegradation is the transformation of a parent compound to carbon dioxide and water, mineral oxides of any other elements present in the test compound, and new cell material. BIOWIN5 (MITI linear model) and BIOWIN6 (MITI non-linear model) are predictive models for assessing a compound's biodegradability in the Japanese MITI ready biodegradation test (OECD 301C). The critical biodegradation evaluations (results of the MITI tests) are either "readily degradable" (value of 1) or "not readily degradable" (value of 0). 0 to 1 is the full probability range. BIOWIN7 (anaerobic biodegradation model) estimates the probability of fast biodegradation under methanogenic anaerobic conditions; specifically, under the conditions of the "serum bottle" anaerobic biodegradation screening test. This endpoint is assumed to be predictive of degradation in a typical anaerobic digester.

The screening criteria for persistence in the environment are BIOWIN2 <0.5 or BIOWIN6 <0.5 and BIOWIN3 <2.25 as described in ECHA's Guidance on Information Requirements and Chemical Safety Assessment – Endpoint specific guidance (ECHA, 2017b).

Apart from the fragment [-CF₃], which is included in the training sets of BIOWIN 1 to 4, BIOWIN is generic when it considers "C bonded to atoms other than H", not being specific to C-F bonds. In addition, the fragment [-F] is included only in the training sets of BIOWIN 5 and 6 (MITI models). These limitations hamper BIOWIN's biodegradability prediction reliability, and the outputs should be interpreted individually and with caution.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

BIOWIN may be used as a supporting tool for aerobic biodegradability predictions, if results are interpreted individually, and all limitations stated. In addition, due to the apparent lack of [-F] and [-CF₃] fragments in the training set of BIOWIN 7, the prediction of PFASs anaerobic biodegradation using BIOWIN should also be interpreted with great care.

OPERA and VEGA returned a low reliability in the predictions of PFAS biodegradability for all subclasses. The results from these models are therefore not used in the assessment and only outputs from BIOWIN (for which the applicability domain is not explicit in the outputs) will be further discussed. For BIOWIN, there is no universally accepted definition of the applicability domain, and therefore different parameters should be considered to evaluate the prediction reliability.

Having these limitations in mind, the main finding of the QSAR modelling study is that all BIOWIN biotic models predict a (very) slow degradation of PFASs. QSAR modelling results of biotic degradation for the individual subgroups are summarized below. For all investigated substances, the estimated values are within the BIOWIN criteria indicating potentially persistent substances as described in ECHA's Endpoint specific guidance (ECHA, 2017b).

The predicted biodegradability of individual PFASs is found in Figure B.4.

Predicted Biodegradability of Six PFAS Categories

ECOSAR BIOWIN v4.11

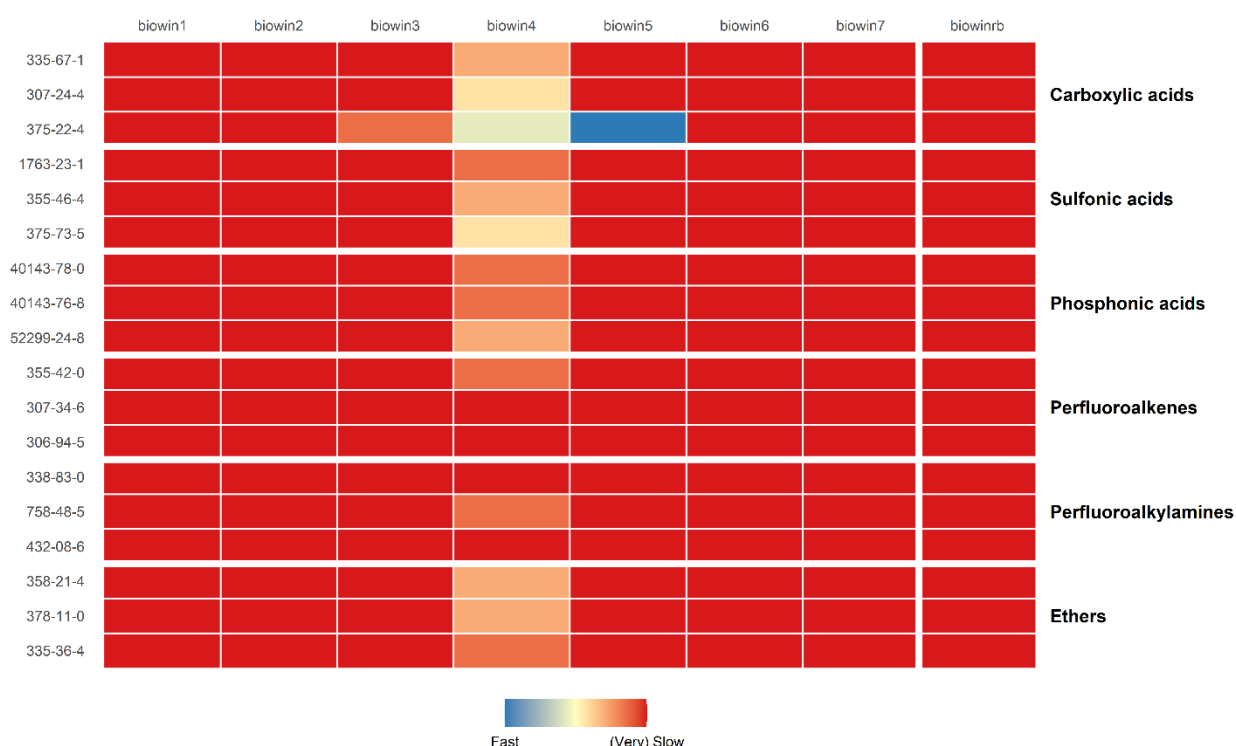


Figure B.4. Predicted biodegradability of the analysed PFAS categories and molecules (numbers on the left are CAS numbers).

The results from the BIOWIN 4 predictions of primary biodegradation show unexpected trends which are not in line with the knowledge from experimental studies for these substances. Hence, these results are regarded as indication that the model has limited suitability for these kinds of compounds.

Perfluoroalkanes

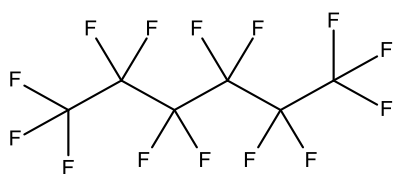


Figure B.5. Example structure: perfluorohexane.

Ravishankara et al. (1993) investigated the atmospheric lifetimes of long-lived halogenated species, including CF_4 , C_2F_6 , $\text{c-C}_4\text{F}_8$, $(\text{CF}_3)_2\text{C-C}_4\text{F}_6$, C_5F_{12} and C_6F_{14} . The possible atmospheric loss processes of these gases were assessed by determining the rate coefficients for the reactions of these gases with $\text{O}(^1D)$, H, and OH and the absorption cross sections at 121.6 nm in the laboratory and using these data as input to a two-dimensional atmospheric model. The lifetimes of all the studied perfluoroalkane compounds were found to be more than 2000 years.

These findings were confirmed by Say et al. (2021) who looked at the global trends and European emissions of tetrafluoromethane (CF_4), hexafluoroethane (C_2F_6) and octafluoropropane (C_3F_8). The fully fluorinated hydrocarbons were described to be potent greenhouse gases with lifetimes in the order of thousands to tens of thousands of years (50 000 years for CF_4).

Thermal decomposition of perfluoroalkanes starts above 800 °C (compounds with tertiary carbon atoms above 600 °C) with the formation of saturated and unsaturated decomposition products and some carbon (Siegemund et al., 2012).

From the group of perfluoroalkanes, perfluorohexane, perfluorooctane and perfluorodecaline were investigated with QSAR biodegradation models. The three substances were predicted to biodegrade slowly (BIOWIN 1, 2, 5, 6 and 7). Ultimate biodegradation (BIOWIN 3) predicted the three substances to be recalcitrant. Primary biodegradation (BIOWIN 4) estimated perfluorooctane and perfluorodecaline to be recalcitrant, while half-life of perfluorohexane was estimated to be months. All perfluoroalkanes were predicted as not readily biodegradable.

Haloperfluoroalkanes

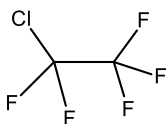


Figure B.6. Example structure: chloropentafluoroethane.

Fully halogenated compounds (Cl and Br in addition to F) with a high fluorine content have excellent thermal stability and are non-flammable. Chlorofluoroalkanes are characterized by high chemical and thermal stabilities, which increase with their fluorine content. At high temperature, thermal cleavage of the C-Br bond of bromoperfluoroalkanes into radicals may occur. The chemical stability of bromofluoroalkanes is slightly lower than that of the corresponding chlorofluoroalkanes. However, as with the chlorofluoroalkanes, stability

increases with the fluorine:bromine ratio. In contrast to chloro- and bromofluoroalkanes, iodofluoroalkanes readily undergo chemical reactions, reacting preferentially by homolytic cleavage of the C-I bond (Siegemund et al., 2012). However, when exposed to ultraviolet light in the upper atmosphere, chloro- and bromofluoroalkanes may suffer cleavage with release of chlorine or bromine radicals that can go on to destroy ozone in catalytic cycles. The atmospheric lifetime of the compound chloropentafluoroethane was reported to be 1 700 years (Forster, 2007). This PFAS subgroup has not been investigated so far with QSAR modelling.

Perfluoroalkylethers (PFAEs)

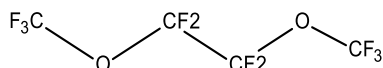


Figure B.7. Example structure: 1,1,2,2-tetrafluoro-1,2-bis(trifluoromethoxy) ethane.

The thermal stability of perfluoroalkylethers (PFAEs) was studied by Helmick (1990) in relation to the potential application of the substances as high temperature engine lubricants. A range of PFAEs was studied and found to have decomposition temperatures in the interval 301 - 389 °C which demonstrates the high thermal stability of the substances. Based on the investigated fluids, the authors concluded that the stability of the PFAEs was not affected by intrinsic factors such as carbon chain length, branching, or cumulated -CF₂- groups.

Hori et al. (2009) investigated the oxygen-induced mineralization of perfluoroalkylether sulfonates in subcritical water. They pointed out that ether linkages originally were inserted into the perfluoroalkyl chains so that the molecules should contain only short perfluoroalkyl fragments. In the first place these molecules were expected to decompose more easily than other PFASs because of the presence of the ether linkages, but no one has confirmed that they do in fact decompose more easily. Indeed, the authors observed that perfluoroalkylether sulfonates decomposed only at 350 °C in the presence of oxygen gas in supercritical water, while below 300 °C no reaction was observed.

Under environmentally relevant conditions perfluoroalkylether chains are similarly resistant to abiotic (photolysis, reactions with OH radicals, and hydrolysis) and biotic degradation as the perfluoroalkyl chains (Wang et al., 2015c).

Three ether substances were investigated with QSAR modelling for biodegradation: perfluorodiethylether, 1,1,2,2-tetrafluoro-1,2-bis(trifluoromethoxy)ethane and 2,2,3,3,4,4,5-heptafluorotetrahydro-5-(nonafluorobutyl)furan. All were predicted not to biodegrade fast (BIOWIN 1, 2, 5, 6 and 7). Ultimate biodegradation (BIOWIN 3) categorized all substances as recalcitrant, while primary biodegradation (BIOWIN 4) was weeks-months for perfluorodiethylether and 1,1,2,2-tetrafluoro-1,2-bis(trifluoromethoxy)ethane, and of months for 2,2,3,3,4,4,5-heptafluorotetrahydro-5-(nonafluorobutyl)furan. All three compounds were predicted as not readily biodegradable. The QSAR models include a negative fragment contribution of the aliphatic ether bond on the degradation potential. This indicates that the ether bond in PFECAs and PFESAs is not expected to decrease the environmental persistence as compared to PFCAs or PFASs.

The ether substance 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid (HFPO-DA/GenX), its salts and its acyl halides were recognized as very persistent by the Member State Committee and the substances identified as substances of very high concern, among others on the basis of an equivalent level of concern having probable serious effects to the environment which give rise to an equivalent level of concern to those of PBT/vPvB substances (ECHA, 2019d).

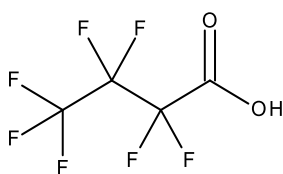
Perfluoroalkylcarboxylic acids (PFCAs)

Figure B.8. Example structure: Perfluorobutanoic acid (PFBA).

The sources, fate and transport of PFCAs were reviewed by Prevedouros et al. (2006). The PFCAs were evaluated as highly water-soluble and persistent with a high potential for long-range aquatic transport to the Arctic. PFCAs were shown to not undergo degradation in the environment. The global historical industry-wide emissions of total PFCAs were estimated to be 3 200-7 300 t. It was assumed that the majority (~80%) of this was released to the environment from fluoropolymer manufacture and use.

Qu et al. (2016) looked at the photochemical decomposition of the environmentally persistent PFCA-class. It was emphasized that the class of PFCAs are chemically inert due to the strong electronegativity of fluorine and very strong C-F bond, making them resistant to normal environmental degradation. In the study, the photodegradation of a series of PFCAs (C₂-C₁₂) in water by a medium-pressure mercury lamp was experimentally and theoretically examined. The PFCAs were mainly decomposed into shorter carbon chain length PFCAs in a stepwise manner, with the accumulation of TFA and fluoride ions as the end products. These findings could enhance the general understanding of the photodegradation of PFCAs, although the conditions investigated are not directly environmentally relevant.

Taniyasu et al. (2013) studied the environmental photolysis of PFASs in natural environment at high altitudes in Mt. Mauna Kea (Hawaii, USA; 4 200 m) and Mt. Tateyama (Toyama, Japan; 2 500 m). They observed decomposition of long-chain PFCAs (and PFSA) with successive dealkylation and formation of short-chain compounds such as PFBA (and PFBS), typically with 20-30% decomposition after 106 days. However, these observations were disputed by Wang et al. (2015b), who argued that the perfluoroalkyl carboxylic and sulfonic acids are too stable to undergo atmospheric photolysis and asked for information on whether adsorption of long-chain substances on the surface of the vials was considered in the experiments.

Among the perfluoroalkylcarboxylic acids, PFOA, PFHxA and PFBA were investigated for biodegradability with QSAR modelling. BIOWIN 1 and 2 predicted all of them not to biodegrade fast. BIOWIN 3 (ultimate biodegradation) predicted that PFOA and PFHxA are recalcitrant, while for PFBA a half-life of months was predicted. For primary biodegradation, BIOWIN 4 predicted semi-quantitative half-lives as PFOA (weeks-months) > PFHxA (weeks) > PFBA (days-weeks). For PFOA and PFHxA BIOWIN 5 and 6 predicted that these compounds do not biodegrade fast. For PFBA the linear model of BIOWIN 5 predicted fast biodegradability, while the non-linear model of BIOWIN 6 predicted that the substance does not biodegrade fast. The overall assessment of biodegradability by BIOWIN for all three perfluoroalkylcarboxylic acids was that they are not readily biodegradable.

BIOWIN 1-4 were reliable to predict all fragments except [-F]. Considering that [-F] contributes positively to biodegradation in BIOWIN 5 (linear MITI model), these results should be interpreted with caution, particularly for PFBA, which was predicted to biodegrade fast by BIOWIN 5, which is an unexpected result that does not match well with the range of observations of PFBA in environmental samples. See Appendix B.4.1.2. for further details of inclusion of fragments in training sets.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Perfluorooctanoic acid (PFOA) as well as six long-chained perfluorinated carboxylic acids (C9-C14 PFCAs) have been identified as substances of very high concern (SVHC) fulfilling the P and vP criteria according to REACH Annex XIII (ECHA, 2012b; ECHA, 2012c; ECHA, 2012d; ECHA, 2012e; ECHA, 2013; ECHA, 2015b; ECHA, 2016b). Furthermore, a REACH restriction on C9-C14 PFCAs including their salts and precursors has recently been adopted (ECHA, 2018a) due to their P and vP properties. A restriction on PFHxA its salts and related substances has been proposed based on its high persistence exceeding by far the P and vP criteria (ECHA, 2019c) and RAC has agreed to the extreme persistence as a key concern.

In 2019, PFOA its salts and PFOA-related substances were listed in the Stockholm Convention, and the restriction is included in the EU POPs regulation since 2020. Just recently a proposal has been submitted for long-chain perfluorocarboxylic acids, their salts and related compounds¹ under the Stockholm Convention.

Trifluoroacetic acid (TFA)

The environmental fate of TFA, together with trichloro-, dichloro-, and monochloroacetic acids, was investigated using field aquatic microcosms and laboratory sediment–water systems (Ellis et al., 2001). TFA was extremely persistent and showed no degradation during a one-year field study.

Biodegradation of mono-, di- and trifluoroacetate by microbial cultures with different origins was investigated by Alexandrino et al. (2018). Microbial inocula samples collected from a site with a long history of industrial contamination and activated sludge obtained from a municipal wastewater treatment plant were used in the study. Defluorination was obtained in the cultures fed with monofluoroacetate, while difluoroacetate and TFA were recalcitrant in all tested conditions. The authors pointed out that the persistence and accumulation of these substances in the environment is a relevant issue that may lead to disturbance in ecosystems.

TFA and its sources, pathways, and consequences for drinking water were assessed by Scheurer et al. (2017). It was pointed out that there are contradictory results in the scientific literature with regards to microbial degradation of TFA. Some studies have observed TFA to be persistent, while some other studies have reported microbial degradation of TFA; Visscher et al. (1994) reported the rapid (in the order of one week) microbial degradation of TFA in sediments under oxic and anoxic conditions, with formation of fluoroform. Kim et al. (2000) performed a long-term (90 weeks) study to assess biodegradation of TFA in an engineered anaerobic reactor. TFA was found to be co-metabolically degradable, and the authors indicated that anaerobic degradation is a potential removal pathway for TFA in freshwater sediments and may limit their accumulation in the environment. In their own study of degradation of TFA in a WWTP, Scheurer et al. (2017) observed no decrease of TFA concentrations over 28 days during biological wastewater treatment in accordance with a modified OECD guideline 302 B Zahn-Wellens test.

TFA is registered in the 1 000 – 10 000 t/y tonnage band in the ECHA database. In the registration dossier, the registrants have concluded, based on experimental evidence, that TFA fulfils both vP and P criteria, and TFA was found to be not readily nor inherently biodegradable, as well as not biodegradable under aerobic conditions. However, it was also stated by the registrant that a 'not assignable study' shows that co-metabolic degradation in anaerobic conditions can happen.

TFA was not investigated specifically in QSAR modelling of biodegradation.

¹ Long-chain PFCAs and their salts are a homologous series of substances with the molecular formula of $C_nF_{2n+1}CO_2H$ (where $8 \leq n \leq 20$). Related compounds are viewed as any substance that is a precursor and may degrade or transform to long-chain PFCAs, where the perfluorinated alkyl moiety has the formula C_nF_{2n+1} (where $8 \leq n \leq 20$) and is directly bonded to any chemical moiety other than a fluorine, chlorine or bromine atom.

Perfluoroalkane sulfonic acids (PFASs)

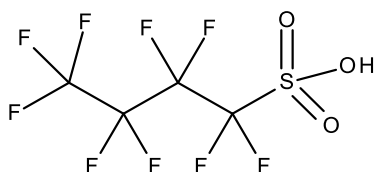


Figure B.9. Example structure: Perfluorobutane sulfonic acid (PFBS).

The Global PFC Group refers to PFASs as very persistent in the environment, while their potential precursors are transformed into PFASs abiotically or biotically (OECD/UNEP, 2013). Due to the high resistance to heat and chemical agents, the perfluoroalkyl substances have been frequently used in products with high versatility, strength, resilience and durability. However, the high persistence allows for a wide distribution in the environment, and many PFASs have been detected globally in the environment.

Perfluoroalkane sulfonic acids (PFASs) are very stable, with a very high thermal and chemical stability. Anhydrous PFASs are stable at 400 °C in the absence of air, but they may form hydrogen fluoride at this temperature when moisture is present. The sulfur atoms in PFASs are at their maximum oxidation state, and cannot be oxidised further (Arp and Slinde, 2018).

Defluorination of fluorinated sulfonates by a *Pseudomonas* strain was investigated by Key et al. (1998). Trifluoromethane sulfonate, PFOS and some related not fully fluorinated substances were subjected to biodegradation by *Pseudomonas* under aerobic, sulfur-limiting conditions. Growth and defluorination were observed for the compounds containing hydrogen on the carbon chain, while it is reported that trifluoromethane sulfonate and PFOS were not degraded.

Saez et al. (2008) studied the degradation of PFASs, including the sulfonic acids PFBS and PFOS, in closed bottle tests with municipal sewage sludge. Bacterial communities from sewage sludge were exposed to a mixture of PFASs under aerobic and anaerobic conditions. Individual PFAS concentrations were determined after solid phase extraction. The experiments were based on the OECD guideline 301D (closed bottle test) with slight modifications. It was found that the PFASs tested in these experiments are non-biodegradable under the conditions used.

A few studies have reported the degradation of PFOS by isolated bacterial strains under special laboratory conditions or by a specific enzyme when incubated with a mediator substance in laboratory conditions. A summary of the studies may be found in the SVHC Support Document for PFBS (ECHA, 2019e). These results show that bacteria may adapt to utilise the energy present in the PFAS substrates. However, such transformations have not been observed at environmentally relevant conditions.

PFOS, PFHxS and PFBS were investigated for biodegradation potential in QSAR modelling. All three substances were predicted not to biodegrade fast (BIOWIN 1, 2, 5, 6 and 7). BIOWIN 3 estimated the compounds to be recalcitrant, while the primary biodegradation model (BIOWIN 4) estimation was PFOS (months) > PFHxS (weeks-months) > PFBS (weeks). All three PFASs were predicted as not readily biodegradable.

It should be noted that the sulfonic acid structure fragment is not included in the MITI models of BIOWIN 5 and 6. Hence, the results from these models should be given little weight in the assessment.

In 2009, PFOS and its derivatives were included in the Stockholm Convention on Persistent

Organic Pollutants to eliminate their use before being restricted in the EU under the POPs Regulation.

PFBS and its salts have been included in the REACH Candidate List meeting the criteria under REACH Article 57(f), due to its very high persistence (ECHA, 2019e).

PFHxS fulfils the criteria for being “very persistent” and has been adopted as SVHC by the Member State Committee in 2017 (ECHA, 2017c). PFHxS, its salts and PFHxS-related compounds were also recently listed on Annex A of the Stockholm Convention without any exemptions for use.

Perfluoroalkyl phosphonic acids (PFPAs)

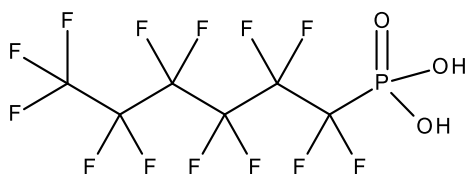


Figure B.10. Example structure: Perfluorohexyl phosphonic acid.

PFPAs are not expected to undergo hydrolysis under environmentally relevant conditions. They are resistant to basic hydrolysis (Emeleus and Smith, 1959) and stable in water at elevated temperatures up to 180 °C (Mahmood and Shreeve, 1986), similarly as PFCAs and PFSAs.

Biotransformation of PFPAs has not been observed. In a metabolism study, rats dosed with C8 PFPAs did not produce 1H-perfluorooctane, which has been observed for the similar substances perfluoroalkyl phosphinic acids at a lower oxidation stage (Joudan et al., 2017). A microbial degradation study conducted according to OECD Test Guideline (TG) 309 examined biodegradation of C6, C8 or C10 PFPAs (Llorca-Casamayor, 2012). Water used in the experiment was wastewater effluent taken from Beuerbach WWTP (Hesse, Germany). The samples were distributed in amber glass bottles and spiked with PFPAs mixture. The bottles were stirred 24 h/d in an orbital digester at 100 rpm and the pH was controlled. Dark conditions were used in order to minimize the algae growth. Aerobic conditions were maintained by aeration 30 min/d. The samples were compared with non-spiked blank samples, as well as with spiked samples treated with NaN₃ to stop all biological activity. Samples were regularly collected from the flasks and analyzed by LC-MS for quantification of the PFPAs substances. The experiment showed that no degradation had occurred for PFHxPA and PFOPA over 30 days. For PFDPA the results were inconclusive due to practical problems and formation of a biofilm on the walls of the experimental flasks.

Wang et al. (2016b) reviewed the environmental properties of e.g. perfluoroalkyl phosphonic acids. Existing evidence demonstrated high resistance of these substances to heat, oxidants, bases and aerobic degradation in surface waters. The authors concluded that the data suggested a high or very high persistence of PFPAs in the environment and biota, and a high long-range transport potential.

PFOPA, PFHxPA and PFBPA were investigated with the QSAR models in BIOWIN v4.11 of EpiSuite for biodegradability. All substances were predicted not to biodegrade fast (BIOWIN 1, 2, 5, 6 and 7). Ultimate biodegradation (BIOWIN 3) categorized all substances as recalcitrant, and primary biodegradation predicted half-life of PFOPA (months) > PFHxPA (months) > PFBPA (weeks-months). All three PFASs were predicted as not readily biodegradable. However, all the BIOWIN models lack coefficients for phosphonate (C-P bond),

which reduces the strength of the BIOWIN modelling results for this subclass.

Perfluoroalkylamines

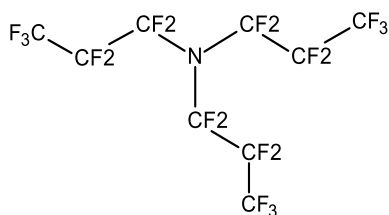


Figure B.11. Example structure: Perfluamine (=perfluoro(tripropyl)amine).

Siegemund et al. (2012) examined the properties of several fluoroorganic compounds. The perfluorinated tertiary amines were found to be chemically inert and thermally stable. The substances are deprived of the usual basic character and reactivity of amines due to the electron-withdrawing nature of the perfluoroalkyl substituents. Tertiary perfluoroalkylamines do not form salts or complexes with strong acids and are not attacked by most oxidizing or reducing agents.

Laboratory experiments were performed by Bernard et al. (2020) in order to assess the atmospheric lifetimes of perfluoroalkylamines $N(C_2F_5)_3$, $N(C_3F_7)_3$, and $N(C_4F_9)_3$. The $O(^1D)$ reaction and UV photolysis loss processes evaluated in this work were used in 2-D atmospheric model simulations to evaluate the global total atmospheric lifetimes. The atmospheric lifetime was found to be more than 3 000 years for all three substances.

Among the perfluoroalkylamines, perfluamine, perfluoromethyldiethylamine and perfluorotrihexylamine were selected for QSAR modelling of biodegradation. All substances were predicted not to biodegrade fast (BIOWIN 1, 2, 5, 6 and 7). Ultimate biodegradation (BIOWIN 3) predicted the three substances to be recalcitrant. Primary biodegradation (BIOWIN 4) estimated perfluamine and perfluorotrihexylamine to be recalcitrant, while the half-life of perfluoromethyldiethylamine was estimated to be months. All perfluoroalkylamines were predicted as not readily biodegradable.

For the compound perfluorotrihexylamine, the number of instances of the fragments [C with 4 single bond and no H] and [-F] exceeds too much the number in the training set. Therefore, the results of the BIOWIN modelling for this substance, should be interpreted with care.

B.4.1.2.4. The effects of chain length, branching and cyclic structure elements

Within each of the above PFAS subclasses the substances differ only in the number of perfluorinated carbon atoms in the carbon chain(s), i.e. the chain length. There is no evidence in the literature that the length of the perfluorinated carbon chain has a significant influence on the degradability/stability of these substances. Hence, all members of the same PFAS subclass are to be considered equally persistent. Neither ultrashort-chain (C1-C3) nor ultralong-chain PFAAs will biodegrade under environmentally relevant conditions, and PFAAs are regarded as highly stable substances in which several precursors ultimately degrade into.

The stability of organic fluorine compounds has been described in detail by Siegemund et al. (2012): "When all valences of a carbon chain are satisfied by fluorine, the zig-zag-shaped carbon skeleton is twisted out of its plane in the form of a helix. This situation allows the electronegative fluorine substituents to envelop the carbon skeleton completely and shield it from chemical (especially nucleophilic) attack. Several other properties of the C-F bond

contribute to the fact that highly fluorinated alkanes are the most stable organic compounds. These include low polarizability and high bond energies, which increase with increasing substitution by fluorine”.

It is not expected that branching of the perfluoroalkyl chain will significantly affect the high persistence of the corresponding unbranched PFAS substances as long as the alkyl chain is fully fluorinated.

Likewise, cyclic perfluoroalkyl structures are expected to be as persistent as linear or branched PFASs, potentially with the exception of very small ring structures with high ring strain (i.e. 3- or 4-membered rings). However, perfluorocyclobutane (PFC-318) has an atmospheric lifetime of 3 200 years, which demonstrates the high persistence even of 4-membered ring structures (Forster, 2007). The cyclic PFAS substance ammonium difluoro[[2,2,4,5-tetrafluoro-5-(trifluoromethoxy)-1,3-dioxolan-4-yl]oxy]acetate (CAS no 1190931-27-1) was shown to be not readily biodegradable (5% DOC removal) in a screening test for ready biodegradability (OECD 301A), see registration dossier².

Monitoring programs have detected the presence of perfluoroethylcyclohexane sulfonate (PFECHS, "cyclic PFOS") in water, sediments and biota from different places in the world, as well as in the Devon Ice Cap, see section B.4.2.7.4 on monitoring data. In the same section it is explained that perfluoropropylcyclopentanesulfonate (PFPCPeS) was found in environmental samples downstream of Beijing airport, which again demonstrates the high environmental stability of the substances.

B.4.1.2.5. Structural elements in combination

As described above, selected PFAS subclasses, or structural elements (different moieties), have been investigated and shown to be persistent and highly stable in the environment. The remarkable stability arises from the high strength of the C-F bond, in combination with structural elements which are not transformed under environmental conditions and which do not inflict sufficient reactivity to neighbouring C-F units. Hence, the PFAS subgroups described represent final degradation products that do not undergo any further degradation in the environment and are designated **arrowhead substances** or **arrowhead subgroups**.

Perfluoroalkyl acids with an acid functional group at its highest oxidation state, i.e. carboxylic, sulfonic and phosphonic acids represent structural endpoints in an oxidative environment. Degradation studies and monitoring data show that these substances are extremely persistent and do not undergo biotic or abiotic degradation in the environment.

It should be noted that all substances in the above assessment are perfluorinated substances with fully fluorinated carbon chains in combination with selected functional groups. If other functional groups or C-H bonds are included in the substance structure, further assessment of the stability may need to be conducted.

Any substance with a combination of the above-mentioned structure elements is also expected to be persistent. There is no reason to expect that these structure elements in combination will induce considerably higher reactivity in a perfluorinated substance as compared to substances containing these elements separately.

Examples of substances that contain a combination of several of the mentioned structure elements include HFPO-DA (GenX), ADONA, F53B, other perfluoroalkyl ether sulfonic acids and perfluoro-N-methylmorpholine (PMM), which can be found in Figure B.12.

² <http://echa.europa.eu/registration-dossier/-/registered-dossier/5712>, date of access: 2022-10-21.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

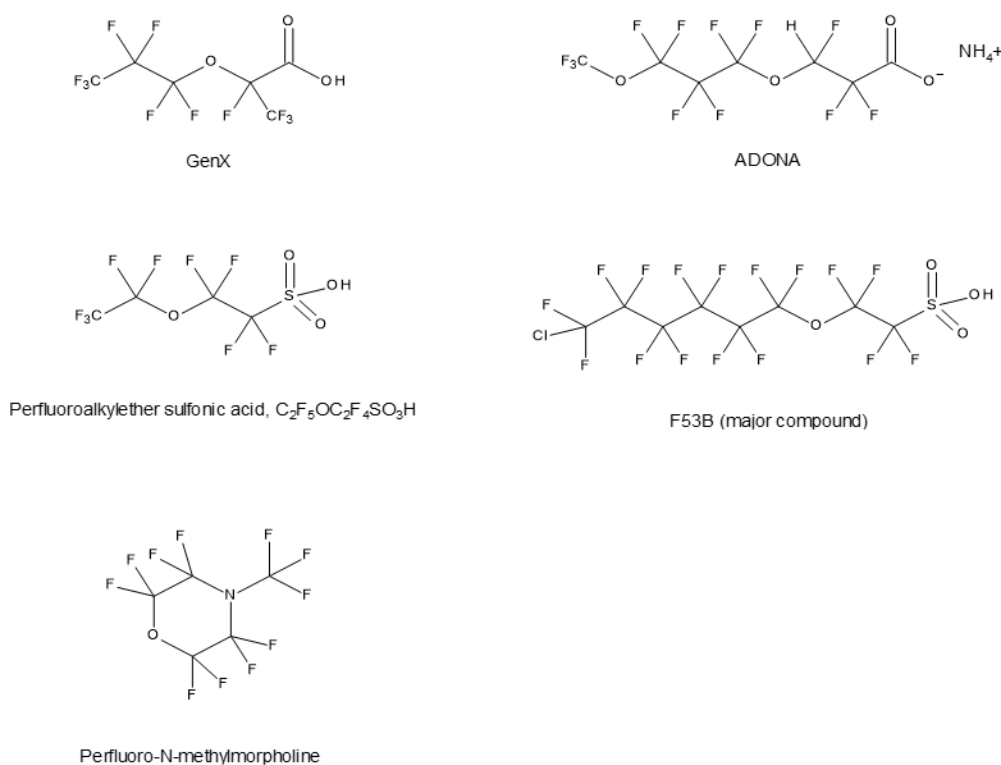


Figure B.12. Examples of substances with a combination of structural elements.

In the SVHC identification of HFPO-DA (GenX) it was concluded, based on available experimental evidence and QSAR information, that the substance exceeds the P and vP-criteria of REACH by far (ECHA, 2019d). Gordon (2011) evaluated toxicological aspects of ADONA and indicated that ADONA is a non-reactive, stable and not readily biodegradable substance that decomposes only at 125–175 °C. Perfluoroalkylether sulfonic acids, including $C_2F_5OC_2F_4SO_3H$, were shown to not undergo any reaction even in supercritical water with oxygen gas for 6 h at temperatures up to 300 °C (Hori et al., 2009). Wang et al. (2013b) looked at the environmental occurrence of F-53B in China and assessed its toxicity and persistence. Ready biodegradability of F-53B was measured in a Closed Bottle Test (CBT) according to OECD Guideline 301D. In addition, the stability of F-53B under various advanced oxidation process (AOP) conditions was assessed. Although the compound showed a slow degradation throughout the test period in the CBT, it did not meet the OECD criteria to satisfy ready biodegradation. Under all AOP test conditions, the degradation of F-53B was very low. The authors concluded that F-53B is not readily biodegradable, and their data suggested that F-53B is as persistent as PFOS. This is supported by the ubiquitous presence of F-53B in the environment in China, US, UK, Sweden, the Netherlands and Korea, while China is the only known location for emissions of the substance. This is a strong indication of high persistence of the substance. However, indications of slow de-chlorination of F-53B were found in an increased molar ratio of the H-analogue as compared to the manufactured mixture (Pan et al., 2018). Perfluoro-N-methylmorpholine (PMM), which contains both an ether structure unit and a tertiary amine in combination, is considered as very persistent by the registrant in the ECHA database (tonnage band: 100–1 000 t/y). The substance was assessed as very persistent by UBA (2019) on the basis of QSAR and biodegradation screening tests, and it has been added to the ChemSec SIN list³ as a very persistent and very mobile substance.

Fluoropolymers and side-chain fluorinated polymers

³ <https://sinlist.chemsec.org/>, date of access: 2022-09-29.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Many of the mentioned structural elements may be combined multiple times in polymeric chains. Again, the combination of persistent structural elements is expected to result in a persistent overall structure, where the number of persistent parts is high. Examples of fluoropolymers constructed from the mentioned persistent structure elements include e.g. polytetrafluoroethylene (PTFE), perfluoroalkoxy polymer (PFA), etc (see Figure B.13).

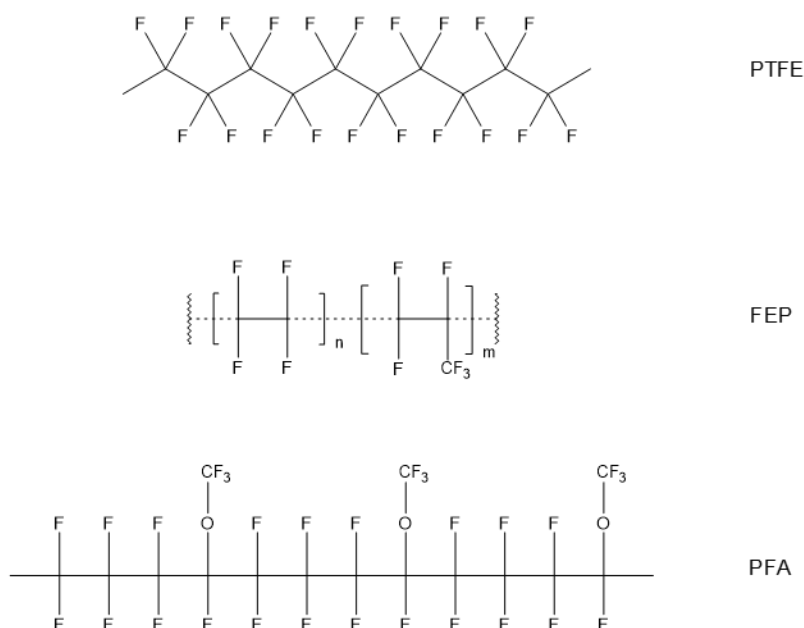


Figure B.13. Examples of fluoropolymers.

Lohmann et al. (2020) investigated whether fluoropolymers may be regarded as polymers of low concern for human and environmental health. With regards to persistence, they pointed out that fluoropolymers are very persistent under environmental conditions, which, in the same way as for other polymers, can lead to a wide array of concerns, particularly with respect to disposal of fluoropolymer-containing wastes and products. Current concern over microplastics present in the oceans is also related to fluoropolymers.

Henry et al. (2018) reviewed regulatory criteria of fluoropolymers in relation to the polymers' physical and chemical properties. It was indicated that fluoropolymers in general have high thermal, chemical, photochemical, hydrolytic, oxidative, and biological stability and that they are persistent. The authors looked in more detail at the four fluoropolymers PTFE (polytetrafluoroethylene), ETFE (ethylene tetrafluoroethylene), FEP (fluorinated ethylene propylene) and PFA (perfluoroalkoxy polymer) and concluded that these are stable under hydrolytic, light, oxidative, biodegrading (aerobic and anaerobic) and thermal conditions. Side-chain fluorinated polymers (SFPs) are different from the fluoropolymers in that they usually contain a non-fluorinated backbone with per- or polyfluorinated alkyl side-chains attached to the backbone via a linker (Buck et al., 2011). These linkers are often labile and may be cleaved under environmental conditions with liberation of well-known PFASs. SFPs are similar to non-polymeric PFAS precursors and are expected to follow the same reactivity pattern. See next section for examples on degradation of SFPs to PFAAs. Further discussion on the degradation of SFPs is provided, e.g. in the restriction proposal of PFHxA, its salts and related substances (ECHA, 2019c).

B.4.1.3. Degradation of precursors into the corresponding PFAS arrowheads

There are many PFASs which contain degradable non-perfluorinated moieties. These precursor substances are not completely persistent themselves but will ultimately degrade to very persistent PFAS arrowheads (PFAAs), through reactions such as atmospheric oxidation, metabolic transformations, and hydrolysis. It is expected that the degradation will primarily target the non-fluorinated parts. During the degradation process the non-fluorinated moieties are transformed and oxidative processes often lead to the gradual conversion of non-fluorinated carbon atoms into oxidized molecules such as CO₂ while the degrading substance structure is gradually getting smaller. In the end most of the non-fluorinated parts are usually lost, while the perfluoroalkyl part is remaining (although defluorination of the carbon atom next to the non-fluorinated part can occur), attached to a functional group at its highest oxidation state (e.g. carboxylic acid). Such functional groups often carry a negative charge which leads to an increased polarity for the degradation products. Hence, the fluorinated degradation products of PFASs may be assumed to have elevated mobility with water compared to precursor substances.

In the coming subsections, relevant available information on degradation of the following precursors is summarised:

PFCA precursors:

- n:2 Fluorotelomer alcohols (FTOHs)
- Other n:2 fluorotelomer derivatives
 - n:2 Fluorotelomer iodides (FTIs)
 - Esters of n:2 fluorotelomer alcohols
 - n:2 Polyfluoroalkyl phosphoric acid mono-/diesters (monoPAPs/diPAPs)
 - n:2 Fluorotelomer urethane (monomers)
 - n:2 Fluorotelomer sulfonic acids (FTSAs)
 - n:2 Fluorotelomer thioether amido sulfonates (FTTAoSs)
 - n:2 Fluorotelomer silanes
 - n:2 Fluorotelomer olefins (FTOs)
 - n:2 Fluorotelomer-based side-chain fluorinated polymers
- Other PFCA precursor
 - Perfluoroalkyl carboxylic acid halides
 - Amides of perfluoroalkyl carboxylic acids
 - n:1 Fluorotelomer alcohols
 - Perfluoroalkyl alcohols
 - Perfluoroalkyl iodides (PFAIs)
 - Perfluorinated olefins (with the formula $C_nF_{2n+1}-CF=CF-C_mF_{2m+1}$)
 - Side-chain fluorinated aromatics

Fluorinated gases:

- Hydrofluorocarbons (HFCs) and hydrofluoroolefins (HFOs)
- Hydrofluoroethers (HFEs)
- Perfluoroalkyl ketones
- Perfluoroalkyl nitrile compounds

PFSA precursors:

- Perfluoroalkane sulfonyl halides
- Perfluoroalkane sulfonic acid esters
- Perfluoroalkane sulfonamides (FSAs)
- Perfluoroalkane sulfide derivatives
- Perfluoroalkane sulfoxide derivatives
- Perfluoroalkane sulfinic acid derivatives
- Side-chain fluorinated polymers based on sulfonic acid derivative

PFPA precursors:

- Perfluoroalkyl phosphinic acids (PFPIAs)

These subsections include degradation data of the various PFAS subgroups in different compartments, such as air, soil, and water and involves different degradation mechanisms and pathways. Hence, the actual fate for a specific PFAS in the environment depends both on available degradation pathways for that PFAS subgroup and the physicochemical properties of the specific substance, like volatility and solubility that determines the partitioning to different compartments. The presence of microorganisms in those compartments is an additional factor that influences the degradation.

B.4.1.3.1. Degradation of PFCA precursors

The degradation pathways of several PFCA precursors into the corresponding PFCAs are extensively described in the Background documents to the Opinion on the Annex XV dossier proposing restrictions on PFOA (ECHA, 2018b), C9-C14 PFCAs (ECHA, 2018a), and PFHxA (ECHA, 2019c). Hence, this section is to a large extent based on the degradation information in these documents which has been discussed and accepted by RAC for the purpose of these restrictions. However, the subsection “Other PFCA precursors” are mainly PFAS subgroups that were not included in the background documents to previous restrictions.

The following PFAS subgroups are expected to degrade into PFCAs:

- n:2 Fluorotelomer alcohols (FTOHs)

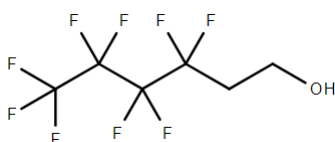


Figure B.14. Example of an n:2 fluorotelomer alcohol: 4:2 FTOH.

Based on the available data it can be expected that n:2 FTOHs will be degraded and transformed into C_x-PFCAs (with x= n-2, n-1, n, n+1; see Appendix B.4.1.3.1. Table B.75). This means that up to three -CF₂- groups can be defluorinated and mineralized to CO₂ and HF until the ultimate persistent PFCA is formed.

The degradation pathways of n:2 FTOHs exemplified by the degradation of 6:2 FTOH:

6:2 FTOH degrades to the corresponding PFCAs under various conditions (see Appendix B.4.1.3.1. Table B.75).

The degradation pathways of 6:2 FTOH in an aerobic river sediment system proposed by Zhao et al. (2013a) are illustrated in Figure B.15 and these pathways are typical for 6:2 FTOHs. In this specific study, after 100 days, 22.4 mol% 5:3 FTCA (5:3 fluorotelomer carboxylic acid; also referred to as 5:3 acid), 10.4 mol% C5-PFCA (PFPeA), 8.4 mol% C6-PFCA (PFHxA), and 1.5 mol% C4-PFCA (PFBA) were detected. Major intermediates during biotransformation of 6:2 FTOH were 6:2 FTCA (6:2 fluorotelomer carboxylic acid; also referred to as 6:2 acid), 6:2 FTUCA (6:2 fluorotelomer unsaturated carboxylic acid), 5:2 ketone, and 5:2 sFTOH (5:2 secondary fluorotelomer alcohol). The recovery of 6:2 FTOH and quantifiable transformation products ranged 71-88 mol% of initially applied 6:2 FTOH. The lower mass balance can be explained by formation of bound residues.

Another study investigated the biotransformation of the intermediate degradation product 5:3 FTCA in activated sludge (Wang et al., 2012). After 90 days 5:3 FTCA biotransformation yielded 14.2 mol% 4:3 FTCA, 5.9 mol% C5-PFCA (PFPeA) and 0.8 mol% C4-PFCA (PFBA).

These results implicate that 5:3 FTCA should not be regarded as an arrowhead, but rather a relatively stable intermediate that will ultimately degrade to the corresponding PFCAs. Still, the degradation rate of 5:3 FTCA is highly dependent on the specific environmental conditions. *E.g.* Liu et al. (2010c) incubated 5:3 FTCA in aerobic soil and after 60 days only 2% 4:3 FTCA was observed. According to the authors, this indicates that 5:3 FTCA is relatively resistant to biodegradation in soil due to its strong tendency to become irreversibly adsorbed to soil.

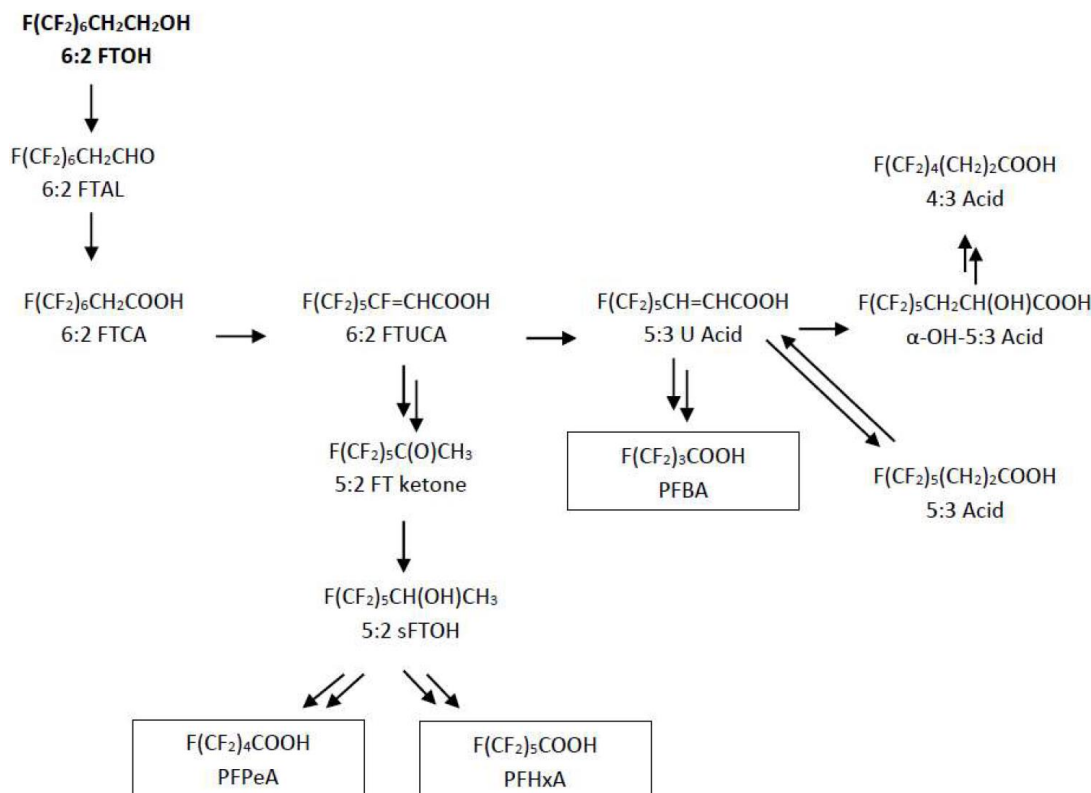


Figure B.15. Proposed 6:2 FTOH biotransformation pathways in aerobic sediment system (based on Zhao et al. (2013a)).

In one biodegradation study with 6:2 FTOH in an aerobic microbial culture (Sun et al., 2020) C2-PFCA (trifluoroacetic acid) (2.3 mol%) was formed along with other degradation products, meaning that in this specific case up to five $-\text{CF}_2-$ groups were defluorinated for a minor fraction of the starting material. However, once the PFCA, for example C4-PFCA (PFBA) is formed, that specific PFCA is persistent and will not show any further defluorination of $-\text{CF}_2-$ groups.

The photooxidation of 6:2 FTOH was investigated at the surface of TiO_2 , SiO_2 , Fe_2O_3 , Mauritanian sand, and Icelandic volcanic ash (Styler et al., 2013). At all surfaces the photooxidation resulted in the production of surface-sorbed PFCAs (PFHpA, PFHxA and PFPeA). These results provide evidence that the heterogeneous photooxidation of FTOHs at metal-rich atmospheric surface may provide a significant loss mechanism for FTOHs and also act as a source of aerosol-phase PFCAs close to source regions. The long-range transport of these aerosols is a possible source of PFCAs to remote areas.

The degradation pathways of n:2 FTOHs exemplified by the degradation of 8:2 FTOH:

8:2 FTOH degrades to the corresponding PFCAs under various conditions (see Appendix B.4.1.3.1. Table B.75). 8:2 FTOH metabolism universally shows the formation of PFOA and, to a smaller fraction, PFNA and lower-chain-length PFCAs (Butt et al., 2014).

The proposed degradation pathways of 8:2 FTOH in soil and activated sludge are illustrated in Figure B.16. These pathways are very similar to those proposed for 6:2 FTOH in Figure B.15. The percentages of the degradation products refer to several studies (Dinglasan et al., 2004; Wang et al., 2005a; Wang et al., 2009; Wang et al., 2005b).

8:2 FTOH metabolism universally shows the formation of PFOA and, to a smaller fraction, PFNA and lower-chain-length PFCAs – mainly PFHPA and PFHxA (Butt et al., 2014). 7:3 FTCA (7:3 fluorotelomer carboxylic acid; also referred to as 7:3 acid) is usually also a major degradation product but should not be regarded as an arrowhead, but rather a relatively stable intermediate that will ultimately degrade to the corresponding PFCAs (Butt et al., 2010; Li et al., 2018b).

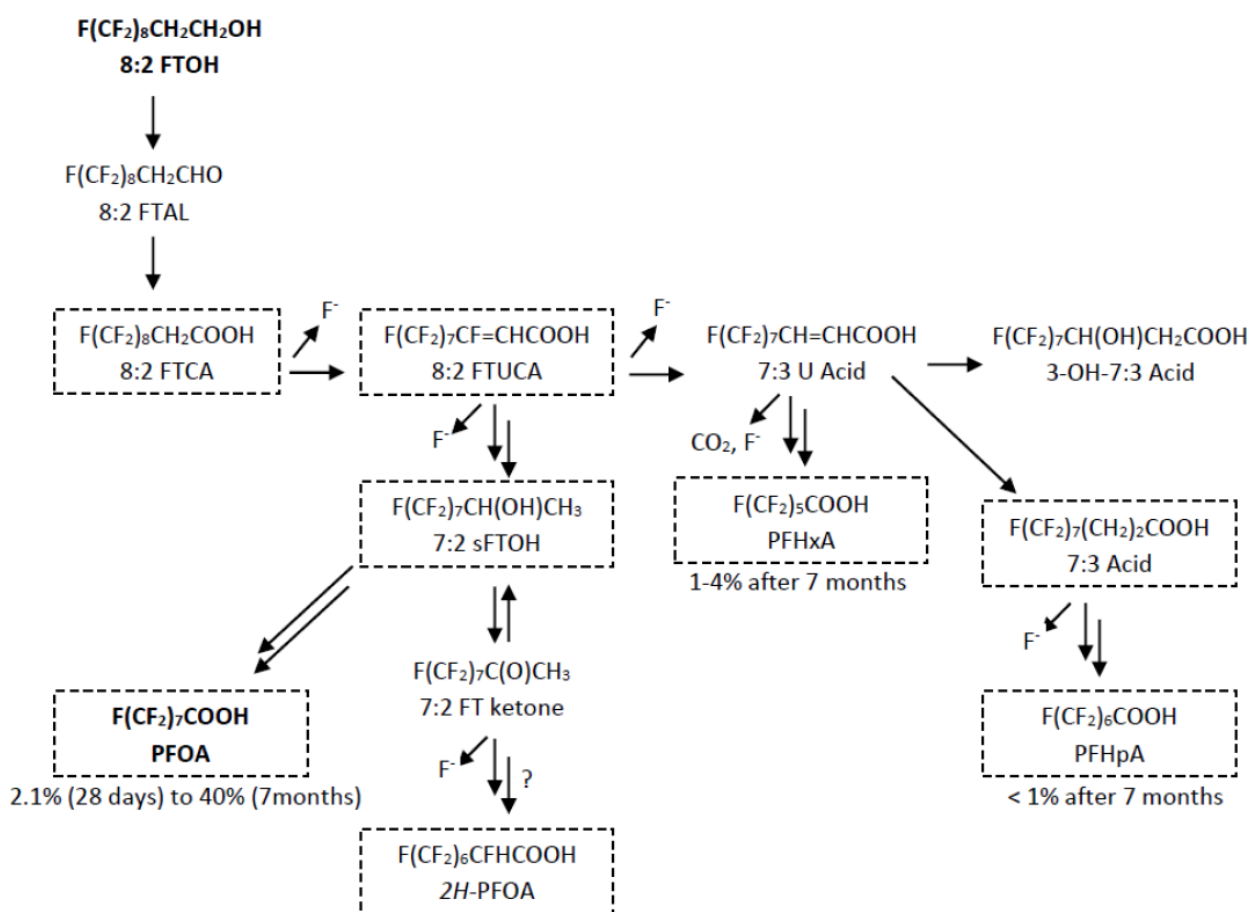


Figure B.16. Aerobic degradation pathways of 8:2 FTOH in soil and activated sludge (figure based on Liu and Mejia Avendano (2013)). Stable and semi-stable compounds are shown inside dashed boxes. 2H-PFOA (2H-C8-PFCA) has been proposed, but it has not been successfully validated.

In one biodegradation study with 8:2 FTOH in an anaerobic activated sludge (Li et al., 2018b) perfluoropentanoic acid (1.2%) and perfluorobutanoic acid (1.9%) were formed along with other degradation products, meaning that in this specific case up to five $-\text{CF}_2-$ groups were defluorinated. However, once the PFCA, for example C6-PFCA (PFHxA) is formed, that specific PFCA is persistent and will not show any further defluorination of $-\text{CF}_2-$ groups.

Atmospheric degradation was studied in a smog chamber (Ellis et al., 2004). Experiments were performed in 750 Torr of air at 296 K. Reaction mixtures were subject to 0.5 to 15 min

UV radiation leading to a consumption of FTOH in the range of 66 to >98%. It was shown that 8:2 FTOH is oxidized, initiated by Cl atoms which represent OH radicals, and forms PFNA, PFOA (1.5% C mass balance of 8:2 FTOH) and PFCAs containing a carbon chain of less than eight carbon atoms. The formation of PFOA is expected to be greater because intermediate transformation products were still observed (e.g. 26% 8:2 FTCA, 6% 8:2 FTAL (8:2 fluorotelomer aldehyde)). The authors stress that the formation of PFOA is small but significant and postulate that FTOH degradation is likely an important source of PFOA and other PFCAs in remote areas.

It can be assumed that the degradation mechanisms for n:2 FTOHs are independent from the chain length (see also section B.4.1.3 concerning the effects of chain length, branching and cyclic structure elements on persistence). A limited number of available degradation studies on n:2 FTOHs and the intermediate products are summarized in Appendix B.4.1.3.1. Table B.75.

- Other n:2 fluorotelomer derivatives
 - n:2 Fluorotelomer iodides (FTIs)

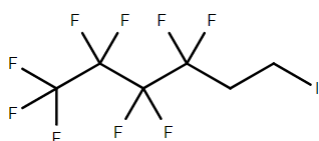


Figure B.17. Example of an n:2 fluorotelomer iodide: 4:2 FTI.

Based on the available data it can be expected that n:2 FTIs will be degraded and transformed into C_x-PFCAs (with x= n-1, n, n+1; see references and % PFCAs in Appendix B.4.1.3.1. Table B.76). n:2 FTIs follow a similar degradation pattern as the n:2 fluorotelomer alcohols forming the corresponding PFCAs, generally via an initial hydrolysis step forming the corresponding n:2 FTOH.

- Esters of n:2 fluorotelomer alcohols

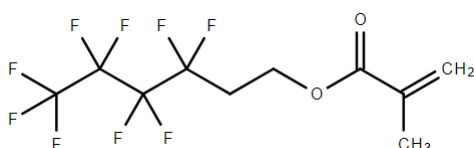
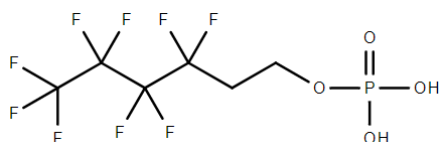


Figure B.18. Example of an ester of an n:2 FTOH: 4:2 fluorotelomer methacrylate (4:2 FTMA).

Based on the available data it can be expected that esters of n:2 fluorotelomer alcohols (e.g. n:2 fluorotelomer (meth)acrylates (FT(M)As), n:2 fluorotelomer stearate monoesters, and n:2 fluorotelomer citrate trimesters) will be degraded and transformed into C_x-PFCAs (with x= n-2, n-1, n; see references and % PFCAs in Appendix B.4.1.3.1. Table B.76). Esters of n:2 fluorotelomer alcohols follow the same degradation pattern as the n:2 fluorotelomer alcohols forming the corresponding PFCAs, generally via an initial hydrolysis step forming the corresponding n:2 FTOH.



Based on the available data it can be expected that n:2 monoPAPs and n:2 diPAPs will be degraded and transformed into Cx-PFCAs (with x= n-2, n-1, n, n+1; see references and % PFCAs in Appendix B.4.1.3.1. Table B.76). n:2 monoPAPs and n:2 diPAPs follow the same degradation pattern as the n:2 fluorotelomer alcohols forming the corresponding PFCAs, generally via an initial hydrolysis step forming the corresponding n:2 FTOH.

COc1ccc(cc1)C(F)(F)F

Based on the available data it can be expected that n:2 fluorotelomer urethane (monomers) will be degraded and transformed into C_x-PFCAs (with x= n-2, n-1, n; see references and % PFCAs in Appendix B.4.1.3.1. Table B.76). n:2 Fluorotelomer urethane monomers follow a similar degradation pattern as the n:2 fluorotelomer alcohols forming the corresponding PFCAs (generally via an initial hydrolysis step forming the corresponding n:2 FTOH).

OS(=O)(=O)CCCC(F)(F)C(F)(F)C(F)(F)C(F)(F)F

Based on the available data it can be expected that n:2 FTSAs will be degraded under aerobic conditions and transformed into Cx-PFCAs (with x= n-2, n-1, n, n+1; see references and % PFCAs in Appendix B.4.1.3.1. Table B.76). n:2 Fluorotelomer sulfonic acids follow a similar degradation pattern as the n:2 fluorotelomer alcohols forming the corresponding PFCAs, generally via an initial de-sulfonation step forming the corresponding n:2 FTOH or the corresponding n:2 FTAL (fluorotelomer aldehyde) directly, depending on the conditions.

- n:2 Fluorotelomer thioether amido sulfonates (FTTAoSs) [belonging to the PFAS subgroup n:2 fluorotelomer-thiol derivatives]

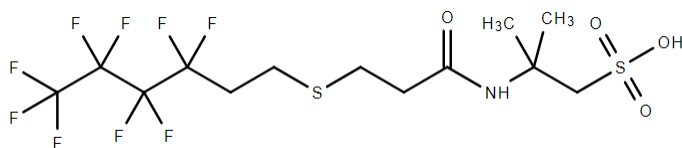


Figure B.22. Example of an n:2 fluorotelomer thioether amido sulfonate: 4:2 FTTAoS (FTTAoSs are used in aqueous film-forming foam (AFF) formulations).

Based on the available data it can be expected that FTTAoS (and similar substances belonging to the PFAS subgroup n:2 fluorotelomer-thiol derivatives) will be degraded under aerobic conditions and transformed into PFCAs (see references and % PFCAs in Appendix B.4.1.3.1. Table B.76). n:2 FTTAoSs follow a similar degradation pattern as the n:2 fluorotelomer alcohols forming the corresponding PFCAs, generally via initial oxidation of the thioether-group into a sulfinyl group followed by an oxidation/C-S-cleavage step to form a n:2 fluorotelomer sulfonic acid, followed by a de-sulfonation step primarily forming the corresponding n:2 FTOH or the corresponding n:2 FTAL (fluorotelomer aldehyde) directly, depending on the conditions.

- n:2 Fluorotelomer silanes

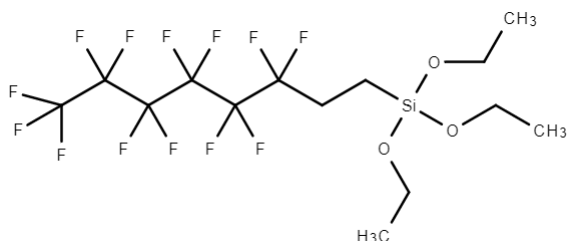


Figure B.23. Example of an n:2 fluorotelomer silane: triethoxy(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silane.

Based on the available data it can be expected that n:2 fluorotelomer silanes will be degraded and transformed into corresponding PFCAs in the atmosphere (see references and % PFCAs in Appendix B.4.1.3.1. Table B.76). Nielsen (2014) proposed a photo-oxidation-mediated mechanism in which the corresponding n:2 fluorotelomer carboxylic acids (n:2 FTCAs) are initially formed by oxidation/Si-C cleavage, followed by further degradation into the corresponding PFCAs (in analogy with degradation of FTOHs).

In a study by Zhu et al. (2019) 8:2 polyfluoroalkyl trimethoxysilane (8:2 PTrMeOSi) was degraded in a hydroxyl radical-based total oxidizable precursor assay, yielding perfluoroheptanoic acid (PFHpA, 49 ± 11%) (-2 CF₂), perfluorooctanoic acid (PFOA, 14 ± 3%) (-1 CF₂), perfluorohexanoic acid (PFHxA, 12 ± 3%) (-3 CF₂), perfluorononanoic acid (PFNA, 2 ± 0.2%) (-0 CF₂) and the other shorter-chain analogues with decreasing molar yields.

○ n:2 Fluorotelomer olefins (FTOs)

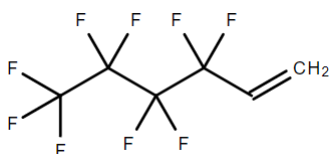


Figure B.24. Example of an n:2 fluorotelomer olefin: 4:2 FTO.

Based on the available data it can be expected that n:2 fluorotelomer olefins will be degraded and transformed into corresponding PFCAs in the atmosphere via a photo-oxidation-mediated mechanism (see Figure B.25 and references in Appendix B.4.1.3.1. Table B.76).

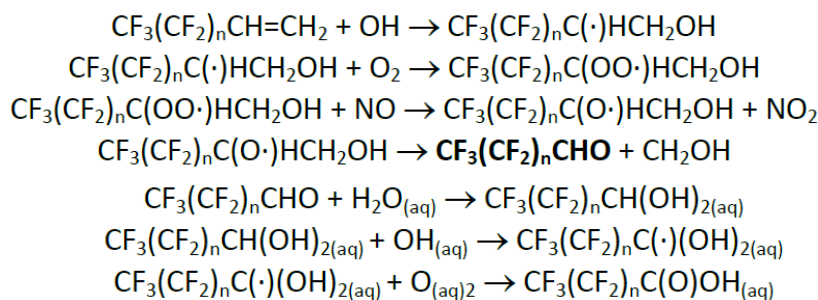


Figure B.25. Proposed atmospheric degradation pathway for n:2 fluorotelomer olefins into PFCAs from Nielsen (2014).

○ n:2 Fluorotelomer-based side-chain fluorinated polymers

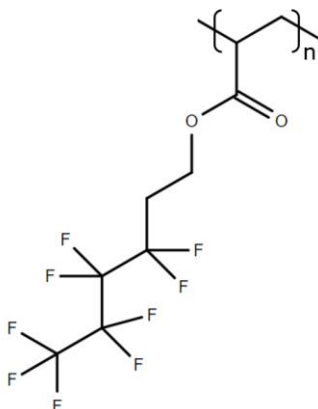


Figure B.26. Example of an n:2 fluorotelomer-based side-chain fluorinated polymer: 4:2 fluorotelomer acrylate polymer.

Based on the available data it can be expected that n:2 fluorotelomer-based side-chain fluorinated polymers will degrade in the same way as the small-molecule precursors into the corresponding PFCAs (Russell et al., 2008; Russell et al., 2010; Washington et al., 2009) (Rankin et al., 2014; Washington and Jenkins, 2015), generally via an initial hydrolysis step forming the corresponding FTOH.

It can be assumed that the degradation mechanisms of the n:2 fluorotelomer derivatives described above are independent from the chain length (see also section B.4.1.2 concerning the effects of chain length, branching and cyclic structure elements on persistence). A limited

number of available degradation studies on fluorotelomer derivatives are summarized in Appendix B.4.1.3.1. Table B.76.

- Other PFCA precursors (majority of these PFAS subgroups were not included in the background documents to previous PFCA restrictions)
 - Perfluoroalkyl carboxylic acid halides

Based on the available data it can be expected that perfluoroalkyl carboxylic acid halides will undergo hydrolysis with formation of the corresponding PFCAs. In the manufacturing of PFCAs, perfluoroalkyl carboxylic acid fluorides, $C_nF_{2n+1}C(O)F$ are hydrolysed in the last synthesis step to yield the corresponding PFCA $C_nF_{2n+1}C(O)OH$ (Buck et al., 2011). Perfluoroalkyl carboxylic acid fluorides, as well as other perfluoroalkyl carboxylic acid halides, are expected to undergo hydrolysis also under environmental conditions (Young and Mabury, 2010).

- Amides of perfluoroalkyl carboxylic acids

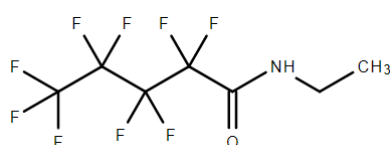


Figure B.27. Example of an amide of a perfluoroalkyl carboxylic acid: N-ethyl-perfluorobutyramide.

Based on the available data it can be expected that amides of perfluoroalkyl carboxylic acids ($C_nF_{2n+1}C(O)NRR'$) can be abiotically degraded (primarily in the atmosphere via a photooxidation-mediated mechanism) and transformed into corresponding PFCAs (mainly $C_nF_{2n+1}C(O)OH$; (Jackson and Mabury, 2013; Jackson et al., 2013)).

- n:1 Fluorotelomer alcohols

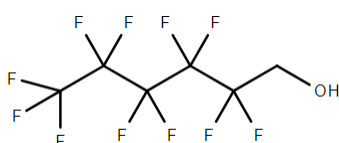


Figure B.28. Example of a n:1 fluorotelomer alcohol: 5:1 FTOH.

Based on the available data it can be expected that in the atmosphere n:1 fluorotelomer alcohols (n:1 FTOHs) can undergo OH-radical-mediated oxidation to form perfluoroaldehydes $F(CF_2)_nC(O)H$, which can be further oxidized to form the corresponding PFCAs (Hurley et al., 2006; Hurley et al., 2004b; Wang et al., 2014c).

In a study by Hurley et al. (2004b), n:1 FTOHs $F(CF_2)_nCH_2OH$ ($n = 1-4$) were reacted with Cl radicals in a smog chamber (UV irradiation of $F(CF_2)_nCH_2OH/Cl_2$ in air; the Cl radicals represent OH radicals). The reaction was followed by FTIR analysis. In all cases, the perfluoroaldehyde, $F(CF_2)_nC(O)H$, was the sole primary product. $F(CF_2)_nCOOH$, $C(O)F_2$, CF_3OH , and $CF_3O_3CF_3$ were observed as secondary products. According to the authors, reaction of $F(CF_2)_nCH_2OH$ ($n = 1-4$) is initiated by the abstraction of hydrogen, followed by reaction with oxygen, leading to formation of the perfluoroaldehyde, $F(CF_2)_nC(O)H$. In a separate study by Hurley et al. (2006), it was suggested that perfluoroaldehydes $F(CF_2)_nC(O)H$ can be further oxidized in the atmosphere via initial formation of perfluoroacyl peroxy radicals $F(CF_2)_nC(O)O_2$ that can react further with HO_2 radicals, forming the

corresponding PFCAs. The perfluoroaldehydes can also degrade via another route, forming $F(CF_2)_n$ radicals and CO, that can react further via a chain shortening mechanism. The authors argued that the relative importance of these two reaction pathways in the atmosphere requires detailed knowledge of the temperature- and pressure-dependence of respective pathway.

○ Perfluoroalkyl alcohols

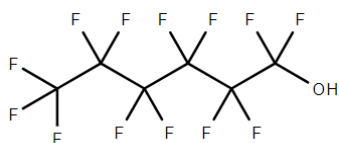


Figure B.29. Example of a perfluoroalkyl alcohol: perfluorohexanol.

Based on the available data it can be expected that in the atmosphere perfluoroalkyl alcohols ($C_nF_{2n+1}OH$) can undergo heterogeneous elimination of HF to give the acyl fluorides $C_{n-1}F_{2n-1}C(O)F$, which can hydrolyze to give the corresponding PFCAs $C_{n-1}F_{2n-1}C(O)OH$ (Ellis et al., 2004).

○ Perfluoroalkyl iodides (PFAIs)

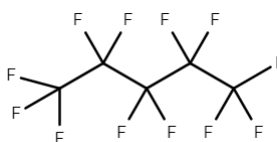


Figure B.30. Example of a perfluoroalkyl iodide: perfluoropentyl iodide.

Based on the available data it can be expected that perfluoroalkyl iodides can be abiotically degraded and transformed into PFCAs. Perfluoroalkyl iodides are known to readily undergo chemical reactions under certain laboratory conditions, such as gas phase photolysis, reacting preferentially by homolytic cleavage of the C–I bond (Nielsen, 2014; Siegemund et al., 2012). Based on this intrinsic property, perfluoroalkyl iodides can be expected to generate the radical C_nF_{2n+1} under certain environmental conditions, e.g. in the atmosphere, via a photooxidation-mediated mechanism. C_nF_{2n+1} is a potential source for PFCAs.

○ Perfluorinated olefins (with the formula $C_nF_{2n+1}-CF=CF-C_mF_{2m+1}$)

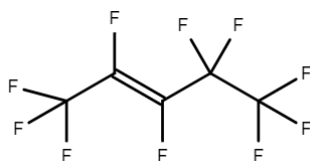


Figure B.31. Example of a perfluorinated olefin: perfluoropent-2-ene.

Based on the available data it can be expected that in the atmosphere perfluorinated olefins ($C_nF_{2n+1}-CF=CF-C_mF_{2m+1}$) can undergo OH-radical-mediated degradation forming the perfluoroacyl fluorides $C_nF_{2n+1}C(O)F + C_mF_{2m+1}C(O)F$ that can subsequently hydrolyse to the corresponding PFCAs $C_nF_{2n+1}C(O)OH + C_mF_{2m+1}C(O)OH$ (Young et al., 2009; Young and Mabury, 2010); see Figure B.32).

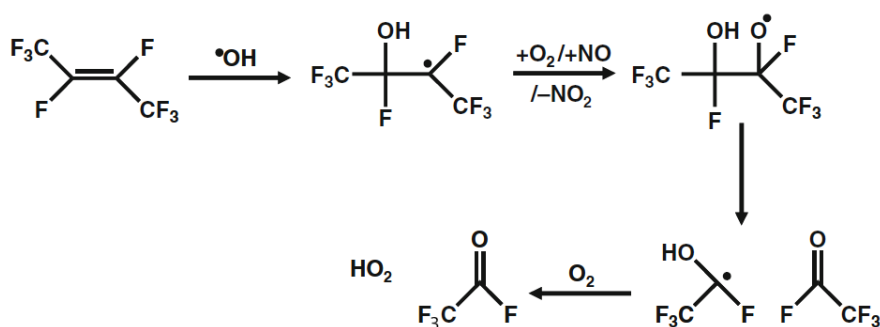


Figure B.32. Mechanism for the atmospheric oxidation of perfluorobut-2-ene (Young et al. 2009).

Young et al. (2009) investigated the expected atmospheric fate of two perfluorobutenes, $\text{CF}_3\text{CF}=\text{CFCF}_3$ and $\text{CF}_3\text{CF}_2\text{CF}=\text{CF}_2$, using smog chamber techniques. Rate constants for reaction with chlorine atoms and hydroxyl radicals were measured with relative rate techniques. The atmospheric lifetimes of $\text{CF}_3\text{CF}=\text{CFCF}_3$ and $\text{CF}_3\text{CF}_2\text{CF}=\text{CF}_2$ are determined by reaction with OH radicals and are approximately 24 and 6 days, respectively. The chlorine atom- and OH radical-initiated oxidation of $\text{CF}_3\text{CF}=\text{CFCF}_3$ in 700 Torr of air gives $\text{CF}_3\text{C}(\text{O})\text{F}$ in a molar yield indistinguishable from 200%, while the oxidation of $\text{CF}_3\text{CF}_2\text{CF}=\text{CF}_2$ gives $\text{CF}_3\text{CF}_2\text{C}(\text{O})\text{F}$ and COF_2 in molar yields indistinguishable from 100%. The atmospheric fate of $\text{CF}_3\text{C}(\text{O})\text{F}$ and $\text{CF}_3\text{CF}_2\text{C}(\text{O})\text{F}$ is hydrolysis to give perfluoroalkyl carboxylic acids (PFCAs), $\text{CF}_3\text{C}(\text{O})\text{OH}$ and $\text{CF}_3\text{CF}_2\text{C}(\text{O})\text{OH}$.

In a review article on atmospheric perfluorinated acid precursors, Young and Mabury (2010) argued that because perfluorinated chain length has not been shown to affect reaction mechanism in experiments with alcohols and acids, it is likely that any alkene, in which a C–F bond and a perfluorinated alkane chain appear on one side of the double bond, would be expected to follow this pathway, producing perfluoroacyl fluorides, and subsequently, PFCAs, in 100% molar yield. Fluorinated alkenes form PFCAs in 100 or 200% yield, under typical atmospheric conditions, in the presence or absence of NOx.

○ Side-chain fluorinated aromatics

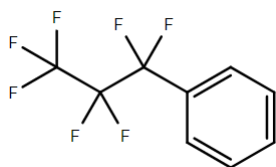


Figure B.33. Example of a side-chain fluorinated aromatic: (Heptafluoropropyl)benzene.

Based on the available data it can be expected that side-chain fluorinated aromatics ($\text{C}_n\text{F}_{2n+1}\text{-Ar}$) can be degraded and transformed into the corresponding PFCAs ($\text{C}_n\text{F}_{2n+1}\text{C}(\text{O})\text{OH}$).

The PFAS subgroup side-chain fluorinated aromatics is a very diverse group defined as “aromatics that have one or more aliphatic fully fluorinated saturated carbon moiety on the side chain(s) attached to the aromatic ring(s)” (OECD, 2021). The aromatic ring can be a phenyl group or any heteroaromatic group, with or without additional substituents. The fluorinated side-chain can have different carbon chain lengths and branching. The trifluoromethyl group is the most widely applied fluorinated side-chain.

There are many pesticides that contain a trifluoromethyl-substituted aromatic ring. The

corresponding PFCA, Trifluoroacetic acid (TFA), has been identified as a significant degradation product in numerous studies conducted as part of the EU evaluation of plant protecting active substances (with a variety of structural features), including:

Flurtamone (Figure B.34): Metabolism of flurtamone in primary crops was investigated in the cereals/grass (wheat, barley) and in oilseeds/pulses (sunflower, peanuts) crop groups, using ^{14}C - flurtamone (EFSA, 2016). TFA metabolite was identified as the most abundant compound of the total residues in wheat grain (86–93% total radioactive residue - TRR), in wheat forage (44% TRR) and in wheat straw (49% TRR), while 3-(trifluoromethyl)benzoic acid metabolite was predominantly identified in sunflower seed (19% TRR). The metabolism of flurtamone in primary crops proceeds mainly by hydroxylation, respectively, of the phenyl and trifluoromethylphenyl rings, followed by conjugation with malonic acid and glucose, N-demethylation, oxidative cleavage of the trifluoromethylphenyl moiety leading to TFA metabolite, and oxidative ring opening of the furanone moiety with subsequent cleavage and degradation of the carbon chain.

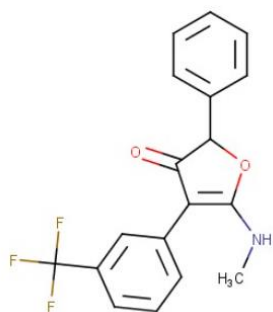


Figure B.34. Structural formula of flurtamone.

Saflufenacil (Figure B.35): Metabolism of saflufenacil in primary crops was investigated in maize, soybean and tomatoes, using ^{14}C - saflufenacil (EFSA, 2014). In maize, TFA was the predominant constituent (30.5% to 88% TRR, in grain it accounted for 0.004 mg/kg). Since the potentially corresponding ^{14}C - phenyl-labelled metabolites as counter parts of TFA were not detected at adequate quantities, the occurrence of TFA was explained by the uptake of this metabolite or a respective precursor molecule from the soil. In soya beans after pre-emergence application to the soil surface, TFA was the major compound identified (65.4%TRR (beans) to 85.2%TRR (forage)). In tomatoes TFA was also found being the predominant constituent (48.6% TRR (in fruit) to 82.2%TRR (in tomato plant)). The occurrence of TFA was explained by the uptake of this metabolite or of a respective precursor molecule from the soil.

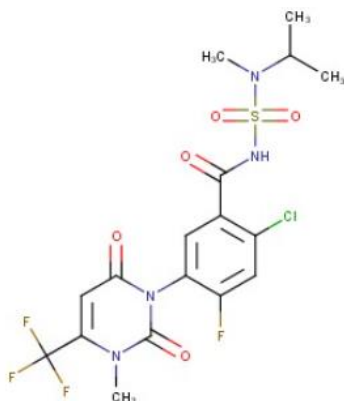


Figure B.35 Structural formula of saflufenacil.

Fluazinam (Figure B.36): Fluazinam is proposed to be used on crops that can be grown in rotation with other crops. In the confined rotational crop studies (EFSA, 2017b), TFA was the only relevant compound in rotational crops (lettuces, barley grains, carrots). Fluazinam or any of its primary metabolites were not found.

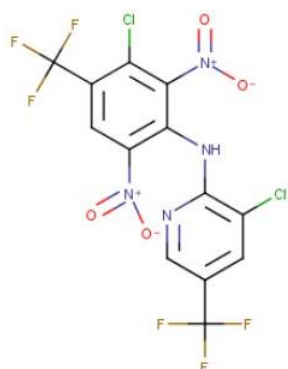


Figure B.36 Structural formula of fluazinam.

Fluometuron, trifloxystrobin and cyflumetofen (Figure B.37) are additional examples of plant protecting active substances where TFA has been identified as a significant metabolite in their respective EU evaluation (EFSA, 2017a; EFSA, 2019b; EFSA, 2021).

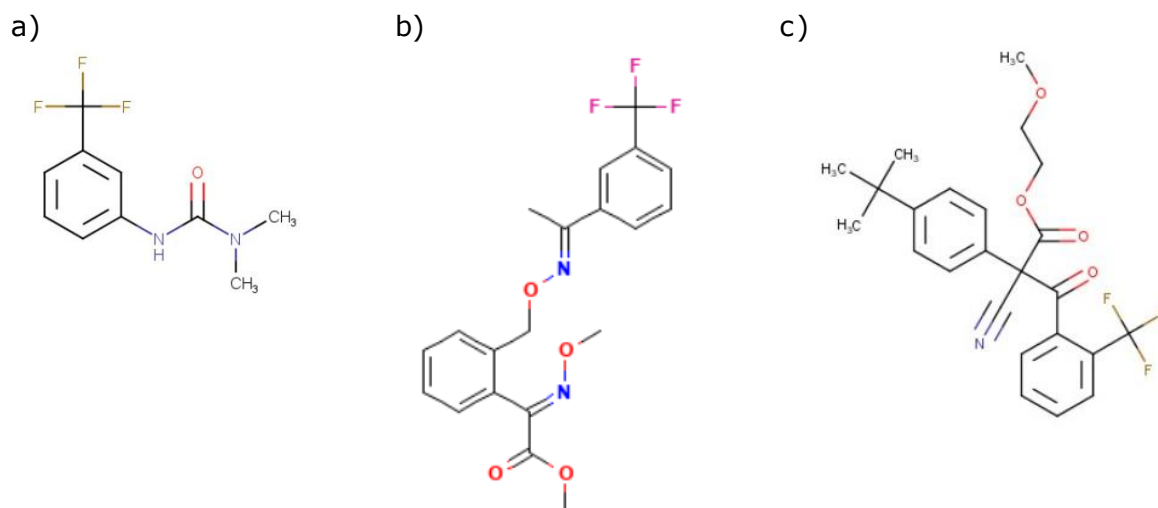


Figure B.37 Structural formulas of fluometuron (a); trifloxystrobin (b); cyflumetofen (c).

In a study by Scheurer et al. (2017) the potential TFA formation in wastewater treatment plants (WWTP) was investigated for a number CF₃-containing compounds, including five trifluoromethyl substituted aromatics: the pharmaceutical active substances fluoxetine and sitagliptine and the plant protecting active substances flufenacet, flurtamone and fluopyram (see Figure B.38).

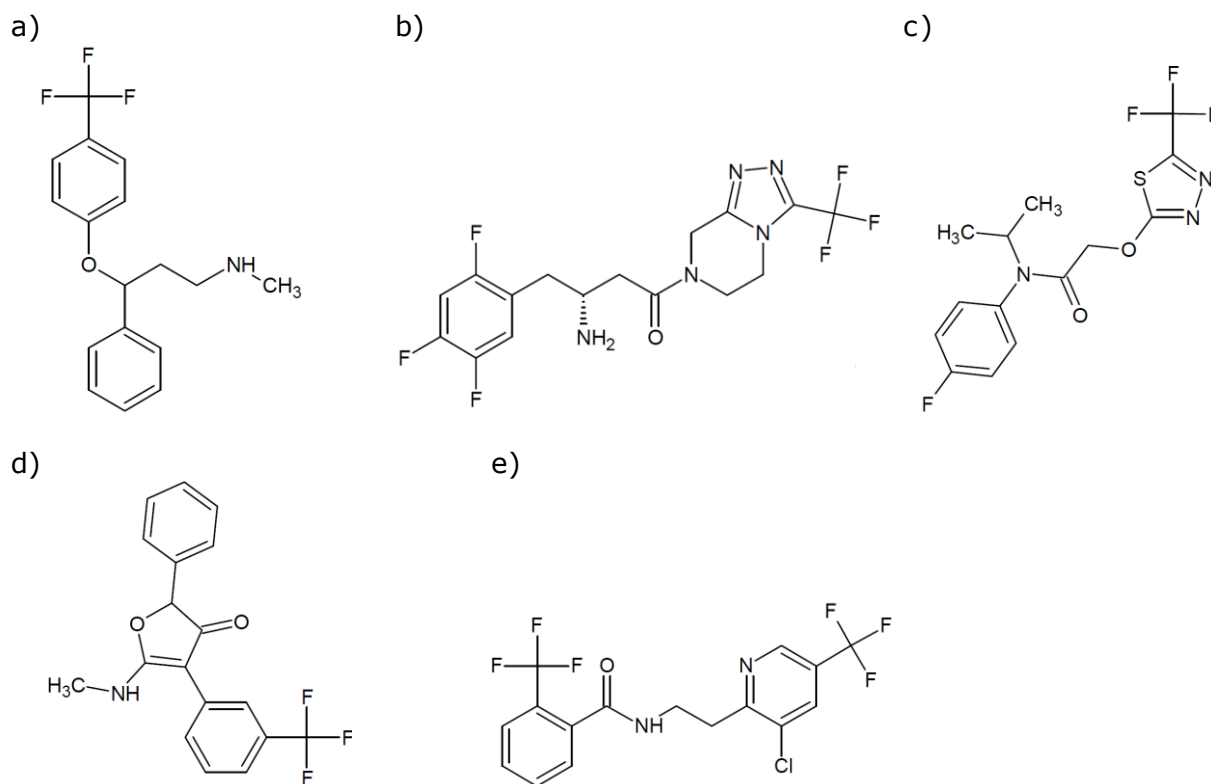


Figure B.38. Pharmaceutical active substances: fluoxetine (a) and sitagliptine (b) and the plant protecting active substances flufenacet (c), flurtamone (d) and fluopyram (e) were examined for their potential degradation to TFA in wastewater treatment plants during activated sludge treatment or upon ozonation (Scheurer et al., 2017).

The TFA-evolution-potential of the test compounds by chemical oxidation were examined. A concentration of 100 µg/L of the test compound was applied in demineralized water and two different ozone dosages (0.4–0.5 mg/L and 4–5 mg/L) were used. Samples were taken after contact times between 5 min and 60 min. Fluoxetine and flurtamone were rapidly degraded by ozone and could not be detected after 5 min contact time at both ozone concentrations applied. Approx. 40% TFA had been formed on a molar base from fluoxetine and flurtamone after 60 min. The respective precursor compounds were completely oxidized after 5 min contact time but a steady increase of TFA over the course of the test indicated that intermediates are formed, which are further oxidized to TFA. A comparatively fast but incomplete oxidation after 60 min was also observed for flufenacet and fluopyram. TFA yields were 19% and 32%, respectively. Sitagliptine was completely degraded after 60 min contact time in the batches with 4 mg/L, but the TFA yield was lower (4%).

The biological degradation of the test compounds was investigated by conducting a modified OECD guideline 302 B Zahn-Wellens test. In the test, sewage sludge directly taken from the activated sludge basin of the local WWTP was used as inoculum and were spiked with an aqueous solution of the test compound to obtain a final concentration of 1 mg/L. Samples were collected at least once a week and at days 27 and 28 according to the guideline. The primary degradation of the compounds and the formation of TFA was followed by LC/MS/MS. At the end of the test (28 d) removal of 67% fluoxetine, 56% flufenacet, 51% flurtamone, 25% fluopyram and 20% sitagliptine was observed. A steady increase of TFA was observed and after 28 d the following TFA concentrations were measured: 1.4 µg/L (fluoxetine), 7.4 µg/L (flufenacet), 1.4 µg/L (flurtamone), 1.2 µg/L (fluopyram), 0.3 µg/L (sitagliptine). These TFA concentrations correspond to up to 5% molar transformation of the degraded parent compounds.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

In a mechanistic study by Khan and Murphy (2021), the microbial degradation pathways of the pharmaceutical active substance fluoxetine by common environmental bacteria were investigated by ^{19}F NMR and GC–MS analyses. After fluoxetine had been incubated with bacteria, TFMP was shown to accumulate, and it is proposed that the ether bond in fluoxetine is initially hydrolysed yielding 4-(trifluoromethyl)phenol (TFMP) and 3-(methylamino)-1-phenylpropan-1-ol. The latter degraded further while TFMP remained in the culture supernatant. In a subsequent experiment, when TFMP was incubated with bacteria separately, it was degraded further and TFA was ultimately formed. In addition to TFA, ^{19}F NMR signals from the meta-cleavage products were detected as well as for fluoride ions. The formation of fluoride ions was explained by a competing photolytic degradation of the meta-cleavage products, resulting in defluorination. The extent of this defluorination pathway was facilitated by the exposure of light. Based on these experimental observations and predicted intermediates from the EAWAG Biocatalysis/Biodegradation Database, the overall degradation pathways for fluoxetine were proposed by the authors (Figure B.39).

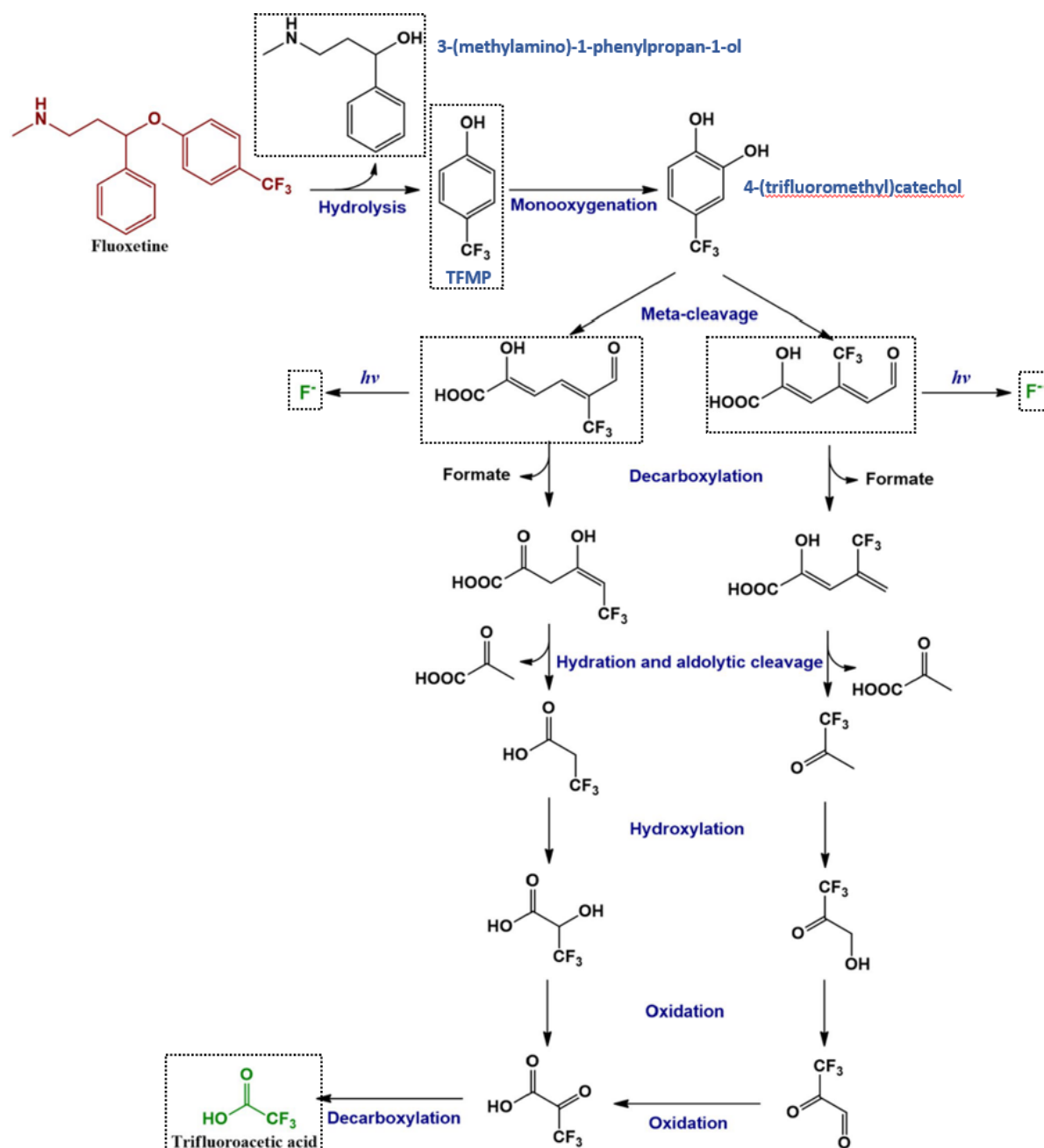


Figure B.39. Degradation pathways for fluoxetine based on the predicted intermediates from the EAWAG Biocatalysis/Biodegradation Database and the experimental observations. Degradation products that were observed with ^{19}F NMR and/or GC-MS analyses are shown inside dashed boxes.

In a study by Tisler et al. (2019), the degradation of fluoxetine by photolysis (solar simulator at 295-3 000 nm) during a 28-h experimental period in phosphate buffered water was monitored by LC-MS/MS analysis. A complex mixture of degradation products was identified including intermediate degradation products retaining the CF_3 -group such as 4-(trifluoromethyl)phenol (TFMP), but also defluorinated degradation products such as hydroxylated benzoic acid. TFA occurrence during direct photolysis was in average 0.3%. During indirect photolysis 1.5% of degraded fluoxetine was transformed to TFA. According to the authors, since TFA can be considered as a mineralization dead-end product, it will presumably occur in low amounts only, if photodegradation is incomplete and the concentrations of intermediates are still increasing. Hence, the level of TFA can be expected

to increase after extended photolysis (>28 hours).

In a mechanistic study by Ellis and Mabury (2000), photolysis degradation experiments of 3-trifluoromethyl-4-nitrophenol (TFM) were carried out at 365 nm in buffered deionized water (pH 7 and pH 9) and analysed by ^{19}F NMR and HPLC–UV. The half-life of TFM at was found to be 22 h at pH 9 yielding 5.1% TFA, and 91.7 h at pH 7 yielding 17.8% TFA. In addition to TFA, the formation of fluoride ions was also observed and explained by competing degradation pathways that seemed to be facilitated by a higher pH (see proposed degradation pathways in Figure B.40). This type of defluorination degradation pathway (via the deprotonated TFM) has been reported previously for *ortho*- and *para* trifluoromethyl phenol (as the only degradation pathway under abiotic degradation conditions; (Sakai and Santi, 1973). This was also verified in separate experiments with *ortho*- and *para* trifluoromethyl phenol within this study.

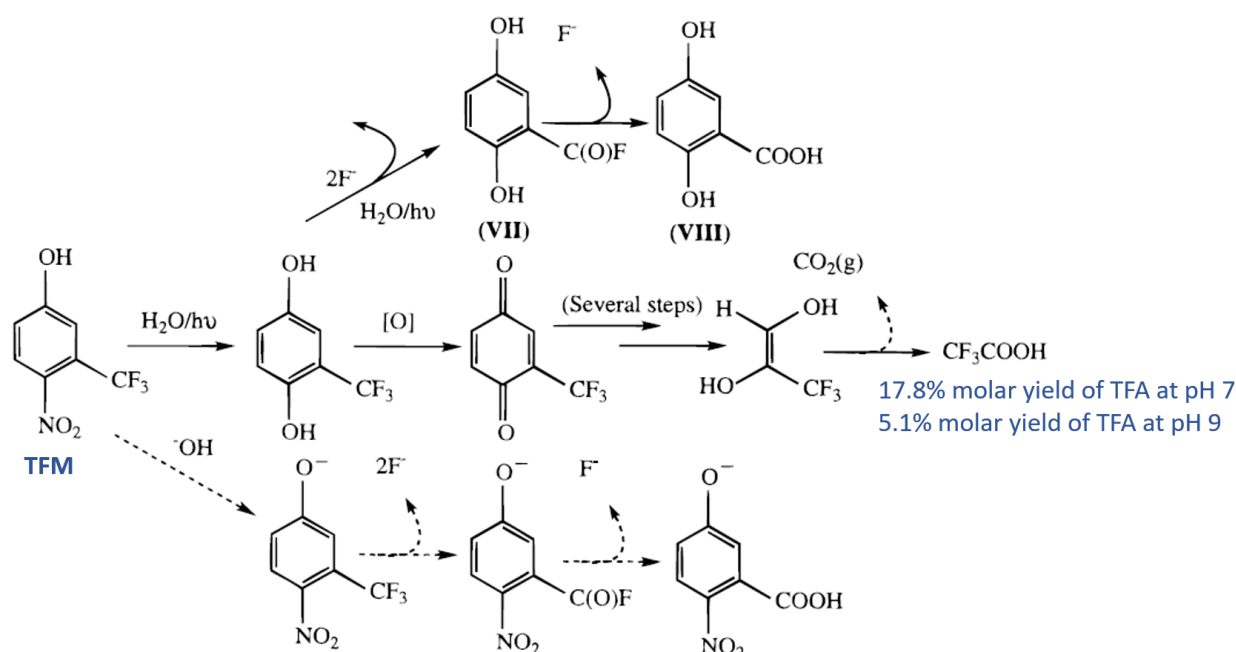


Figure B.40. Photolysis degradation pathways of TFM proposed by Ellis and Mabury (2000).

Conclusions on degradation of PFCA precursors

In conclusion, all PFCA precursor share the same basic structural features: a perfluorinated aliphatic part ($\text{F}(\text{CF}_2)_n-$) (linear/branched/cyclic) attached to a degradable moiety, including for example $-\text{CH}_2-\text{R}$, -aromatic group, $-\text{C}(\text{O})\text{NRR}'$. These substances can be degraded to PFCAs by abiotic and/or biotic processes in the environment. However, there may be a large variation in the degradation rates, pathways and to what extent the corresponding PFCAs are formed depending on the specific environmental conditions. For those substances where no specific degradation studies are available, degradation pathways can in many cases be assumed based on the chemical similarity with related substances, irrespective of chain length or branching of the perfluoroalkyl moieties. Still, physicochemical properties like volatility and solubility of a specific substance will influence the partitioning to different compartments in the environment and thus affect the environmental fate.

The above conclusions are to a large extent based on the reasoning in the Background documents to the Opinion on the Annex XV dossier proposing restrictions on PFOA (ECHA, 2018b), C9-C14 PFCAs (ECHA, 2018a), and PFHxA (ECHA, 2019c) which has been discussed and accepted by RAC for the purpose of these restrictions.

B.4.1.3.2. Degradation of fluorinated gases

A part of the PFAS universe are fluorinated gases which end up in the atmosphere after releases and therefore degrade under different conditions, as compared to PFAS that mainly partition to water and soil. Following release into the environment, fluorinated gases reside in the atmosphere where they are oxidized into a variety of degradation products. Some degrade easily in the atmosphere, while others are more stable and require much longer times. Some degradation routes lead to formation of TFA as a single product in high yields which precipitates with rain and snow. In some cases, intermediate degradation products form, which may degrade further via several pathways. For example certain fluorinated gases have more complex degradation mechanisms which partly lead to complete degradation and formation of degradation products like CO₂ and HF, while TFA formation is a minor degradation product.

- Hydrofluorocarbons (HFCs) and hydrofluoroolefins (HFOs)

When evaluating the degradation of fluorinated gases like HFCs and HFOs, there are some key intermediates which are formed from several different starting gases. These include trifluoroacetaldehyde (CF₃CHO), trifluoroacetyl fluoride (CF₃COF) and trifluoromethanol (CF₃OH), see Figure B.41 below. For example, fluorinated gases containing one or more C-H bonds are susceptible to attack by OH radicals in the lower atmosphere (Wallington et al., 1994). These radical processes lead to carbonyl compound intermediates, e.g. trifluoroacetaldehyde (CF₃CHO) or trifluoroacetyl fluoride (CF₃COF). It is known that the atmospheric decomposition of e.g. HFO-1234ze (CHF=CH-CF₃) yields trifluoroacetaldehyde (CF₃CHO) with 100% molar yield (Hansen et al., 2021; Nilsson et al., 2009; Qing et al., 2018).

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

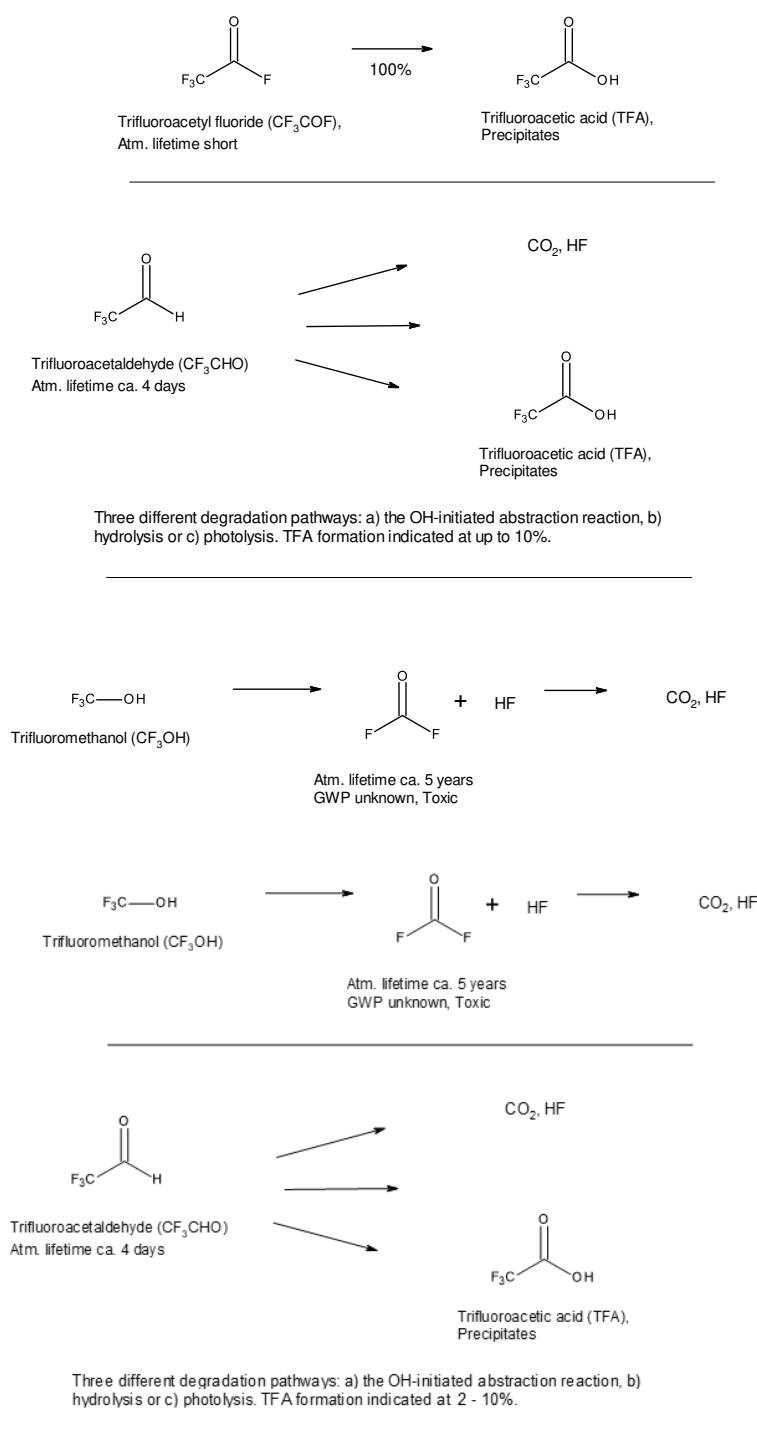


Figure B.41. Degradation routes of some key intermediates from fluorinated gases.

The sequence of gas-phase reactions that follow from an initial attack of OH radicals on the parent halocarbon are sufficiently rapid that heterogeneous and aqueous processes play no role. In contrast, the lifetimes of the carbonyl products are relatively long (weeks) and hydrolysis in water droplets may be relevant for the removal of halogenated halogen compounds (Wallington et al., 1994).

For trifluoroacetaldehyde (CF_3CHO) reaction with OH radicals is important, while trifluoroacetyl fluoride (CF_3COF) is removed almost entirely into water droplets. Although acid fluorides are almost insoluble in water, they hydrolyze quickly with formation of HF and the corresponding carboxylic acid which are very water soluble. Hence, hydrolysis removes trifluoroacetyl fluoride (CF_3COF) from the gas phase irreversibly as TFA. For trifluoroacetaldehyde (CF_3CHO) further gas-phase oxidation processes are important.

The atmospheric degradation of trifluoroacetaldehyde (CF_3CHO) can occur via three competing reactions: a) the OH-initiated abstraction reaction, b) hydrolysis or c) photolysis ((UBA, 2021c), page 106, and references therein). TFA may be the outcome of some of these processes and subprocesses (e.g. path b, hydrolysis, Figure B.41), with CO_2 and HF indicated as the final end products in the other processes. How important the three different degradation processes are relative to each other is unclear, while up to 10% formation of TFA from trifluoroacetaldehyde (CF_3CHO) has been estimated by UBA (2021c), page 109.

Buszek and Francisco (2009) looked at the gas-phase decomposition of trifluoromethanol (CF_3OH) with water. They pointed out that it is known that trifluoromethanol quickly degrades into carbonyl fluoride (CF_2O) and HF at room temperature, while the photolytic lifetime of the substance in the atmosphere below 40 km is very long, see section B.4.1.4. Hence, trifluoromethanol in the atmosphere is acting as a sink for hydrofluorocarbons (HFCs) and hydrofluoroethers (HFEs). However, the authors identified a catalytic mechanism with water and OH radical to be relevant for the decomposition of trifluoromethanol and formation of carbonyl fluoride (CF_2O) and HF.

Sulbaek Andersen et al. (2018) investigated the atmospheric degradation of HCFO-1233zd(E), E- $\text{CF}_3\text{CH}=\text{CHCl}$ in a 3-dimensional global atmospheric chemistry and transport model. Atmospheric degradation of E- $\text{CF}_3\text{CH}=\text{CHCl}$ is initiated by reaction with OH radicals, which leads to several chemical oxidation products. The atmospheric lifetime was estimated to ca. 36 days, and GWP at <5. The degradation pathways were shown to go via CF_3CHO as a key intermediate, which over time degrades further to HF and CO_2 or TFA. In this model TFA formation was indicated at approximately 2%. As HFO-1234ze also degrades via the intermediate CF_3CHO , a similar yield of TFA is expected, while HFO-1336mzz(Z) degrades with formation of 2 molecules of CF_3CHO and would therefore give approximately 4% TFA.

In a comprehensive overview of the current knowledge on HFO degradation to TFA and the consequences for human health and the environment following from increasing TFA-concentrations in the environment, the group ATMOSphere pointed at the strong evidence for TFA levels increasing in the environment as a result of increasing HFO use (ATMOSphere, 2022). They strongly underlined the urgent need for policymakers to take action, as it is impossible to remove TFA from the environment at a later stage.

In conference presentations and in a preprint publication Hansen et al. (2021) looked further into the atmospheric photodissociation of trifluoroacetaldehyde (CF_3CHO) as a degradation intermediate from HFO-1234ze. They found indications that although photolysis of trifluoroacetaldehyde (CF_3CHO) with formation of trifluoromethyl (CF_3) and formyl (CHO) radicals, which is further transformed into CO_2 and HF, is the dominating decomposition pathway (79%), up to 11% of the trifluoroacetaldehyde (CF_3CHO) in the atmosphere could decompose with formation of CO and fluoroform (CHF_3 , HFC-23). Fluoroform has a GWP = 12 690, while its parent HFOs may have GWPs of less than 1 (e.g. HFO-1234ze). However, the authors point at uncertainties in the study and call for experiments to investigate these considerable findings further. The atmospheric lifetime of fluoroform (HFC-23) is ca. 228 years (Stanley et al., 2020).

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

In a recent study of the tropospheric photolysis of CF_3CHO , Sulbaek Andersen and Nielsen (2022) came to a different conclusion when they, in a chamber study, used broadband actinic radiation and FTIR spectroscopy for detection of the photolysis products. No formation of CF_3H (HFC-23), was observed under any of the experimental conditions and an estimated upper limit for the yield of HFC-23 of 0.3% was established.

The atmospheric chemistry of short-chain haloolefins (e.g. HFO-1234ze) was investigated by Wallington et al. (2015). They concluded that haloolefins containing the $\text{CF}_3\text{CF}=\text{group}$ leads to TFA as a persistent degradation product, while haloolefins containing the $\text{CF}_3\text{CH}=\text{group}$ were reported to degrade with formation of CF_3CHO as the primary key intermediate. This general rule will identify among others the substances HCFO-1224yd(Z) ($\text{CF}_3\text{CF}=\text{CHCl}$), HFO-1234yf ($\text{CF}_3\text{CF}=\text{CH}_2$) and HFO-1216 ($\text{CF}_3\text{CF}=\text{CF}_2$) as TFA-precursors.

The report by UBA on persistent degradation products of halogenated refrigerants and blowing agents (UBA, 2021c) investigates the degradation of e.g. hydrofluorocarbons (HFCs). For HFC-134a (CF_3CFH_2) degradation to 7-20% TFA is reported, while for HFC-227ea ($\text{CF}_3\text{CHF}_2\text{CF}_3$) 100% yield of TFA is stated. Trifluoroacetyl fluoride (CF_3COF), which hydrolyses to TFA in droplets, is reported as the key intermediate also for HFC-236ea ($\text{CHF}_2\text{CHF}_2\text{CF}_3$). For HFC-43-10mee ($\text{CF}_3\text{CF}_2\text{CHF}_2\text{CF}_3$) degradation to TFA, as well as PFPrA, is indicated in high yields. For HFC-125 (pentafluoroethane, CF_3CHF_2), Young and Mabury (2010) observed that TFA was formed as a degradation product under conditions of limited NO_x .

○ Hydrofluoroethers (HFEs)

Tsai (2005a) looked into the degradation of hydrofluoroethers (HFEs) as these are being used as third generation replacements to chlorofluorocarbons (CFCs), hydrochlorofluorocarbons (HCFCs) and perfluorocarbons (PFCs). With regards to atmospheric degradation, the author uses HFE-7100, $\text{C}_4\text{F}_9\text{OCH}_3$, as a typical example and explains that OH radical initiated hydrogen abstraction is common. Following oxidative reactions then lead to the corresponding formate ester $\text{C}_4\text{F}_9\text{OC(O)H}$. Such substances are rather unreactive towards further radical processes but may undergo hydrolysis in droplets. Nohara et al. (2001) found that for the formate esters such, as $\text{C}_4\text{F}_9\text{OC(O)H}$, the formate group is cleaved off with formation of the corresponding alcohol $\text{C}_4\text{F}_9\text{OH}$, which suffers loss of F-atoms from the carbon atom attached the hydroxyl group and formation of the carboxylic acid $\text{C}_3\text{F}_7\text{CO}_2\text{H}$ (PFBA) with one perfluorinated C-atom less in the fluoroalkyl chain, i.e.: $\text{C}_n\text{F}_{2n+1}\text{OCH}_3 \rightarrow \text{C}_{n-1}\text{F}_{2n-1}\text{CO}_2\text{H}$.

○ Perfluoroalkyl ketones

According to a study by Taniguchi et al. (2003) the ketone substance $\text{CF}_3\text{CF}_2\text{C(O)CF(CF}_3)_2$ (FK-5-1-12) in the atmosphere suffers photolytic cleavage which results in $\text{CF}_3\text{C(O)F}$ and COF_2 . As indicated above, $\text{CF}_3\text{C(O)F}$ will be incorporated into rain/cloud/seawater where it will undergo hydrolysis to give TFA, while COF_2 will be converted to CO_2 and HF. The half-life of trifluoromethanol (CF_3OH) with respect to decomposition into COF_2 was found to be 4-5 h in this study. Ren et al. (2019) found that photolysis of FK-5-1-12 was the dominant loss pathway in the troposphere, with the substance having an atmospheric lifetime of 3-11 days. TFA and PFPrA were identified as degradation products. According to information from the manufacturer 3M (3M, 2017), the fluoroketone $(\text{CF}_3)_2\text{CFC(O)CF}_3$ (C5-FK) will quickly hydrolyze in contact with water with TFA as the primary hydrolysis product, and 3M recommends against uses of the compound where substantial amounts are intentionally released.

○ Perfluoroalkyl nitrile compounds

The atmospheric chemistry of the nitrile compound $(\text{CF}_3)_2\text{CFCN}$, (C4-FN) was studied by Sulbaek Andersen et al. (2017) in FTIR/smog chamber experiments and ab initio quantum calculations. They estimated the atmospheric lifetime of C4-FN at approximately 22 years and GWP at 1 490. The sole atmospheric degradation products were found to be NO, COF_2 , and $\text{CF}_3\text{C(O)F}$. The latter is known to hydrolyze in droplets with formation of TFA. The yield of

formation of $\text{CF}_3\text{C}(\text{O})\text{F}$ from C4-FN was indicated at 100%.

Conclusions on degradation of fluorinated gases

In conclusion, fluorinated gases have a complex atmospheric chemistry often based on radical oxidation processes via trifluoroacetaldehyde (CF_3CHO) or trifluoroacetyl fluoride (CF_3COF) as intermediates. The latter of these key intermediates is further hydrolyzed in high yield to trifluoroacetic acid (TFA) in water droplets which precipitates with rain and snow, while trifluoroacetaldehyde may degrade to TFA in 2 to 10% yield in one of three degradation pathways. Other key degradation products from fluorinated gases include longer chain substances like PFBA which may be formed e.g. from the hydrofluoroether HFE-7100 ($\text{C}_4\text{F}_9\text{OCH}_3$).

B.4.1.3.3. Degradation of PFSA precursors

The degradation pathways of several PFSA precursors into the corresponding PFSA (mainly C4, C6 and C8 perfluoroalkane sulfonic acids) are described in the Annex XV restriction report for the restriction proposal on perfluorohexane sulfonic acid (PFHxS, (ECHA, 2019b)). Hence, this section is based on the information in the PFHxS Annex XV restriction report. It can be assumed that the degradation mechanisms for PFSA of other chain lengths are the same as for C4, C6 and C8 PFSA precursors.

In a literature study carried out by the University of Oslo (Nielsen, 2017), the formation of PFBS and PFHxS through abiotic degradation of precursors was investigated. PFBS/PFHxS-related substances were found to include PFBS/PFHxS sulfonic acid halides, sulfonic esters (alkyl, olefinic and aryl) and sulfonamides, side-chain fluorinated polymers containing the PFBS/PFHxS moiety, as well as subclasses of PFBS/PFHxS-related substances like sulfones and sulfinic acids.

Abiotic degradation of the identified precursors to PFSA may proceed either via reaction with water or via oxidative radical processes in the atmosphere. However, in the radical processes, for the sulfonyl group may also be cleaved off in a different degradation pathway with formation of perfluoroalkyl radicals that may suffer sequential CF_2 -loss and formation of shorter chain-length PFCAs (this pathway has been reported for perfluoroalkane sulfonamides, (D'Eon J et al., 2006; Martin et al., 2006); see Figure B.42). To what extent the precursors will end up as PFSA or PFCAs may vary with the environmental conditions and is difficult to predict. The rate of degradation may vary for the different precursors, and in some cases the process may take years. Little information about the rate of degradation of such substances has been published.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

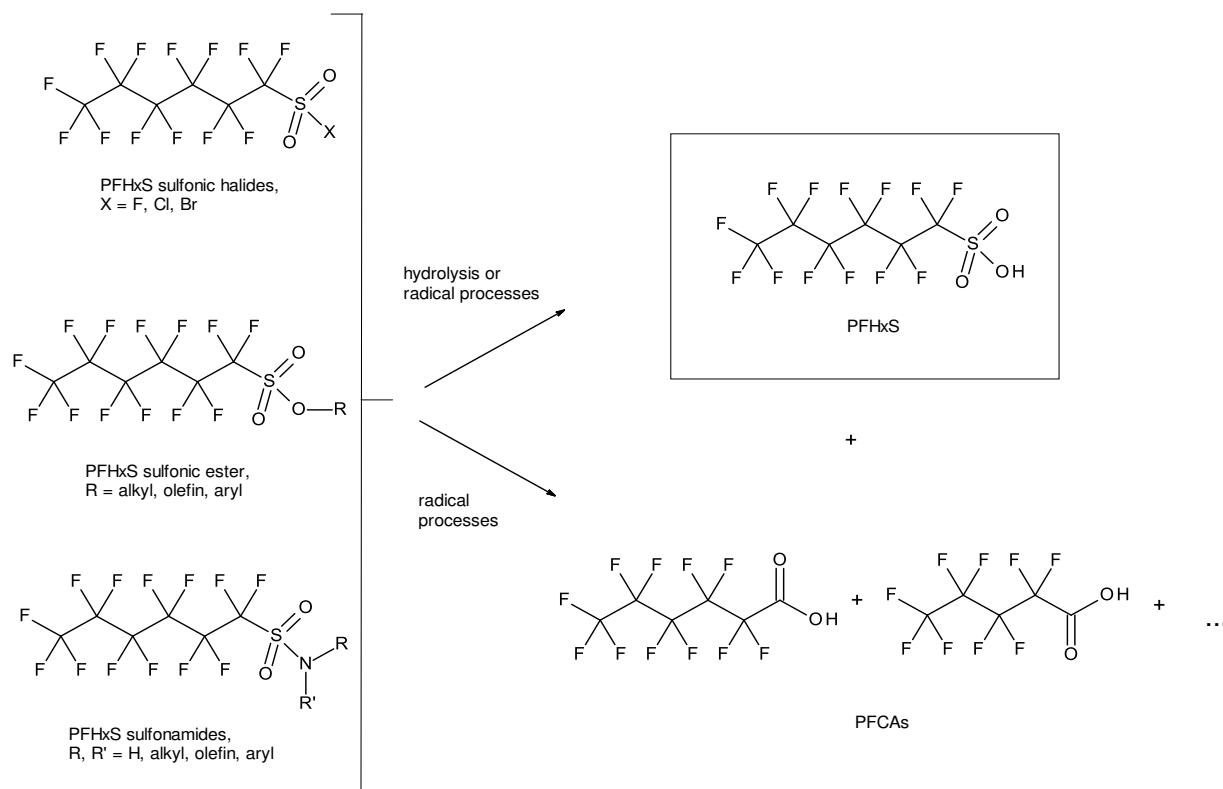


Figure B.42. Degradation scheme of a selection of PFSA precursors, exemplified by PFHxS precursors.

A review article on the atmospheric oxidation of organic sulfur-containing substances shows that dimethyl sulphide is oxidized in radical initiated oxidation processes in the atmosphere via dimethylsulfoxide and methane sulfinic acid to methane sulfonic acid as the end product (Barnes et al., 2006). Oxidation of the relevant sulfinic acids to PFBS and PFHxS is also described in a study of potential precursors to PFBS and PFHxS (Nielsen, 2017). The findings suggest sulphides, thiols and intermediate oxidation products as precursors to PFSA, as shown in Figure B.43.

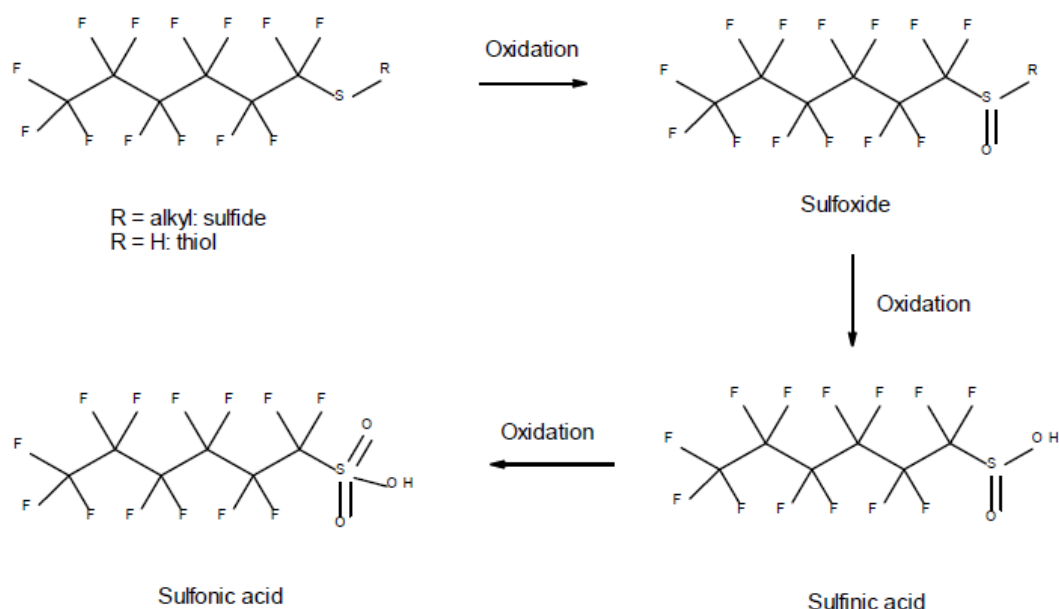


Figure B.43. Oxidation processes from sulphides/thiols to the corresponding PFSA s.

A review of the microbial degradation of polyfluoroalkyl chemicals in the environment points out that perfluoroalkane sulfonamido derivatives may undergo aerobic biodegradation, via the relatively stable intermediate sulfonamides, to the corresponding PFSA s as the final degradation products (Liu and Mejia Avendano, 2013). Liu et al. (2019a) investigated the biotransformation of perfluoroalkane sulfonamide compounds in aerobic soil and looked specifically at differences between the linear and branched isomers in the transformation of PFOS-precursors to PFOS. However, as there are several degradation pathways for the different precursors, there was no clear overall trend that differentiates between the linear and the branched precursors.

In biological systems it has been demonstrated that perfluoroalkane sulfonamides like N-EtFOSA are precursors to PFOS in fish (Tomy et al., 2004) and N-EtFOSA was biotransformed by earthworms to PFOS after in vivo and in vitro exposure (Zhao et al., 2018b). Further in vitro depletion of PFOS precursors (N-EtFOSA and perfluorooctane sulfonamide (FOSA)) was confirmed in a liver microsomal assay approach in polar bear, ringed seal and laboratory rat (Letcher et al., 2014). Perfluoroalkane sulfonamido alcohols like N-EtFOSE are degraded to PFOS in activated sludge (Rhoads et al., 2008) and levels of PFSA-precursors in sludge from WWTP exceeded those of PFSA s itself (Eriksson et al., 2017a).

Conclusions on degradation of PFSA precursors

In conclusion, all molecules that contain a $C_nF_{2n+1}SO_2^-$, $C_nF_{2n+1}SO^-$ or $C_nF_{2n+1}S^-$ moiety (Figure B.44) can form the corresponding PFSA s ($C_nF_{2n+1}SO_3H$) through abiotic and/or biotic degradation in the environment. However, concerning perfluoroalkane sulfonamides, the sulfonyl group may also be cleaved off in a different degradation pathway in the atmosphere with formation of perfluoroalkyl radicals that may suffer sequential CF_2 -loss and formation of shorter chain-length PFCAs. For those substances where no degradation studies are available it can be assumed that based on the chemical similarity, irrespective of chain length or branching of the perfluorinated moieties, they will most likely be degraded in a similar way (see also section B.4.1.2 concerning the effects of chain length, branching and cyclic structure elements on persistence). It was also concluded in the Annex XV restriction report for PFHxS that side-chain fluorinated polymers containing .e.g. perfluoroalkane sulfonamide-based side-chains, will degrade in the same way as the corresponding small-molecule precursors.

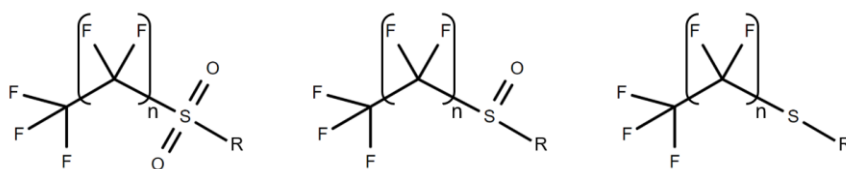


Figure B.44. Generic structures of PFSA precursors. R = any chemical group, n = 0 or higher.

PFAS subgroups that are considered as PFSA precursors includes, e.g.:

- Perfluoroalkane sulfonyl halides
- Perfluoroalkane sulfonic acid esters
- Perfluoroalkane sulfonamides (FASAs)
- Perfluoroalkane sulfide derivatives
- Perfluoroalkane sulfoxide derivatives
- Perfluoroalkane sulfinic acid derivatives
- Side-chain fluorinated polymers based on sulfonic acid derivatives (mainly sulfonamides)

B.4.1.3.4. Degradation of PFPA precursors

- Perfluoroalkyl phosphinic acids (PFPIAs)

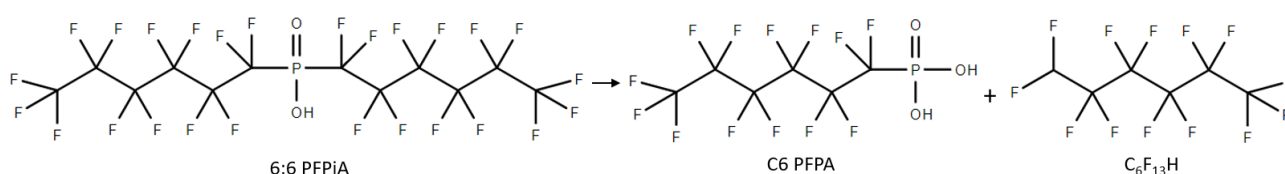


Figure B.45. Degradation pathway of 6:6 perfluoroalkyl phosphinic acid (6:6 PFPIA).

In a review by Wang et al. (2016b), available information on degradation of perfluoroalkyl phosphinic acids (PFPIAs) were evaluated. PFPIAs were found to degrade to perfluoroalkyl phosphonic acids (PFPAs) and 1H-perfluoroalkanes $C_nF_{2n+1}H$ under various laboratory conditions. The environmental relevance of this degradation remains however somewhat unclear. Biodegradation of PFPIAs into PFPAs were found in some *in vivo* studies, while no degradation of PFPIAa was observed in a 28-day OECD 301-F test on ready biodegradability. 1H-Perfluoroalkanes can also potentially be oxidized to form corresponding PFCAs (e.g. via reaction with OH radicals in the atmosphere (Wang et al., 2014c; Young and Mabury, 2010).

Conclusions on degradation of PFPA precursors

Based on the available data it can be expected that perfluoroalkyl phosphinic acids can be abiotically or biotically degraded and transformed into the corresponding perfluoroalkyl phosphonic acids (PFPAs) and 1H-perfluoroalkanes $C_nF_{2n+1}H$. 1H-Perfluoroalkanes could potentially degrade further to form the corresponding PFCAs.

B.4.1.3.5. Degradation of other precursors

Structural elements in combination:

Above, the degradation patterns of different structural elements in per- and polyfluorinated substances have been investigated for representative PFAS substances. Most often perfluoroalkyl chains remain mainly intact, while degradation processes take place elsewhere

in the precursor molecules, especially in non-fluorinated moieties. In many cases degradation stops when a perfluoroalkyl group attached to a functional group at its highest oxidation step has been reached, i.e. PFAAs. However, in some cases molecules suffer loss of fluorine from the carbon atom next to the non-fluorinated part of the substance. Persistent final degradation products, i.e. arrowheads, have been investigated in detail in section B.4.1.2.

The degradation processes of molecules are dictated by their chemical structure and the conditions that prevail where the substances are found. Hence, it is important to take into consideration if a substance partitions to air, soil or water. However, under identical conditions one specific type of functional group often behaves in the same way with similar neighbouring groups in a molecule. The length of a perfluoroalkyl chain, branching or the presence of cyclic structures is not expected to affect the reactivity and degradation of a functional group considerably. The same applies for the different types of polymers within the PFAS scope, which are in general assumed to follow the same degradation pattern for each specific functional group. The degradability of a substance can often be assessed by looking at one reactive structure element at the time, when these elements are separated by non-reactive moieties, like in many PFASs.

Based on the understanding of the reactivity of structural elements in per- and polyfluorinated substances, one can assess expected degradation routes of similar compounds for which experimental studies of degradation have not been published. In combination with the knowledge summarised in section B.4.1.2 on persistent structural elements, one can estimate the degradation patterns, and in many cases the final degradation products, of a large part of the PFAS universe.

B.4.1.4. Fully degradable PFASs

Generally, PFASs are either very persistent themselves or will ultimately degrade to very persistent degradation products which are still PFASs (arrowheads). There are, however, a few specific PFAS subgroups with certain structural elements in combination that are fully degradable and cannot form persistent PFAS arrowheads (such as perfluoroalkyl acids). For the vast majority of PFASs regulatory standard tests for persistence are missing, and the assessment of full degradability is based on the general scientific literature and expert judgement. In this section, relevant available degradation data on substances belonging to these PFAS subgroups are summarised: *fully degradable trifluoromethoxy-derivatives, fully degradable trifluoromethylamino-derivatives, fully degradable difluoromethanedioxy-derivatives*. First a brief chemical overview of degradation pathways is given, followed by experimental observations.

B.4.1.4.1. Trifluoromethanol, trifluoromethylamine and difluoromethanediol

In the first instance, the three parent compounds, trifluoromethanol, trifluoromethylamine and difluoromethanediol, are all inherently unstable compounds that spontaneously decompose, as shown in Figure B.46.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

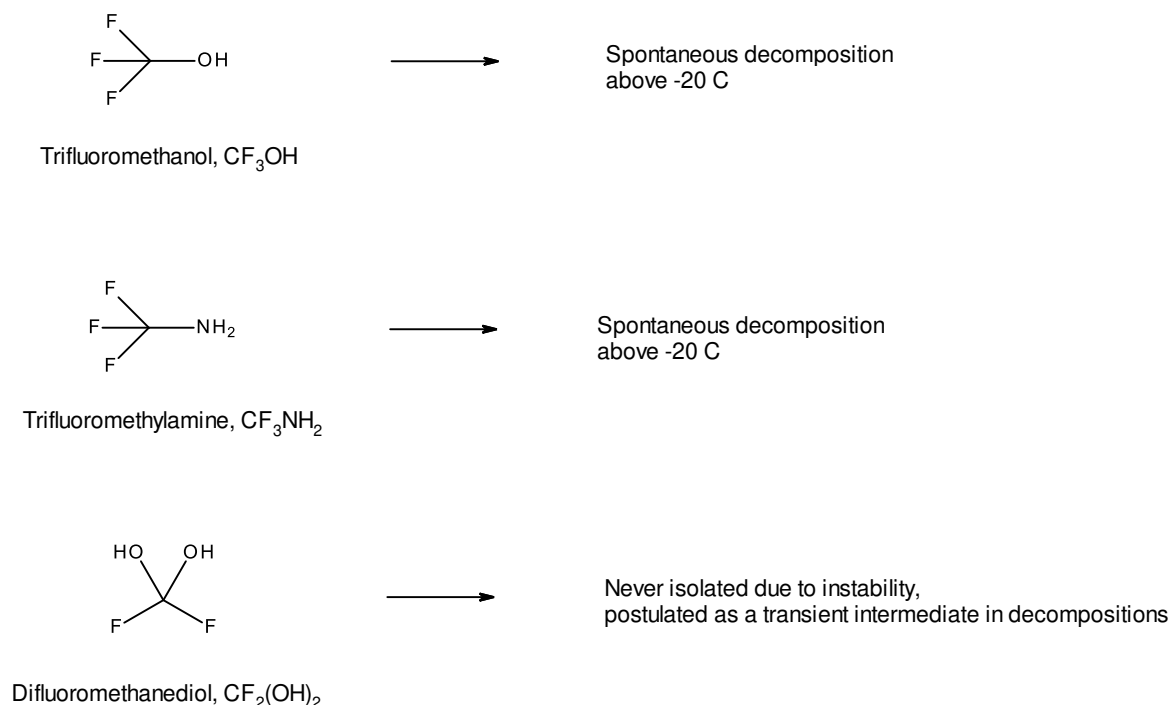


Figure B.46. Inherently unstable key fluorinated compounds.

Trifluoromethanol (CF₃-OH) is a chemically unstable gas at room temperature and decomposes spontaneously (slow decomposition was found already at -20 °C). It degrades via the initial elimination of hydrogen fluoride (Christe et al., 2007; Redwood and Willis, 1965; Seppelt, 1977; Taniguchi et al., 2003) to form carbonyl difluoride that, in the presence of water, subsequently hydrolyses to yield carbon dioxide and hydrogen fluoride ((Francisco, 1993; Taniguchi et al., 2003; Uchimaru et al., 2004); see Figure B.47).

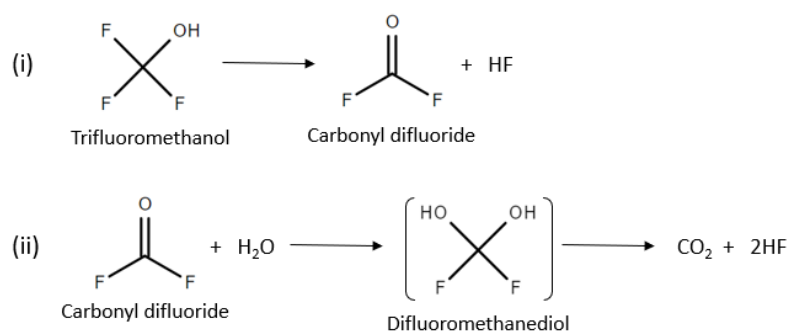


Figure B.47. Degradation pathway of trifluoromethanol.

Trifluoromethylamine (CF₃NH₂) is a chemically unstable gas at room temperature and decomposes spontaneously at temperatures above -20 °C via HF elimination (see Figure B.48).

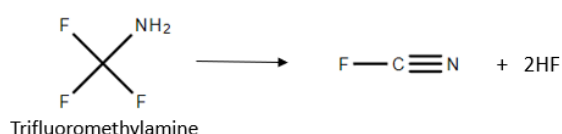


Figure B.48. Degradation pathway of trifluoromethylamine proposed by Klöter and Seppelt (1979).

Difluoromethanediol (CF₂(OH)₂) has never been isolated as such due to its low stability, but it has been postulated as a transient intermediate in the hydrolysis of carbonyl difluoride by Francisco (1993). It is considered a chemically unstable substance and decomposes spontaneously. Hence, it leads to full mineralization to HF and CO₂ (see Figure B.49).

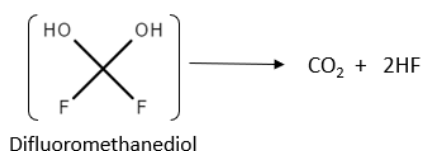


Figure B.49. Postulated hydrolysis via difluoromethanediol by Francisco (1993).

As the above three key perfluorinated compounds are chemically unstable, all compounds that lead to these substances during degradation, and no other perfluorinated degradation products, will degrade under any relevant environmental conditions. The perfluorinated part of these substances will eventually fully mineralize. Below, different substances that degrade via the three key substances with full mineralization are discussed.

- Fully degradable trifluoromethoxy-derivatives

A larger molecule containing a trifluoromethoxy-group attached to a degradable moiety (CF₃-X, where X = -OR and where R = methyl (-CH₃), methylene (-CH₂-), an aromatic group or a carbonyl group (-C(O)-)) is expected to degrade with formation of trifluoromethanol. As this substance is inherently unstable, it will quickly mineralize under environmental conditions as described above. Hence, it cannot be persistent in itself nor degrade to a persistent PFAS

arrowhead.

- Fully degradable trifluoromethylamino-derivatives

A larger molecule with a trifluoromethylamino-group attached to a degradable moiety ($\text{CF}_3\text{-X}$, where $\text{X} = \text{-NRR}'$ and where R and $\text{R}' = \text{hydrogen (-H), methyl (-CH}_3\text{), methylene (-CH}_2\text{-), an aromatic group or a carbonyl group (-C(O)-)}$) is expected to degrade with formation of trifluoromethylamine. This substance is inherently unstable, as described above, and will mineralize under environmental conditions. Hence, it cannot be persistent in itself nor degrade to a persistent PFAS arrowhead.

- Fully degradable difluoromethanedioxy-derivatives

A larger molecule containing a difluoromethanedioxy-group attached to a degradable moiety ($\text{X-CF}_2\text{-X}'$, where $\text{X} = \text{-OR}$ and $\text{X}' = \text{-OR}''$ and where R and $\text{R}'' = \text{methyl (-CH}_3\text{), methylene (-CH}_2\text{-), an aromatic group or a carbonyl group (-C(O)-)}$) is expected to degrade to difluoromethanediol. This substance is inherently unstable, as described above, and will quickly mineralize under environmental conditions. Hence, it cannot be persistent in itself nor degrade to a persistent PFAS arrowhead.

In the following text examples of experimental observations of the degradation of compounds in the groups trifluoromethoxy-, trifluoromethylamino- and difluoromethanedioxy-derivatives are presented. Although the experiments have generally not been run under standard persistence test conditions, the results are regarded as supporting evidence for the above assessment based on general chemical principles.

- Experimental observations - fully degradable trifluoromethoxy-derivatives

In a study by Peschka et al. (2008), 10-(trifluoromethoxy)decane-1-sulfonate was exposed to a fixed bed bioreactor (FBBR) that was run with surface water from lakes and rivers and the biodegradation pathways were investigated by LC-MS, TOF-MS and ion chromatography (IC) analyses. Two degradation pathways were proposed by the authors (Figure B.50).

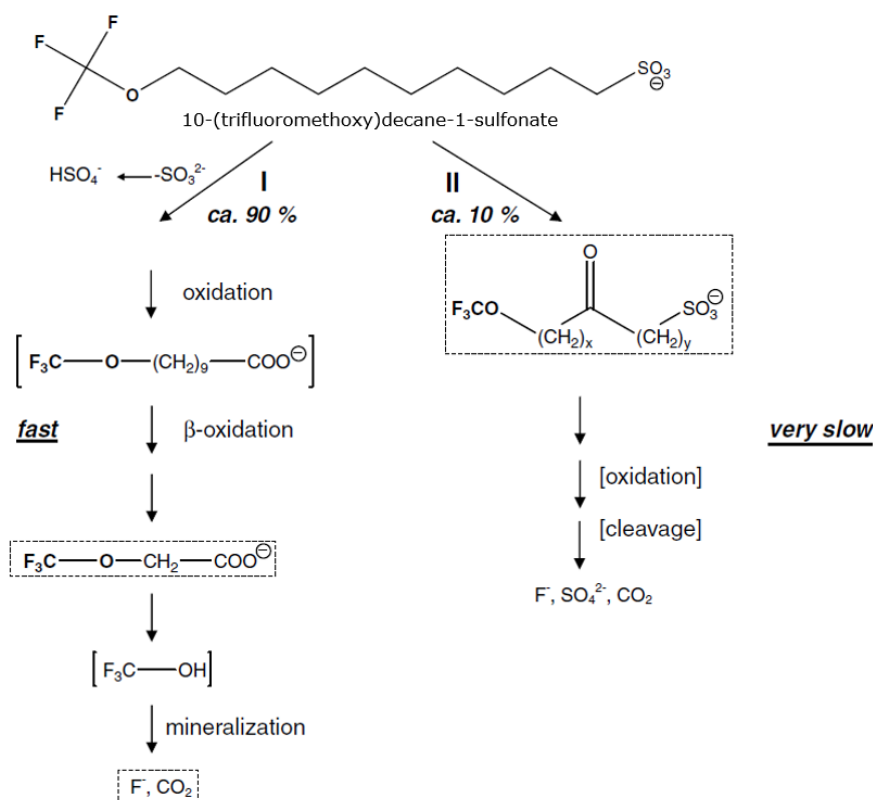


Figure B.50. Degradation pathways of 10-(trifluoromethoxy)decane-1-sulfonate proposed by Peschka et al. (2008).

The main degradation pathway (I) proceeds via a desulfonation step, oxidation and chain shortening via β -oxidation. Trifluoromethanol is subsequently formed and degrades immediately to inorganic fluoride and carbon dioxide. The minor degradation pathway (II) proceeds via oxidation of the alkyl chain forming the proposed oxo-10-(trifluoromethoxy)decane-1-sulfonate, that was slowly degraded further, with assumed mineralization into fluoride, sulfate and carbon dioxide as final degradation products. The degradation via pathway I was nearly complete after 28 days, while a slow release of fluoride was continuing to the end of the experiment (87 days) which was presumably ascribed to a slow degradation of the oxo-10-(trifluoromethoxy)decane-1-sulfonate (pathway II). The overall mineralization of 10-(trifluoromethoxy)decane-1-sulfonate was ca 90% complete after 87 days based on the measured fluoride ion concentration. These results represent a water test that indicate biotic degradation of the substance in the environment.

Biodegradation of two trifluoromethoxy-substituted alcohols, 6-(trifluoromethoxy)-hexan-1-ol (TFMHxOH) and 3-(trifluoromethoxy)-propan-1-ol (TFMPrOH) were examined by Frömel and Knepper (2015). Experiments were carried out under aerobic conditions with effluent water from a municipal wastewater treatment plant and the biodegradation pathways were investigated by LC-MS and ion chromatography (IC) analyses. TFMHxOH was almost completely mineralized after 37 days as judged from the fluoride release. 6-Trifluoromethoxy hexanoic acid (TFMHxA) and trifluoromethyl carbonate (TFMC) were identified as transient transformation products (proposed degradation pathways in Figure B.51).

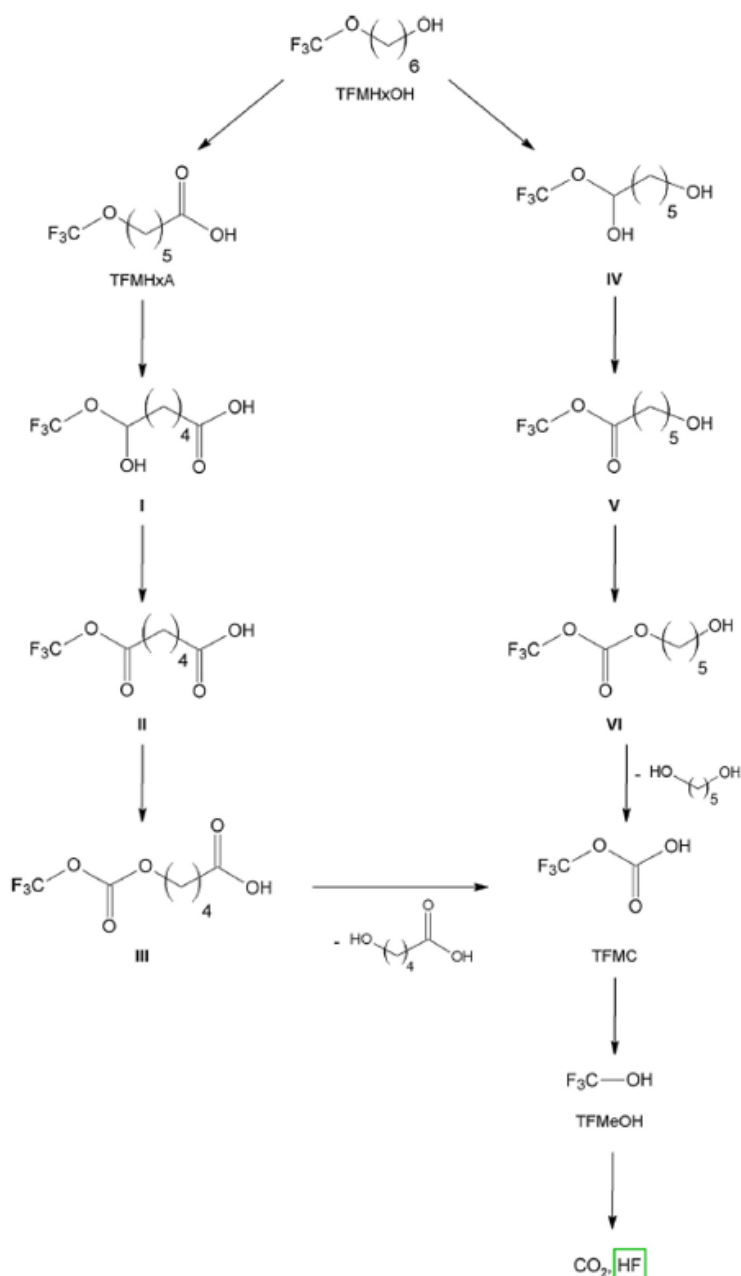


Figure B.51. Degradation pathways of TFMHxOH proposed by Frömel and Knepper (2015).

TFMPrOH on the other hand only mineralized to a 15% extent as judged from the fluoride release. TFMHxOH was also detected during biotransformation of TFMPrOH, however, the major transformation product was 3-trifluoromethoxy-propanoic acid (TFMPrA), which did not show any further degradation under these conditions within a 47 days period (proposed degradation pathways in Figure B.52). The authors pointed out that the long-term fate of the remaining major transformation product TFMPrA is questionable and cannot be assessed without further laborious studies. However, based on the chemical structure of TFMPrA (non-perfluorinated methylene groups), it should not be regarded as an arrowhead, but rather a relatively stable intermediate that is likely to mineralize under environmentally relevant conditions over time. EAWAG-BBD pathway prediction⁴ of TFMPrA reveals plausible degradation pathways for

⁴ EAWAG-BBD Pathway Prediction System predicts plausible pathways for microbial degradation of chemical compounds. Predictions use biotransformation rules, based on reactions found in the EAWAG-BBD database or in the scientific literature. <http://eawag-bbd.ethz.ch/predict/>, date of access: 2022-09-29.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

microbial degradation into trifluoromethanol. The results indicate biotic degradation of the substance in the environment.

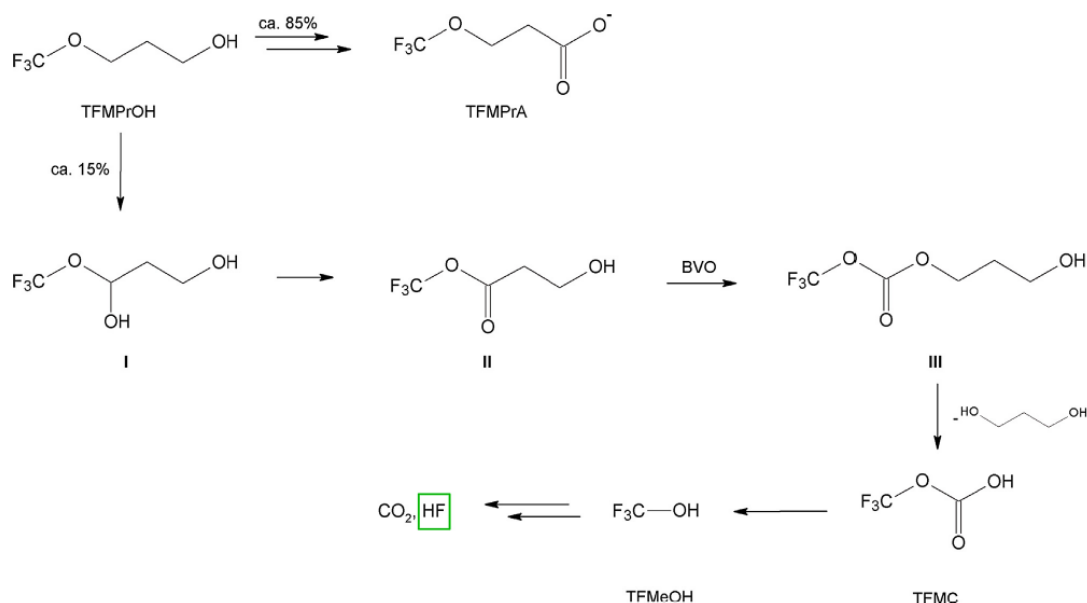


Figure B.52. Degradation pathways of TFMPrOH proposed by Frömel and Knepper (2015).

In a study by Dihel et al. (2009), Sprague Dawley rats were given a single oral dose of the preclinical candidate OSI-930. LC-MS/MS analysis of the rat plasma revealed a substantial metabolite peak that was assigned to a glucuronide conjugate of OSI-930 (dTFM + Glucuronide, see Figure B.53). Based on these findings and further experiments of OSI-930 *in vitro* (in rat and human hepatic microsomes), the authors concluded that this biotransformation is CYP-mediated and they proposed an ipso-substitution mechanism for the displacement of the trifluoromethoxy group from the phenyl moiety (producing trifluoromethanol), followed by a rapid glucuronidation. CYP3A4 was found as the major facilitator of this pathway with a contribution from CYP2D6. These results show that trifluoromethoxy substituted aromatic substances may be metabolized with full mineralization of the perfluoroalkyl part by mammals in the environment. Although this study applies only to certain specific conditions, the results are taken as indications that biotic degradation may take place in the environment.

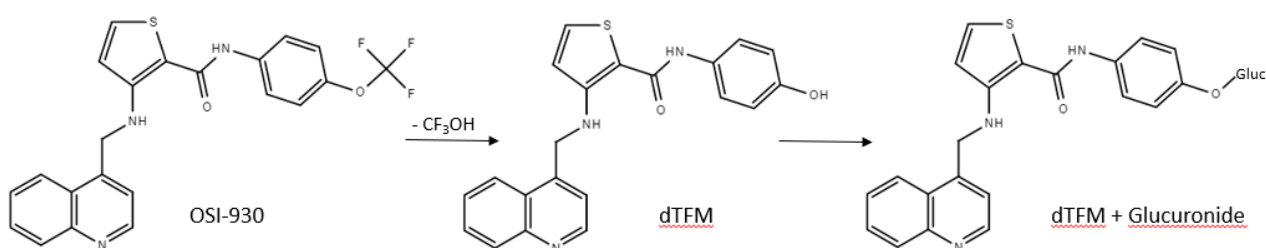


Figure B.53. CYP-mediated degradation of OSI-930.

One stakeholder has initiated a biodegradation study on the ^{14}C radiolabelled 4-(^{14}C -trifluoromethoxy)benzoic acid in Q2 2022 (CropLife Europe (2022), see Figure B.54). A summary of the interim results (data collected at day 14) is presented below. This aerobic

soil degradation study is conducted according to OECD guideline 307 (OECD, 2002). According to the study protocol, soil samples were treated with the radiolabelled test item at 0.67 mg/kg (dry weight equivalent) and incubated under controlled and dark conditions at 20 °C. A closed incubation system with continuous aeration was used with an attached trapping system for the determination of volatile compounds. The incubations were performed in three different soils with 8 samplings over a planned period of 28 days. At each sampling date, evolved and trapped volatiles (e.g. $^{14}\text{CO}_2$ in NaOH trapping solution) were quantified by LSC (liquid scintillation counting). For each soil and sampling time, two replicates were taken and extracted with acetonitrile/water mixtures and acetone, and the extracts were analysed by LSC and radio-HPLC in order to determine the amount of test substance remaining in soil and the number and amount of potential metabolites. The non-extractable residues were quantified by combustion in an Oxidizer and subsequent LSC measurement. All quantitative measurements of ^{14}C are expressed as % of the total applied radioactivity (% TAR).

Interim results after 14 days are available for two of the soils and show that the parent compound was almost completely degraded (<2% TAR of parent recovered in extracts). For both soils, the major degradation product was $^{14}\text{CO}_2$ accounting for 57–58% TAR, meaning that complete defluorination/mineralization of the O- CF_3 -group has occurred to this extent after 14-day incubation. No other volatile ^{14}C -containing metabolite could be detected. Non-extractable residues (NER) were observed for both soils which reached maximum levels of 46% TAR at day 6 and 51% TAR at day 3, respectively, before they decreased again to levels of 32 and 36% TAR at day 14. According to the authors of the report, this indicates that part of the parent test item was bound to the humic matrix in soil. They argue further that the proceeding defluorination and mineralization (increasing $^{14}\text{CO}_2$ -levels) also show that this does not stop the further degradation of trifluoromethoxy-group, but just slows it down to a certain extent.

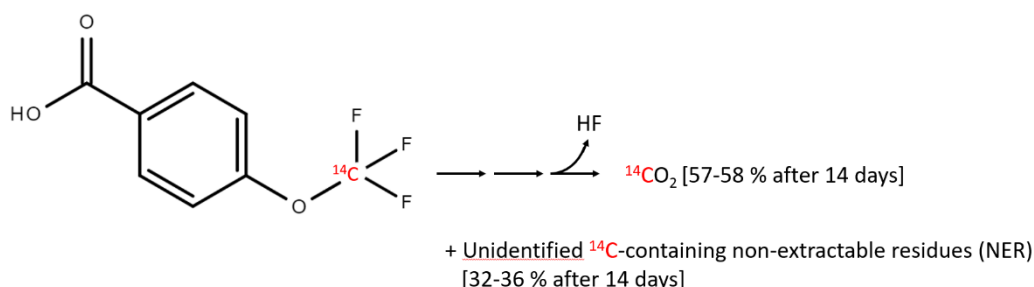


Figure B.54. Degradation pathways of 4-(^{14}C -trifluoromethoxy)benzoic acid in a soil degradation study conducted according to OECD guideline 307.

The above assessment explains that substances that degrade via trifluoromethanol (and no other perfluoroalkyl fragments) are not to be considered as persistent PFASs, as there are no possible stable PFAS that may be formed from the indicated substances. Furthermore, examples of degradation of specific substances have been included to show that there is experimental data to support this consideration.

- Experimental observations - fully degradable trifluoromethylamino-derivatives

Schiesser et al. (2020) investigated the hydrolytic stability of twelve trifluoromethylamino-derivatives in aqueous media (2 mM water/dimethyl sulfoxide 4:1 solution at room temperature; degradation monitored by LC-MS analysis). All trifluoromethylamino-derivatives were found hydrolytically unstable as they were hydrolysed to a significant degree already after 24 hours under these mild conditions (100% completion for ten of the derivatives and 75% and 10% completion respectively for two of the derivatives), yielding the corresponding carbamoyl fluorides ($\text{RR}'\text{NC}(\text{O})\text{F}$), which are no longer PFAS, by elimination of 2 HF (see Figure B.55).

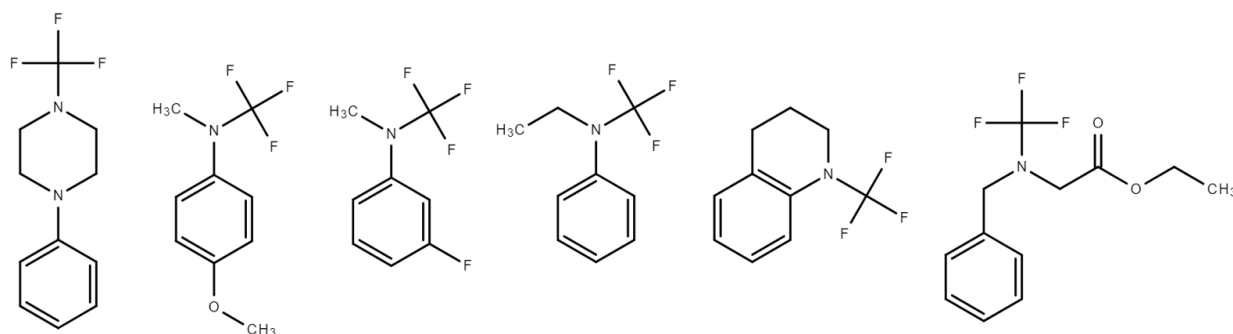


Figure B.55. Representative examples of trifluoromethylamino-derivatives that were found hydrolytically unstable (Schiesser et al., 2020).

The above assessment explains that this type of trifluoromethylamino-derivatives are not to be considered as persistent PFAS as there are no possible stable PFAS that may be formed from the indicated substances. Furthermore, examples of degradation of specific substances have been included to show that there is experimental evidence to support this consideration.

- Experimental observations - fully degradable difluoromethanedioxy-derivatives

In a mechanistic study by Bygd et al. (2021), the microbial degradation of model compound 2,2-difluoro-1,3-benzodioxole (DFBD) by *Pseudomonas* strains was investigated by ^{19}F NMR, ^1H NMR, and GC-MS analyses. It was found that for bacterial strains expressing toluene dioxygenase (e.g. *Pseudomonas putida* F1), a rapid fluoride release was observed that declined within hours. The authors proposed a degradation pathway with the initial formation of 4,5-dihydro-dihydroxy-DFBD (4,5-DD-DFBD) and subsequent reactions producing fluoride ions (Figure B.56). This major path is highlighted by darker arrows. The three intermediates between 4,5-DD-DFBD and fluoride plus pyrogallol are expected to have a very short lifetime and represent a proposed mechanism for fluoride release. The minor products (thin arrows) were found stable under these conditions and within the timeframe for this study. These results only demonstrate degradation under certain specific conditions. However, the results are taken as indications that biotic degradation of such substances may take place in the environment. The *Pseudomonas* genome database and other databases revealed hundreds of bacteria with enzymes sharing high amino acid sequence identity to toluene dioxygenase from *P. putida* F1, which according to the authors suggest that the mechanism revealed here may apply to the defluorination of DFBD-containing compounds in the environment.

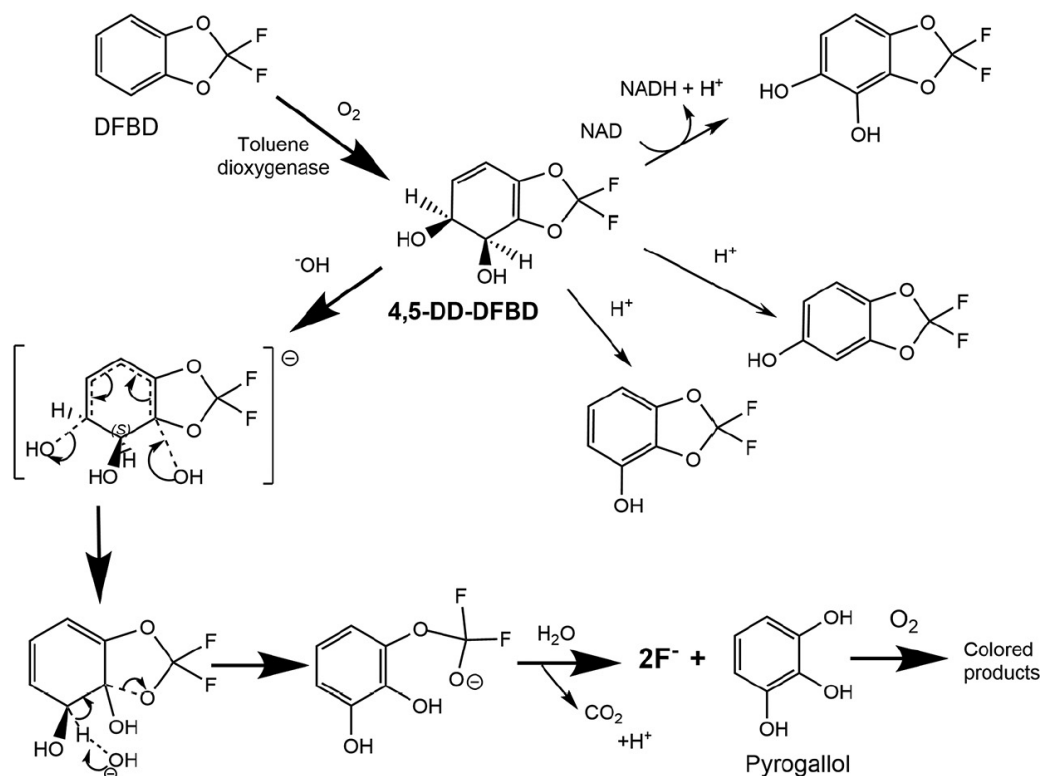


Figure B.56. Biodegradation pathways of 2,2-difluoro-1,3-benzodioxole (DFBD) proposed by Bygd et al. (2021).

In a study by Alexandrino et al. (2020), the biodegradation of fludioxonil by microbial consortia enriched from estuarine sediment and agricultural soil was investigated by potentiometry and HPLC analyses (see Figure B.57). After an enrichment period of 6 months, four microbial consortia were able to completely remove and defluorinate fludioxonil under co-metabolic conditions in concentrations up to 10 mg/L, in a maximum of 21 days. Results suggest that defluorination is not a primary catabolic step, as fludioxonil removal was always faster than its defluorination. Three of the four enriched consortia had similar biodegradation performances in the absence of sodium acetate as a co-substrate. According to the authors, estimated half-life values were significantly lower than those reported in literature, highlighting the unique metabolic performance of the obtained consortia. Analysis of their microbial composition revealed that they integrate several bacterial species belonging to the Proteobacteria phylum, with the most common genera being *Pseudomonas*, *Ochrobactrum* and *Comamonas*. The environmental relevance of the degradation in these consortia was not further elaborated by the authors.

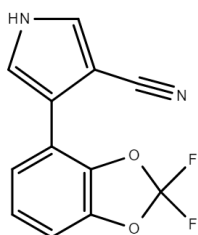


Figure B.57. Fludioxonil.

The above assessment explains that substances that degrade via difluoromethanediol (and no other perfluoroalkyl fragments) are not to be considered as persistent PFAS as there are no possible stable PFAS that may be formed from the indicated substances. Furthermore, examples of degradation of specific substances have been included to show that there is experimental data to support this consideration.

B.4.1.4.2. Conclusions on fully degradable PFASs

In conclusion, it can be expected that PFASs from the subgroups described above can fully mineralize in the environment with basis in the understanding of the reactivity of key structural elements. Mineralization pathways have been identified and persistent arrowheads, such as perfluoroalkyl acids, cannot be formed along the expected degradation pathways of these PFASs.

B.4.1.5. Persistence of PFASs under regulatory and scientific scrutiny

The European Environment Agency stresses that the major concern of PFASs is due to their persistence, and that PFASs either are, or degrade to, persistent chemicals, with many of them accumulating in humans and animals, and all of them ultimately accumulating in the environment (EEA, 2020).

The Global PFC Group points out that PFAAs are very persistent in the environment, whereas their potential precursors are transformed in the environment abiotically or biotically into PFCAs and/or PFSAs. PFAAs and their potential precursors are ubiquitous in the environment, even in remote regions. Several PFASs have lately been recognised as very persistent, potentially bioaccumulative and toxic (OECD/UNEP, 2013).

According to the Californian toxic substances' authorities, all PFASs or their degradation, reaction, or metabolism products, are environmentally persistent. And for this reason, PFASs as a class are regulated in certain consumer products in California (Balan et al., 2021). It is emphasised by these authorities that persistence of a chemical in the environment promotes sustained exposure and contributes to accumulation in the environment. Because persistence is an inherent property of a chemical in the environment that results in increased exposure to the chemical and consequently potential for health risks, it can appropriately be identified as a hazard trait.

In the Helsingør Statement on PFASs a group of scientists pointed out that the current knowledge demonstrates that the perfluorinated parts of any PFAS are recalcitrant and will form terminal transformation products, including PFCAs and PFSAs, which are persistent in the environment (Scheringer et al., 2014). Extensive and increasing use and emissions of fluorinated alternatives will lead to increasing levels of PFCAs, PFSAs and other stable perfluorinated degradation products in the environment, biota and humans. In the follow-up Madrid statement, it was warned that PFASs are very persistent man-made substances found everywhere. PFASs contain perfluorinated chains that only degrade very slowly, if at all, under environmental conditions (Blum et al., 2015).

The high persistence of PFASs allows for a wide distribution in the environment, and many PFASs have been detected globally in the environment. A large group of scientists has reached a consensus that PFASs are the most environmentally persistent substances among organic chemicals and support a broad scope in restricting the use of PFAS in society (Cousins et al., 2020b). PFAS has been given the nickname "forever chemicals" in the popular press.

Cousins et al. (2019) investigated the consequences of persistence for organic substances and provided case studies for three different classes of very persistent substances: chlorofluorocarbons, polychlorinated biphenyls, and PFASs. They argue that high persistence has important implications for the behaviour of chemicals in the environment. Persistent chemicals are distributed widely, often globally, and reach (much) higher concentrations than

short-lived chemicals emitted at the same rate.

Looking more at detail at the Cousins et al. (2019) paper the Dossier Submitters find the following:

The implications of high persistence for the levels and time trends of chemicals in the environment were modelled using a simple multimedia environmental fate model. The model was a so-called unit-world model with three compartments: the global troposphere (height 6 000 m, volume $3.06 \times 10^{18} \text{ m}^3$), the global surface ocean water (depth 100 m, volume $3.62 \times 10^{16} \text{ m}^3$), and the global surface soil (depth 0.1 m, volume $1.48 \times 10^{13} \text{ m}^3$). In each compartment, a first-order degradation process takes place. In addition, there are three non-degradative losses: diffusion to the stratosphere, settling to deep ocean water, and burial in deep soil.

Substances C and D were assigned the following properties (see Table B.6):

Table B.6. Properties of compared substances.

	Log K_{aw}	Log K_{ow}	t_{1/2} (d)
Substance C	-1	8	2
Substance D	-1	8	2 000

A half-life of 2 000 days or 5.5 years is long, but not excessively high. PFASs, for example most PFAAs, can have much longer half-lives. If PFAAs degrade, they do it so slowly that it is not observable and their half-lives could be on the order of decades, centuries or even greater. Log K_{ow} for the two substances compared in the study was 8, which is typical for more lipophilic substances.

In a first emission scenario, the same constant emission rate to air (100 mol h^{-1}) was assumed for each chemical and the concentrations in air, water and soil calculated at steady-state and in a dynamic scenario where the initial concentrations in all media are equal to zero. The model showed that an increase in the degradation half-life by a factor of 1 000 (from 2 days to 2 000 days) leads to an increase in the time to steady-state by a factor of 600–880 (from 20 days to 33–48.5 years). Similarly, the increase in the total inventory of chemical in the model system is only around a factor of 550 to 600 because of the increasing effect of the non-degradation losses. The long-lived chemical (chemical D) shows a marked overshoot with increasing concentrations for more than 4 years after the emission peak in year 10 (concentration peak in year 14.5, see Figure B.58 below). Moreover, the decreasing concentrations form a long tail that extends for many years after the stop of the emissions in year 20. An important finding from the model results is that the K_{ow} is of less importance and does not modify the general implications of high persistence.

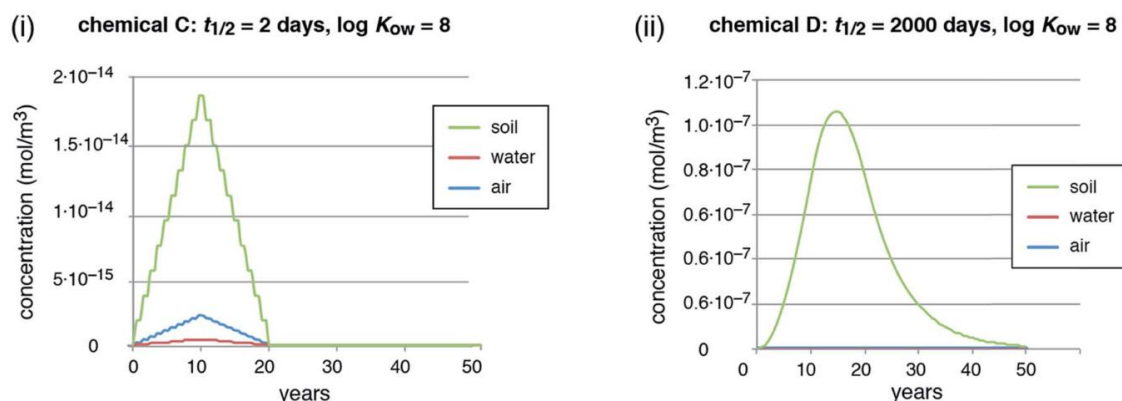


Figure B.58. Implications of high persistence. Concentrations of chemicals C (panel (i)) and D (panel (ii)) as function of time in the scenario with dynamic emissions. For both chemicals, emissions start in year 0, increase by 10 mol h⁻¹ every year, peak in year 10 at a value of 100 mol h⁻¹, then decrease by 10 mol h⁻¹ every year, and end in year 20. Note the much higher levels of chemical D compared to chemical C.

In the case that unexpected effects are caused by a short-lived chemical, it is possible to rapidly cease environmental contamination by restricting or banning its use, which then also means that no additional effects will be caused by that chemical. In contrast, in the case of very persistent chemicals, it is not possible to cease environmental contamination within a reasonable time frame by simply restricting or banning their use. Environmental contamination by very persistent chemicals – and the effects related to this contamination – will continue for years to decades. This poor reversibility of contamination is because very persistent chemicals are, by definition, difficult to degrade.

In summary, the main concerns with very persistent chemicals according to Cousins et al. (2019) are:

- (1) The continuous release of very persistent chemicals will lead to widespread, long-lasting, and increasing contamination.
- (2) Increasing concentrations will result in increasing probabilities that known and unknown effects occur, be it by a single chemical and/or in a mixture with other substances.
- (3) Once adverse effects are identified, it will be technically challenging, energy intensive, and thus costly, to reverse the chemical contamination and therefore the effects. These measures are limited to contamination hotspots, whereas, for most of the environment, no remediation or clean-up will be possible.

It is argued that high persistence should be given particular emphasis in chemicals assessment and management and that very persistent chemicals should be regulated on the basis of their persistence alone (P-sufficient approach).

Monitoring results underline the above listed main concerns of persistent chemicals

PFASs' ubiquitous presence in the environment confirms their widespread occurrence. PFASs which have been monitored are present in soils, ground- and freshwater as well as drinking water across the world (see B.4.2). PFASs are even found in remote areas without anthropogenic activity. This also demonstrates their long-range transport potential (see B.4.2.8). Though their transport potential is also determined by other properties their persistence is crucial.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

The poor reversibility of contamination within reasonable time due to persistence can be demonstrated by time trends (see B.4.2.7.9). Though industry has voluntarily phased out PFOS and it is also regulated globally as a POP environmental monitoring data do not show a clear downward trend. Though concentrations of marine predators in Europe level off, increasing PFOS (and PFCAs) concentrations were reported for biota living in contaminated regions with slow water exchange such as the Baltic Sea which indicates a dilution in the environment rather than a degradation (see B.4.2.7.9).

B.4.2. Environmental distribution

B.4.2.1. Adsorption/desorption/mobility in water

B.4.2.1.1. Factors influencing adsorption potential of PFASs

Chain length

Adsorption happens dominantly via hydrophobic attraction. An increase in sorption with increasing chain length at least for longer chain PFASs (C5- C15) has been observed across the main PFAA subclasses (PFCAs, PFSA, PFPAs, PFPIAs), in sediments (Higgins and Luthy, 2006), sludge (Arvaniti et al., 2014; Zhou et al., 2010a) and soil (Lee and Mabury, 2017). Elmoznino et al. (2018) demonstrated that an increase in log K_{OC} correlates to the alkyl chain length for PFCAs (C7-C10) and PFSA (C6 and C8). Baduel et al. (2017) demonstrated a predictable pattern for the effect of alkyl-chain length on mobility in soil for PFSA (C1-C11), PFCAs (C4-C10), PFSA (C3-C8) and ketone PFSA (C6-C11) where the vertical distribution is a function of the alkyl chain length with higher mobility for shorter chain lengths. In sewage sludge, Zhang et al. (2013c) also recorded an increased sorption with increasing chain length for PFCAs (C3-C12) and PFSA. Milinovic et al. (2015) reported that among three studied PFASs (PFOS, PFOA and PFBS), PFOS was the most strongly adsorbed by six different soils. The authors attributed the strong interaction of PFOS with soil particles to hydrophobic interaction, as indicated by a strong correlation between the log K_{OW} values of the three PFASs, the functional hydrophilic group, i.e. sulfonic vs. carboxylic acid, and the log K_{OC} values of the soils. Campos Pereira et al. (2018) showed that the PFCA and PFSA sorption was further found to increase with increasing perfluorocarbon chain length with 0.60 log K_{OC} units per CF_2 moiety for C3-C10 PFCAs and 0.83 log K_{OC} units per CF_2 moiety for C4, C6, and C8 PFSA. Shorter-chained PFASs such as PFBA, PFPeA and PFBS were weakly sorbed (less than 10% on average), while longer-chained PFASs (PFOS, FOSA, C9-C11 and C13 PFCA) sorbed strongly (on average, 99- 100%).

In general, the shorter the chain length the more important the polar-polar interaction becomes (Zhao et al., 2012). For C2-C4 PFAAs, the adsorption on sludge increases with decrease in chain length (Zhang et al., 2013c). The interpretation of this phenomenon given by the authors is that the hydrophobicity of short-chain PFCAs and PFSA decreases with decreasing chain length so that electrostatic interaction was dominant for sludge-water interactions for C2-C4 PFAAs in contrast to hydrophobic interactions, which dominate the sorption for longer chain PFAAs. Therefore, electrostatic interactions are also an important factor though adsorption/desorption to soils is commonly normalised to the organic carbon fraction (i.e. K_{OC} value) assuming hydrophobic interaction mainly governing adsorption/desorption. However, the clay fraction is for instance also considered a relevant sorption phase for organic cations such as the PFAAs (Droge and Goss, 2013).

Functional groups

Elmoznino et al. (2018) observed that PFSA would partition more strongly to effluent-derived suspended particulate matter than PFCA with the same number of perfluorinated carbons. The authors attribute this to differences in sorption, as log K_{OC} values are one and two units lower for PFHxS and PFBS, respectively, than for PFOS. Also Campos Pereira et al. (2018) found that PFSA sorbed more strongly than PFCA.

Lee and Mabury (2017) concluded that PFPAs are more sorptive than PFCAs at equal chain length by comparing the K_d values calculated for PFPIAs and PFPAs via aqueous loss method and direct soil analysis in a soil-sorption experiment with those reported in literature for other PFAAs. The differences between the sorption of PFPAs and PFSA of equal perfluorocarbon chain length were not consistent between the direct soil analysis and aqueous loss method. Although there is no data available to compare the K_d of PFPIAs with other PFAAs of the same chain length, based on the data from Lee and Mabury (2017) it is expected that PFPIAs are at

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

least as sorptive as other PFAAs. Differences in sorption between sediment soil and sludge and the water phase have been reported for PFCAs, PFSA and PFPAs with the same chain length. The partition coefficients between sediments and the overlaying water phase by direct analysis have been reported to be higher for PFOS than PFOA (Ahrens, 2011). In soil, Campos Pereira et al. (2018) demonstrated that the sorption of PFSA was stronger than of PFCAs and the sorption increased with increasing perfluorocarbon chain length. An increase of 0.60 and 0.83 log K_{OC} units per CF_2 moiety for PFCAs and PFSA, respectively, was observed. Higher partition coefficient of PFSA than PFCAs has also been reported in sorption experiments via the aqueous loss method in sediments (Higgins and Luthy, 2006) and activated sludge (Zhou et al., 2010b).

Cyclic structure and ether groups

Based on modelled data (COSMOlogic), cyclic PFAAs (C5-C7) can be (highly) adsorbed by soil ($\log K_{OC} > 3.5$), with increasing sorption with increasing number of perfluorinated carbons.

The presence of ether groups in the carbon chain does not alter the electron density in the carbon chain. Thus, short-chain PFECAs and PFESAs are expected to behave similar as PFCAs and PFSA, with shorter chain substances having low adsorption potential, which is expected to increase with increasing chain length. The high mobility of HFPO-DA (5 Carbons) is described in the Annex XV dossier on the proposal for identification of HFPO-DA as a substance of very high concern (ECHA, 2019d).

Role of the sorbent

Soils consist of organic matter, minerals and pore spaces filled with air and water (Bradry, 2010; Hellsing et al., 2016). Sand, silt and clay all provide minerals and surface area for the sorption of PFASs. Sand, silt and clay differ in their particle size, and smaller clay particles have colloidal properties carrying positive and/or negative charges.

Influence of ions and pH versus fraction of organic components

PFAS sorption is influenced by the soil pH and soil solution ionic strength. Campos Pereira et al. (2018) investigated the effect of solution pH and concentrations of Al^{3+} , Ca^{2+} and Na^+ on the sorption of PFCAs and PFSA in soils. The K_{OC} showed a negative relationship to both pH ($\Delta \log K_{OC} / \Delta pH = -0.32 \pm 0.11$ log units) and the soil organic matter (SOM) bulk net negative charge ($\Delta \log K_{OC} = -1.41 \pm 0.40$ per log unit $mol\ g^{-1}$). The effects of cation treatment and SOM bulk net charge were evident for many PFASs with low to moderate sorption (C5–C8 PFCAs and C6 PFSA). However, for the most strongly sorbing and most long-chained PFASs (C9–C11 and C13 PFCAs, C8 PFSA and perfluorooctane sulfonamide (FOSA)), smaller effects of cations were seen, and instead sorption was more strongly related to the pH value. Hellsing et al. (2016) found that a negatively charged silica surface was not able to adsorb anionic PFASs such as PFHxA, PFOA, PFOS, and PFNA. On the contrary, positively charged alumina surface adsorbed significant amounts of these compounds, indicating that an electrostatic mechanism might come into partial effect for adsorbing PFCAs (C8–C11), PFSA (PFOS and PFDS) and N-EtFOSAA, N-MeFOSAA on electrically charged soil components (Higgins and Luthy, 2006). One study investigated sorption to the phyllosilicate clay minerals illite, kaolinite, and bentonite (Droge and Goss, 2013). The authors point out that clays and minerals can have widely differing available surface areas for sorption and cation-exchange capacity values. It therefore would be challenging to include a generic parameter to account for clay sorption. It has been proposed that an increase in the fraction of organic components in the soil leads to more pronounced hydrophobic interaction as shown for PFOs, PFOS and 8:2 FTOH and PFBS (Brusseau, 2018; Milinovic et al., 2015).

Influence of humic acid and formation of complexes

Humic acid or other dissolved organic matter might form complexes with PFASs in the soil solution and inhibit sorption of those chemicals on to soil components such as clay minerals

and particulate organic matter. In river water, PFAAs like PFHxS, PFHxA, PFBS and PFOA were shown to be co-transported with dissolved organic carbon (DOC). These PFCAs and PFSAs carry a negative charge in natural waters, and the correlation was observed only for the shorter chained ($\leq C7$ for PFCAs and $\leq C6$ for PFSAs) and more hydrophilic substances. The authors suggest that one possible explanation for the observed phenomenon could be that these PFASs readily bind to positively charged ions that are complex bound to DOC (e.g. Ca^{2+}) with negatively charged head groups, while the longer chained PFAAs ($\geq C7$ for PFCAs and $\geq C6$ for PFSAs) rather partition to even more hydrophobic phases in the water, such as the organic carbon fraction of suspended particulate matter (Nguyen et al., 2019).

Influence of proteins

Protein binding as discussed in B.4.2.9 can also be an important factor influencing the adsorption for instance to sewage sludge. The presence of protein may lead to an increased adsorption of PFCAs (C2-C15) to sludge (Zhang et al., 2013a). For PFSAs, unlike PFCAs, carbohydrates were found to lead to an increase of adsorption.

B.4.2.1.2. Adsorption and desorption of arrowhead PFASs

As pointed out in section B.4.1., most PFASs degrade to their corresponding arrowhead PFASs in the environment. These arrowhead PFASs are therefore looked at with regard to adsorption potential. Physicochemical properties of PFASs are characterised in section B.1.2.

pKa values

With regard to electrostatic interactions it is important to differentiate between neutral and charged PFASs. PFCAs, PFSAs and PFPAs have low pKa values and are therefore almost completely dissociated at environmental relevant pH-values and therefore have a negatively charged headgroup. In contrast, perfluoroalkylamines have very high pKa values and thus will exist predominantly in the neutral form. Perfluoroalkylamines are therefore volatile depending on their molecular mass and water solubility (B.4.2.4). Van der Waals interactions will however play a role for both groups, PFAAs and amines, dependent on the length of the hydrophobic fluorinated carbon chain.

Because soils are generally anionically charged, anionically charged PFAAs become more mobile whereas cationic charged bases such as perfluoroalkylamines become less mobile as they can be retained by cation exchange processes. However, for some soil types, such as those with metal oxides, which can have a large anionic exchange capacity, this general rule of thumb may not apply. In sum, an assessment merely on the K_{OC} value may underestimate mobility of negatively charged PFAAs (UBA, 2019).

K_{OC} values

According to the physicochemical data for PFCAs, PFSAs and PFPAs there is a trend of increasing K_{OC} values with increasing chain length. The increasing adsorption potential pattern from PFCAs over PFPAs to PFSAs, as reported in the previous section, however, is not that clearly reflected in the K_{OC} values.

Perfluoroalkanes, which lack a functional group, have higher K_{OC} values than the PFAAs of the same chain length. It is thus expected that PFASs without a functional group will be more adsorptive. It should, however, be noted that up to a chain length of 4 carbons perfluoroalkanes have boiling points below 0 °C and their Henry's Law constants indicate that they are volatile (see B.4.2.4 on volatilisation). It is thus more likely that these short-chained perfluoroalkanes evaporate into the air when released to the environment. The same applies to the shorter chained perfluoroethers without any other functional groups. The two C4 perfluoroethers (1,1,1,2,2-Pentafluoro-2-(pentafluoroethoxy) ethane and 1,1,2,2-Tetrafluoro-1,2-bis(trifluoromethoxy)ethane) have boiling points below 2.5 °C and 13 °C and their Henry's Law constants indicate that they are volatile (see B.4.2.4 on volatilisation).

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

HFPO-DA, a branched C5 PFECA with an additional carboxylic acid functional group is described in the Annex XV dossier on the proposal for identification of HFPO-DA as a substance of very high concern (ECHA, 2019d). In the dossier log K_{OC} values for HFPO-DA are 2.48 and 1.92 based on molecular connectivity indices and on estimated log K_{OW} , respectively. Also, ADONA, a diether with five perfluorinated carbons and a carboxylic acid functional group can be considered mobile on the basis of its estimated log K_{OC} <1.3.

With respect to the carbon chain length, it should be noted that precursor substances which have a non-fluorinated moiety are expected to degrade to arrowhead PFASs with less carbons (see section B.4.1). Hence, those precursors are expected to form more arrowhead PFASs once they have been released to the environment.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.7. Log Koc for PFAAs (sediment organic carbon-normalised distribution coefficient) shown in dependence of the carbon chain length.

	1 Carbon	2 Carbons	3 Carbons	4 Carbons	6 Carbons	8 Carbons	9 Carbons	10 Carbons	11 Carbons
Perfluoroalkylcarboxylic acids		TFA		PFBA	PFHxA	PFOA	PFNA	PFDA	PFUnDA
log Koc (sediment organic carbon-normalised distribution coefficient)		0.437 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66))		1.767 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66))	1.63 – 2.35 (Sepulvado et al., 2011)	2.06 (Higgins and Luthy, 2006) 1.09 (Ahrens et al., 2010b; Ahrens et al., 2010c)	2.39 (Higgins and Luthy, 2006) 2.4 (Ahrens et al., 2010b; Ahrens et al., 2010c)	2.76 (Higgins and Luthy, 2006) 3.6 (Ahrens et al., 2010b; Ahrens et al., 2010c)	3.3 (Higgins and Luthy, 2006) 4.8 (Ahrens et al., 2010b; Ahrens et al., 2010c)
Perfluoroalkane sulfonic acids	C ₁ -PFSA	C ₂ -PFSA	C ₃ -PFSA	2.345 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	3.675 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))				

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

	1 Carbon	2 Carbons	3 Carbons	4 Carbons	6 Carbons	8 Carbons	9 Carbons	10 Carbons	11 Carbons
log K _{oc} (sediment organic carbon-normalised distribution coefficient)	0.352 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	1.016 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	1.681 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))						
Perfluoroalkyl phosphonic acids				PFBPA	PFHxPA				
	PFMPA		PFEPA	n.a.	3.977 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))				
log K _{oc} (sediment organic carbon-normalised distribution coefficient)	0.654 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))		1.318 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))						

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.8. Log K_{oc} for PFCs shown in dependence of the carbon chain length (sediment organic carbon-normalised distribution coefficient).

Perfluoroalkanes							
	1 carbon	2 carbons	3 carbons	4 carbons	5 carbons	6 carbons	8 carbons
	C-PFC	C ₂ -PFC	C ₃ -PFC	C ₄ -PFC	C ₅ -PFC	C ₆ -PFC	C ₈ -PFC
log K _{oc} (sediment organic carbon-normalised distribution coefficient)	1.687 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	2.352 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	3.016 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	3.681 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	n.a.	5.010 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	6.339 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.9. Log Koc for perfluoroalkylamines and perfluoroethers (sediment organic carbon-normalised distribution coefficient).

Perfluoroalkylamines						
Acronym	PFMAm	PFEAm	PFPPrAm	PFBAm	PFHxAm	
molecular formula	C ₃ F ₉ N;	C ₆ F ₁₅ N;	C ₉ F ₂₁ N;	C ₁₂ F ₂₇ N;	C ₁₈ F ₃₉ N;	C ₅ F ₁₃ N
	[(CF ₃) ₃ N]	[(C ₂ F ₅) ₃ N]	[(C ₃ F ₇) ₃ N]	[(C ₄ F ₉) ₃ N]	[(C ₆ F ₁₃) ₃ N]	
log Koc (sediment organic carbon-normalised distribution coefficient)	3.104 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	5.098 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	n.a.	n.a.	n.a.	4.433 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))
Perfluoroethers						
molecular formula	C ₂ F ₆ O	C ₄ F ₁₀ O	C ₄ F ₁₀ O ₂	C ₆ F ₁₄ O ₃	C ₂ F ₄ O	C ₃ F ₆ O
log Koc (sediment organic carbon-normalised distribution coefficient)	1.330 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	2.660 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	4.706 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	1.946 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	0.932 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	1.596 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))

Conclusion on sorption

Several studies have confirmed a relationship between sorption and perfluorocarbon chain length. Although generally there is a linear relationship between the carbon chain length and $\log K_{oc}$ value, it should also be noted that for the substances with shorter carbon chain length, the polar-polar interaction, determined by a functional group such as carboxylic acid or amine, gains importance. Most of the studies investigating distribution focussed on PFCAs and PFSAAs but also PFPAs, PFPiAs, PFECAs and PFESAs, additionally cyclic PFAAs (C5-C7) have been investigated to some extent. PFPAs are more sorptive than PFCAs at equal chain length. Sorption differences of PFPAs and PFSAAs did not follow a systematic pattern. PFAAs have both hydrophobic fluoroalkyl chains and hydrophilic ionizable functional group and thus show complex behaviours in the environment in terms of their sorption and desorption processes (Ahrens, 2011; Kannan, 2011). Neutral PFASs are more likely to adsorb to organic matter or partition into the gas phase. It is difficult to predict the sorption of the PFASs universe from a single sorbent bulk property. The properties of the sorbent needs to be considered as well.

B.4.2.1.3. Mobility in water

Specific criteria have been proposed for identifying mobile or very mobile substances and are currently under consideration for including into legislation. For example, the German Environment Agency (UBA) has proposed the following: M is indicated by water solubility ≥ 0.15 mg/L and $\log K_{oc} \leq 4.0$ or $\log K_{ow} \leq 4.0$, and vM by water solubility ≥ 0.15 mg/L and $\log K_{oc} \leq 3.0$ or $\log K_{ow} \leq 3.0$ (UBA, 2017a). In the continuing discussion water solubility has been considered not to be a suitable property to set a threshold for the assessment of mobility. The principal reasons are difficulties when assessing ionic and ionizable substances, in which water solubility is dependent on counter ions (Rüdel et al., 2020; UBA, 2019). For the purpose of this restriction proposal no specific cut off values are proposed to be used but the comparisons below are for background information.

With respect to the suggested mobility criteria described above and on the basis of their K_{oc} , all PFCAs up to a chain length of 11 carbons can be considered either vM ($\leq$ C10-PFCA, PFDA) or M (PFUnDA). Likewise, all PFSAAs up to 6 carbons can either be considered vM ($\leq$ C4-PFSA, PFBS) or M (PFHxS) based on their K_{oc} values. The same can be concluded for the PFPAs. Considering the perfluoroalkylamines, only 1,1,1-Trifluoro-N,N-bis(trifluoromethyl)methanamine (PFMAm) fulfils the M criterion based on the K_{oc} value. With the exception of C₄F₁₀O₂ all perfluoroethers fulfil either the vM or M criterion based on their K_{oc} values. It is noted that perfluorinated olefins, and alkenes in general are expected to degrade to PFCAs (see section B.4.1.3), which are mobile. Perfluoroalkanes up to four carbons would be considered mobile. However, as mentioned above, it should be noted that up to chain length of 4 carbons perfluoroalkanes have boiling points below 0° C. It is thus more likely that these short chained perfluoroalkanes evaporate into the air when released to the environment. The same applies to the short-chain perfluoroethers without any other functional groups. (see also B.4.2.1.2)

Three PFASs have been accepted as being mobile so far:

- PFBS has been identified as a substance of very high concern based on its equivalent level of concern as compared to PBT/vPvB substances: very high persistence, high mobility in water and soil, high potential for long-range transport, and difficulty of remediation and water purification as well as moderate bioaccumulation in humans (ECHA, 2019e)
- HFPO-DA has been identified as a substance of very high concern based on its equivalent level of concern due to its mobility and persistence (ECHA, 2019d);
- RAC has agreed that PFHxA, its salts and related substances possess properties, in particular very high persistence combined with mobility, that can be considered to constitute an intrinsic hazard (ECHA, 2021a).

Many PFASs are precursors of PFAAs, which have been demonstrated above to be either mobile or very mobile. Hence a large part of PFASs can be considered as mobile in water, either by themselves or as result of their degradation into PFAAs. However, no or insufficient data are available on physico-chemical properties and fate of many PFASs (especially precursors). Therefore, uncertainties remain regarding mobility of several PFASs in water.

Several PFASs have been detected in fresh and ocean water as well as ground and drinking water indicating their mobility. Though routine target analyses mainly focus on PFCAs and PFSAAs and some of the precursors of these PFAAs, other PFASs can also be present in these compartments, which is further supported by the large fraction of unknown organofluorine compounds in aquatic samples (see B.4.2.6.1). For example, less studied PFASs, such as HFPO-DA, HFPO-TA, ADONA, 6:2 Cl-PFESA, 8:2 Cl-PFESA, 6:2 H-PFESA and 6:2 FTSA, have been ubiquitously detected in worldwide surface waters (Wang et al., 2019c). In addition, studies on the aquatic environment published between 2009 and 2017 have (tentatively) identified 455 new PFASs (nine fully and 446 partially fluorinated compounds), although for most of these compounds there are no quantitative monitoring data due to the lack of reference standards (Xiao, 2017) (see also B.4.2.6.3).

The review of review papers by Sims et al. (2022) on surface water monitoring data note that >C9 PFCAs and PFSAAs were generally detected at lower concentrations compared to shorter-chained PFCAs and PFSAAs in both surface waters and groundwater (see B.4.2.7.2). Physico-chemical properties and environmental partitioning dynamics clearly affect fate in the environment as discussed in B.4.2.1.1 and B.4.2.1.2. Shorter-chained PFAAs are more likely to be distributed to drinking water than longer-chained PFAAs based on their properties. However, also for PFASs considered not as mobile due to their adsorptive properties it cannot be excluded that they, due to the high persistence, enter drinking water. In this context it has to be also noted that ultra-short chained PFAAs (C1-C3) are often lacking in monitoring programs as they are analytically challenging (Björnsdotter et al., 2020). However, available data indicate that TFA generally occurs in considerably higher concentrations than other PFASs in aquatic samples. Other ultra-short PFAAs may also significantly contribute to the total amount of PFASs in water samples (see B.4.2.7.3 and Table B.77 to Table B.80).

Mobility as a concern

Mobility is a contributing factor for

1. Potential for long range transport via water (see section B.4.2.8)
2. Potential for drinking water contamination (see also next subsection)
3. Uptake in plants and crops (see section B.4.4)
4. Making very persistent substances available for increasing internal concentrations in biota along the increase of the environmental exposures (see section B.4.2.9, "Persistence compensating low bioaccumulation potential" and section 1.1.4. of the main report "High potential for ubiquitous, increasing and irreversible exposure of the environment and humans").

For substances mobile in water phase, there are no local or intermittent sinks for the pollution stock, and therefore mobile substances have a high potential for continuously increasing environmental concentrations and exposure of wildlife and humans. Oceanwater is important as a sink and for transport of these compounds. The occurrence of high concentrations of PFASs in coastal waters could possibly be problematic because the substances will be bioavailable and can accumulate in the marine food chain (Cai et al., 2012). Furthermore, it is difficult in practice to manage exposures due to high mobility and exposures at different locations and times. Mobile PFASs may end up in drinking water, posing a potential risk to human health. Apart from soil as a long-term source of

groundwater contamination, statistical analysis showed a correlation between the major contaminants in the river and those in the groundwater, indicating the potential linkage of PFASs in the groundwater to the surface water ((Li et al., 2020a), see also B.4.2). Reemtsma et al. (2016) concluded that persistent and mobile organic compounds may be of concern for water quality because they are persistent in the environment and are not removed from water by sorption processes due to their high polarity and excellent water solubility. A problem which has been underestimated due to an analytical gap in the past.

Raw water which is used for drinking water is obtained either from groundwater, bank filtration or surface waters. On average about 50% of the water for drinking water production is taken from groundwater, whereas the amount from surface water is about 36% (EC, 2016). With regard to groundwater and bank filtration, adsorption and desorption in soil and sediment are thus crucial parameters for drinking water quality. Due to their persistence, the residence time of PFASs in groundwater is at least the residence time of groundwater (>40 days up to an order of millennia (Małoszewski and Zuber, 1982; McGuire et al., 2005)) because transport away from the site in water is the only removal mechanism. As a consequence, PFAS-contaminated groundwater can act as a long-lasting source, leading to poorly reversible exposure (Cousins et al., 2016). Human exposure via drinking water is further discussed in B.9.21.2.

Cases of contaminated sites provided below in this section and in Annex E illustrate the long-lasting problems and hardly reversible contaminations with groundwater and drinking water contamination. However, not only incidences cause elevated levels of PFAS in drinking water.

A three-year monitoring campaign (2010–2013) investigated the occurrence, sources and fate of nine PFCAs and three PFSA, in the most industrialized region of Italy (Castiglioni et al., 2015), also discussed in section B.4.2.3 (soil). Samples were collected in influents and effluents of wastewater treatment plants (WWTPs), in the main rivers flowing through the basin, and in raw groundwater and finished drinking water. The mass balance of the emissions in the River Lambro basin showed continuously increasing contamination from north to south and differences in the composition of homologues in the west and east sides of the basin. Ground and drinking water were contaminated in industrial areas, but these substances were removed well in Milan. Contamination from industrial sources was prevalent over urban sources, contributing to 90% of the loads measured at the closure of the basin. The River Lambro was confirmed as one of the main sources of contamination in the Po River. Moreover, an epidemiological investigation was carried out on the population living in an area contaminated by PFASs in drinking water and possibly affecting the food chain. The ongoing investigation shows an important set of a priori evidenced adverse health effects (Mastrantonio et al., 2018) (see B.5).

Several studies have demonstrated PFAS contamination of water bodies due to the use of aqueous film forming fire-fighting foams (AFFF) at e.g. airports. For example, contamination away from its point source (which was likely a military airport in the north of the city) was demonstrated in Uppsala, Sweden. The PFAA levels in groundwater measured in 2012–2014 decreased downstream from the point source, although high Σ PFAA levels (>100 ng/L) were still found several kilometres from the point source in the Uppsala aquifer (Gyllenhammar et al., 2015).

Several studies have also shown that fluorochemical production facilities are potential point-sources of several PFASs, including perfluoroalkyl ethers, to surrounding environmental compartment including water bodies (see B.4.2.7 and B.4.2.3).

WWTPs are also an important source for contamination. For example, the effluent of WWTP in Halle was found to contain four times higher levels of PFAAs than river water and was dominated by PFBS with 32 times higher concentration than the riverine level. In this case annual flux of PFAAs from River Saale was estimated to be 164 ± 23 kg/y (Shafique et al., 2017).

Drinking water contamination

Following summarized monitoring data on detection of PFASs in drinking water underline that drinking water contamination is a concern already not limited to a few locations but ubiquitously. Further monitoring data for specific PFAS groups are also summarized in B.4.2.6, B.4.2.7, and Appendix B.4.2.1.3. Mobility in water Table B.79.

Jian et al. (2017) reviewed the global distribution of PFASs in drinking water from Europe in France, Spain, Norway, Netherlands, Faroe Islands and Germany and Thailand, Korea, Japan, Ghana and the US (Boiteux et al., 2017; Domingo, 2012; Eriksson et al., 2013; Eschauzier et al., 2013; Haug et al., 2010a; Llorca et al., 2012a; Schwanz et al., 2016). The reviewed monitoring programs of targeted analysis mainly focussed on PFAAs. In this review, PFAS levels varied in the order of well water > tap water > bottled water > drinking water > raw water. The highest PFAS contamination in well water indicated that point sources could be the main cause. For results diverging from this order, the authors assume that greater PFAS concentrations in tap and drinking water than in raw water indicate a role of drinking water treatment⁵ processes in PFAS contamination. As discussed in section B.4.5, shorter-chain PFASs are generally less efficiently removed during water treatment process compared to the longer-chain PFASs. For example, Eschauzier et al. (2012) demonstrated that granular activated carbon (GAC) could efficiently reduce longer-chain PFAAs, but had little effect on shorter-chain PFAAs such as PFBA and PFBS. It was proposed that the degradation of precursor compounds and long-chain chemicals could lead to PFAS increase at the WWTP (Eriksson et al., 2013). Thus, purification processes greatly influence PFAS levels in post-treatment water, while the carbon chain lengths of PFASs in untreated water also have significant influence on the purification efficiency (Schwanz et al., 2016).

Castiglioni et al. (2015) analysed drinking water collected in the whole Lambro basin in Milan, Italy. This study confirmed PFAAs as ubiquitous contaminants in the aqueous environment and identified the main sources and the environmental fate of these substances in the most industrialized and heavily inhabited area in Italy. All the substances (C4-C12 PFCA, C4, C6 and C8 PFSA) were detected in drinking water at frequencies higher than 60% in northern Milan (an industrialized area), around 30–50% in the metropolitan area of Milan (except long-chain PFCA, which was not detected) and were never detected in southern Milan (agricultural area). In comparison to the above-mentioned studies, the levels of longer-chained PFASs such as PFOA, PFOS and PFHxS in the Milan area were the highest (up to 1 886 ng/L for PFOA, 150 ng/L for PFOS and 141 ng/L for PFHxS in drinking/tap water according to data given in the IPCHEM database). Same observations are made for shorter-chained PFASs - the highest concentrations have been measured in Italian drinking/tap water: up to 556 ng/L (PFBA), 347 ng/L (PFBS), 267 ng/L (PFPeA), 240 ng/L (PFHxA) and 100 ng/L (PFHpA) according to data given in the IPCHEM database⁶. In comparison PFBA has been detected up to 27 ng/L maximum and 10 ng/L average in tap water in Spain; PFBS up to 36 ng/L maximum and 8.3 ng/L average in Spain, PFHpA up to 16 ng/L maximum and 8.1 ng/L average in Spain and 1.2 ng/L average concentration in France, PFHxA up to 11 ng/L maximum and 4.7 ng/L average in Spain and 3.7 ng/L average and France, and PFPeA up to 17 ng/L maximum and 3.8 ng/L average in Spain and 2.7 ng/L average in France (Kaboré et al., 2018; Llorca et al., 2012a). Other PFASs have been also detected in tap water but the concentrations have been mostly below 1 ng/L.

Schwanz et al. (2016) investigated bottled drinking water (n=38) from France, Spain and Brazil. The profile of compounds in bottled water was significantly different for the samples from the three studied markets. For example, PFOS was only detected in France (present in 26% of the samples), PFBS was detected in France and Brazil but not in Spain, whereby, Spain was the only country where PFHxA was quantified in 20% of the samples. The median

⁵ <https://www.sciencedirect.com/topics/earth-and-planetary-sciences/water-purification>, date of access: 2022-09-29.

⁶ <https://ipchem.jrc.ec.europa.eu/>, date of access: 2022-09-29.

concentration of the total PFASs in bottled water was as follows: Brazil > France > Spain with 15.0, 14.9 and 11.3 ng/L, respectively. However, the highest level of contamination in a single sample was found in a bottled water sample that was commercialised in France, with 116 ng/L as the sum of all individual PFASs. In the present work, in bottled water the most frequently detected compound was PFHpA, which was detected up to 47% in the samples from France and 40% in Spain. While French and Brazilian samples showed contamination by various PFAS, above the limit of detection, in Spanish samples only PFHxA, PFHpA, PFOA and PFNA were found. However, the authors hypothesise that the source of contamination is the migration from the dopants used in the polymers (in general, PET) in the fabrication of water bottles and in the ink from labels can be the source of part of PFASs in water though residual environmental contamination can be a source. PFASs have also been detected in bottled drinking water from Ireland (Harrad et al., 2019) as well as Germany (Llorca et al., 2012a). The detection frequency of bottled water from Ireland (n=21) was 87% for PFOA, 29% for PFOS, 29% for PFBS, 19% for MetFOSA and PFNA and 42% for MetFOSE. The detection frequency was 100% (n=2) for PFHpA in bottled water from Germany. The concentration in these samples was 6.6 and 12 ng/L, and one of them contained also PFOS at 1.0 ng/L. Likewise it was hypothesized that the origin of PFHpA is the plastic of the bottles, although there is no available data to confirm it.

A recent global survey found a widespread distribution of short-chain PFAAs in drinking water (Kaboré et al., 2018), with PFBA being detected in 58% of bottled water and 92% of tap water, PFPeA detected in 32% of bottled water and 68% of tap water, PFHxA in 50% of bottled water and 64% of tap water, PFHpA in 42% of bottled water and 90% of tap water, PFBS in 47% of bottled water and 88% of tap water.

All the above-mentioned studies have focussed on analysing PFCAs and PFSA in targeted analysis. However, the ban on PFOA has led to the production and use of alternative fluorinated compounds, such as HFPO-DA which now has been identified as a substance of similar concern due to its persistence and mobility. HFPO-DA and other perfluoroalkyl ethers have been detected in drinking water especially in the vicinity of fluoropolymer production plants (see B.4.2.7.6), but also further away from the point-sources which illustrates the problem of mobile PFASs.

Taken together, the concentrations and relative contributions of different conventionally analysed PFAAs in drinking water differ between studies, but the individual levels of the most abundant PFAAs, i.e. PFOA, PFOS, PFHpA, PFBA, PFPeA, PFBS, PFNA are generally within the same order of magnitude. Furthermore, studies of ultrashort PFAAs show that TFA (shortest PFCA) is present in drinking water at roughly 2 orders of magnitude higher concentrations compared to the above mentioned PFAAs and other ultrashort PFAAs have been found in largely comparable levels to the conventionally measured PFAAs (see B.4.2.7).

Besides the few routinely analysed PFASs, a large fraction of the total organofluorine in drinking water remains unidentified (see B.4.2.6). Apart from target analyses, studies of total organic fluorine as well as screening studies show that other, but not yet reliably identified and quantifiable PFASs are present in drinking water (see B.4.2.6). In a study by Kaboré et al. (2018), 104 suspect-target PFASs were screened in drinking water samples from Canada and other countries (Burkina Faso, Chile, Ivory Coast, France, Japan, Mexico, Norway, and the USA). The study is the first to observe perfluoroalkane sulfonate (PFECs) and C4–C6 perfluoroalkane sulfonamides (FBSA, FHxSA) in drinking water. In addition, Guardian et al. (2021) was the first study to show the presence of 2-(N-methylperfluorooctanesulfonamido) acetic acid (N-MeFOSAA) in drinking water and 3 novel PFASs (C₅H₅OF₈, C₆H₄O₂F₆, and C₉H₂O₂F₁₆) were detected using suspect screening in source water in Philippines and Thailand.

Conclusion on mobility of PFASs

Mobility is of concern for several reasons as these properties contribute to the LRTP, uptake in plants and crop and the potential to contaminate drinking water. There are no local or intermittent sinks for the pollution stock, and therefore mobile substances have a high potential for continuously increasing environmental concentrations and exposure of wild life and humans. As discussed above many of the arrowhead PFASs can be considered as mobile or very mobile based on their K_{oc} values with respect to the suggested mobility criteria. Several PFASs have been detected in fresh and ocean water as well as ground and drinking water indicating their mobility. Monitoring data on detection of PFAS in drinking water underline that drinking water contamination is a concern already not limited to a few locations but ubiquitously.

B.4.2.2. Sewage sludge

Sewage sludge is a by-product of wastewater treatment in municipal and industrial sewage treatment plants and has been identified as relevant anthropogenic source for the release of PFASs into the environment (Bossi et al., 2008; Kallenborn et al., 2004). The recycling of sewage sludge as amendment for agricultural soils is a regular practice in the EU (Hudcová et al., 2019; Kacprzak et al., 2017) and is widely considered a potent release pathway of PFASs from sewage sludge (Aro et al., 2021b; Bossi et al., 2008; Navarro et al., 2016; Schultz et al., 2006; Semerád et al., 2020). PFAS contamination of agricultural soil has been directly linked to sewage sludge amendments in the US (Washington et al., 2010) and China (Wen et al., 2014). EU regulations do not require testing of sewage sludge for PFAS contamination before application (Hudcová et al., 2019). Therefore, data is limited.

Bossi et al. (2008) and Semerád et al. (2020) hypothesized that soil amendments with PFAS contaminated sewage sludge can lead to the contamination of agricultural soils and leaching into ground water (see also B.4.2.3). The uptake of PFASs from sewage sludge contaminated soil into plants has been demonstrated for PFAAs (Lee et al., 2014; Wen et al., 2014), similar to the uptake into soil organisms (Navarro et al., 2016). The migration of pollutants from soil to plants or soil organisms could facilitate a probable entry pathway into the food chain (Navarro et al., 2016).

B.4.2.3. Soil

A recent review demonstrated that PFASs are present in soils across the globe, and indicated that soil is a significant reservoir for PFASs (Brusseau et al., 2020). A major aspect of concern is the long-term migration potential to surface water, groundwater, and the atmosphere as well as potential human exposure via the soil-groundwater-drinking water-path or the soil-groundwater-nutrition (plant or animal) path.

Brusseau et al. (2020) compiled data on soil concentrations of PFASs for “uncontaminated” sites (to derive background concentrations of PFASs in soil), contaminated sites as well as secondary source sites. Contaminated sites include PFAS manufacturing sites, fire training sites and other AFFF-associated locations at airports and military installations, and an airplane crash site. The secondary-source sites include sites that are adjacent to PFAS-contaminated primary-source sites, or sites for which PFAS-contaminated media were used for different purposes e.g. for irrigation or as fertilizer. Examples of such cases are described below.

The potential importance of soil as a global reservoir for PFASs was first quantified by Strynar et al. (2012) who measured the concentrations of 13 PFAAs (PFTTrDA, PFTeDA, PFDoA, PFUdA, PFDA, PFNA, PFOA, PFHpA, PFHxA, PFDS, PFOS, PFHS, PFBS) in samples of surface soil collected from 60 locations in 6 countries. Strynar et al. estimated global soil loadings of 1 860 and >7 000 t of PFOA and PFOS, respectively. Rankin et al. (2016) reported concentrations of 32 PFASs (PFCAs and PFSAs) in surface soil samples collected

from 62 locations across all continents. Quantifiable levels of more than one PFAS were present in all samples tested, including soils collected from remote locations. Washington et al. (2019) used data from Rankin et al. (2016) to calculate global soil loadings for eight PFAAs (PFCAs with chain lengths C6 – C12 and PFOS). The combined estimated load for all eight PFAAs ranged from 1 500 to 9 000 t, with mean estimates of approximately 1 000 t for both PFOA and PFOS. These results indicate that soil has the potential to be a substantial reservoir for PFASs.

Another study reported a meta-analysis of PFASs soil-to-groundwater concentration ratios for samples collected from 324 AFFF source-zone sites across 56 military installations distributed throughout the U.S. (Hunter Anderson et al., 2019). The results demonstrated that soil is a significant reservoir for PFASs at these contaminated sites. Transport modeling conducted at individual contaminated sites also indicates that soils and the vadose zone serve as a significant long-term source of PFASs (Weber et al., 2017).

In this context it is worth noting that point-source contamination may be challenging to identify unless locations of use or production has been identified or is suspected in an area. Results from groundwater monitoring near point sources indicate that PFAS concentrations in groundwater and aquifers are highly variable even within a few kilometres, at least based on the currently available information, which inherently is influenced by site-specific geological factors. For example, levels of PFOA around an industrial park in China were on average around 15 000 ng/L, however, when compared to observations only 1-4 km away, mean PFOA dropped to 23 ng/L, and then further decreased to 2.6 ng/L when sampled 4-10 km away from the facility (Liu and Liu, 2016). A similar gradient was seen by Filipovic et al. in Stockholm, Sweden for groundwater contamination by AFFF at a former air force base. Concentrations of PFOS in some wells reached 42 200 ng/L while others within a few kilometers were as low as 7 ng/L (Filipovic et al., 2015).

Another point of interest is the relative ranges of soil versus groundwater concentrations reported for PFASs (Hunter Anderson et al., 2019) in order to estimate the potential for groundwater contamination via soil-leaching. In this context soil monitoring studies investigating depth profiles of PFASs can reveal how PFASs with different properties distribute in soil and subsequently their potential for leaching into groundwater. The basic assumption is, that the differing physico-chemical properties of different PFASs lead to differences in their distribution within the soil column (.e.g. (Baduel et al., 2017; Buck et al., 2011; Casson and Chiang, 2018; Dauchy et al., 2019; Sepulvado et al., 2011; Washington et al., 2010)). This leads to different PFAS concentrations depending on the sampling depth. Brusseau et al. (2020) - based on findings from the above-mentioned studies - described a trend according to which the greatest concentration of longer-chain PFASs $\geq C7$ (referring to Buck et al. (2011)) are mostly found closer towards the surface (within 1 m, according to Baduel et al. (2017)). Accordingly, maximum concentrations for short-chain PFASs are measured at greater depths (>2 m according to Baduel et al. (2017)). Brusseau et al. (2020) summarized the observations from different studies as follows: "The majority of depth-profile data sets show high concentrations present at shallow depths and exponential decreases at greater depths". Hunter Anderson et al. (2019) described positive $c_{\text{soil}}/c_{\text{groundwater}}$ ratios for the vast majority (87%) of data they took into account, reflecting greater soil than groundwater concentrations. In this context soil concentrations ~ 100 -times greater than groundwater were observed. This may pose a long-term source for groundwater contamination due to leaching.

The following examples for PFAS contamination in soil are provided to support the link between the mobile and persistent properties of PFASs and the type of contamination. Further monitoring data from contaminated areas are presented in Appendix B.4.2.3. Table B.81.

B.4.2.3.1. Examples from Europe

Cases of land application of industrial-waste derived amendment are for instance described in the study by Wilhelm et al. (2008). Industrial waste with high concentrations of PFASs was manufactured into a soil improver by a recycling company and spread by farmers on agricultural land of the rural area Sauerland, Germany. This led to substantial environmental pollution and had an impact on drinking water.

A second site with a similar cause of contamination is located in Baden-Wuerttemberg, Germany. In the surroundings of Rastatt, 480 hectares of former arable land are contaminated with short-chain PFASs. The pollution was detected in 2013 and has probably been caused by the longstanding application of compost mixed with sludge from paper production, contaminated with various precursors. Over time, shorter-chained PFASs (e.g. PFBS, PFBA, PFHxA) and precursors (e.g. 4:2 FTOH, 6:2 FTOH) in the soil wash out into the groundwater. Two groundwater wells for drinking water production had to be closed. Until now, no practicable solution for removing the short-chain PFASs from the soil or groundwater has been found. Furthermore, there are still high concentrations of PFASs (Brendel et al., 2018).

In Italy, on January 2014, drinking water contamination in an area of the Veneto Region was detected mainly due to the drain of fluorinated chemicals by a manufacturing company operating since 1964. More details on the drinking water contamination are provided in B.4.2.1.3

Drinking water works in the municipality of Kallinge, Sweden were immediately closed down after contamination of the groundwater was discovered near a Swedish Air Force and civil aviation base where PFAS-containing AFFFs have been used (Jakobsson et al., 2014).

Field investigations were carried out in the vicinity of four sites where AFFFs are or were intensively used (two airports, a training center for firefighters and an oil storage depot after a large explosion). In case of the incident of a fire at an oil storage depot 28 years had passed until the field investigation. PFAS profiles were influenced by parameters such as route of PFAS transport after use (runoff, seepage, direct discharge), time elapsed since the cessation of firefighting activities, and firefighting foam composition. The authors conclude that the PFAS concentrations found around the investigated sites are the highest recorded in France (Dauchy et al., 2017).

A study investigating the impact of two fluoropolymer manufacturing facilities on downstream contamination of a river and drinking water resources clearly demonstrated the impact on the water quality of the drinking water resources (Bach et al., 2016a).

Landfills have also been shown to contaminate adjacent areas. For example, in a survey of leachates from 117 Swedish landfills, all samples contained detectable levels PFAAs. The most abundant PFAAs were PFBA, PFBS, PFPeA, PFHxA and PFOS with mean concentrations between 427 and 1 242 ng/L (maximum concentrations of 22 800 – 74 600 ng/L). PFAAs were also found in nearby ground water at mean concentrations ranging between 67 to 129 ng/L and in surface water at generally lower mean concentrations ranging between 15 and 30 ng/L (Miljösamverkan Sverige, 2022). Another Swedish study has shown that ultrashort (C1-C3) PFAAs also contribute significantly to the total PFAA content in leachate (Björnsdotter et al., 2019).

It should be noted that most of these cases were discovered by chance. Other cases may be yet undetected. Consequently, the use of PFAS-contaminated media such as biosolids and irrigation water can result in soil contamination, subsequent distribution to other media, and ultimately the potential for human exposure at locations far from the original PFAS source (Lindstrom et al., 2011; Liu et al., 2017).

B.4.2.3.2. Examples outside Europe

In June 2000, 22 000 L of fire-retardant foam containing perfluorinated surfactants was accidentally released at L. B. Pearson International Airport, Toronto, ON, and subsequently entered into Etobicoke Creek, a tributary to Lake Ontario (Moody et al., 2002). A few years later, the same creek was subject to contamination with approx. 48 000 L of AFFF which were applied to a burning aircraft, which had overrun the runway (Oakes et al., 2010). This incidences may be seen as an involuntary long-term field study on the distribution of PFASs. For instance, even a decade after the first spill, sediment PFOS concentrations were still elevated in Spring Creek Pond which received the foam discharge (Awad et al., 2011).

The decades-long disposal of manufacturing waste containing PFASs in landfills in Minnesota resulted in contamination of groundwater serving as the drinking water supply for the eastern Twin Cities metropolitan region. In 2004, local and state agencies in Minnesota were alerted to the presence of PFAAs in the drinking water supplies of several eastern Twin Cities suburbs. A study conducted in 2010, six years after the discovery, measured PFASs in garden produce due to past/ongoing water contamination (Scher et al., 2018).

B.4.2.3.3. Conclusion on soil distribution

PFASs are present ubiquitously in soils, not only at contaminated sites but they are also found in “uncontaminated” sites far from point sources. At the most contaminated sites, PFAS concentrations in soil range up to ppm levels. Many cases of soil contamination with PFASs are known inside and outside of Europe and the assumption is that many contaminated sites are yet to be discovered. Soil can thus be seen as a global reservoir for PFAS contamination and human exposure via drinking water or food. PFASs in agricultural soils are a potential point of entry into the food web via crops or animals. Additionally, PFASs are retained at high concentrations in the vadose zone where they eventually can reach groundwater which is a potential source for drinking water.

B.4.2.4. Volatilisation

The threshold for volatile substances is Henrys Law Constant $>250 \text{ Pa} \cdot \text{m}^3/\text{mol}$, according to REACH Guidance R.16 (ECHA, 2016a). For PFASs which are below this threshold aqueous compartments are more relevant regarding their distribution compared to the atmosphere.

Neutral PFASs can have a relatively high vapour pressure whereas dissociated, charged PFASs have a negligible vapour pressure, are soluble in water, and have a very low air–water partition coefficient (Barton et al., 2007; Kaiser et al., 2005). Vierke and co-workers concluded in their work on PFCAs that the extent of volatilization of PFCAs in the environment will depend on the water pH and their pKa. Knowledge of the pKas of PFCAs is therefore vital for understanding their environmental transport and fate (Vierke et al., 2013).

PFAAs may exist as neutral PFASs with higher volatility and lower water solubility or ionic PFAS with lower volatility and higher water solubility. Considering their low pKa values, it can be assumed that the PFAAs almost completely dissociate at environmentally relevant pH values and are therefore charged, have a low vapour pressure and higher water solubility than their neutral forms and their volatility can be regarded as negligible. In their review on distribution modelling the authors consider volatilization not a major concern for most PFASs with functional groups which dissociate such as PFAAs (Sima and Jaffé, 2021).

Furthermore, it can be expected that larger molecules with a high molecular weight are non-volatile. The largest molecules among the PFASs, e.g, side-chain fluorinated polymers, gradually degrade into the PFAAs, and are therefore expected to have negligible volatilisation (see also section B.4.1.3). Same applies to other PFASs which contain a large

non-fluorinated aromatic moiety.

Neutral PFASs such as the perfluorinated olefins, perfluoroethers, perfluoroalkylamines and halofluoroalkanes are volatile depending on their molecular size and water solubility (see section B.1.2). As discussed in the section on long-range transport (B.4.2.8) precursors such as fluorotelomer alcohols (FTOHs) are very volatile due to their high vapour pressures and non-ionic status (Chen et al., 2020a). Similarly, uncharged PFASs like perfluoroalkane sulphonamides (FASAs), perfluoroalkane sulfonamidoethanols (FASEs) are less water-soluble and more volatile. For many of these PFASs, degradation to a less volatile and more water-soluble arrowhead PFAS applies as well, depending on the chain length of the resulting arrowhead (see section B.4.1.3).

B.4.2.5. Distribution modelling

Not assessed.

B.4.2.6. Monitoring of unknown PFASs in environmental compartments

Targeted PFAS analysis commonly includes up to 40 individual PFASs. However, given the much larger number of PFASs in total, methods that measure unspecific organic fluorine are used to estimate the total amount of PFASs in a sample. In this section, environmental monitoring data for PFASs of unknown identity are summarised, including analyses by extractable organic fluorine (EOF), adsorbable organic fluorine (AOF), the total oxidizable precursor assay (TOPA) as well as non-target and suspect screening. For a description of the analytical methods and their applicability see Annex E.4.

B.4.2.6.1. EOF/AOF

Adsorbable organofluorine (AOF) and extractable organofluorine (EOF) analysis provide two different sum measures of the organic fluorine in the sample, including known and unknown organofluorine compounds (including non-PFAS compounds) with different physico-chemical properties. The covered organofluorine compounds may vary depending on which of the two methods is used. Fluorine mass balance analysis of EOF/AOF and the sum of identified PFASs via targeted analysis allows the estimation of the fraction of unidentified organic fluorine (UOF) in a sample.

Available measurements of EOF/AOF in the environment cover a wide range of environmental media, including surface water, drinking water, ground water, wastewater, sediment, sludge, soil, dust, and wildlife. For a detailed list of studies, including main results, see Appendix B.4.2.6.1. Table B.82 and Table B.83. For human matrices, see section B.9.22. Below follows a summary of the main results from selected environmental studies.

EOF/AOF and fluorine mass balance analyses in abiotic environmental matrices show varying, but significant, fractions of unidentified PFASs (40-99.9%). The varying fractions could be due to sample location (e.g. a contaminated area), but also to e.g. sample characteristics, study design, choice of analytical method (e.g. extraction method, detection limit) and the number of PFASs included in the targeted analysis. While in most studies, a few to a few dozen analytes were measured in the targeted analysis, a recent study (Aro et al., 2021b) on effluent and sludge water in the Nordic environment monitored 73 PFASs in addition to EOF.

Surface- and groundwater overall displayed a large fraction of UOF. In samples without known point-sources, the UOF fraction was generally >90%, whereas contaminated water samples normally contained a lower but highly variable fraction of UOF. One study reported in European surface waters without known contamination, EOF levels in the range <30-849 ng F/L in Finland, Sweden, Iceland, Denmark, Greenland, Norway and the Faroe Islands, and an average UOF of 92% (Kärrman et al., 2019). The EOF concentrations in

this study were similar to two studies of German rivers reporting EOF levels (without targeted analysis) of 40–60 ng F/L in Moselle, 50–300 ng F/L in Rhine (Metzger et al., 2019), and 50–550 ng F/L in river Spree (Gehrenkemper et al., 2021). The highest overall European EOF concentrations (800–4 000 ng F/L) were detected in contaminated river and lake surface waters in Norway, where UOF was on average 99% (Aro et al., 2021b). Outside Europe, the highest level of EOF in surface water (440 000 ng F/L) was reported from the Cape Fear River in the US, downstream a fluoropolymer manufacturing plant (Han et al., 2021a). The EOF was largely composed of perfluoro-2-methoxyacetic acid, used in fluoropolymer manufacturing, demonstrating that UOF can be low in areas contaminated with specific PFASs.

EOF/AOF and fluorine mass balance analyses in biota show, similar to the abiotic samples, varying fractions of UOF (range 10–99%). Kärrman et al. (2019) analysed EOF as well as 78 targeted PFASs in samples of biota (n=51) from the Nordic countries. The results showed average EOF levels ranging from 221–707 ng F/g (Figure B.59). Despite the relatively large number of targeted PFASs analysed, significant and varying fractions of UOF were present in the samples, ranging from 32% UOF in bird eggs to 82% in reindeer. In a study on marine mammals from the northern Hemisphere, the EOF could in most of the samples be explained by the sum of target PFASs, and in particular the bioaccumulative long-chain PFAAs (Spaan et al., 2020). However, for samples taken at the US east coast, 30–75% of the EOF remained unidentified, which indicates sources of unidentified organofluorine. In another study (Schultes et al., 2020b), samples of killer whales from east Greenland showed that although most of the EOF in liver, blood, kidney, lungs and ovaries could be explained by targeted and known PFASs, almost none of the EOF in blubber, which displayed the highest concentration of EOF, was attributed to PFASs in the targeted analysis.

	Average F (ng/g) (range)	Average mass balance, target PFAS/EOF (range)
Marine mammals	707 (<40–2056)	37% (10–62%)
Reindeer	249 (<76–427)	18% (3–42%)
Brown bear	233	28%
Bird eggs	221 (<40–649)	68% (33–102%)
Marine fish	243 (<132–355)	42% (14–92%)
Fresh water fish	241 (<140–488)	26% (5–51%)
Sludge	663 (<556–767)	9% (3–21%)
Effluent	437 (<123–893)	11% (2–44%)
Surface water	239 (<30–849)	8% (2–17%)

Figure B.59. EOF (ng F/g) detected in different matrices and comparison between target PFASs and EOF, expressed as mass balance (% of known PFASs) (Kärrman et al., 2019).

In the different studies, PFASs detected via targeted analysis in biota are predominantly the long-chain PFASs (especially PFOS) and PFCAs, most likely due to their bioaccumulating properties. Conversely, ultrashort-chain PFAAs (C1–C3 PFAAs), that are often not included in the target analyses, may contribute significantly to the fluorine mass balance in abiotic and aqueous samples, due to their high water solubility and low adsorption. PFAAs detected in environmental samples may to a varying degree originate from degradation of known or unknown precursor compounds. These precursors are also likely to yield several intermediate products before degrading into their respective stable arrowhead PFAAs. Since only fractions of the original precursors degrade fully into PFAAs, the unknown intermediates are likely significant contributors to the fluorine mass balance and UOF. In the study by Kärrman et al. (2019), there was an indication of decreasing UOF from abiotic samples to biotic samples (Figure B.59), indicating possible metabolism of precursors to arrowhead PFAAs. In addition, by increasing the oxidation in a sample using the total

oxidizable precursor assay (TOPA), as discussed in section B.4.2.6.2, more arrowheads are being formed, decreasing the UOF.

In conclusion, studies on EOF/AOF combined with targeted PFAS analyses show that varying but significant fractions of organofluorine in environmental samples are unknown and not captured by conventional monitoring using only targeted PFAS analysis. There are indications that higher trophic levels have lower fractions of UOF, possibly due to metabolism of precursors into the stable PFAAs which are often included in the targeted analyses and among which many tend to biomagnify within food webs.

B.4.2.6.2. TOPA

The total oxidizable precursor assay (TOPA), which estimates the amount of unknown oxidizable PFCA precursors in a sample, has been applied to abiotic samples such as water, soil and suspended particular matter as well as to biotic samples. Overall, studies show that unknown PFASs constitute varying fractions of the total PFAS content in environmental samples, ranging from small to very large. A number of relevant studies are provided below.

Joeris et al. (2020a) analysed PFASs in river water from Germany and China. Samples were collected close to seven suspected point sources and analysed for 29 individual PFASs, with and without pre-treatment with TOPA. Upon oxidative conversion by TOPA, a marked increase in C4-C7 PFCAs was observed in the samples from Germany ($59 \pm 19\%$), with an $88 \pm 30\%$ increase of PFBA (C4 PFCA), demonstrating the presence of unknown precursor substances to unregulated PFASs. The increase in C4-C7 PFCAs was less marked in the samples from China ($15 \pm 10\%$).

In one study, 83 freshwater, marine and soil samples from the German environmental specimen bank were analyzed for 32 PFASs using target analysis, before and after TOPA treatment (Gockener et al., 2021). After TOPA, only C4-C14 PFCAs were analysed based on the assumption that all precursors are oxidized to PFCAs. The result showed that the concentrations of primarily C4-C10 PFCAs increased in most samples, by factors of up to 90, demonstrating that substantial fractions of precursor substances were present in the samples which would not have been detected without the use of TOPA. A follow-up study (Gockener et al., 2022) on 100 samples of suspended particular matter from the German environmental specimen bank, collected between 2005-2019, where 41 PFASs were analysed, showed that Σ PFASs were 1.3 – 145 times higher after direct oxidizable precursors assay (dTOP) as compared to the targeted analysis, demonstrating large amounts of unknown precursors in the samples.

Simonnet-Laprade et al. (2019) examined the trophic transfer of PFASs in the Orge River near Paris, France, with the aim to investigate the contribution of precursors to the biomagnification of PFAAs. 30 PFASs were analyzed in samples that were subject to treatment with TOPA in water (n=1), sediment (n=1) and biota (n=15), including biofilm, invertebrates, and fish. The result showed that substantial proportions of extractable unknown precursors were present in all samples (15–80% of the sum of PFASs) and that a systematic increase in the sum of PFCAs was observed (+15–424%) following TOPA. The largest relative increases were found at the base of the trophic web, in biofilm (424%), sediment (319%), leaf litter (298%), and macrophytes (196%) whereas lower relative increases were found in fish (15–22%), pointing to biotransformation of unknown pre-PFAAs in the trophic web to known PFAAs.

In a feeding experiment with laying hens and feed grown on a PFAS-contaminated site, 25 PFASs were analyzed in the feed and eggs with/without TOPA to assess the transfer of PFASs into eggs (Gockener et al., 2020a). The results showed that application of TOPA demonstrated the presence of significant fractions of precursor substances in the feed and in the eggs. In the feed, the levels of C4-C8 PFCAs increased after TOPA, ranging from 232% (PFPeA) to 786% (PFOA). Similarly, in the egg yolk PFOA increased by 647%,

whereas C5-C7 PFCAs increased by more than 1 000% from levels below LOQ. Altogether this demonstrated the presence of unknown precursor substances in the feed as well as in the eggs.

Janda et al. (2019) analysed the impact of TOPA treatment on concentrations of PFCAs including ultrashort C2-C3 substances. From a soil core of the PFAS-contaminated Upper Rhine Valley area in Germany, samples at different depths were analysed for C2-C14 PFCAs as well as C4-C8 and C10 PFASs, with and without TOPA treatment. After the TOPA, concentrations of C2-C14 PFCAs increased considerably in the upper soil layers (0-30 cm), with total molar PFAA-concentrations increasing by factors of 1.6 to 5.0. More than 40 cm below the surface, precursors of TFA, PFPrA and PFBA (i.e. C2-C4 PFCA) accounted for >50% of the measured PFASs, showing their importance in mass balances based on TOPA.

Chen et al. (2019a) analysed 39 precipitation samples from 28 cities in mainland China for 22 PFASs, including the ultrashort TFA and PFPrA (C2-C3 PFCAs), with and without TOPA treatment. The result showed that unknown precursors accounted for 6-56% of the total molar concentrations of PFASs, demonstrating an underestimation of PFAS mass load from precipitation if only monitoring data on known PFASs were analysed. TFA and PFPrA constituted large fractions (22-91%) of the Σ PFASs after TOPA treatment. Similarly, in leachates from municipal solid waste facilities in China, Wang et al. (2020b) showed from the use of TOPA that unknown C2-C12 PFAA-precursors constituted 0.35 – 68 molar% of the leachates and that unknown precursors to C2-C3 PFCAs represented major fractions.

In conclusion, studies of abiotic and biotic samples utilizing TOPA demonstrate that considerable fractions of PFASs in the samples may be comprised of unknown oxidizable PFASs that are not detected in routine target analyses, including precursors to C2-C3 PFCAs that are rarely analysed. Thus, environmental samples commonly contain PFASs with unknown identity and regulatory status and the total PFAS mass balances may be underestimated without treatment with TOPA.

B.4.2.6.3. Non-target and suspect screening of PFAS

Non-target and suspect screening are qualitative or semi-quantitative analytical methods that have been used to identify unknown PFASs. In suspect screening analysis (SSA), the accurate mass of molecular features obtained from HRMS are compared to databases with known PFASs (Koch et al., 2020), e.g. the Norman Network PFAS Suspect List, the OECD's New Comprehensive Global Database for PFASs⁷ and the USEPA CompTox Chemistry Dashboard. Further confirmation of the structure will then be compared with available mass spectra from literature and databases, such as the MassBank⁸. Non-target screening (NTS) applies different data filtration/data mining techniques to identify compounds without a priori knowledge about which substances that may be present in a sample. Non-target and suspect screening have been applied to environmental samples, including water, sediment, sludge, air, soil, airborne particulate matter and biota. For screening of human matrices, see section B.9.21. The paragraphs below summarise the results from a selection of relevant papers.

In a review by Liu et al. (2019d), on NTS studies published until October 2018, it was shown that NTS methods using chromatography coupled to high-resolution mass spectrometry (HRMS) had been used to (tentatively) identify more than 750 PFASs belonging to more than 130 classes with small (e.g. C₂F₄) to very large (e.g. C₄₄F₇₉) PFAS moieties in selected environmental samples, biofluids or commercial products. Different PFCAs, PFASs, fluorotelomers and per/polyfluoroalkyl sulfonamides together composed 82% of all discovered PFAS subclasses and 74% of all PFAS analytes. This estimate of total PFAS discoveries may still underestimate the total number of PFASs molecules observed

⁷ <http://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/>, date of access: 2022-09-29.

⁸ www.massbank.eu, date of access: 2022-09-29.

because of unresolved structural isomers and a possibility of the occurrence of coelution (i.e. inadequate chromatographic separation of similar substances).

In 2019, Ng et al. (2022) investigated a large number of PFASs by target and suspect screening in 95 samples of river water, wastewater, ground water, sediment and biota from the Danube River Basin (passing through 11 European countries). For the targeted PFAS screening, 56 commercially available reference standards were used. The suspect screening covered 4 777 PFASs retrieved from the NORMAN Substance Database⁹. In total, 82 PFASs were detected in the samples, of which 10 were detected by targeted screening and 72 via the suspect screening. This demonstrated that targeted PFAS analyses with reference standards only covered a small fraction of all PFASs in the studied environmental compartments of the Danube River Basin and indicates a potentially large-scale migration of PFASs in Europe.

Spaan et al. (2020) performed a fluorine mass balance on 25 liver tissues from 11 different species in the northern hemisphere, sampled between the years 2000 to 2017, using a combination of targeted PFAS analysis, EOF and total fluorine determination, and suspect screening. In 7/25 samples the EOF was significantly greater than the sum of the targeted analytes, with 30–75% of the EOF unidentified. Of the identified 63 PFASs, the suspect screening provided 37 PFASs that were not part of the targeted analysis, demonstrating the value of a multiplatform approach for determining PFAS mass balance in environmental samples.

Barrett et al. (2021) employed non-target and suspect screening to examine temporal trends of 22 legacy PFASs as well as unregulated PFASs in livers of 98 beluga whales in Canada collected from 2000 to 2017. In total, 54 PFASs were identified via integration of non-target (34 identified PFASs) and suspect screening (39 identified PFASs), demonstrating the advantage of using the two complementary screening methods. 21 of the 54 PFASs were confirmed via traditional targeted analyses using reference standards.

In conclusion, non-target and suspect screening have identified hundreds of different PFASs in various environmental samples. These substances would go undetected if only targeted analyses with available reference standards were performed. Consequently, the targeted analyses underestimate the number of PFASs as well as the total PFAS mass balance, however the suspect and non-target screening can only provide qualitative data of substances, and not quantitative, giving limited value to mass balance calculations.

B.4.2.7. Monitoring of specific PFASs in environmental samples

In this section monitoring data are summarised for specific PFAS groups, with focus on PFASs that are not covered by existing or proposed restrictions under REACH and/or the POPs Regulation ((EU) No 2019/1021). The data presented here is not a complete review of studies. Instead, key studies have been selected to exemplify environmental occurrence of PFASs, especially of those not routinely included in monitoring studies. Reported concentrations of PFASs in these studies are presented in Appendix B.4.2.1.3. Mobility in water, Appendix B.4.2.3. and Appendix B.4.2.7.

Environmental matrices discussed here include biota as well as abiotic matrices, such as water (ground-, raw-, surface- and drinking water rain, snow, ice), suspended particulate matter, air, soil and sediment as well as wastewater influent, effluent and sludge. Concentrations of PFASs in humans, food, indoor air and dust are discussed B.9.21 and B.9.22. The current section of targeted analyses does not cover monitoring of precursors. Instead, occurrence of precursors in the environment is discussed in section B.4.1.3.5 and B.4.2.6.2.

⁹ <https://www.norman-network.com/nds/susdat/>, date of access: 2022-09-29.

B.4.2.7.1. $\geq$ C4 PFCAs and $\geq$ C4 PFSA covered by existing or proposed restrictions

PFASs covered by existing or proposed restrictions under REACH and/or the POPs Regulation include PFOA, PFOS, PFHxS, PFHxA and C9-C14 PFCAs, as well as their salts and related compounds. These PFAAs (especially PFOS and PFOA) have been thoroughly monitored and thus there is a wealth of data on their occurrence in the environment. Monitoring data for these compounds are partly presented in sections B.4.2.1-B.4.2.4 to substantiate the environmental fate properties of PFASs.

In brief, PFOS and PFOA are generally the PFAAs detected at highest levels in soil, sediment and sludge (see B.4.2.3), whereas PFOS and C9-C14 PFCAs are dominating in biota (see B.4.2.9). The higher concentrations of the longer chain PFAAs in these matrices, in comparison to the shorter chain PFAAs, are partly due to differences in sorption and bioaccumulation, which is further discussed under B.4.2.1 and B.4.2.9.

PFOA, PFOS, PFHxS and PFHxA are among the most abundant PFASs in aquatic compartments and can generally be found in the majority of analysed ground-, surface- and tap water samples from various countries, which has been summarised by e.g. Sims et al. (2022). For further details, see B.4.2.1.3.

In summary, despite the phase-out of PFOS and PFOA they are still abundantly detected worldwide, including Europe and remote regions, which illustrates that once released environmental contamination with PFASs is poorly reversible. Furthermore, the presence of PFAA precursors (including slowly degradable side-chain fluorinated polymers) will remain a long-lasting source of PFAAs in the environment.

B.4.2.7.2. $\geq$ C4 PFCAs and $\geq$ C4 PFSA not covered by existing or proposed restrictions

C4-C7 PFCAs and PFSA that are not included in existing or proposed restrictions include PFBA, PFPeA, PFHpA, PFBS, PFPeS and PFHpS. These compounds are found in surface water from the global oceans, rivers, and lakes (Muir and Miaz, 2021; Sims et al., 2022), groundwater, tap water and raw water (Kaboré et al., 2018; Llorca et al., 2012a; Sims et al., 2022), soil and sediment (Brusseau et al., 2020; Janda et al., 2019), the atmosphere (Wong et al., 2021), and in snow and ice of remote regions (Kwok et al., 2013; MacInnis et al., 2017). Furthermore, these compounds are found in influent, effluent and sludge of WWTPs (Lenka et al., 2021) and in landfill leachates (Hamid et al., 2018). This is further exemplified below.

PFBA and PFBS are the dominating $\geq$ C4 PFAAs in European and Arctic surface waters (Muir and Miaz, 2021; Pan et al., 2018; Zhao et al., 2015). In general, the levels of these compounds are in the same order of magnitude as those of PFOA and PFOS (Sims et al., 2022). In a recent review of the occurrence of PFAAs in global surface and ground water, PFBA, PFPeA, PFHpA, PFBS and PFPeS were each detected in 35-79% of the samples (Sims et al., 2022). Furthermore, $\geq$ C9 PFCAs and PFSA were present in lower concentrations compared to the shorter-chain homologues in both surface waters and groundwater. In a monitoring study of surface water from the lake Mälaren (Sweden), Thames River (UK) and Rhine River (Germany) the combined concentration of C4-C7 PFCAs and PFBS represented approximately half of the total PFAS content (Pan et al., 2018). In another example from the North Sea, PFBS and PFBA accounted for approximately 50% of the sum of PFASs (Zhao et al., 2015). Similarly, PFBA, PFPeA, PFHxA, PFHpA and PFBS accounted for approximately 60% of the sum of PFASs in coastal waters of the German Bight and Baltic Sea (Joerss et al., 2019).

Poor correlation between PFBS/PFBA and other PFAAs in aquatic environments suggests that these compounds have other sources than longer chain PFAAs, which could reflect a different use pattern and/or environmental behaviour (Joerss et al., 2019; Zhao et al., 2015). For example, in a study investigating source-specific patterns of PFASs in river

samples up- and downstream potential industrial point-sources, PFBS represented 66-70% of the total PFAS in rivers downstream pharmaceutical and pesticide intermediate manufacturing sites, which is probably due to the use of PFBS in these industries (Joerss et al., 2020a).

A survey of drinking water from several countries showed that PFBA, PFPeA, PFHpA and PFBS were each detected in 68-92% of the tap water and in 32-58% of the bottled water samples. The sum of these compounds constituted approximately half of the total PFAS concentration in the drinking water (Kaboré et al., 2018). The ubiquity of these short chain PFAAs in drinking water support that they are highly mobile and well distributed in the freshwater environment, even far away from point sources and that they are poorly removed by current drinking water treatment technologies (see B.4.2.1).

In the atmosphere at locations far away from point-sources, PFBA has been shown to be the dominant $\geq C_4$ PFAA (Fredricsson et al., 2021; Wong et al., 2018). In contrast to other studied PFAAs, the levels of PFBA in these remote areas were comparable to reported levels in urban environments, which indicates that PFBA is uniformly distributed in the global atmosphere (Wong et al., 2018). This could be explained by PFBA being more susceptible to long-range transport or/and that PFBA is being formed from fluorinated gases, such as HFE-7100, in the atmosphere (see B.4.1.3.2 and B.4.2.8). In the air directly above landfills, incineration plants, transfer stations and WWTPs, reported levels of PFASs (dominated by FTOHs) are considerably higher (up to 30 times) compared to reference sites (Ahrens et al., 2011; Tian et al., 2018; Wang et al., 2020b). PFBA was generally the dominant $\geq C_4$ PFAA in the air above these sites, although the levels of PFOA or PFOS occasionally reached or even exceeded the PFBA concentration.

In biota, the concentrations of shorter chained PFAAs are often below the reporting limits or, when detected, considerably lower compared to longer chained PFAAs. This is probably a consequence of their shorter biological half-life and lower potential to partition into protein and lipids (see B.4.2.9). For example, PFBS has been found in livers from arctic polar bears and killer whales, however in concentrations five orders of magnitude lower than those of PFOS (Gebbink et al., 2016).

In soil, the shorter chain PFAAs are generally found at lower concentrations than longer chain PFAAs. However, whereas the longer PFAAs strongly dominate at the shallow depths, the shorter PFAAs become increasingly more abundant at the deeper depths. This is due to their higher mobility in soil compared to the longer PFAAs, which increases the risk for these substances to reach the water table over time (Brusseau et al., 2020). In the meantime, the soil is a significant reservoir for these and other PFASs.

PFASs in wastewater influents and effluents have been reviewed by Lenka et al. (2021). For PFCAs, the sorption is expected to increase with carbon chain length and PFCAs with less than 10 carbon are therefore expected to be present in treated wastewater, whereas longer chain PFCAs and PFOS are expected to sorb on sewage sludge (Arvaniti et al., 2014). In general, the majority of studies demonstrate poor removal of most PFASs, which is demonstrated by the concentrations of PFASs generally being higher in the effluents after wastewater treatment, which can result in considerable releases into the environment (Lenka et al., 2021) (see also B.4.5). In a study of Nordic WWTP effluent samples, C₄-C₇ PFAAs contributed with 43% to the Σ PFAS, whereas the longer chained PFCAs and PFOS together accounted for 26% (Aro et al., 2021b). C₄-C₆ PFAAs were also the dominant class in WWTP influents and effluents in the U.S., contributing with $55 \pm 19\%$ of the Σ PFAS (Tavasoli et al., 2021). In contrast, longer chained PFAAs are relatively more abundant than shorter chained PFAAs in WWTP sludge, even though shorter chained PFAAs are also detected in these matrices (Aro et al., 2021b; Tavasoli et al., 2021). In addition to WWTPs, landfills constitute another point-source of PFASs. A review of PFASs in landfill leachate from several continents concluded that C₄-C₇ PFAAs were more abundant than their longer-chain ($>C_8$) homologues in leachate (Hamid et al., 2018).

The text above regards what is often referred to as short-chain PFCAs and PFSAAs. However, there are also longer chained PFAAs that are not covered by existing or proposed restrictions and are sometimes included in target analysis of environmental samples. Examples of these are $\geq C_9$ PFSAAs, such as PFNS (C_9) and PFDS (C_{10}). In general, these compounds are of relatively low importance in aquatic samples.

In conclusion, $\geq C_4$ PFCAs and PFSAAs that are not subject to existing or proposed restrictions constitute a large part of the total PFAA levels in European aquatic environments, including drinking water. Furthermore, PFBA is the dominating $\geq C_4$ PFAA in the atmosphere. However, these compounds are found in lower levels in top-layers of soil, sludge and biota compared to the longer chain PFCAs and PFOS.

B.4.2.7.3. C1-C3 PFCAs and PFSAAs

C_2 - C_3 PFCAs (i.e. TFA, PFPrA) and C_1 - C_3 PFSAAs (i.e. TFMS, PFEtS and PFPrS), often referred to as ultrashort PFAAs, have not usually been included in monitoring studies, which could partly be explained by analytical limitations (Björnsdotter et al., 2020). Among these compounds, most monitoring and source information is available for TFA. Studies reporting detectable levels of TFA in deep ocean waters and in pre-industrial glacier ice and firn samples have indicated that there can be natural sources of TFA (Frank et al., 2002; Scott et al., 2005; von Sydow et al., 2000). However, whether non-anthropogenic sources of TFA exist is still debated (Joudan et al., 2021; Nielsen et al., 2001). In any case, natural sources will only apply for TFA in the oceans, while TFA in fresh water and in the terrestrial environment originates from anthropogenic sources. It is known that TFA is formed through atmospheric oxidation of some hydrofluorocarbons (HFCs), hydrochlorofluorocarbons (HCFCs) and hydrofluoroolefins (HFOs). TFA can also be formed during fluoropolymer thermolysis and through oxidation of precursor compounds, such as other PFASs as well as pharmaceuticals or pesticides containing a carbon-bound trifluoromethyl moiety (Cui et al., 2019; Freeling et al., 2020). Industries that manufacture TFA or use TFA in the production of e.g. plant protection agents are also potential point sources (Scheurer et al., 2017). Information about the sources of the other ultrashort PFAAs is limited, but PFPrA could potentially arise from impurities and byproducts in either TFA or PFBA-chemistry, whereas PFETs and PFPrS have been found in AFFFs and can be present as a residual formulation and/or by-product from products manufactured by electrochemical fluorination (Björnsdotter et al., 2020).

Two Swedish studies have investigated the presence of C_1 - C_3 PFAAs in waters close to potential point sources, such as airports, landfills and waste management facilities (Björnsdotter et al., 2019; Ericson Jogsten and Yeung, 2017). In the study by Björnsdotter, concentrations of ΣC_1 - C_3 ranged up to 84 000 ng/L and represented more than 30% of the Σ PFAS in 20 out of 32 analysed samples (Björnsdotter et al., 2019). The Ericson study, which only analysed PFETs and PFPrS, found that all samples contained at least one of these compounds and that PFPrS contributed with 0.4 to 17% to the Σ PFASs in these samples. In addition, leachate from seven municipal solid waste disposal facilities in Tianjin, China showed that TFA contributed with 52-68% to total PFAS concentration in leachate from incineration plants and transfer stations, whereas PFPrA was dominant (49-83% of Σ PFAS) in leachate from landfills (Wang et al., 2020a).

C_1 - C_3 PFAAs have also been found in aquatic matrices without known historic PFAS contamination. For example, in two Swedish drinking water samples without known contamination PFPrA, TFMS and PFPrS were detected in levels up to 28, 7.8 and 0.18 ng/L, respectively, which resulted in a combined contribution of 43% and 84% to the Σ PFAS (Björnsdotter et al., 2019). In a study of US bottled drinking water, PFPrA was detected in 22 out of 101 samples and accounted for 42% of the total PFAS content on a mass basis, whereas PFPrS contributed with less than 1% (Chow et al., 2021). In a multinational study of drinking water, PFPrS and/or PFETs were detected in samples from Burkina Faso, Ivory Coast and China but not from Norway, Chile, Canada and USA (Kaboré et al., 2018). The drinking water studies above did not include TFA in their analyses. However, in a recent

study of direct or indirect source water for drinking water production, TFA was found at a median concentration of 900 ng/L, representing more than 90% of the total PFAS content (Neuwald et al., 2022). In addition, TFMS, PFPrA, and PFPrS were detected in more than 80% of these samples. In another study of Danish ground water, TFA was detected in 89% of the 247 analysed samples. The TFA levels were mostly below 1 000 ng/L but concentrations up to 2 400 ng/L were detected (Miljøstyrelsen, 2020).

TFA mainly enters the terrestrial environment via precipitation, where it has been reported to be the most abundant known PFAS. For example, in a nation-wide German study including 1 187 wet deposition samples taken over a year (2018-2019), the precipitation-weighted average of TFA was 335 ng/L (Freeling et al., 2020). Higher levels were observed in the summer, which was suggested to result from higher concentrations of photochemically generated oxidants (e.g. hydroxyl radicals) in the troposphere, which enhances transformation of TFA precursors. In a study of precipitation from mainland China, TFA was found in concentrations of 9-1 800 ng/L, which was 1-2 orders of magnitude higher than those of any other individual PFAA. The sum of TFA and PFPrA accounted for 22-91% of the total PFASs in these samples (Chen et al., 2019a). Another Chinese study reported average TFA levels of 643±169 and 282±68 ng/L in Beijing urban landscape water and snow, respectively (Zhai et al., 2015).

C2-C3 PFAAs have also been detected in WWTP effluents. In a Nordic study, PFEtS, PFPrS and PFPrA were found in all WWTP effluent (dissolved + particle phase) samples and accounted for 6% of the total PFAS concentration in the samples from Finland, Sweden, Denmark, Norway, and Faroe Islands (Kärman et al., 2019). In Greenland and Norway they were the most abundant class of PFAAs with a mean contribution of 39%. In another study of fluorine mass balance analysis of Nordic WWTP effluent samples, C2-C3 PFAAs was the group with the largest contribution (on average 35%) to the identified extractable organofluorine (Aro et al., 2021b).

In 144 air samples collected during a year (2012-13) in Beijing, China, the annual mean concentration of TFA was 1 580±558 pg/m³ (Wu et al., 2014). In addition, TFA was the dominant PFAA in the air above Chinese landfills and constituted 80% of the ΣPFCA, whereas the levels of PFPrA were in the same range as PFBA (i.e. the most abundant ≥4C PFAA). TFA was also the most abundant PFAA in plant leaves and dry deposition the at these sites (Tian et al., 2018).

In a study of the Nordic environment, C2-C3 PFAAs were not detected in any of the biota samples including bird eggs, fish and terrestrial and marine mammals, which probably reflects their relatively low bioaccumulation potential (Kärman et al., 2019).

In conclusion, TFA has been detected at high levels in aquatic environments (including drinking water) and precipitation worldwide, whereas there is less information about other C1-C3 PFAAs. The few available studies reveal that C1-C3 PFAAs are being released into the environment and constitute a considerable fraction of the total content of known PFASs in aquatic matrices, including drinking water. The presence of these compounds in drinking water also reflects the difficulties to remove them with common water treatment methods (see B.4.5).

B.4.2.7.4. Cyclic PFAAs

Perfluoro-4-ethylcyclohexanesulfonate (PFECBS), which is a cyclic C8-PFSA, is the most monitored cyclic PFAA. It has been used as an erosion inhibitor in aircraft hydraulic fluids (De Silva et al., 2011) and could also be present as an impurity in POSF-based products, such as AFFFs (MacInnis et al., 2017).

PFECBS has been detected, together with other PFASs, in water, sediment and biota in the vicinity of airports in China, Canada and the Nordic countries, probably as a consequence of its use in aircraft hydraulic fluids (de Solla et al., 2012; Kärman et al., 2019; Lescord

et al., 2015; Wang et al., 2016a). Furthermore, PFECHS has been found in Chinese coastal water and sediment, for which the primary source was suggested to be erosion inhibitor factories (Liu et al., 2019d). PFECHS has also been found in Nordic WWTP effluent samples, which indicates that consumer products, other than aircraft hydraulic fluids, may be source of PFECHS (Kärman et al., 2019).

PFECHS has been detected in all surface water samples from the North American Great Lakes (De Silva et al., 2011) and in 86% of Baltic Sea coastal water samples, but in none of the water samples from the German Bight (Joerss et al., 2019). In the Baltic Sea, levels of PFECHS were in the same magnitude as those of PFOS which indicates that a direct source (e.g. hydraulic fluids) is more likely than PFECHS being an impurity in POSF-based products (Joerss et al., 2019). PFECHS has also been detected in tap water samples from 2 source locations from the Great Lakes but not in other analysed samples from other countries included in a study by Kaboré et al. (2018).

PFECHS, together with other PFASs, has also been detected on the Devon Ice Cap (1 800 m above sea level) (MacInnis et al., 2017). The presence of PFASs in the ice cap is suggested by the authors to be attributable to atmospheric deposition due to the high altitude, which source could be the direct emission due to leakage of the compound from aircraft during usage.

In biota, PFECHS has been detected in polar bears in the Canadian Arctic (Letcher et al., 2018) and in marine mammals from the Denmark and Greenland (Kärman et al., 2019), however in concentrations several orders of magnitude lower compared to PFOS. Furthermore, PFECHS has been detected in herring gull eggs and in top predator fish in the Great Lakes of Canada (De Silva et al., 2011; Letcher et al., 2015), but not in bird eggs in a study of the Nordic environment (Kärman et al., 2019).

The Dossier Submitters have found few monitoring studies on other cyclic PFAAs. Downstream of Beijing international airport, perfluoropropylcyclopentanesulfonate (PFPCPeS) was found in surface water, sediment and Crucian carp but at lower detection frequencies and levels than those of PFECHS (Wang et al., 2016a). None of these compounds were found in the aquatic reference samples. In another study of fish from the Great Lakes of Canada, perfluoromethylcyclohexane sulfonate (PFMeCHS), was detected in the dissolved phase but not above the detection limits in fish tissue (De Silva et al., 2011).

In conclusion, PFECHS has been detected in aquatic environments, especially in connection to aviation activities. PFECHS has also been found in low levels in biota and ice of remote areas. Monitoring of other cyclic PFAAs is scarce.

B.4.2.7.5. Perfluoroalkyl phosphonic acids (PFPAs)

Perfluoroalkyl phosphonic acids (PFPAs) have been included only in a limited number of studies, where they generally have been detected at lower levels and detection frequencies than frequently analysed PFCAs and PFSAAs (Xiao, 2017). For example, PFPAs have been detected in surface water in the Netherlands (Esparza et al., 2011) and Canada (D'eon et al., 2009), in Spanish and German tap water and in German WWTP effluent water (Llorca et al., 2012a). The lower concentrations and detection frequencies could be explained by a lower global historical use and releases of these substances compared to PFCAs and PFSAAs (Wang et al., 2016b).

B.4.2.7.6. Perfluoroalkyl ethers (PFAEs)

The most studied PFAEs to date are HFPO-DA, ADONA and Cl-PFESAs. Other PFAEs have rarely been measured with targeted (semi-)quantitative analyses in environmental samples. Further insight on the occurrence of additional PFAEs can be gained by applying non-target or suspect screening methods which are further discussed in B.4.2.6.3.

HFPO-DA has been found in surface waterbodies, including the marine environment in Europe (Heydebreck et al., 2015; Pan et al., 2018), in the US (Sun et al., 2016) and China (Pan et al., 2017). For example, HFPO-DA was detected in all surface water samples from the lake Mälaren (Sweden), Rhine River (Germany) and Thames River (UK), which showed occurrence in European waters not limited to fluorochemical industry zones (Pan et al., 2018). Furthermore, the HFPO trimer acid (HFPO-TrA) was detected in 73% of these samples but in levels generally lower than those of HFPO-DA. In contrast, in the highly contaminated Xiaoqing River Estuary, China, HFPO-TrA was found at higher detection frequencies and concentrations in surface water, invertebrates and fish compared to HFPO-DA (Li et al., 2021e). In a study by Joerss et al. (2019), the levels of HFPO-DA in the German Bight coastal water were three times higher than those of PFOA and contributed with 27% to the Σ PFAS. On the contrary, the same study reported negligible levels of HFPO-DA in the Baltic Sea, probably reflecting the lower water exchange and fewer point-sources. HFPO-DA has also been detected in Arctic seawater (albeit in considerably lower levels than in European coastal waters) and snow (Joerss et al., 2020b; Xie et al., 2020b).

The occurrence of HFPO-DA has also been studied in the vicinity of fluorochemical production plants in Europe. For example, HFPO-DA was detected in all samples downstream from a fluorochemical production plant in Dordrecht, the Netherlands, with the highest level (812 ng/L) being 13 times higher than the sum of PFAAs. In contrast, the levels were below the reporting limit at the control sites and in two out of three samples taken upstream from the plant. HFPO-DA was also found in tap water within 50 km from the fluoropolymer manufacturing plant (Brandsma et al., 2019; Gebbink et al., 2017). In the same area, HFPO-DA was detected in all grass and leave samples collected within 3 km from the plant (Brandsma et al., 2019), but not in a reference area 85 km away. This indicates that locally grown foods may contain HFPO-DA, which was confirmed by Mengelers et al. (2018) who showed that HFPO-DA could be detected in 40% of 74 vegetable samples within 4 km from the plant. Both in leaves/grass and river water, there was a declining concentration gradient in relation to the distance from the plant, which further strengthens that the manufacturing plant was the source of HFPO-DA to the adjacent environment.

Another example of the impact of point-sources on environmental HFPO-DA levels was investigated by Joerss et al. (2020a), who found detectable levels in all 29 German river samples up- and downstream potential point-sources. Levels were particularly high downstream from a German fluoropolymer manufacturing site, where HFPO-DA constituted approximately 50% of the total PFASs in the samples.

In a study by Pan et al. (2018), ADONA was found only in the German Rhine River but not in other surface waterbodies in Europe, US and China. Furthermore, in another study by Joerss et al. (2020a) ADONA was detected in 73% of the analysed German river samples up- and downstream potential point-sources. The levels were markedly high (up to 2 500 ng/L) downstream from a German fluoropolymer manufacturing site where ADONA constituted approximately 40% of the total PFASs. In a study of the Nordic environment, ADONA was not detected in either water or biological samples (egg birds, fish and marine and terrestrial mammals) in areas without known contamination (Kärman et al., 2019).

China is the only known emission source of 6:2 Cl-PFESA, where it is ubiquitously present in the environment (Pan et al., 2018). In European surface waters, 6:2 Cl-PFESA has either been below the reporting limit (Gebbink et al., 2017; Joerss et al., 2020a) or detected at low levels (Pan et al., 2018). 6:2 Cl-PFESA has also been detected in Greenland marine mammals (Gebbink et al., 2016). These data strongly suggest that 6:2 Cl-PFESA can undergo long-range transport to the Arctic and has the potential for global distribution and to a certain degree to bioaccumulate.

Several PFECAs have been detected in the Cape Fear River in the US downstream from a fluorochemical manufacturer plant (Strynar et al., 2015; Sun et al., 2016) where a sulfonated tetrafluoroethylene based fluoropolymer-copolymer was produced. Due to the

lack of authentic standards, the concentration of these PFECAs could not be quantified. Based on the comparison of chromatographic peak areas Sun et al. (2016) determined that the dominant PFECA was perfluoro-2-methoxyacetic acid (PFMOAA), with a peak area ~100 times that of HFPO-DA, followed by perfluoro-3,5-dioxahexanoic acid (PFO2HxA; peak area ~25 times that of HFPO-DA) and perfluoro-3,5,7-trioxaoctanoic acid (PFO3OA; peak area ~5 times that of HFPO-DA). Hopkins et al. (2018) estimated the added concentration of PFAEs in the Cape Fear River to be 40 000 ng/L with contributions from PFMOAA >> PFO2HxA > PFO3OA ~ HFPO-DA > Nafion byproduct 2 > PFO4DA. When the manufacturer began to capture the process wastewater, the sum concentration of targeted PFAEs in the river dropped sharply to an estimated concentration of approximately 4 200 ng/L. Furthermore, analysis of water samples taken at the water treatment plant located 80 km downstream from the industry showed similar levels of PFAEs in the ingoing raw water and the treated drinking water, which demonstrates the difficulties to remove these compounds from drinking water. Studies of increased blood levels of these PFAEs in the population consuming the contaminated drinking water are further discussed in B.9.21.2.

Song et al. (2018c) identified the presence of several PFAEs in the Xiaoqing River, which receives water discharge from one of the major fluoropolymer manufacturing facilities in China. They identified a total of 42 PFASs, including 3 HFPO oligomers (dimer acid, DA; trimer acid, TA and tetramer acid, TeA) and numerous tentatively detected isomers of C9–C14 PFECAs. The water concentrations of HFPO-TrA and HFPO-DA were approximately 1 and 2 orders of magnitude lower than the concentrations of PFOA. Besides the HFPO oligomers, monoether PFECAs and polyether PFECAs were the most abundant emerging PFASs, whereas the levels of polyhydrogen-substituted PFCAs, monohydrogen-substituted PFCAs and monochlorine-substituted perfluoroalkyl carboxylic acids were significantly lower.

In conclusion, studies clearly demonstrate significant releases of well-known as well as less studied PFAEs from fluorochemical industries resulting in high levels of these compounds in the adjacent environments, including drinking water. Furthermore, there is evidence of PFAEs also being found in water environments without known point-sources.

B.4.2.7.7. Fluorinated Gases

Atmospheric levels of fluorinated gases are routinely monitored for example in the Advanced Global Atmospheric Gases Experiment (AGAGE, 2022). Time trends from these monitoring programs are presented B.4.2.7.9.

B.4.2.7.8. Polymeric PFASs

Polymeric PFASs (including fluoropolymers, perfluoropolyethers and side-chain fluorinated polymers (SCFP)) can generally not be quantified by standard analytical methods used for low-molecular weight non-polymeric PFASs as reference standards are not available and the methods are unsuitable (see E.4.). However, there are methods that can be used to determine the type of polymer, the molecular weight and the layer thickness of the polymer (NCM, 2022). Furthermore, some total fluorine methods can include fluorine originating from polymeric PFASs (although polymeric PFASs will be lost if extraction methods are applied, in e.g. EOF analysis). Furthermore, TOPA can to a certain degree be applied to side-chain fluorinated polymers to cleave off and release PFAAs, which can subsequently be measured by conventional analytical methods (NCM, 2022).

Using mass spectrometry, two side-chain fluorinated polymers have been quantitatively analysed. The active components of the common fabric protector Scotchguard™, one perfluorooctane sulfonamide-based urethan side-chain polymer used until 2002 and perfluorobutane sulfonate-based urethan side-chain polymer used after 2002, have been detected in several matrices including aquatic sediment and agricultural soil (Chu and Letcher, 2017) as well as biosolids from WWTPs in the US (Letcher et al., 2020) and in

WWTP sludge and landfill leachates in Sweden (Fredriksson F et al., 2020). At all sites, the levels of these side-chain fluorinated polymers greatly exceeded the sum of all other individual non-polymeric PFASs (22-83 analysed by targeted analysis in the different studies). side-chain fluorinated polymers in the environment is the detection of the fluorinated siloxanes D₃F and D₄F (which are degradation products of and impurities in silicone side-chain fluorinated polymers) close to a fluorinated methylsiloxane manufacturing plant in China. The concentrations of D₃F and D₄F in surface water near the plant ranged between 3.3-291 ng/L and 7.0-168 ng/L, respectively, and in sediment between 12-5 478 ng/g and 17-6 277 ng/g, respectively (Zhi et al., 2018). D₃F and D₄F have also been detected in sediment, sewage sludge and WWTP effluent in Europe (McLachlan et al., 2014; van Bavel B. et al., 2016).

According to a review of Lohmann et al. (2020), incomplete polymerization during the synthesis of fluoropolymers may result in residual monomers, oligomers and smaller “polymers” with up to about 100 monomer units, which may be released to air upon heating during manufacturing and processing and to water through wastewater streams. In one example, a series of polyfluorinated carboxylic acids differing by one 1,1-difluoroethene (CF₂CH₂) unit, which were likely used as building blocks for production of PVDF, were found close to a manufacturing facility in the US (Lohmann et al., 2020). In another example, PFAS oligomers were detected in stack emission samples at a fluorochemical production site.

Fluoropolymer microparticles have been found in the environment and biota, even in remote areas, which is further discussed in B.7.5.

In addition to the release of polymers to the environment, several examples of the release of other PFASs (such as HFPO-DA and PFOA) from fluoropolymer production facilities are given in the sections above.

B.4.2.7.9. Environmental time trends

Temporal trend analysis of PFASs in the environment is challenging due to the statistical power of individual studies often being too low to identify significant trends. Furthermore, comparison of different studies is hampered by the use of different study designs including geographical regions, time intervals, sampled matrices and analytical as well as statistical methods. For example, recent changes in the environment may be masked in longer time series (sometimes several decades), unless the time trends before and after identified change-points (i.e. a timepoint when the trend changes direction) are assessed separately.

It is important to mention that phased-out PFASs that may show declining trends in Europe are not disappearing on a global scale due to their potential for long-range transport and persistency in various compartments, which is further discussed in B.4.2.8.

Time trends for PFASs covered by existing or proposed restrictions

Global environmental trends for PFASs have been reviewed by Land et al. (2018). Overall, they concluded that while there are clear declining trends for PFOS and PFOA in humans (see B.9.22.5), the trends in biota are mixed and often not significant (which can be influenced by biota being more heterogenous). For example, monitoring of biota from North America, Europe and the Arctic revealed no clear trend for PFASs (i.e. PFOS, its precursor FOSA and PFHxS) or PFOA, whereas longer chained PFCAs (PFNA, PFDA, PFUnDA, PFDoDA, PFTTrDA and PFTeDA) showed increasing or insignificant temporal trends. Another review of time series of Arctic biota, which included the 1980s/1990s, generally found increasing PFOS/PFSA trends but these seem to be levelling off from the mid-2000s, which becomes apparent when trend analysis only considers more recent years (Muir et al., 2019). Similar results were obtained for PFCAs, but the decline of certain PFCAs in biota seems to be delayed and weaker compared to the trends for PFOS. In individual studies, increasing PFOS (and PFCA) concentrations have been reported for biota living in contaminated

regions with slow water exchange, such as the Baltic Sea (Faxneld et al., 2016; Huber et al., 2012; Roos et al., 2013; Schultes et al., 2020b; Sun et al., 2019). In summary, the results indicate that the phase-out of PFOA and PFOS did not result in clear declining trends in biota on a global scale yet, which is likely attributable to their high persistence.

Regarding time trends of PFASs in abiotic matrices, the review by Land et al. (2018) found declining trends for PFOS and PFOA in surface waters, whereas most studies on sediment cores reported increasing concentrations. The authors concluded that the PFOS and PFOA restrictions resulted in decreasing concentrations especially in surface waters with high water exchange, whereas remote areas might have a delayed response to regulatory measures.

A recent review by Muir and Miaz (2021) compiled data on global temporal trends of PFASs in ocean and coastal waters. Significantly declining trends were observed for Σ C7-C12 PFCAs in recent years in the North Sea and Baltic Sea (2015-2017) and in the North American Great Lakes (2004-2017). For the Mediterranean Sea, PFOA and PFOS showed significantly declining trends in 2012-2018. Furthermore, mass discharge estimates indicated continued emissions of C7-C12 PFCAs to the Chinese Coasts in recent years, whereas the European riverine discharges have been reduced.

In Germany, levels of commonly targeted PFASs in suspended particulate matter (SPM) from the main river systems showed declining trends between 2005-2019, whereas the decline was less pronounced after applying the direct total oxidizable precursors (dTOP) assay. This indicates that declining trends of legacy PFASs may be overestimated when precursors are not taken into account (Gockener et al., 2022).

Analyses of European wastewater sludge have shown decreasing levels of PFOA and PFOS over time (Alder and van der Voet, 2015; Ulrich et al., 2016). For example, in a study of 4 981 sludge samples collected between 2008-2013 from 1 165 German WWTPs, the estimated load of PFAA in the sewage sludge decreased by 90% over the study period (Ulrich et al., 2016).

In conclusion, in contrast to clear decreasing trends of PFOA and PFOS in humans, the trends of these compounds in biota are conflicting. In addition, there is indication of potentially increasing levels of longer chain PFCAs in biota from contaminated regions with slow water exchange. Regarding time trends in aquatic environments, the levels of PFOS and PFOA seem to be decreasing in European and North American coastal, sea and river waters.

Time trends for PFASs not covered by existing or proposed restrictions

While there are numerous time trend studies for the most studied PFAAs, such as PFOA and PFOS, there is very limited time trend information available for the majority of PFASs, including precursors, PFAEs, PFPAs and shorter chain PFCAs and PFSAs.

In the review of temporal trends by Land et al. (2018), no firm conclusions could be drawn for non-restricted PFAAs in biota as these compounds are rarely analysed in biota and often are close to or below the detection limits. For PFBA (C4 PFCA) and PFHpA (C7 PFCA), there were mostly insignificant trends. For PFDS (C10 PFSA), there was a tendency towards increasing trends in mammals, decreasing trends in fish and mixed trends for birds.

Some studies have indicated a shift from longer chain to shorter chain PFAAs over time. For example, a recent study of temporal trends in Canadian beluga whale livers showed that unregulated C4-C7 PFASs, H-PFCAs, and odd-chain FTCAs increased between 2000 and 2017, whereas longer chain PFASs significantly decreased over time (Barrett et al., 2021). In another example, time trends of PFAAs in suspended particulate matter (SPM)

from German main river systems were examined with direct TOP analysis (dTOP)¹⁰, which accounts for precursors (Gockener et al., 2022). There were no significant trends for C4-C7 PFCAs between 2005-2019 but declining trends for C8-C18 PFCAs and PFSAAs (Figure B.60). In a study by Pickard et al. (2020) PFBA increased in ice cores from the Canadian Arctic between approximately 1990 and 2015 (Figure B.60). In concordance, Kirchgeorg et al. (2013) reported that PFBA was the most abundant $\geq$ C4 PFAA in a firn core sample from the European Alps and that the levels significantly increased between the years 1997 and 2007. At the same time, decreasing trends were seen for PFOA and PFHpA.

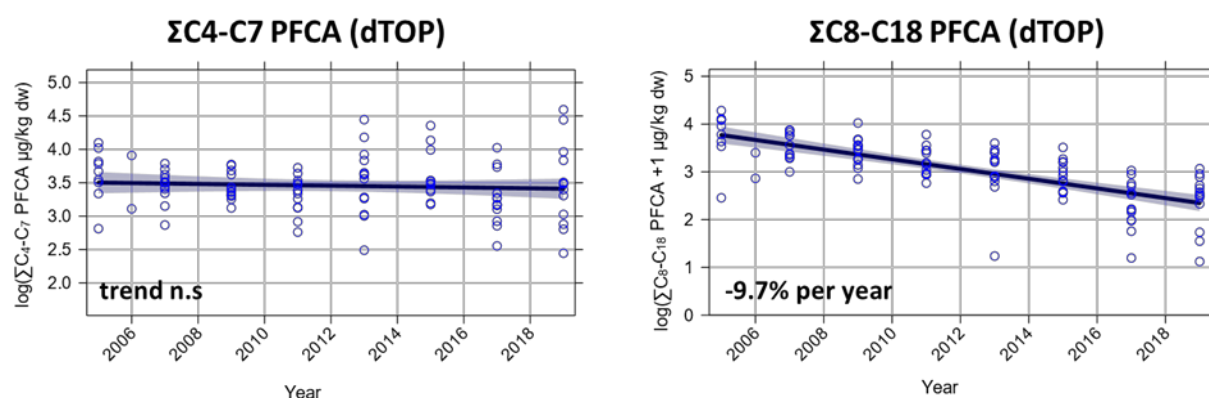


Figure B.60. Time trends (percent per year) in suspended particulate matter (2005-2019) sampled in the main German rivers and important tributaries (Danube, Elbe, Mulde, Rhine, Saale, Saar) presented by Gockener et al. (2022). Samples were analysed by direct Total Oxidizable Precursor (dTOP) Assay. Trend analysis took variations in river system and total organic carbon content into account. n.s. = non-significant trend.

In the arctic atmosphere, the concentration of PFBA was reported to be 1 to 2 orders of magnitude higher than that of other individual PFAAs and an increasing trend of PFBA with a doubling time of 2.5 y was reported at the Alert station in Canada between 2006 and 2014 (Wong et al., 2018). Increasing concentrations were also reported for PFOA, PFOS, and FTOHs at the Alert station with doubling times of 3.7, 2.9 and 5-7 years, respectively. In contrast, decreasing or non-changing levels of PFOA and PFOS, with half-times of 1.9-7.5 and 11-67 years, respectively, were reported from two stations in Northern Norway (PFBA was not monitored at these sites) (Wong et al., 2018).

There are few time trend studies of C1-C3 PFAAs. Pickard et al. (2020) studied atmospheric deposition of TFA and PFPrA using two Arctic ice cores. They concluded that the deposition fluxes for these compounds have increased since approximately 1990. The mean fluxes of TFA were almost one order of magnitude higher in the post-2000 samples, compared to the pre-2000 samples (Figure B.61). The authors concluded that the trend is in consistency with the production rate of fluorinated gases (HCFCs and HFCs) that degrade to TFA, which suggests that these are the major sources to TFA in arctic ice cores.

¹⁰ The dTOP assay is a modification of the TOP assay in which the sample is directly and fully oxidized in a more concentrated oxidation solution compared to the original method where extracts are oxidized.

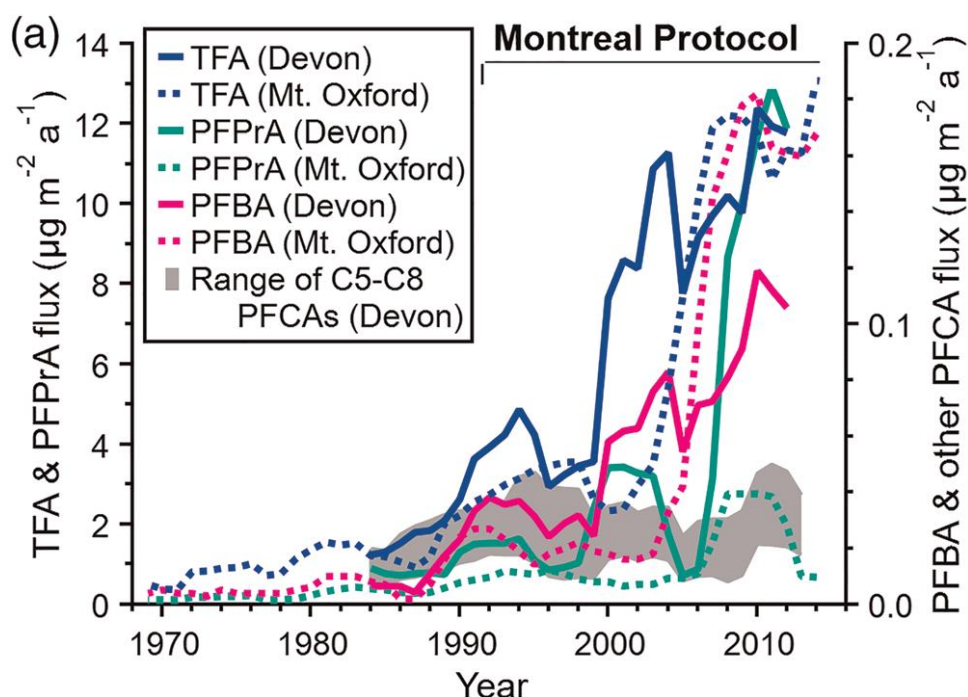


Figure B.61. Five-year moving average deposition fluxes of TFA, PFPrA, and PFBA from Devon Ice Cap (solid lines) and Mt. Oxford icefield (dashed lines) ice cores (taken from Pickard et al. (2020)).

In studies of TFA in German precipitation, the precipitation-weighted average concentrations in 2018-2019 (Freeling et al., 2020) were 3 to 4 times higher compared to 1995-1996 (Klein, 1997). These results indicate a substantial increase of wet-deposited TFA during the past two decades in the German environment. An even stronger increase was observed for urban landscape waters in Beijing, China, where TFA concentration showed up to 17-fold increase between 2002-2012 (Zhai et al., 2015). An increase in TFA concentrations has not only been observed in abiotic matrices but also in leaves of European beech in Germany between 1989-2020 (Figure B.62) and in leaves of black poplar (UBA, 2021b). A positive trend was also indicated in coniferous shoots from the European spruce and in shoots from pines (Freeling et al., 2022). Based on these results, the authors concluded that TFA concentrations continue to increase in Germany, which may result in an increased exposure to the wider environment including other biota.

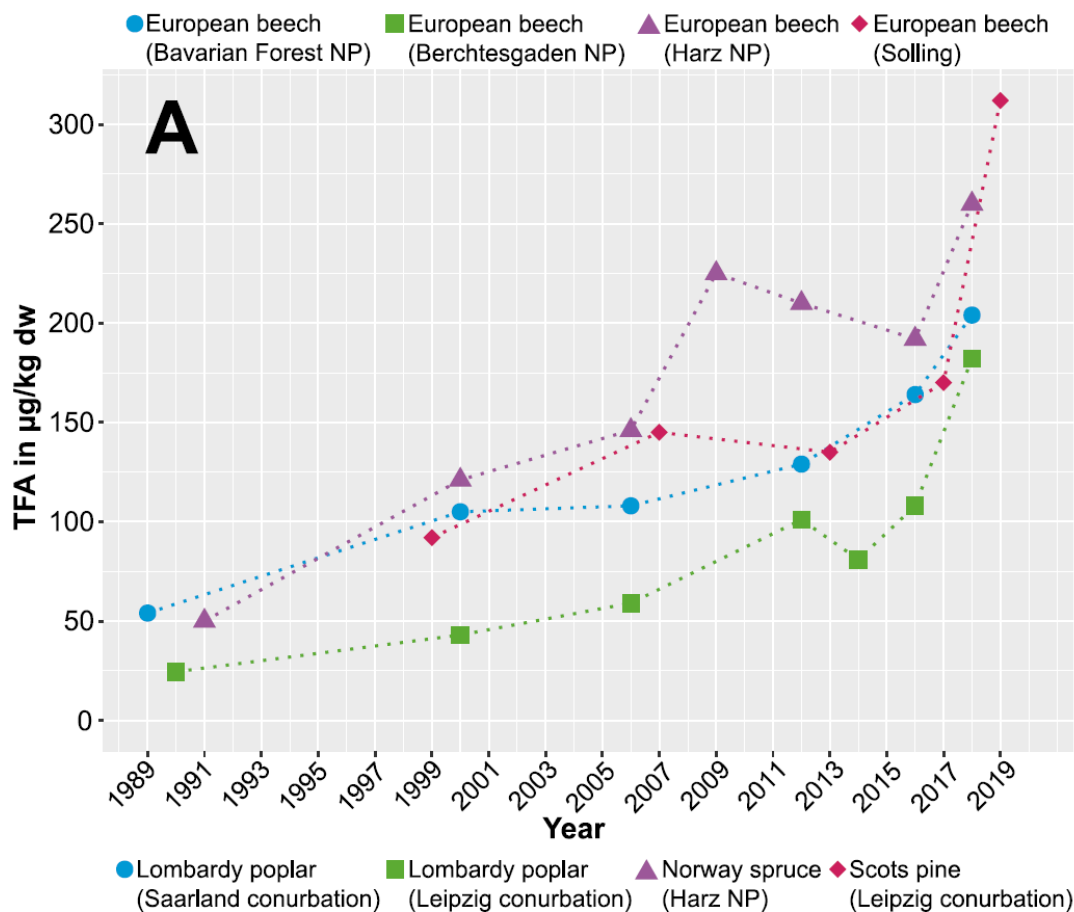


Figure B.62. Time trends of trifluoroacetic acid (TFA) in leaves ($\mu\text{g/g}$ dry weight) of the European beech from four locations in Germany (taken from Freeling et al. (2022)).

The Zeppelin station in Svalbard represents a background site for global climate gas monitoring and is used to study the transport of polluted air episodes. At this location, increasing trends for the majority of the 13 investigated fluorinated gases in air were reported (NILU, 2021). The results demonstrate that four gases, namely HFC-125, HFC-134a, HFC-152a, and HCFC-141b, showed increasing trends from 2001-2020 ranging between 0.4–5.19 ppt/y (see Figure B.63 for HFC-134a). The other nine gases were analysed between 2010-2020 and eight of these (HFC-32, HFC-43-10mee, HFC-143a, HFC-227ea, HFC-236fa, HFC-245fa, HFC365mfc, and HFC-23) showed increasing trends between 0.01-2.31 ppt/y. The only fluorinated gas showing a declining trend was HCFC-124 with -0.056 ppt/y between 2010-2020 (NILU, 2021). Similar results were reported globally under the Advanced Global Atmospheric Gases Experiment (AGAGE), which includes monitoring data from coastal or mountain sites in Norway (the Zeppelin station mentioned above), Italy, Ireland, Switzerland, American Samoa, Barbados, the US, and Australia (AGAGE, 2022). Taken together, the results available for fluorinated gases show overall increasing concentrations in air.

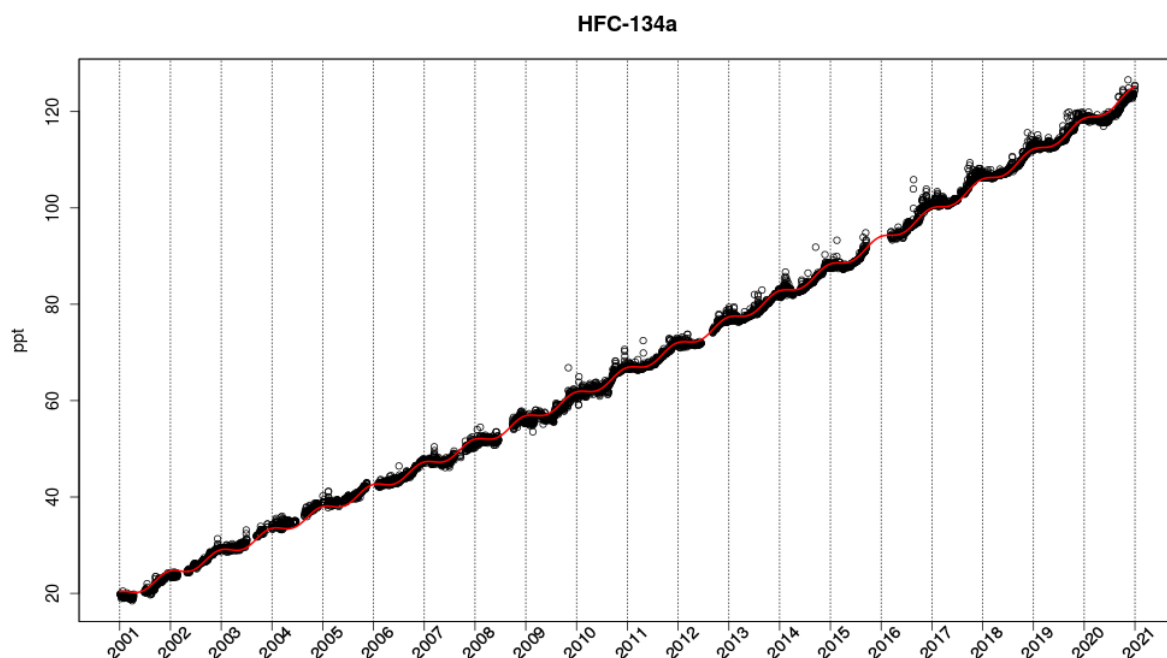


Figure B.63. Time trend of HFC-134a (+5.19 ppt per year) in air sampled at the Zeppelin station in Svalbard between 2001-2020 in ppt (NILU, 2021).

In conclusion, time trend studies clearly demonstrate steadily increasing levels of fluorinated gases increasingly used after the implementation of the Montreal Protocol in 1989. Concurrently, a clear increase of TFA in air, precipitation, ice cores and plants has been observed, which is likely a result of the growing abundance of TFA-yielding gases. In addition, analyses of ice/firn cores show increasing levels of PFBA and PFPrA over time. Regarding non-restricted PFAAs in biota, no firm conclusions can be drawn due to few existing time trend studies combined with low concentrations and detections frequencies. However, limited environmental evidence from individual studies of different environmental matrices suggests a shift from longer chain to shorter chain PFAAs in the environment. However, more evidence is needed to draw clear conclusions.

B.4.2.7.10. Conclusions for environmental monitoring

Studies on EOF/AOF and mass balance analysis show that varying but significant fractions of organofluorine in environmental samples are unknown and are therefore not captured by monitoring using only targeted PFAS analysis. There are indications that higher trophic levels display a lower fraction of unknown organofluorine, possibly due to metabolism of precursors into the stable PFAAs which are often included in the targeted analyses. Studies of abiotic and biotic samples utilizing TOPA demonstrate that considerable fractions of PFASs in the samples may be comprised of unknown oxidizable PFASs that are not detected in routine target analyses, including precursors to C1-C3 PFCAs that are rarely analyzed. Thus, environmental samples commonly contain PFASs with unknown identity and regulatory status and the total PFAS mass balances may be underestimated without treatment with TOPA.

Non-target and suspect screening methods have been applied with the aim to identify the compounds constituting the unknown organofluorine fraction. These screening methods have (tentatively) identified hundreds of different PFASs in various environmental samples. These substances would go undetected if only targeted analyses with available reference standards were performed. However, the suspect and non-target screening can only

provide qualitative and semi-quantitative data of substances, and not quantitative, giving limited value to mass balance calculations.

Although the information above clearly demonstrates that targeted analyses of individual PFASs do not provide the full picture of PFASs contamination, the vast majority of studies have applied such methods. While most of these studies have analysed a limited number of compounds, limited data are available on the occurrence and/or concentration of other PFASs, such as PFAEs and C1-C3 PFAAs.

PFASs are ubiquitously found in European environments and biota. Furthermore, numerous examples of drinking water highly contaminated from different types of point-sources have been reported and many more cases are likely to go undetected. The sum of shorter chain PFAAs have been shown to often account for a major part of the total known PFAS content in water samples, including drinking water. In the light of the high persistence of these non-restricted compounds, their high mobility, low adsorption to organic carbon and the difficulty to remove them from water (section B.4.2.2), the concentrations of these compounds will increase if emissions of these compounds and/or their precursors to the environment continue.

Targeted monitoring studies of PFASs in environmental matrices show that PFOS and PFOA, which are restricted, still are the dominating PFASs in soil, sediment, sludge and biota, and among the most abundant PFAAs in aquatic environments. Thus, despite the phase-out of PFOS and PFOA, they are still detected in high levels worldwide, which illustrates that contamination of PFASs is poorly reversible and underpins the need to ban also other PFASs to avoid similar problems in the future. Furthermore, the presence of precursors, such as side-chain fluorinated polymers, will remain a long-lasting source of PFAAs in the environment even after a phase-out of production.

The bans of PFOS and PFOA have resulted in a transition to other PFASs, such as shorter chain PFAAs and PFAEs. For example, HFPO-DA is widely detected in the European environment, whereas 6:2 Cl-PFESA is found in high levels in China, but currently not in Europe. Besides these most studied PFAEs, studies have clearly showed the presence of other, sometimes even more abundant PFAEs in the vicinity of fluorochemical industries. However, little is known about the environmental levels of these and other PFAEs. Furthermore, very little is known about the levels of polymeric PFASs in the environment.

Whereas time trends of PFOA and PFOS are decreasing in humans, the trends in biota are inconsistent. Regarding time trends in aquatic environments, the levels of PFOS and PFOA seem to be decreasing in European and North American coastal, sea and river waters. However, it has to be noted that phased-out PFASs that may show declining trends locally are not disappearing on a global scale due to their potential for long-range transport and persistence in various compartments. For most PFASs, including PFAEs and shorter chain PFAAs, there is limited or no temporal trend data. The clearest ongoing time trend is observed for the fluorinated gases that have been increasingly used after the implementation of the Montreal Protocol. A simultaneous increase of TFA in air, precipitation and plants is likely a result of the increase of TFA-yielding gases. In addition, analyses of ice/firn cores show increasing atmospheric deposition of TFA, PFPrA and PFBA over time.

B.4.2.8. Long-range transport potential

The potential for environmental long-range transport (LRTP) is one major concern for persistent pollutants. By long range transport a shift of potential risks occurs off of the point of emission and often time-delayed.

According to the OECD definition, long-range transport (LRT) refers to the transport of substances within the moving mass to locations distant from its sources (mainly for a distance greater than 100 kilometres). LRTP is indicated, if these substances are measured

in distant locations in concentrations that are of “potential concern”. The moving mass could be air, water or particles, as discussed below.

B.4.2.8.1. Transport pathways

As outlined below contamination is not geographically limited, so PFASs are found ubiquitously in the environment. Because of non-degradability, the movement of their carriers leads to global drift of PFASs over long distances from the point of release. Depending on their specific physiochemical properties PFASs distribute between the respective compartments. Three main hypotheses are currently proposed for the global transport of PFASs.

- Non-charged, volatile precursor compounds could undergo long-range atmospheric transport and be degraded to persistent arrowhead PFASs being deposited via wet or dry atmospheric deposition in atmosphere and reaching remote areas (Ellis et al., 2004; Martin et al., 2006; Schenker et al., 2008; Wong et al., 2018).
- ionic and water soluble PFASs could be transported directly by river waters into estuaries and coastal waters.
- additionally, PFASs can be transported by particles to which they are adsorbed or absorbed, such as dust, sediments, or through matrices in which they are included as additive, e.g. in polymers. Moreover, a long-range transport of PFASs may occur by biota e.g. migratory birds.

Further, due to complex interactions between a substance and the compartments and a broad variety of environmental conditions the transport into remote areas is not limited to a single pathway. PFASs distribute to different compartments depending on their physicochemical properties, as well as the environmental conditions (e.g. temperature or pH). By changing environmental conditions, a substance-shift between the compartments may occur.

Most existing studies focus on legacy PFASs but emerging and novel per- and polyfluoroalkyl substances currently come into research focus (e.g. Gomis et al. (2015)). This will narrow the gap of knowledge regarding other PFASs.

Air and water

Generally, charged short-chain PFASs have a higher LRTP in aquatic environments (Muir et al., 2019). The physicochemical characteristics also influence the type of long-range transport in the aqueous environment, e.g. sea spray, microlayer, surface water, deep ocean water (Ahrens et al., 2010a; Ahrens et al., 2010c).

Early modelling studies indicated that PFAAs are more likely to be transported via oceanic currents than by the atmosphere (Armitage et al., 2006; Wania, 2007) but a recent study by Yeung et al. (2017) suggested that atmospheric input accounts for the majority of measured PFOA in the Arctic Ocean. Global transport by marine ocean currents was indicated as the major pathway of PFASs delivery to non-emission regions by both monitoring and modelling results (Stemmler and Lammel, 2010; Yeung et al., 2017) though the single processes are not yet fully understood.

PFASs are globally distributed in the marine environment (Yamashita et al., 2011). The movement of PFASs, from coastal areas that are influenced by urban emissions, to sub-Arctic and Arctic Ocean waters, was illustrated by Ahrens et al. (2010c), who found C₆–C₁₀ PFCAs averaging about 700 pg/L in coastal seawater of southern Norway and at detection limits (~10 pg/L) in the open Norwegian Sea. As well industrial coastal areas as river based large industrial metropolitan areas and atmospheric deposition are considered as main sources of PFASs in sea water. Ocean currents and related dilution effects have a crucial

influence on global PFAS distribution in marine ecosystems (Ahrens et al., 2010a). Above that, ocean waters are important sinks for PFASs (Lohmann et al., 2013; Yeung et al., 2017)

The transport of PFASs with water also could be time delayed. PFAS-loaded river water often runs not directly into oceans, but into more or less enclosed estuaries and adjacent seas, like into the North Sea, the Baltic Sea or the Mediterranean. Despite the North Sea having a wide-open connection to the Atlantic Ocean, the exchange between both seas is partially limited due to the morphology of the North Sea. The water circulates in the shallow North Sea continental shelf and the formation of thermo- and haloclines further hampers the water exchange. It is assumed that the North Sea water is totally exchanged within one or two years (Gyory J., 2013). The trapping effect of persistent pollutants is much higher in areas with lower exchange rates with the oceans due to deep basins and narrow links or due to natural barriers to the ocean. So, the water in the Baltic Sea is exchanged every 25-35 years (Kraatz, 2004). The residence time of water in the Mediterranean of approximately 100 years, making the Mediterranean ecosystem especially sensitive to the increase of the pollution stock of highly persistent substances like PFASs (Millot, 1989). Depending on water exchange rates from the adjacent seas with the oceans the translocation of PFASs sulfonfyl group. Particularly volatile precursors, such as FTOHs, can undergo long-range atmospheric transport (Ellis et al., 2004). The detection of FTOHs for instance in the Arctic and Antarctic air agreed with the model prediction and conclusion, which supported the hypothesis of atmospheric transport toward remote regions (Bengtson Nash et al., 2010; Dreyer et al., 2009; Paul et al., 2009).

Finally, sea spray aerosols (SSA) could be an important source of PFASs to the atmosphere and, over certain areas where sea spray deposition is important, a significant source to terrestrial environments, too (Johansson et al., 2019). SSA formation and their subsequent atmospheric transport and deposition have been suggested to play a prominent role in the occurrence of ionizable PFASs in the maritime Antarctica and other remote regions. However, field studies on SSA's role as vector of transport of PFAS are lacking. The effective enrichment of certain PFASs, such as PFAAs and possibly other PFASs in sea spray aerosols was recently demonstrated in laboratory studies, suggesting that SSA is a potential source of PFAAs to the atmosphere (Sha et al., 2022). The first field work by Casas et al. (2020) assessed the simultaneous occurrence of PFASs simultaneously at South Bay (Livingston Island, Antarctica) in seawater (SW), the sea-surface microlayer (SML) and SSA. Average PFASs concentrations were 313 pg L⁻¹, 447 pg L⁻¹, and 0.67 pg m⁻³ in SW, the SML and SSA, respectively. The enrichment factors of PFASs in the SML and SSA ranged between 1.2 and 5, and between 522 and 4 690, respectively. This amplification of concentrations in the SML is consistent with the surfactant properties of ionic PFASs, while the large enrichment of PFASs in atmospheric SSA may be facilitated by the large surface area of SSA and the sorption of PFASs to aerosol organic matter.

The measured large amplification of concentrations in marine aerosols supports the role of SSA as a relevant vector for long-range atmospheric transport mainly of charged PFASs. The transport via SSA may impact large areas of inland Europe and other continents in addition to coastal areas. Thus, SSA may currently be an important source PFASs to the atmosphere and, over certain areas, to terrestrial environments triggering also long-range transport.

Particles and plastic debris

Several PFASs may adsorb to particles. These particles such as dust or sediments may be easily drifted by air and water, and could be deposited far away from the point of release. Longer chain PFASs, in particular those with a sulfonfyl group like PFSAAs, EtFOSAA and FOSA are preferentially distributed in biota or the abiotic environment such as sediments, which could act as a sink for PFASs (Muir et al., 2019). However, considering the persistent nature of PFASs or their degradation products it is important to note, that sinks can become sources again.

Dust can be transported vertically and horizontally. The main anthropogenic sources for particulate organic matter are the transport and the industrial sector. About 3.1 Mt/a of these particles are emitted in Europe annually (Koolen and Rothenberg, 2019). Global annual dust emissions are currently estimated to range between 1 000 and 3 000 Mt/a, whereas, beside anthropogenic sources, major dust source regions include the Sahara, the Arabian and Asian deserts (Tegen and Schepanski, 2009). Anthropogenic as well as natural particles could be loaded with PFASs. Dust deposition in remote areas occurs through both dry deposition and wet deposition associated with cloud and precipitation processes. As such, deposition involves a complex set of physical processes. Global dust deposition rates are strongly interlinked with the origin of the particles and with the meteorological and seasonal conditions (Knippertz and Todd, 2012).

Rivers carry enormous amounts of sediments into coastal areas. For example, the annual transfer of sand, gravel and cobbles from the hinterland towards the Rhine delta was estimated by Frings et al. (2014) with 0.66 Mt/y. Not only natural sediments are transported by rivers and marine currents. The long-range transport of plastic debris and microplastics in the marine environment has been extensively documented (Eriksen et al., 2014; Howell et al., 2012; Maximenko et al., 2012; Obbard, 2018; Van Sebille et al., 2020). Plastics enter the oceans in massive amounts every year (4.8 to 12.7 Mt) (Jambeck et al., 2015) and accumulate in the oceans as plastic gyres (Eriksen et al., 2014) or in sediments.

The transport of PFASs often does not take the direct and fastest routes from the point of release to remote areas. Depending on particles size, particles could remain for long times in the atmosphere and a deposition may occur even many years later.

Adsorptive PFASs undergo long-range marine transport via plastic debris to a vast extent (Rani et al., 2017; Tanaka et al., 2020a; Tanaka et al., 2020b). A large share of microparticles as well as larger particles found in the environment already consists of plastic debris. Non-fluorinated as well as fluorinated plastics absorb large amounts of non-polymeric PFASs. Consequently, both polymeric PFASs and non-polymeric PFASs like additives can be transported as and with plastic debris. Larger plastic particles become suspended microplastics over time by mechanical crushing and by chemical transformation processes, which much easier could be moved to remote areas. Due to its density PE and PP float in the ocean surface and are easily transported by surface ocean currents and winds, whereas PVC tends to deposit near sources.

An estimated amount of about 35 000 t of microplastics are floating in the world's oceans (Cózar et al., 2014; Eriksen et al., 2014). However, according to Koelmans et al. (2017), this represents less than 1% of the floating accumulated plastic discharge. The remaining share is settled below the surface, at deep seafloor and in coastal sediments. The floating particles are transported with the ocean currents and a large part is trapped in the five subtropical gyres for about 40 years. It is estimated, that plastic debris are transported across the global oceans for more than 70 years (Wu et al., 2021). The Arctic Ocean appears to be a dead-end for plastic debris due to the poleward transport from sub-polar North Atlantic Ocean. The Arctic Ocean seafloor (e.g. Barents Seas) is thus an important sink of marine plastics (Cózar et al., 2014). It can be concluded, that PFASs associated with plastic debris are transported over long distances for many decades.

As mentioned in chapter B.7.6, plastic debris (macro- as well as microparticles) is ingested by migratory species e.g. seabirds (Tanaka et al., 2020b).

Partially, these organisms cover long distances on their extended migrations.

So, migratory organisms have to be considered as important vector for PFASs and for long-range transport. Moreover, substances are subject to complex exchange processes between the different compartments. Thus, sediments may serve as temporary sinks for a certain time for instance for substances which are adsorbed to particles.

B.4.2.8.2. LRTP based on physicochemical data

PFASs can be expected to be more volatile the higher their air water coefficient $\log K_{AW}$ is. Volatile PFASs can undergo long-range atmospheric transport. It is highly likely that, e.g. fluorinated gases, short-chain fluorotelomer alcohols and perfluorinated olefins are transported this way due to their volatility. Of these the PFASs which gradually degrade into ionic PFCAs (see sections B.4.1.3 and B.4.2.1 "Mobility in water") may change their route of long-range transport from air to water, depending on the chain length of the resulting PFCA. In general, uncharged PFASs like perfluoroalkane sulphonamides (FASAs), perfluoroalkane sulfonamidoethanols (FASEs) and fluorotelomer alcohols (FTOHs) are less water-soluble and more volatile than ionic PFASs. Once released in the environment, these PFASs can be (bio)degraded in the atmosphere or in other compartments under aerobic conditions to PFCAs and PFSAAs (Ellis and Mabury, 2003; Martin et al., 2006; Rhoads et al., 2008; Schenker et al., 2008) (see also section B.4.1.3).

PFCAs and PFSAAs are PFAS subgroups that exist in anionic form in water. Therefore, these substances are highly water soluble. They could be transported by river waters and by ocean currents to remote regions (Armitage et al., 2009; McMurdo et al., 2008; Prevedouros et al., 2008). See also sections B.1.2 and B.4.2.1 for data on the properties relevant for LRTP.

Substances with higher $\log K_{OC}$ -values (>3.5) like long-chain PFASs and cyclic PFAAs can be (highly) adsorbed by particles. For ionic and ionizable substances, the water solubility and/or the sorption potential is dependent on counter ions (section B.4.2.1). So, cationic charged PFAS like perfluoroalkylamines also may adsorb to particles because of mainly anionically charged soil particles. Depending on natural circumstances, such substances could be moved either by water or adsorbed with particles. Not only natural particles serve as PFAS acceptor. As described above, particles of plastic debris are an important vector for highly adsorptive PFASs. Because of their small size, especially microplastics (<1 mm) have a large ratio of surface area to volume. That promotes adsorption of chemical contaminants to their surface. Microplastic particles therefore have a very high capacity to facilitate the transport of PFASs.

Using substance physicochemical property data, the potential for long-range transport can be estimated. Different models use different matrices as basis for calculation. The OECD Tool (LRTP-Tool; ©OECD, 2009), which is used for the LRTP estimates, is a generic multimedia box model that yields estimates of numerical indicators for LRTP like the Characteristic Travel Distance (CTD [km]) for screening purposes. CTD is defined as the point in space at which the concentration as a function of place has decreased to $1/e$ (about 37%) of the initial value. The CTD is applied for water and for air (CTD_{water} , CTD_{air}) (Bennett et al., 1998).

High CTD values were calculated for fluorotelomer alcohols. For the calculation an atmospheric lifetime of about 20 days was used from Ellis et al. (2003). For degradation half-life in water a value of 93 h from Gauthier and Mabury (2005) for 8:2 FTOH was used for all FTOHs¹¹. The respective $\log K_{AW}$ values based on Arp et al. (2006) (Episuite calculation) and the $\log K_{OW}$ values based on Arp's COSMOTHERM estimations were used as input parameter to estimate the LRTP with the OECD-tool for fluorotelomer alcohols. The models standard setting was retained for the calculation. Based on their $\log K_{OW}$ and the $\log K_{AW}$, FTOHs are mainly emitted to air. It is noted that with increasing chain length the CTD is decreasing (see Table B.10).

¹¹ It is noted that this value is only used here for the purpose of LRTP calculation whereas it is not provided here for the purpose of the degradation assessment.

Table B.10. Estimated characteristic travel distances of fluorotelomeric alcohols and the respective input parameter for the OECD tool.

	[unit]	4:2 FTOH	6:2 FTOH	8:2 FTOH	10:2 FTOH
CAS-Nr.		2043-47-2	647-42-7	678-39-7	865-86-1
CTD air	km	9 405	6 727	3 816	2 839
CTD water	km	11	9	10	10
molecular weight	g x mol ⁻¹	264.09	364.10	464.12	564.13
logK _{aw}		-1.35	-2.39	-3.25	-4.23
logK _{ow}		3.21	4.44	5.66	6.91
degradation half-life air	h	480	480	480	480
degradation half-life water	h	107	93	93	93
half-life soil	h	72	72	72	72

Because FTOHs are forming corresponding PFCAs (see section B.4.1.3), PFCAs may be released into the environment secondarily from a release of FTOHs within a very long distance.

For PFCAs the respective calculated logK_{AW} values (EpiSuite) and the log K_{OW} values calculated with COSMOTHERM based on Arp et al. (2006) were used as input parameters for the OECD-tool to estimate the LRTP for perfluoroalkyl carboxylic acids. The standard half-life's for non-degradable substances of 10⁶ h for all compartments, provided in the OECD tool, were used for the calculation.

Table B.11. Estimated characteristic travel distances of selected PFCAs and the respective input parameter for the OECD tool.

	[unit]	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA
CAS-Nr.		2706-90-3	307-24-4	375-85-9	335-67-1	375-95-1	335-76-2
CTD air	km	398 785	667 771	852 725	1 010 029	1 042 881	1 045 656
CTD water	km	25 917	18 187	11 993	6 598	4 005	2 249
molecular weight	g x mol ⁻¹	264.05	314.05	364.06	414.07	464.08	514.09
log K _{aw}		-3.04	-2.66	-2.37	-2.03	-1.79	-1.52
log K _{ow}		3.43	3.26	3.82	4.30	4.84	5.30
half-life air	h	1 000 000	1 000 000	1 000 000	1 000 000	1 000 000	1 000 000
half-life water	h	1 000 000	1 000 000	1 000 000	1 000 000	1 000 000	1 000 000
half-life soil	h	1 000 000	1 000 000	1 000 000	1 000 000	1 000 000	1 000 000

CTD estimations show, that PFCAs theoretically could be transported by air multiple times across the globe, due to their non-degradability. Because, PFCAs partition to air occurs only to a very limited extent, transport via water appears more relevant. Shorter chain PFCAs like PEPeA are distributed with water more than 20 000 km. Assuming a multidirectional substance distribution, that means a distribution over the complete earth

surface. With increasing chain length, the CTD in water decreases, however, long-chain PFACs are still transported for several thousand kilometres (see Table B.11).

As described in chapter B.4.2.1, PFASs with high $\log K_{OC}$ and $\log K_{OW}$ strongly adsorb to particles. Highly adsorptive PFASs are PFOS, PFOA and PFBS. Especially cyclic PFAAs (C5-C7, and greater) strongly adsorb to soil and particles. For these substances a particle mediated long-range transport is highly likely. It is not common to provide CTD values for particles. But looking at data provided before, particle associated PFASs, especially those which are adsorbed to plastic debris, may be transported over the whole earth surface for many decades, too.

B.4.2.8.3. LRTP evaluation based on monitoring data

Generally, field data are accepted as evidence for the long-range transport of a chemical if (1) measured levels are available in locations distant from the sources of its release; (2) monitoring data show that long-range environmental transport of the chemical may have occurred via air, water, or migratory species. However, the mere detection of a chemical in a remote region cannot necessarily be understood as evidence of long-range transport, as the potential influence of local sources has to be considered as well (Scheringer, 2009), since both long-range transport as well as local pollution may contribute to the presence of PFASs.

Various PFASs are already ubiquitously detectable in remote areas like in arctic-, antarctic- or glacier firms, at open sea or even in the higher atmosphere (see B.4.2.7, Appendix B.4.2.3. and Appendix B.4.2.7.). All these data confirm the long-range transport. While little information on PFASs in Antarctica is available, new data show a wider range of PFASs in the Arctic since 2009. Several novel PFASs were detected in biota, water and air from Nordic and Arctic countries showing the wide distribution and potential for long-range transport of precursors and PFASs. Precursor -PFASs contribute to the total PFASs detected in all environmental compartments of remote areas and were frequently detected in many matrices.

Data for tracking PFASs along the way from its point of release to remote areas are rare. Following, the results of such a study are discussed in regard to LRTP of PFASs. In their comprehensive studies Möller et al. (2010) investigated the distribution and sources of 40 PFASs in the river Rhine watershed in the Rhine-Waal-Scheldt-Estuary and at open North Sea. PFOS, PFOA, PFBS and PFBA usually were the main detected substances.

In the North Sea, about 175 kilometres offshore, an average summarised PFAS concentration of 0.35 ng/L was provided in this publication. The measured concentration of PFASs in the North Sea seems to be low, however, if linked to the volume of the North Sea of 54 000 cubic kilometres (areal of the North Sea 575 000 square kilometres with an average depth of 94 m) it results in 2 000 t PFAS. Many large rivers, carrying high loads of pollutants, drain into the North Sea. The river basins are densely populated and large industries occur in this area. Going from open sea via river estuaries upstream the rivers, an increasing PFAS concentration could be measured. Along the Dutch coast, in the Rhine-Waal-Scheldt-Estuary, an average PFAS concentration of about 12 ng/L could be detected. The average PFAS concentration at the mouth of the rivers Rhine and Waal, in the Haringvliet, is 121 ng/L. Going further upstream the rivers, a high amount of PFASs is released into the Nederrijn and in the river Waal (average concentration of summarised PFAS: 260 ng/L). Large amounts of PFASs are also drained into the North Sea by the river Scheldt. At the Scheldt rivers' mouth (Western Scheldt) an average PFASs concentration of 95 ng/L was measured. The highest mean concentration of PFASs was measured in the river Scheldt with 498 ng/L. In the river Ruhr (into which the river Moehne is drained) at the inflow into the Rhine an average PFASs concentration of 47 ng/L was detected. Downstream Leverkusen the mean concentration of summarised PFASs raised to 181 ng/L instantaneously, compared to the average summarised PFASs concentration of about 21 ng/L in the Rhine upstream Leverkusen.

The respective increasing PFASs concentration in the rivers Rhine, Waal and Scheldt was caused by direct industrial emissions or indirectly via wastewater treatment plants or by the inflow of contaminated water from the several tributaries. Another source of PFASs contamination in river water may result from application of contaminated sludge to fields. The PFASs are eroded from the soil by rain. The substances are transported via river effluent over long distances into the Rhine-Waal-Scheldt-Estruary. So, for example, the linear distances from the point of emission are >200 km, from Leverkusen to a monitoring point in the North Sea or >300 km from contaminated soil in the river Moehnes drainage area to the same monitoring point at the open sea. On the one hand, the substances are diluted within the North Sea due to the large amount of marine water, but also trapped in the North Sea for a while.

The studies from Möller et al. (2010) not only show an increased PFAS concentration in the vicinity of heavy industrialised and dense populated areas but also indicate that composition of measured PFASs concentrations at different sampling points along the River Rhine watershed and in the North Sea is very distinct. Whereas in the North Sea and in the Lake Constance a high share of PFOS was detected, the share of PFHxS and PFBA is much higher in the river sections. Due to the restriction of PFOA and PFOS the industries substituted these substances with shorter chain PFASs already some years ago. So, the high share of PFOS in the Lake Constance and in the North Sea mainly could be related to previous environmental releases. In contrast to this, the measured concentration of short-chain PFASs in the river sections represent current PFAS releases. This is an indication that enclosed water bodies may serve as temporary sinks for PFASs, too. Due to trapping effects PFASs are transported time delayed e.g. from large lakes into the rivers or from estuaries and adjacent seas into the oceans.

Conclusion: Many PFASs have potential for long-range transport mainly due to their high persistence. Mobility in water and volatility contribute to the LRTP as well. Some precursors, such as FTOH, are themselves long-range transported. The same can be expected for other volatile PFASs. Precursor PFASs degrade over time to PFAAs which can be expected to be long-range transported, based on their physicochemical properties and high persistence. This was demonstrated with model calculation for selected PFCAs. The LRT pathways are different, depending on the PFASs, and may change when a precursor degrades to the corresponding arrowhead. Volatile PFAS such as fluorinated gases and uncharged PFASs like perfluoroalkane sulphonamides (FASAs), perfluoroalkane sulfonamidoethanols (FASEs) and partially fluorotelomer alcohols (FTOHs) are mainly transported via air. The long-range transport via water is the predominant pathway for anionic PFASs like PFCAs and PFSAAs). An important vector to remote areas is plastic debris for adsorptive PFASs. Further, all compartments (e.g. air, water and sediments) may serve as a temporary sink for PFASs. And, the combination of different sinks and considering the persistent nature of PFASs or their degradation products, sinks can become sources for environmental releases again over very long periods of time. However, for the majority of PFASs no data on transport pathways or point sources are available and thus substantial uncertainties on the concern of the long-range transport potential remain.

B.4.2.9. Bioaccumulation

For this dossier, a review of recent peer-reviewed articles and scientific reports was carried out. The recent data illustrate the specific mechanisms of bioconcentration and biomagnification and list in particular results of non-regulated or assessed PFASs. In the following, data from modelling, laboratory and field studies as well as from monitoring campaigns are presented.

B.4.2.9.1. Toxicokinetics of PFASs in animals

The overall body burden and target site concentration of a chemical and its metabolites is governed by its toxicokinetics (i.e., processes of absorption, distribution, metabolism, and excretion, ADME). Yet, available toxicokinetic data primarily focus on PFAAs (De Silva et

al., 2021; Kudo, 2015; Kudo and Kawashima, 2003). In a recent preliminary study targeted as well as non-targeted and suspect screening of striped dolphins of the Mediterranean Sea stranded along Tuscany coasts revealed a broader spectrum of PFAS uptake (Roscioli C et al., 2022). Non-target analysis allowed identifying FOSA as well as n:3 PFCAs. FOSA was the most abundant followed by FHxSA and FBSA in all the tissues. n:3 FTCA were mainly detected in high levels in liver and only in traces in some blood samples. This suggests that they are generated from precursors such as FTOHs and FTS present at high concentration in liver cells, but they are not distributed to different tissues through the bloodstream (Roscioli C et al., 2022). Overall, there are more robust data regarding the ADME of PFASs in humans and rodent model species than in other species. Furthermore, PFOA and PFOS are the most frequently studied PFAS. As discussed in the chapter on toxicokinetic processes (see section B.5.1), studies with mammalian species show that PFCAs and many other PFASs are readily absorbed and distributed especially among protein-rich tissues like liver, serum, and kidney (Kudo and Kawashima, 2003). Due to the high sorption capacities (e.g. (Armitage et al., 2012; Luebker et al., 2002)), the toxicokinetic behaviours of many PFASs (uptake, translocation, bioaccumulation, biotransformation, elimination, etc.) differ considerably from the common hydrophobic and persistent organic pollutants (Ng and Hungerbühler, 2013). Indeed, PFAAs were found to serum albumin, α globulins, and fatty acid-binding proteins. For instance, PFOA and PFOS preferentially distribute to the liver in most species; PFBA and PFHxS appear to preferentially distribute to the serum and, to a lesser extent, to the liver in animals (reviewed by Ebert et al. (2020)).

The enterohepatic circulation of PFAAs likely contributes to their extended elimination half lives in humans. It was demonstrated that PFBS, PFHxS, and PFOS were transported into hepatocytes both in a sodium-dependent and a sodium-independent manner by Na^+ /taurocholate co-transporting polypeptide (NTCP). PFBS, PFHxS, PFOS and PFCAs with 7-10 carbons are substrates of organic anion transporting polypeptides (OATPs). Chinese Hamster Ovary and Human Embryonic Kidney cells were used to demonstrate that human OATPs can transport PFBS, PFHxS, PFOS and the 2 PFCAs (C8 and C9). In addition, it was shown that rats possess different OATPs able to transport all 3 sulfonates. This study suggests that besides NTCP and the human apical sodium-dependent bile salt transporter, OATPs are also capable of contributing to the enterohepatic circulation and extended human serum elimination half-lives of PFBS and other PFAAs (Zhao et al., 2016).

As outlined in chapter B.5.1 on toxicokinetics, in mammals the major route of excretion for PFASs is renal elimination and to a smaller extent biliary and faecal (ATSDR, 2021; Consoer et al., 2014; EFSA, 2020; Kudo and Kawashima, 2003). Likewise, elimination of PFOA in rainbow trout occurred primarily via the renal route, which is consistent with numerous studies also in mammals suggesting that fish possess membrane transporters that facilitate the movement of PFOA from plasma to urine (Consoer et al., 2014).

In both, humans and animals, PFASs are transferred to the foetus via the placenta and to the offspring via breast milk (e.g. DeWitt (2015)). PFAAs do not readily cross the mature blood-brain barrier. This is supported by findings from Harada et al. (2007) in which PFOA and PFOS cerebral spinal fluid concentrations in adult humans were more than 500-fold lower than serum concentrations. However, high levels of PFASs and PFCAs were found in the brain of wild mammals and birds, e.g. in polar bears or gulls (Leranth et al., 2008; Verreault et al., 2005). PFASs are transferred to offspring, milk and eggs in many taxa, including livestock species (see review by Death et al. (2021)). For instance, Sharpe et al. (2010) showed that when zebrafish underwent a reproductive cycle in the presence of PFOS, approximately 10% of the adult PFOS body burden was transferred to the developing embryos, resulting in a higher total PFOS concentration in eggs ($116 \pm 13.3 \mu\text{g/g}$) than in the parent fish ($72.1 \pm 7.6 \mu\text{g/g}$). Gronnestad et al. (2017) demonstrated in hooded seals (*Cystophora cristata*) how 8 PFASs were transferred from mother to offspring via maternal transfer via both milk and the placenta, of which placental transfer is the dominant pathway reaching high levels in pub plasma.

Also in birds, maternal transfer is a major exposure route (Gockener et al., 2020b; Jouanneau et al., 2021; Kowalczyk et al., 2020) though little is known about the extent of the transfer of the different PFASs to the eggs, especially for alternative fluorinated compounds. A recent study by Jouanneau et al. (2021) showed that contamination of females and their eggs were dominated by linPFOS, then PFUnA or PFTriA. They measured PFASs, including HFPO-DA, ADONA, and F-53B, in the plasma of prelaying black-legged kittiwake females breeding in Svalbard. There was a linear association between females and eggs for most of the tested PFASs and maternal transfer ratios in females and eggs suggest that the transfer is increasing with PFAAs carbon chain length, therefore the longest chain PFCAs were preferentially transferred to the eggs.

PFCAs and PFSAAs are not metabolised in animals (Kudo, 2015). Studies on PFOA as well as PFSAAs such as PFOS (C8-PFSA) and PFDS (C10-PFSA) in rats have shown that they are excreted untransformed without forming any metabolites or conjugates. Thus, PFCAs are believed to represent metabolically inert and stable end-stage products. However, certain precursors have been shown to transform, to various extents in rodents, e.g. into their perfluorinated carboxylate “backbone structures”, such as 8:2 FTOH that is metabolised into e.g. PFOA and PFNA (C9-PFCA) (Henderson and Smith, 2007). Neutral volatile atmospheric precursors such as FTOH and FASA can biotransform in humans and wildlife, contributing to overall exposures of the arrowhead PFAAs (including PFOS and PFOA) (De Silva et al., 2021).

Based on the available literature on elimination half-lives in animal experiments, it can be assumed that several replacement substances have similar bioaccumulative properties as the arrowhead PFASs (Brantsaeter et al., 2013). Still, data providing evidence for bioaccumulative potential of less-well studied PFASs is rare. Rice et al. (2021) reported that HFPO-DA and ADONA may have bioaccumulative potential, but no clear conclusion could be drawn based on available data in rats. Polychlorotrifluoroethylene (PCTFE) oligomers accumulated preferentially in the liver during long-term oral exposure of rats (Kinkead et al., 1991). 6:2 FTSA, but not 6:2 FTCA, was detected at high levels in serum and liver following repeated-dose exposure of mice (Sheng et al., 2017), whereas 6:2 Cl-PFESA accumulated in serum and gut (Pan et al., 2019b) and liver of mice (Pan et al., 2021). Similarly, sodium *p*-perfluorooctanesulfonate (OBS) bioaccumulated in mouse liver, but also in the gut (colon, ileum). At the highest dose, OBS was also detected in serum, kidney and faeces (Wang et al., 2019a).

It is challenging to demonstrate bioaccumulation of PFAAs in humans, because of the lack of constant exposure over several years. However, findings from several studies provide indirect evidence. For example, a study on predictors of selected PFASs in pregnant women found that reported time since the most recent pregnancy was positively associated with measured blood concentrations of PFOA, PFNA and PFOS, thus indicating bioaccumulation during the time between pregnancies (Brantsaeter et al., 2013). In a study on levels of 6:2 Cl-PFESA and 8:2 Cl-PFESA in metal plating workers, lower median values were observed in individuals which had been employed less than one year (18.6 ng/mL) as compared to those with more than one year of employment (1 347 ng/mL) (Shi et al., 2016), which indirectly indicates bioaccumulation.

Conclusion: Many PFASs are readily absorbed and distributed especially among protein-rich tissues (especially liver, serum, kidney) and, thus, the toxicokinetic behaviours of PFASs differs considerably from the traditional hydrophobic chemicals. Many PFASs are transferred to the fetus via the placenta and via eggs, and to the offspring via breast milk.

B.4.2.9.2. Characteristics influencing bioaccumulation and toxicokinetic behaviour

Protein binding

Some PFASs, mainly PFAAs, have been discussed as being proteinophilic rather than

lipophilic substances questioning the usual bioaccumulation assessment scheme.

As discussed in the PFHxA background document, the relationship between structure (e.g. chain length) and affinity to proteins is complex and thus still a matter of research.

In mammals, serum albumin, fatty acid binding proteins (FABPs) and organic anion transporters (OATs) have been identified as important to the tissue distribution, species-specific accumulation, and species- and gender-specific elimination rates of PFCAs and PFSAAs (Zhang et al., 2013d).

Several biological matrices with high sorption capacities and the corresponding distribution coefficients or binding affinities have been reported for some PFAAs. These include serum albumin as a transport protein in blood, phospholipids as the major component of cellular membranes, alpha globulins, and liver fatty acid binding proteins (FABPs) that belong to the intracellular lipid-binding protein superfamily (Allendorf et al., 2019; Allendorf et al., 2021; Armitage et al., 2012; Bischel et al., 2011; Droge, 2019; Luebker et al., 2002; Weaver et al., 2009). Unlike the accumulation in adipose tissue, binding to proteins and accumulation in specific organs has a higher potential to cause adverse effects, since organ toxic effects may arise (see B.5.1).

Several PFCAs and PFSAs bind to albumin and other proteins (EFSA, 2020). Protein binding contributes to the distribution of PFASs to blood rich organs and liver. PFOA and PFOS have a high affinity for human uptake transport proteins such as organic anion transporters OAT1, OAT3 and urate transporter URAT1 (EFSA, 2020). The data for PFECAs is more limited. A recent study showed that HFPO-DA binds to human liver fatty acid-binding protein (Sheng et al., 2018a). There are no studies available investigating direct binding between HFPO-DA and albumin, and therefore it currently remains unknown whether HFPO-DA interacts with albumin directly or not. However, highest concentrations of HFPO-DA in rodents are found in the liver and the blood, indicating that HFPO-DA follows the same pattern of protein binding as other PFASs (Chen and Guo, 2009; Sheng et al., 2016). In addition to this, no data is available on OAT efficacy for HFPO-DA. It is therefore not known what effect HFPO-DA has on the functioning of the OATs and if resorption of HFPO-DA in the lumen of the kidney will occur in humans or not.

Differences in protein affinity may have implications for renal reabsorption of PFASs by the organic anion transporter in which higher affinity may imply higher reabsorption (Lu et al., 2021). Lu et al. (2021) estimated binding affinities of various PFASs on OAT4 which indicated that the affinity increased with carbon chain length. PFASs can also bind to hL-FABP and it is reported that binding affinity increases in the order of 6:2 fluorotelomer carboxylic acid (FTCA) < 6:2 fluorotelomer sulfonic acid (FTSA) < HFPO-DA < PFOA (Sheng et al., 2018a). Higher binding affinity of (6:2 Cl-PFESA) and HFPO-DA compared to PFOA was reported (Rice et al., 2021; Sheng et al., 2018a).

Bischel et al. (2011), investigated with equilibrium dialysis the binding of PFCAs (C2–C12) and PFSAs (C4, C6, and C8) to bovine serum albumin (BSA). An increase in the protein water distribution (K_{PW}) with increasing chain length was observed for PFCAs with four to six perfluorinated carbons. Log K_{PW} values for C4 to C12 PFAAs range from 3.3 to 4.3. Affinity for BSA increases with PFAA hydrophobicity but decreases from the C8 to C12 PFCAs, likely due to steric hindrances associated with longer and more rigid perfluoroalkyl chains. With the exception of PFDoDA over 90% of all PFAAs were bound to BSA (Bischel et al., 2011).

Allendorf (2021) analysed a consistent set of distribution coefficients for a series of PFAAs and 4 other PFASs (HFPO-DA, DONA, 9Cl-PF3ONS and PFECBS) to physiologically relevant matrices including albumin, membrane lipids, structural proteins, and storage lipids. The results of the physiologically based distribution calculations showed that albumin with the highest partitioning coefficients as well as membrane lipids, and structural proteins are of major relevance in estimating the accumulation of PFAAs in different organs.

Log K_{pw} values for C7 to C11 PFCAs range from 4.6 to 4.86. For PFSAAs with four to eight carbons (C4, C6, and C8) Log K_{pw} values are 3.34, 4.94 and 4.81, respectively. For HFPO-DA, DONA, 9Cl-PF3ONS and PFECBS Log K_{pw} values are 3.19, 4.06, 5.14 and 4.68, respectively. The albumin/water partition coefficients for the alternatives are in the same range as for classical PFAAs. Structural modifications such as the introduction of ether groups into the chain do not reduce sorption to albumin, whereas the chlorine atom in 9Cl-PF3ONS seems to even increase the sorption to albumin (Allendorf et al., 2019). This study concludes that the introduced ether groups do not considerably alter the distribution properties compared to PFCAs.

Apart from serum albumin the binding to other proteins may have an impact. In the study by Zhang et al. (2013d) the binding strength to a fatty acid binding protein, a high-abundance protein in liver, was found to be dependent on the length of the fluorocarbon tail and the polar headgroup. According to the authors, this dependence can be rationalized by the binding mode inside the protein's ligand-binding cavity, as revealed by molecular docking analysis. The authors conclude that based on their calculation, the potential disruption of the uptake and transport of fatty acids cannot be ignored.

Affinity to serum proteins increases with decreasing chain length (Bischel et al., 2011). This might, besides placental transfer, also affect other aspects of accumulation, such as passage of the blood-cerebral barrier. Notably, a previous comparative study demonstrated occurrence of PFASs in human brain, using autopsies of various organs that had been sampled from 20 subjects (Perez et al., 2013). In this study, the concentrations of 21 PFASs (C4-C18 PFCAs, C4, C6 and C8 PFSAs, and perfluorohexyl ethanoic acid (FHEA), perfluorooctyl ethanoic acid FOEA, and perfluorodecyl ethanoic acid FDEA; perfluorooctanesulfonamide (PFOSA)) were analysed in 99 samples of autopsy tissues (brain, liver, lung, bone, and kidney) from subjects who had been living in Tarragona (Catalonia, Spain). Note that PFBA levels in lung and kidney tissues are likely overestimated by Perez et al. (2013) as discussed under B.5.1.2 samples showed detectable values of at least two of the investigated compounds. Although PFASs accumulation followed different trends depending on the specific tissue, some similarities were observed between liver and brain, on one hand, and between kidney and lung, on the other hand. In liver, PFHxA, PFOS and FHEA were the most prevalent compounds, with median concentrations of 68.3, 41.9 and 16.7 ng/g, respectively. PFOS was present in 90% of the samples, while PFOA could be quantified in 45% of the samples (median: 4.0 ng/g). In brain, PFHxA was the main compound, being detected in all the samples at concentrations ranging from 10.1 to 486 ng/g. The contributions of PFNA (median: 13.5 ng/g) and PFDA (median: 12.4 ng/g) were also relatively important in brain samples. In contrast, PFOS was only quantified in 20% of the samples (median: 1.9 ng/g), whereas PFOA was not detected in any of them. In general terms, lung was the tissue showing the highest accumulation of PFASs. In contrast, detection of PFHxS and other PFASs was much lower in the investigated brain samples (Ao et al., 2019). Again, further studies are required to clarify whether this effect is related to neurological or neurobehavioural health risks.

Protein binding is assumed as one of the main mechanisms explaining facilitated tissue distribution. This hypothesis is supported by the findings of Numata et al. (2014). Four PFSAs and 3 PFCAs were quantifiable in feed, plasma, edible tissues, and urine of pigs. Unexcreted PFAAs accumulated in plasma (up to 51%), fat, and muscle tissues (collectively, meat 40–49%), liver (under 7%), and kidney (under 2%) for most substances. An exception was PFOS, with lower affinity for plasma (23%) and higher for liver (35%) in the body of pigs. Nevertheless, the potential to bind to BSA may not fully explain the toxicokinetics. Transporter proteins as described above may also have an impact on toxicokinetics. Apart from this, a study has shown that PFAAs bind to peroxisome proliferator-activated receptors. This plays a role in lipid metabolism, induces conformational changes of this receptor and may thus change the function of the protein (Zhang et al., 2014).

Conclusion: Protein binding is assumed as one of the main mechanisms explaining facilitated tissue distribution. The relationship between structure (e.g. chain length) and affinity to proteins is complex and thus still a matter of research. Several biological matrices with high sorption capacities and the corresponding distribution coefficients or binding affinities have been reported for some different groups of PFAS. These include serum albumin as a transport protein in blood, phospholipids as the major component of cellular membranes, alpha globulins, and liver fatty acid binding proteins (FABPs) that belong to the intracellular lipid-binding protein superfamily.

Chain length and chemical structure

Depending on chain length and functional groups, PFASs vary in their ability to bioaccumulate. This has been mainly investigated for PFCAs and PFSAAs. As discussed in the PFHxA background document, the affinity of PFAAs to proteins is chain-length dependent and increases up to a certain number of perfluorinated carbons depending on the protein (Ng and Hungerbühler, 2014; Zhang et al., 2013a).

Shi et al. (2018b) investigated how the differential tissue distribution and bioaccumulation behaviour of 25 PFASs in crucian carp from two field sites impacted by point sources can provide information about the processes governing uptake, distribution and elimination of PFASs. Transformation of concentration data into relative body burden demonstrated that blood, gonads, and muscle together accounted for >90% of the amount of PFASs in the organism. Functional group was a relatively more important predictor of internal distribution than chain-length for PFASs. PFCAs and PFSAs with six or more perfluorinated carbons displayed a positive trend in BAFs with increasing chain-length and distinct differences for PFASs with different functional groups (sulfonic acid > sulfonamide > carboxylic acid). Branched isomers of PFOS and PFOA had consistently lower BAFs compared to the linear isomer while the inclusion of an ether bond and/or terminal chlorine leads to a higher BAF for C8 Cl-PFESA compared to *n*-PFOS. This may be one reason why whole-body bioaccumulation factors (BAFs) for short-chain PFASs deviated from the positive relationship with hydrophobicity observed for longer-chain PFASs. Overall, the study suggests that BAF patterns were most consistent with protein-binding mechanisms, although partitioning to phospholipids may contribute to the accumulation of long-chain PFASs in specific tissues (Shi et al., 2018b).

Ahrens and Bundschuh (2014) published a review paper on the behaviour and impacts of different PFASs in aquatic systems, including bioaccumulation in various taxa. They showed that the average sum of PFOS and PFOA concentrations were typically in the ranges of 0.1-10 µg/kg ww for invertebrates, 1-100 µg/kg ww for fish and reptiles, 1-500 µg/kg ww for birds and 5-10 000 µg/kg ww for mammals. PFOS concentrations were typically up to 3 orders of magnitude higher compared with PFOA. The lower bioaccumulation potential of PFOA in comparison to PFOS was believed to be driven by both a shorter C-chain and differences in the functional group (e.g. carboxylic acids vs. sulfonates). Branched isomers were measured and were generally more readily excreted than linear isomers, which lead linear isomers to appear as more bioaccumulative than the comparable branched isomers in the addressed aquatic taxa.

De Silva et al. (2009) conducted dietary exposure studies in rainbow trout, administering PFOA isomers (manufactured with Electrochemical Fluorination (ECF)), linear PFNA, and branched PFNA for 36 d. Throughout exposure and depuration phases, blood and tissue sampling ensued. The accumulation ratio revealed similar accumulation propensity of *n*-PFOA and two minor branched PFOA isomers; however, the majority of branched isomers (*n*=5) had lower accumulation ratio values than *n*-PFOA.

Sharpe et al. (2010) investigated the bioaccumulation of branched and linear PFOS isomers in rainbow trout and zebrafish. They found the branched PFOS isomers to bioaccumulate significantly less than the linear PFOS isomers, which may explain the relative lower concentration of branched PFOS isomers in some aquatic species in the field. The study

remained unclear about whether this observed difference was due to differences in the uptake phase or in the elimination phase.

A different study on fish found linear PFOS isomers to accumulate more readily than the branched PFOS isomers, possibly being the result of a more efficient elimination of the branched PFOS isomers (number of branched isomers: $n=5$, (Hassell et al., 2020)).

Conclusion: It is evident that protein binding of various PFASs efficiently distribute them into different organs and tissues, allowing for passage across brain and placental barriers, yielding in maternal- offspring transfer also via the milk. Due to surfactant properties of some PFASs and the broad range of chemical structures, the affinity of different PFAAs for proteins varies widely, suggesting binding site-specific interactions, while the toxicokinetic behaviour is complex.

B.4.2.9.3. Modelling partitioning and bioaccumulation behaviour

Mechanistic bioaccumulation models developed for neutral lipophilic contaminants such as polychlorinated biphenyls and organochlorine pesticides have been widely used by academics, risk-assessment professionals, and regulatory authorities (Amot and Gobas, 2004). Strong relationships between empirically derived bioaccumulation metrics (BCF, BAF, TMF) and distribution ratios for protein–water (DPW) and membrane–water (DMW) of individual PFAAs have been demonstrated for some ecosystems (Anderson et al., 2019; Byrne et al., 2017). DPW and DMW are key parameters that may be useful for predicting PFAS bioaccumulation potential. However, distinction between proteins is warranted, since different protein types can exhibit different sorptive capacities (Henneberger et al., 2016). Accordingly, simple equilibrium partitioning-based models may require utilizing a series of distribution coefficients for different proteins (e.g. transporter protein–water distribution ratios and structural protein–water distribution ratios). This approach was e.g. used to assess tissue-specific bioaccumulation of PFAAs and other ionic compounds in laboratory exposed fish (Chen et al., 2016; Chen et al., 2017a). Chen et al. (2017a) showed a positive linear relationship between $\log BCF_{ss}$ values and physicochemical properties such as octanol–water distribution coefficients ($\log D_{ow}$), membrane–water distribution coefficients ($\log D_{mw}$), albumin–water distribution coefficients ($\log D_{BSAw}$), and muscle protein–water distribution coefficients ($\log D_{mpw}$), indicating the importance of lipid–, phospholipid–, and protein–water partitioning.

A chemical activity–based approach to ecological risk assessment bridges some gaps between traditional empirical modelling efforts and mechanistic models (Gobas et al., 2018a; Gobas et al., 2018b; Gobas et al., 2020b). This approach was used to assess bioaccumulation and exposure risks of several PFASs in wildlife at AFFF-impacted sites (Gobas et al., 2020a). The chemical activities of PFOS and other PFAAs indicated that these compounds tend to primarily biomagnify in food webs composed of air-breathing wildlife (birds, mammals, terrestrial reptiles) compared to those comprising only aquatic organisms. An advantage of this approach that is particularly relevant to PFAS is that it can be used effectively for both neutral and ionic substances, including anionic, cationic, and zwitterionic compounds (De Silva et al., 2021).

Beyond simple partitioning-based models for substance screening, more sophisticated approaches may be required for higher-resolution modelling. For example, ionic compounds binding to intra- and extracellular protein (serum albumin, L-FABP), as well as membrane-associated organic anion transporters, may act to provide both enhanced sorption capacity and advective transport across biological membranes (Ng and Hungerbühler, 2013). This affects uptake and elimination rates as well as tissue distribution and helps explain the long elimination half-lives of PFAA in organisms.

Wang et al. (2011c) conducted studies employing the COSMOtherm model to estimate physicochemical properties for 130 individual PFASs, namely perfluoroalkyl acids (including branched isomers for C_4 – C_8 perfluoroalkylcarboxylic acids), their precursors and some

important intermediates. The estimated physico-chemical properties are interpreted using structure-property relationships and rationalised with insight into molecular interactions. Within a homologous series of linear PFASs with the same functional group, both air–water and octanol–water partition coefficients increase with increasing perfluorinated chain length, likely due to increasing molecular volume. For PFASs with the same perfluorinated chain length but different functional groups, the ability of the functional group to form hydrogen bonds strongly influences the chemicals' partitioning behaviour). The partitioning behaviour of all theoretically possible branched isomers can vary considerably; however, the predominant isopropyl and monomethyl branched isomers in technical mixtures have similar properties as their linear counterparts (differences below 0.5 log units). Even with the large number of studies available, physiologically based toxicokinetic models for predicting the bioaccumulation of PFASs are, however, still in developmental phases (Armitage et al., 2017) and thus highly uncertain.

Two fish bioaccumulation models have been developed that account for some of the physico-chemical characteristics of PFASs. One is the BIOconcentration model for Ionogenic Organic Compounds (BIONIC) (Armitage et al., 2013), and the other is a protein-partitioning bioaccumulation model from Ng and Hungerbühler (2013); Ng and Hungerbühler (2014). Due to data availability, these models were built on training sets limited to PFCAs with carbon chain lengths greater than 7. Both models focused on predictions in freshwater fish. Given the lack of protein-partitioning values for fish, the protein-partitioning component of the bioaccumulation model (i.e., Ng and Hungerbühler (2013) used rat and human protein-partitioning values. The BIONIC model (Armitage et al., 2013) considers phospholipids, rather than proteins, as the primary repository for PFASs, but the model does recognize the ionization potential of these substances. However, because PFCAs and PFSAAs bind primarily to fatty acid-binding proteins and lipoproteins/albumin, and then are sequestered in protein-rich tissues, these proteins are important to consider. However, the protein-partitioning model underestimated the bioaccumulation of PFHxS (6 carbons) and generally underestimated whole-body bioaccumulation (Ankley et al., 2021). Thus, it is possible that the active clearance and reabsorption processes described in the protein-partitioning model do not operate in the same way or to the same extent in fish as in rats or humans (Ankley et al., 2021). None of these models offer predictions for short-chain (less than 7 carbon) PFCAs and PFSAAs, but available empirical data from Martin et al. (2003a) and Martin et al. (2003b), used in both models, showed that short-chain PFCAs (i.e., PFHxA, PFHpA) did not bioconcentrate in any rainbow trout tissue.

Physiologically based toxicokinetic (PBTK) models incorporating absorption, distribution, metabolism, and excretion metrics have been developed to assess the toxicokinetic of PFOS and PFOA in various animal models, including fish and mammals (Andersen et al., 2008; Consoer et al., 2014; Khazaee and Ng, 2018), but are still in the developmental phase.

Conclusion: Several modelling studies indicated that simple equilibrium partitioning-based models may require utilizing a series of distribution coefficients for different proteins. Positive linear relationships BCF values and physicochemical properties such as octanol–water distribution coefficients, membrane–water distribution coefficients, albumin–water distribution coefficients, and muscle protein–water distribution coefficients. Even with the large number of studies available, physiologically based toxicokinetic models for predicting the bioaccumulation of PFASs are, however, still in developmental phases and thus highly uncertain.

B.4.2.9.4. Laboratory and field studies on bioaccumulation

A recent review article by Burkhard (2021) evaluated literature for bioconcentration factors (BCFs) and bioaccumulation factors (BAFs) for PFASs in freshwater species from 22 taxonomic classes. The assembled data were evaluated for quality, and for gaps and limitations in bioaccumulation information for the PFAS universe of chemicals. For BCFs, measurements have been focused on perfluorohexane sulfonic acid (PFHxS), PFOS,

perfluorooctanoic acid (PFOA), PFNA, and PFDA. Accordingly, in general, carbonyl and sulfonyl PFAS classes are relatively data rich, whereas phosphate, fluorotelomer, and ether PFAS classes are data limited for fish and non-existent for most other taxonomic classes. Laboratory studies are limited to species with standardized testing protocols. Taxonomic classes with the most measurements were, in descending order, Teleostei (fish), Bivalvia, and Malacostraca. The numbers of PFAS chemicals with available measured BCFs (and BAFs) are summarized in Table B.12 by structure category, and these counts cover all tissue types (BCFs and BAFs for whole body, muscle, fillet, liver, and other organs). The BCFs reported were measured in the laboratory using standardized protocols with aquatic organisms and a water-borne exposure procedure. Steady state was demonstrated for all tests. Tests are typically run with a 28-d uptake phase followed by a depuration phase running from 14 to 28 d depending on the chemical. As commonly noted in the literature, BCFs and BAFs with 8 or more carbons increase uniformly with increasing number of carbons in the alkyl chain (Babut et al., 2017; Kwadijk et al., 2010). For the other taxonomic groups, a similarly large increase in BCFs and BAFs generally occurs between PFOA and PFNA. BCF values of different PFASs groups followed the order phosphinic acids > PFCAs > PFSAAs > others. Among the 43 PFASs compounds for which BCF and BAF studies are available in different aquatic species 62% (27 compounds) have a median $\pm$ SD BCF and/or BAF values above the REACH threshold for B ($\log$ BCF >3.3).

Table B.12 and Figure B.64 show large inter- and intra-species variability and that differences between individual studies and the medians across all studies exist for BCFs, as also confirmed by Wassenaar et al. (2020). These may have several reasons: there is an inherent variability in BCF and BAF measurements, which is commonly observed in BCF and BAF measurements for a chemical (Arnot and Gobas, 2006; Wassenaar et al., 2020). Furthermore, bioaccumulation of PFAS chemicals appears to have a slight dependency on concentration of the chemical (Chen et al., 2016; Dai et al., 2013; Hoke et al., 2015; Inoue et al., 2012), though other reporting demonstrated significant correlation of concentrations for PFOA (RIVM, 2017) and different studies have different exposure concentrations. Laboratory measurements suggest that BCFs decline with increasing exposure concentration (Chen et al., 2016; Dai et al., 2013; Hoke et al., 2015; Inoue et al., 2012). For example, Inoue et al. (2012) reported BCFs of 720 and 1300 with aqueous concentrations of 16 and 1.88 $\mu\text{g/L}$, respectively, for PFOS with common carp, a 1.8-fold increase in BCF with an 8.5-fold decrease in exposure concentration. As reviewed by Burkhard (2021), within a study, most often, lower concentrations provide higher measured BCFs, for example, studies with PFOS in 3 amphibian species (Abercrombie et al., 2019), PFASs with common carp (Inoue et al., 2012), and with zebrafish (Chen et al., 2016), and with *Daphnia magna* (Dai et al., 2013). Cause(s) of the decrease in BCFs with higher concentrations are unknown. However, PFAS residues are known to be controlled by a combination of passive diffusion and active transport processes (Ankley et al., 2021) and are generally not concentration dependent, which suggests there might be some type of capacity limitation in the active transport processes.

Table B.12. Overview on bioconcentration factors (BCFs) and bioaccumulation factors (BAFs; L/kg wet wt) for fish for whole-body, muscle/fillet, and liver tissues (median $\pm$ standard deviation, n) provided by Burkhard (2021). Bold numbers = above the B criterion of REACH Annex XIII. SS = steady state; OECD = Organisation for Economic Co-operation and Development.

Chemical	Tissue B metric CAS no.	Whole body Log BCF SS and Log BCF kinetic	Muscle/fillet Log BCF SS and Log BCF kinetic	Liver Log BCF SS Log BCF kinetic	Whole body Log BAF	Muscle/fillet Log BAF	Liver Log BAF
Carbonyl compounds:							
Carboxylic acids:							
PFBA	45048-62-2	1.18 $\pm$ 0.08 (2)	-0.22 $\pm$ 1.15 (5)	1.80 $\pm$ 1.23 (5)	2.16 $\pm$ 1.68 (6)	0.47 $\pm$ 0.96 (40)	0.37 $\pm$ 1.11 (3)
PFPeA	45167-47-3	-0.05 $\pm$ — (1)	-0.64 $\pm$ 1.21 (3)	1.15 $\pm$ 1.53 (3)	1.74 $\pm$ 2.45 (5)	0.15 $\pm$ 1.46 (18)	1.48 $\pm$ 1.43 (4)
PFHxA	92612-52-7	0.98 $\pm$ 0.3 (3)	0.40 $\pm$ 1.01 (5)	1.73 $\pm$ 0.99 (5)	1.40 $\pm$ 1.51 (11)	0.09 $\pm$ 1.34 (19)	2.79 $\pm$ 1.62 (6)
PFHpA	12088-5-29-2	1.26 $\pm$ — (1)	0.51 $\pm$ 1.24 (3)	1.78 $\pm$ 1.20 (3)	1.80 $\pm$ 1.24 (10)	-0.16 $\pm$ 1.27 (32)	0.92 $\pm$ 0.99 (6)
PFOA	45285-51-6	1.38 $\pm$ 0.61 (14)	0.82 $\pm$ 1.18 (7)	1.93 $\pm$ 1.00 (14)	2.16 $\pm$ 0.87 (48)	0.90 $\pm$ 1.14 (105)	1.97 $\pm$ 1.05 (48)
PFNA	72007-68-2	2.78 $\pm$ 0.51 (6)	2.80 $\pm$ 0.40 (4)	3.79 $\pm$ 0.24 (4)	2.80 $\pm$ 1.15 (41)	2.07 $\pm$ 0.76 (88)	2.84 $\pm$ 0.73 (20)
PFDA	73829-36-4	3.79 $\pm$ 0.48 (3)	3.81 $\pm$ 0.54 (4)	2.98 $\pm$ 0.93 (8)	3.45 $\pm$ 0.62 (43)	3.06 $\pm$ 0.49 (72)	3.72 $\pm$ 0.65 (30)
PFUnDA	19685-9-54-8	3.57 $\pm$ 0.31 (5)	3.97 $\pm$ 0.88 (4)	3.41 $\pm$ 0.74 (8)	3.47 $\pm$ 1.01 (21)	3.89 $\pm$ 0.77 (54)	4.34 $\pm$ 0.72 (28)
PFDODA	17197-8-95-3	3.64 $\pm$ 0.60 (8)	4.12 $\pm$ 0.83 (4)	4.46 $\pm$ 1.16 (4)	2.18 $\pm$ — (1)	4.50 $\pm$ 1.57 (28)	4.32 $\pm$ 1.52 (17)
PFTTrDA	86237-4-87-6	4.34 $\pm$ 0.46 (2)	4.51 $\pm$ 0.85 (2)	5.22 $\pm$ 1.08 (2)	—	4.66 $\pm$ 0.16 (3)	5.43 $\pm$ — (1)
PFTeDA	36597-1-87-5	4.40 $\pm$ 0.56 (4)	4.96 $\pm$ 0.62 (2)	4.74 $\pm$ 1.09 (3)	—	4.38 $\pm$ — (1)	5.08 $\pm$ — (1)
PFHxDA	67905-19-5	3.68 $\pm$ 0.01 (2)	—	—	—	—	—
PFOcDA	16517-11-6	2.57 $\pm$ 0.09 (2)	—	—	—	—	—
Sulfonyl compounds:							
Sulfonic acids:							
PFBS	375-73-5	1.06 $\pm$ 0.49 (7)	0.09 $\pm$ 1.15 (4)	1.74 $\pm$ 1.06 (5)	2.00 $\pm$ 1.13 (5)	1.35 $\pm$ 0.84 (16)	1.18 $\pm$ 0.34 (5)
PFHxS	355-46-4	2.07 $\pm$ 0.25 (6)	1.34 $\pm$ 0.19 (2)	2.41 $\pm$ 0.4 (4)	2.30 $\pm$ 0.74 (25)	1.28 $\pm$ 0.86 (56)	2.18 $\pm$ 0.58 (17)
PFHpS	375-92-8	—	—	—	—	2.20 $\pm$ — (1)	3.20 $\pm$ 0.10 (3)
PFOS	1763-23-1	3.01 $\pm$ 0.66 (21)	3.27 $\pm$ 0.96 (7)	3.17 $\pm$ 0.88 (18)	3.52 $\pm$ 0.78 (81)	3.09 $\pm$ 0.60 (155)	3.74 $\pm$ 0.84 (61)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Chemical	Tissue B metric CAS no.	Whole body Log BCF SS and Log BCF kinetic	Muscle/ fillet Log BCF SS and Log BCF kinetic	Liver Log BCF SS Log BCF kinetic	Whole body Log BAF	Muscle/fillet Log BAF	Liver Log BAF
PFDS	335-77-3	—	—	3.21 ± — (1)	1.30 ± — (1)	—	4.20 ± 0.15 (3)
PFECHS	—	—	—	—	—	—	—
Sulfonamides:							
FOSA	754-91-6	—	—	—	3.70 ± 0.53 (12)	2.95 ± 0.94 (24)	4.00 ± 0.2 (11)
Sulfonamidoacetic acids:							
MeFOSAA	2355-31-9	—	—	—	4.10 ± 0.16 (2)	—	—
EtFOSAA	2991-50-6	—	—	—	3.50 ± 0.06 (2)	—	3.45 ± 0.21 (2)
Perfluoroalkane sulfonyl amido ethanols, phosphate esters (SAmPAPs):							
SAmPAP	2965-52-8	1.42 ± — (1)	—	—	—	—	—
Perfluoroalkyl phosphate compounds:							
Phosphonic acids:							
PFHxPA	40143-76-8	1.46 ± 0.36 (2)	1.44 ± 0.14 (2)	2.83 ± 0.35 (2)	—	—	—
PFOPA	40143-78-0	1.92 ± 0.13 (2)	1.74 ± 0.12 (2)	2.66 ± 0.18 (2)	—	—	—
PFDPA	52299-26-0	2.21 ± 0.13 (2)	1.87 ± 0.04 (2)	3.36 ± 0.67 (2)	—	—	—
Phosphinic acids:							
C6/C6 PFPiA	40143-77-9	5.12 ± 0.71 (2)	5.51 ± 0.16 (2)	5.50 ± 0.69 (2)	—	—	—
C6/C8 PFPiA	—	7.36 ± 1.24 (2)	7.03 ± 0.88 (2)	7.35 ± 0.93 (2)	—	—	—
C8/C8 PFPiA	40143-79-1	8.30 ± 0.89 (2)	7.44 ± 1.43 (2)	7.36 ± 1.65 (2)	—	—	—
C6/C10 PFPiA	—	8.52 ± 1.01 (2)	7.78 ± 1.43 (2)	7.43 ± 1.36 (2)	—	—	—
C8/C10 PFPiA	—	5.79 ± 0.07 (2)	2.71 ± 3.80 (2)	1.85 ± 2.28 (2)	—	—	—
C6/C12 PFPiA	—	6.30 ± 0.98 (2)	5.35 ± 1.56 (2)	4.89 ± 2.73 (2)	—	—	—
Fluorotelomer-related compounds:							
Fluorotelomer alcohols:							
8:2 FTOH	678-39-7	2.50 ± 0.42 (2)	—	—	—	—	—
n:2 Fluorotelomer alcohol, phosphate esters (PAPs):							
6:2 diPAP	57677-95-9	—	—	3.50 ± — (1)	—	—	—
8:2 diPAP	678-41-1	—	—	2.39 ± — (1)	—	—	—
Fluorotelomer sulfonate:							
4:2 FTSA	75712-4-72-4	—	—	—	4.14 ± — (1)	1.49 ± — (1)	—

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Chemical	Tissue B metric CAS no.	Whole body Log BCF SS and Log BCF kinetic	Muscle/ fillet Log BCF SS and Log BCF kinetic	Liver Log BCF SS Log BCF kinetic	Whole body Log BAF	Muscle/fillet Log BAF	Liver Log BAF
6:2 FTSA	27619-97-2	1.54 ± 0.62 (3)	—	—	—	—	—
8:2 FTSA	39108-34-4	—	—	—	4.86 ± 0.41 (2)	3.94 ± 0.56 (4)	—
Per- and polyfluoroalkyl ether-based compounds:							
PFESAs, salts, and esters–monoethers:							
4:2 Cl-PFESA	—	—	—	—	—	—	3.27 ± — (1)
F-53B (6:2 Cl-PFESA)	73606-19-6	2.85 ± 1.16 (6)	—	3.43 ± 0.20 (4)	4.33 ± 0.19 (5)	3.85 ± 0.42 (6)	4.76 ± 0.4 (6)
8:2 Cl-PFESA	83329-89-9	0.40 ± — (1)	—	—	—	4.69 ± — (1)	5.64 ± — (1)
PFECAs, salts and esters–diethers:							
HFPO-DA	13252-13-6	—	—	—	—	0.61 ± — (1)	0.50 ± — (1)
HFPO-TA	13252-14-7	—	—	—	—	1.05 ± — (1)	1.75 ± — (1)

A synthesis of 513 laboratory-based and 931 field-based measurements indicates that long-chain PFCAs with a 12 to 14 carbon-chain length generally exhibit the highest bioaccumulation potential, with whole-body BCF values ranging between 18 000 and 40 000 L/kg (Gobas et al., 2020b). Laboratory-based whole-body BCFs of PFCA with 8 to 11 carbon-chain lengths are generally lower (BCF range 4.0–4 900 L/kg).

As described in the monitoring section B.4.2.4, field studies show that air-breathing organisms are more likely to bioaccumulate PFAAs compared to gill breathing organisms since they cannot eliminate PFAAs via ventilation. Accordingly, certain PFASs like C8–C10 PFCAs and C6 PFSA are more likely to bioaccumulate in air-breathing organisms, including humans, as compared to gill breathing organisms and that trophic magnification occurs in certain food webs in the environment where air breathing organisms are top-predators in the food chains (e.g. (De Silva et al., 2021)).

Conclusion: For BCFs, measurements have been focused on PFHxS, PFOS, PFOA, PFNA, and PFDA. However, also for other members of these substance classes BCFs have been reported in several studies. Accordingly, in general, carbonyl and sulfonyl PFAS classes are relatively data rich, whereas phosphate, fluorotelomer, and ether and all other PFAS subgroups are data limited for fish and non-existent for most other taxonomic classes. Generally, measured BCF values show extremely large inter and intra species variability for the same compounds indicating large uncertainties. Among the 43 PFASs for which BCF and BAF studies are available in different aquatic species, 62% (27 compounds) have a median ± SD BCF and/or BAF values above the REACH threshold for B (log BCF >3.3). BCF values of PFAS groups follow the order phosphinic acids > sulfonyl acids > carbonyl acids > others. In general, BCFs decline with increasing exposure concentration, while BCFs/BAFs of PFASs with 8 or more carbons increase uniformly with increasing number of carbons in the alkyl chain, with highest bioaccumulation potential of compounds with 12 to 14 carbon-chain length. However, aqueous testing underestimates the potential of bioaccumulation of PFASs, since air-breathing organisms are more likely to bioaccumulate PFASs compared to gill breathing organisms. Thus, established assessment methods of bioaccumulation based on bioconcentration testing in aquatic organisms do not suffice to

assess the bioaccumulation behaviour of PFASs.

B.4.2.9.5. Bioaccumulation and trophic magnification in wildlife

Analyses of biota at different trophic levels of the ecosystem show clearly that many PFASs that do not accumulate in aqueous species, bioaccumulate and biomagnify to high concentration levels in air breathers including top predator animals like polar bears, whales and seals (for example De Silva et al. (2021) and Chen et al. (2021b)). In top-predators dietary uptake routes indeed are important in PFASs toxicokinetics, especially for uptake in mammalian and top predator species. The recent review by De Silva et al. (2021) demonstrated that elevated exposures of wildlife to PFAS represent a concern for their health directly and for human populations that consume wildlife (Fair et al., 2019; Guillette et al., 2020). PFASs were detected in endangered species like green turtles and polar bears (Eggers Pedersen et al., 2015; Wood et al., 2021). In 2001, the first report on the global occurrence of PFOS in wildlife was released, illustrating widespread presence in biological tissues even in remote regions such as the Arctic (Giesy and Kannan, 2001). Concentrations of PFOS and other PFAA have been detected in invertebrates, fish, amphibians, reptiles, birds, and mammals worldwide (Ahrens et al., 2011; Houde et al., 2011; Muir et al., 2019). Several comprehensive reviews (Ahrens et al., 2011; Houde et al., 2011; Muir et al., 2019) have summarized data from available biomonitoring studies.

The highest PFAS concentrations in wildlife tend to be associated with proximity to contaminated sites. For example, one of the highest reported fish PFOS concentrations (maximum 9 349 ng/g dry wt in whole fish tissue) was from an AFFF-impacted site downstream from Barksdale Air Force Base in Louisiana (Lanza et al., 2017). Many biomonitoring studies have identified elevated exposures to legacy and emerging PFASs as the result of industrial activities (Death et al., 2021; Groffen et al., 2019; Guillette et al., 2020; Liu et al., 2017).

As shown by Burkhard (2021), for species commonly consumed by humans (e.g.e.g. fish, clams, mussels, oysters, and scallops, lobsters, crabs, shrimp, and prawns and winkles), there are BCF and BAF measurements for the PFCAs (n-PFHxA through n-PFUnDA), PFASs (n-PFBS, n-PFHxS, and n-PFOS) and FOSA (except for Gastropoda). For other chemicals, BCF and BAF data are limited, and measurements for chemicals beyond the PFASs just listed are needed. Comparison of laboratory BCFs with field BAFs revealed that 60% (26 of 43 comparisons) of the BAFs are greater than their corresponding BCFs, and similar proportions exist for BAFs based on whole body, muscle, and liver (Burkhard, 2021), Table B.12, Figure B.64). The BAFs include all exposure routes and, as suggested by the modelling efforts of Larson et al. (2018), sedimentary sources of the PFAS can cause BAFs to be greater than BCFs. Trophic magnification factors (which are food web average biomagnification factors) are slightly >1 for some PFAS compounds (Fang et al., 2014; Loi et al., 2011; Martin et al., 2004; Munoz et al., 2017). These field data suggest that BAFs for some PFASs should be larger than their BCFs for aquatic species because of biomagnification processes within the food web.

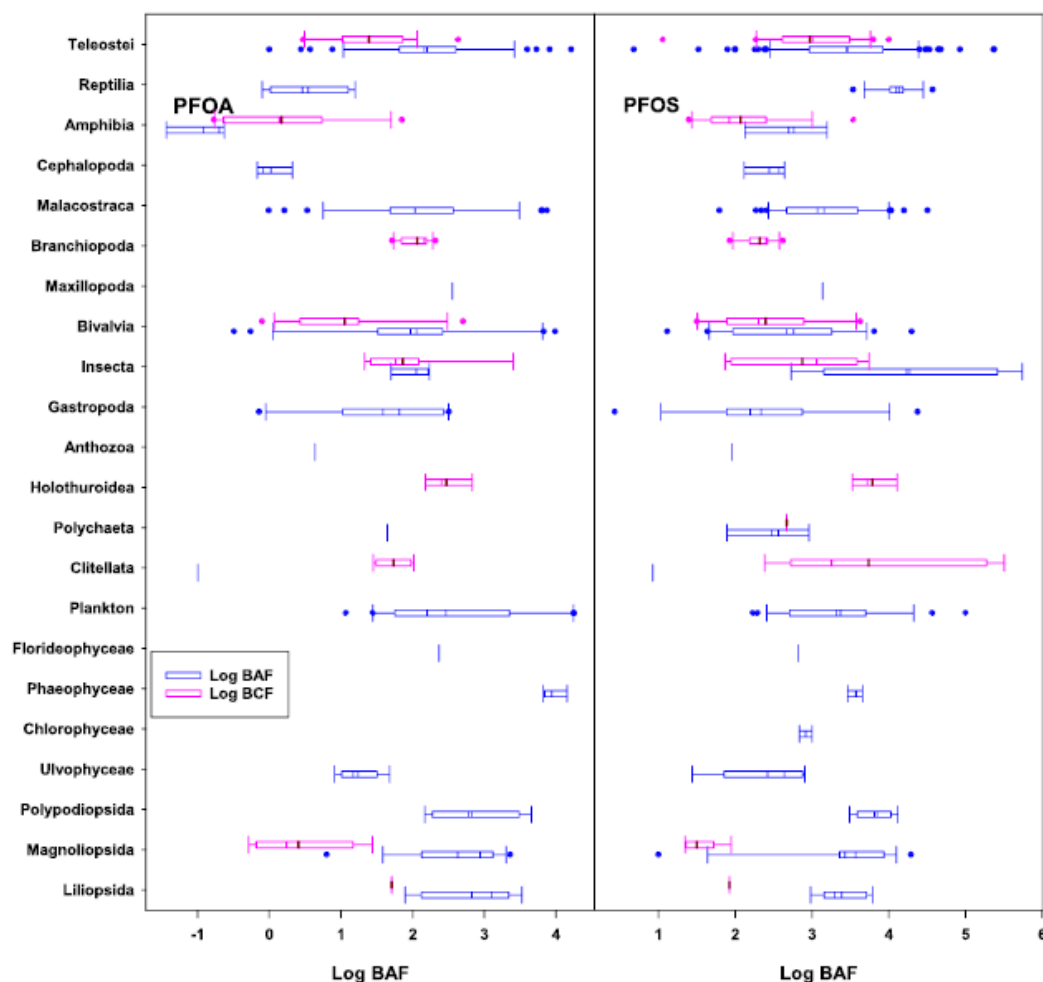


Figure B.64. Measured BCFs and BAFs in log units from different aquatic species (provided in Burkhard (2021)).

Avian and marine mammalian food webs exhibit the highest reported trophic magnification factors (TMFs) for PFAAs (Kelly et al., 2009). In aquatic piscivorous food webs, TMFs tend to be much lower. For example, TMFs of PFOS in the Lake Ontario aquatic piscivorous food webs including air breathing top predators, e.g. dolphins range between 1.9 and 5.9 (Houde et al., 2008). In particular, PFOS and several other PFAS of concern, which are likewise moderately hydrophobic and poorly metabolizable substances, may not biomagnify extensively in aquatic food webs because of efficient respiratory elimination to water via gills (De Silva et al., 2021; Kelly et al., 2009). Conversely, these substances can biomagnify to a high degree in food webs containing air-breathing animals because elimination of these substances via lung–air exchange is negligible.

The contribution of PFAA precursors to field-based measurements of BAFs represents a major gap in understanding of PFAS bioaccumulation. For example, one study noted higher than expected accumulation of PFCA with 5 and 6 carbons in marine plankton from the north-western Atlantic and posited that this reflects the accumulation of degraded precursor compounds (Zhang et al., 2019d). Another study that included liver tissues from marine mammals from the same region found a large fraction (30–75%) of unidentified organofluorine (Spaan et al., 2020).

Occurrence and accumulation of PFAS in apex species

PFOS is the dominant PFAS in apex predators, with an average proportion of approximately 60%, and the proportion of PFOS in many cases (>25%) is above 80%. Meanwhile, long-chain PFCAs (C9-C14) are major PFASs in apex predators as well (Chen et al., 2021c). In particular, PFOS/PFOA as well as PFCAs of C8/9-C11/12 chain length have shown to biomagnify in terrestrial (e.g. Müller et al., 2011; Zhao et al., 2013c) and aquatic food webs (Kelly et al., 2009; Xu et al., 2014). As a consequence, species of high trophic position (e.g. apex predators) accumulate high concentrations of certain PFASs in their tissues (Chen et al., 2021c). Among European predators, especially Eurasian otters (*Lutra lutra*) have shown to have comparably high PFOS levels compared to other predators (Androulakis et al., 2022; Badry et al., 2022). The fact that PFOS is still the most dominant PFAS in biota was suggested to be related to its persistence and the continued use of PFOS precursors like fluorotelomer alcohols and polyfluoroalkyl phosphate (Houde et al., 2011). Apex predators of aquatic food webs have shown to accumulate high PFOS levels in proximity of potential point pollution sources (e.g. Badry et al., 2022). More detailed information on occurrence and concentrations of regulated and non-regulated PFASs are provided in section B.4.2.6 and B.4.2.7.

Conclusion: As outlined in this section, analyses of biota at different trophic levels of ecosystems clearly show that many PFASs bioaccumulate and biomagnify to high concentration levels in top predator animals. Comparison of laboratory BCFs with field BAFs revealed that in most cases the BAFs are greater than their corresponding BCFs likely due to multiple exposure pathways in wildlife. Avian and marine mammalian food webs exhibit the highest reported TMFs for PFAA while in aquatic piscivorous food webs TMFs tend to be much lower. In particular, PFOS, which are likewise moderately hydrophobic and poorly metabolizable substances, may not biomagnify extensively in aquatic food webs because of efficient respiratory elimination to water via gills but can biomagnify to a high degree in food webs containing air-breathing animals because elimination of these substances via lung-air exchange is negligible. Especially PFOS and long-chain PFASs are frequently detected in protein-rich tissues of almost all wildlife species, whereas novel analytical techniques demonstrate the presence of emerging PFASs such as 7:3 FTCA or 6:2 Cl-PFESA.

B.4.2.9.6. Substance-specific bioaccumulation data

Bioaccumulation of long-chain (C8-C14) PFCAs and (C6-C8) PFSA

- C11-C14 PFCAs have been assessed to fulfil the vB-criterion of REACH Annex XIII.
- C8-C10-PFCA, as well as their salts meet the B-criterion (vB not assessed).
- C6-PFSA has been assessed to meet the vB criterion of REACH Annex XIII.
- PFOS and its salts have been assessed to meet the POP criterion for bioaccumulation due to its potential to bioaccumulate and biomagnify in mammals and piscivorous birds

Details of the assessment can be found in the supporting documentation of the listing in the Candidate List (ECHA, 2012b; ECHA, 2012c; ECHA, 2012d; ECHA, 2012e; ECHA, 2013; ECHA, 2015b; ECHA, 2016b; ECHA, 2017c)¹².

Bioaccumulation of short-chain (C4-C6) PFCAs and PFSA, and C7 PFCA

For the shorter-chain PFCAs and PFSA no bioconcentration in aquatic organisms due to uptake from the aqueous phase by diffusion via the gills is expected. Due to their high water-solubility SC-PFAAs are, unlike C8-C10-PFCAs and C6-PFSA, expected to be quickly excreted via gill permeation (Martin et al., 2003a; Martin et al., 2003b). A study was conducted on both bioconcentration and biomagnification in rainbow trout (Martin et al., 2003a; Martin et al., 2003b). Both studies investigated a homologous series of PFCAs and

¹² <http://chm.pops.int/TheConvention/ThePOPs/TheNewPOPs/tabid/2511/Default.aspx>, date of access: 2022-12-22.

PFASs and perfluoroalkyl chain lengths shorter than eight and six carbons, respectively, could not be detected in most tissues and were considered to have insignificant bioconcentration factors (BCF).

SC-PFCAs and SC-PFSAs are to some extent bioaccumulative in air breathing organisms, as far as this has been possible to assess. Elimination half-lives of short-chained-PFAAs, which have been recently used for long-chained PFAAs as a metric to estimate bioaccumulation potential in air-breathing organisms, are shorter in comparison with long-chained PFAAs. Depending on the species, half-lives range from a couple of hours to several days in mammals (Chengelis et al., 2009a; Gannon et al., 2016; Numata et al., 2014) and up to over a month-almost a year in humans (Bolan et al., 2021), see toxicokinetic section B.5.1.1.4).

Bioaccumulation of cyclic PFAAs

De Silva et al. (2011) estimated the Bioaccumulation factors (BAFs_{whole-body}) for two fish species (lake trout and Walleye), of several PFAAs, including PFECHS based on the ratio of fish to water concentrations measured in samples from the Great Lakes. The mean log BAF (whole body homogenate, wet weight) values for fish corresponded to 2.8 for PFECHS, 2.1 for PFOA, and 4.5 for PFOS. BAFs are calculated with the assumption that the concentration of the pollutant observed in the fish is the result of exposure to the same pollutant in the water and diet. As such, if the pollutant in the fish is the result of biotransformation of a precursor, then the resulting BAF may be an overestimate. It is not probable that the fishes could have been exposed to precursors to PFECHS, as no precursors to this substance are known. A trend in tissue/blood ratios (liver > kidney > bladder > muscle) was observed for PFECHS, PFPCPeS, br-PFOS, lin-PFOS, and F-53B suggesting that these compounds share similar mechanisms for uptake and distribution in the body (Wang et al., 2016a). Overall, the trend of mean Log BAF_{whole-body} F-53B (4.6) $\approx$ lin-PFOS (4.6) > br-PFOS (3.8) > PFECHS (2.7) > PFPCPeS (1.9) appeared to follow the hydrophobicity pattern, with lowest BAF for the less hydrophobic cyclic PFAAs. Isomer-specific differences in the tissue/blood distribution ratios and BAF whole-body for PFECHS and PFPCPeS indicate that ring structure and position of the sulfonic acid group affect the bioaccumulation potential. No studies of the biomagnification or trophic magnification of PFECHS or other cyclic PFAAs have been identified.

Bioaccumulation of PFECAs and PFESAs

Few laboratory studies are available on the bioaccumulation potential of PFECAs in fish (see Appendix B.4.2.9.). Additional data on field studies for HFPO-DA are presented in section B.4.2.7.6 and in the Annex XV dossier on the proposal for identification of HFPO-DA as a substance of very high concern (ECHA, 2019d).

According to the SVHC support document for HFPO-DA (ECHA, 2019d), the BCFs for HFPO-DA are below 2 000. Based on the structural similarities with PFOA, it can be expected that bioaccumulation factors are higher at low environmental concentrations. Although bioaccumulation of HFPO-DA is still low at environmental concentrations, fish consumption could be a relevant exposure route for humans as it is for PFOA (ECHA, 2019d).

Chlorinated polyfluoroalkyl ether sulfonic acid (Cl-PFESA) is regarded as a Chinese perfluorooctane sulfonate (PFOS) alternative with a commercial name of F-53B, in which the main component is 6:2 Cl-PFESA with its two homologues (8:2 and 10:2 Cl-PFESA) as impurities (Jin et al., 2020c). Shi et al. (2015) recently reported on the first detection of F-53B in biological samples and determined the tissue distribution and whole-body bioaccumulation factors (BAF_{whole body}) in crucian carp (*Carassius carassius*). Tissue/blood ratios showed that distribution of F-53B primarily occurs to the kidney, gonad, liver, and heart. Median Log BAF_{whole body} values for F-53B exceeded regulatory bioaccumulation criterion and were significantly higher than those of PFOS in the same data sets. On the basis of its apparent omnipresence and strong bioaccumulation propensity, it was

hypothesized that F-53B could explain a significant fraction of previously unidentified organofluorine in biological samples from China. However, no laboratory study on the bioaccumulation of F-53B is available.

The available data indicate that bioconcentration factors and bioaccumulation factors (BAF) are low for shorter-chain PFECAs. Similarly, as for LC-PFCAs, it can be expected that PFECAs with more than the seven perfluorinated carbons would show a higher potential for bioconcentration. However, there are no bioconcentration studies available for longer chain PFECAs.

The only PFESA that has been commercialised is 6:2 Cl-PFESA, the major component of F-53B, a substitute for PFOA used for decades in China in the chrome plating industry see Annex A chapter 3.5. In a Chinese field bioaccumulation study 6:2 Cl-PFESA (substitute of PFOS) was detected in the tissues (kidney, gill, muscle, brain, heart, gladder, gonad, liver) and blood of all sampled Crucian carp (n=43) from two different locations (Shi et al., 2015). The median Log BAF_{whole body} (L/kg ww) values for 6:2 Cl-PFESA ranged from 3.80 to 5.23.

Wang et al. (2016a) conducted a study on the bioaccumulation factors and tissue distribution of and other PFAAs in Crucian carp (*Carassius carassius*) downstream of the Beijing Airport in China. The median concentration for F53-B was highest in blood (11.42 ng/g ww) followed by kidney (10.02 ng/g ww), liver (8.73 ng/g ww) and bladder (8.54 ng/g ww) and lowest in muscle (1.75 ng/g ww). The mean concentration in the surface water for the sampling sites ranged from <MLQ to 5.32 ng/L. The median Log BAF_{whole body} (L/kg ww) for F-53B was 4.59.

In another Chinese field study by Chen et al. (2018c), 6:2 Cl-PFESA was detected in muscle tissue of invertebrates, fishes, seabirds and mammals collected from the Bohai Sea (n=152, detection frequency of 81.3%). The logarithm BAFs of 6:2 Cl-PFESA reported in this study for fish were in the range of 2.41–3.80, with an average value of 3.00, which is about one order of magnitude than the values reported by Shi et al. (2015) in freshwater crucian carp. Chen et al. (2018c) estimated the value for trophic magnification factor (TMF) for 6:2 Cl-PFESA was 3.94 in the studied marine food web, indicating the potential for this substance to biomagnify in the marine food chain. A first report of a field study of the estuarine food web of the Xiaoqing River, China measured PFECAs and other PFAS in water, sediment, plankton, bivalves, crustacean, gastropods and fish (Li et al., 2021e). Highest concentrations in water samples were measured for PFOA, PFO2HxA, PFMOAA, PFO3OA, HFPO-TrA, and HFPO-DA. The highest concentrations in biota were observed for PFMOAA and HFPO-TrA. The detection frequency of PFMOAA was 100% with highest concentrations found in gastropods in a range of 15 900–16 700 ng/g dw. HFPO-TrA was found at a detection frequency of 100% with highest concentrations in crustacea in a range of 20.9–138 ng/g dw and fish in a range of 11.9–188 ng/g dw. Logarithmic BAFs were 1.15±1.06 for PFMOAA and 0.65±0.67 for HFPO-TrA. The authors found that BAFs values of PFECAs were dependent on carbon chain length and increase with longer chains. Trophic magnification was observed for HFPO-TrA (TMF= 5.25), HFPO-TeA (TMF = 2.95), PFO5DoA (TMF = 5.62), HPFMO2OSA (TMF = 2.69) and PFOS (TMF = 1.62). Based on BAFs, long-chain PFECAs are expected to accumulate to a greater extent than short-chain PFECAs.

Bioaccumulation of PFPIAs and PFPAs

Bioaccumulation potential of PFPIAs and PFPAs has been assessed under IMAP (2018), and a review of available data their bioaccumulation has also been done by Wang et al. (2016a), which are summarised below: Similar to other PFAAs, PFPAs and PFPIAs, do not follow the behaviour of traditional hydrophobic compounds with partitioning into fatty tissues, but instead have high affinities for proteins (i.e., they are proteophilic) and they tend to partition to protein-rich tissues (Ng and Hungerbühler, 2014). In a bioconcentration study conducted according to OECD TG 305 (Chen et al., 2016), zebrafish were exposed to a technical mixture of PFPAs (C6-10 PFPAs) and PFPIAs (C6/C6, C6/C8, C8/C8, C6/C10, C8/C10, C6/C12 PFPIAs). Measured bioconcentration factor (BCF) values indicated that

PFPIAs had very high bioconcentration potential, with a lowest measured whole-body BCF for C6/C6 PFPIA (12 perfluorinated carbons) of 41 700 L/kg, meeting the B and vB criteria of REACH Annex XIII. The study suggests that aqueous exposure will result in a high bioaccumulation potential of longer-chain PFPIAs in gill-breathing organisms. It is noted that the results from this study appear to follow the same pattern as observed for PFCAs, where the total number of the perfluoroalkyl carbons is indicative of the bioaccumulation potential in gill breathers. The results should, however, be considered to be only an indication of the expected aquatic bioconcentration pattern.

In a biomagnification study, dietary exposure of a mixture of C6/C6, C6/C8 and C8/C8 PFPIAs in juvenile rainbow trout gave biomagnification factors (BMF) of less than one for each congener (Lee et al., 2012).

The bioconcentration and biomagnification potential of PFPAs were also investigated in the studies discussed above (Chen et al., 2016; Lee et al., 2012). PFPAs were found to have low bioconcentration potential in zebrafish when exposed to the technical mixture of PFPAs and PFPIAs, with a measured whole-body BCF of 204 L/kg for C10 PFPA (Chen et al., 2016), which is below the numerical criteria 2000/5000 of REACH annex XII for B and vB. BCF values in plasma (67 L/kg), liver (1 400 L/kg), muscle (80 L/kg) and ovary (200 L/kg) were also reported.

B.4.2.9.7. Overall conclusion on bioaccumulation

By now, C11-C14 PFCAs and C6-PFSA have been shown to fulfil the vB-criterion and C8-C10-PFCA the B criterion of REACH Annex XIII. For the shorter chain (SC) PFCAs and PFSAs no high bioconcentration factors in aquatic organisms due to uptake from the aqueous phase by diffusion via the gills is expected (ECHA, 2018b). However, short-chained-PFCAs and PFSAs are to some extent bioaccumulative in air breathing organisms, as far as this has been possible to assess. Due to the binding to serum albumin the blood estimation of true bioaccumulation potential of SC-PFASs is not possible with conventional methods related to lipid adsorption. Currently no systematic approach for assessing bioaccumulation potential in particular for air-breathing species for this kind of substances is available. Studies on the bioaccumulation factors and tissue distribution of F-53B and other PFAAs in fish indicate that F-53B and p-perfluorooctanesulfonate (OBS) are in the range of fulfilling the B/vB criteria of Annex XIII to REACH. No studies on the biomagnification or trophic magnification of PFECHS or other cyclic PFAAs have been identified. As for long-chained PFCAs, it can be expected that PFECAs with more than the seven perfluorinated carbons will show a higher potential for bioconcentration. However, there are no bioconcentration studies available for longer chain PFECAs. Measured bioconcentration factor (BCF) values indicated that PFPIAs had very high bioconcentration potential, with a lowest measured whole-body BCF for C6/C6 PFPIA (12 perfluorinated carbons) of 41 700 L/kg, meeting the B/vB criteria of REACH Annex XIII. Studies suggest that PFPIAs are B/vB in gill-breathing organisms. The investigated PFPAs were found to have low but not negligible bioconcentration potential in fish, as expected based on the total number of the perfluorinated carbons. However, it is finally noted that a low bioconcentration in gill-breathing organisms and the accumulation in lipids is not the most relevant endpoint to consider for PFASs. It must be, however, noted that the Dossier Submitters current understanding of PFAS bioaccumulation and other hazards is based on a relatively small number of compounds, and little is known about the properties and behaviour of most of the thousands of PFASs as individual chemicals or as the much more commonly present complex mixtures.

B.4.3. Persistence compensating low bioaccumulation potential for mobile substances

As outlined in the Microplastics Restriction Dossier (ECHA, 2020), when considering persistence-based concerns, it is important that they are framed within an appropriate time scale. It is important to consider that accumulation in environmental media (water, sediment, soil, air) is a time-dependent process that depends on the rate of input (release, transport from other compartments, uptake in case of biota), rate of removal (degradation, transport to other compartments, elimination in case of biota; see also section on mobility B.4.2.1.3). Assuming a continuous release rate, the ultimate steady-state concentration reached in a given environmental compartment is a balance of these parameters (Crookes and Fisk, 2018). Accordingly, Crookes and Fisk (2018) investigated how the concentrations of mobile and persistent chemicals in the environment develop over time and compared their findings with the bioaccumulation criteria of the Stockholm Convention. They found that substances that are both persistent and mobile in the environment have the potential to be transported long distances from the point of emission. If such substances accumulate over time in the environment, they can reach levels that may have effects on both ecosystems and human health. In other words, persistence is key to increasing environmental exposure while mobility in the environment (particularly the aquatic environment) is a prerequisite for a rapid widespread distribution and thus for broad exposure.

Crookes and Fisk (2018) modelled the expected time-trend for concentrations in biota of substances with a certain combination of half-life in water and bioconcentration factors, see Figure B.65 for the reproduction of their simulation below. Persistence in this model relates to the life-time in the relevant compartment, water, and degradation as well as sedimentation and other processes that remove the substance from the compartment is included in P. The authors found that for a given mass emission rate, as the half-life increases, the steady-state concentration predicted in biota for substances with relatively low BCF values can, over extended periods of time, approach that of a substance that is considered to have a high bioaccumulation potential, and the steady-state concentration ultimately reached is a function of both, persistence and BCF.

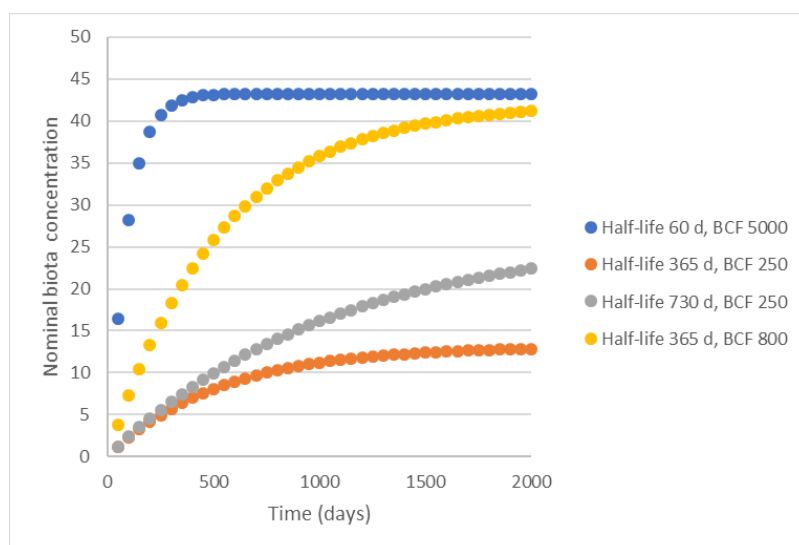


Figure B.65. Reproduction of model for biota concentration development from Crookes and Fisk (2018). Impact of persistence on the concentration of a substance in biota in relation to bioaccumulation potential.

UBA (2019) have discussed the quantifier of mobility with regard to the persistence criteria under REACH. With regard to PFASs which may remain in the environment for centuries,

persistence gains more importance than mobility. This has for instance been discussed by Gellrich and Knepper (2011) who observed that in groundwater, PFASs with short-chain lengths (<7 fluorinated carbon atoms) are usually detected in higher concentrations than long-chained. However, the concentrations of PFOA and PFOS, i.e. longer-chained and more adsorptive in water and other environmental matrices, are likely to increase because of (1) the continuous desorption of PFOS and PFOA that are still bound to soil particles, and (2) the slow transformation of precursors of these compounds in environmental compartments (Frömel and Knepper, 2010). Model results (unit-world model) show that the higher the persistence of a chemical, the longer the time-to-steady state, the higher the steady-state concentrations, and the greater the overshoot and long-lasting contamination tail at the end of the emissions irrespective of the values of the partition coefficients (Cousins et al., 2019).

Conclusion: Substances that are both persistent and mobile in the environment have the potential to be transported long distances from the point of emission. If such substances accumulate over time in remote regions they can reach levels that may have effects on both ecosystems and human health. When the model from the report by Crookes and Fisk (2018) is used for PFASs, the concentrations of very persistent and mobile subgroups in biota may be expected to ultimately exceed the biota concentrations which increases the risk of being persistent and bioaccumulative.

B.4.4. Accumulation in plants

Many PFASs are highly water soluble, and are thus easily absorbed, transferred and to a certain degree also bioaccumulated in plants (Brown et al., 2020; Zhang et al., 2020b; Zhang et al., 2021). Consumption of PFAS-contaminated agricultural products represents a feasible pathway for the trophic transfer of these toxic chemicals along food webs, leading to risks associated with human and animal health (Wang et al., 2020b). Considering that agricultural crops constitute a major portion of livestock and human diets, consumption of the PFASs-laden food represents an important route responsible for the accumulation of PFASs in animals and humans (Blaine et al., 2014a; Brambilla et al., 2015; Pérez et al., 2014).

Root uptake from nutrition matrixes and foliar absorption from atmosphere are two prevailing pathways for organic chemicals transported to plants (Collins and Finnegan, 2010; Paterson et al., 1994). The volatile or particle-bound PFAS precursors can be absorbed via plant leaves from air and subsequently metabolized into PFCAs and PFSAAs (Ghisi et al., 2019). For instance, Tian et al. (2018) demonstrated that foliar uptake of PFASs from the atmosphere was an important exposure route for Chinese pine (*Pinus tabulaeformis* Carr.), oriental plane (*Platanus orientalis* Linn), and white poplar (*Populus alba*) surrounding the landfill sites.

Consumption of plant material, e.g. grains and vegetables either as roots or above ground plant parts, function as source of PFASs to humans. This is of relevance for example when agricultural soil is contaminated with PFASs, leading to the contamination of agricultural plants. Via plants, PFASs enter the food chains of humans and animals.

Several studies investigated the uptake of PFASs from the surrounding environment into plants (e.g. agricultural crops, vegetables). An overview of the studies and further details on the studies as well as results can be found in Appendix B.4.4.). The studies were conducted under strictly controlled laboratory conditions, under semi-natural conditions and under environmental conditions (field studies). The results of the studies are not directly comparable due to the different conditions (e.g. hydroponic systems, soil systems, varying exposure times, plant physiology etc.). Furthermore, the uptake and accumulation of PFASs in plants may be affected by various abiotic and biotic factors, e.g. soil properties like pH, temperature, salinity, organic carbon and clay content (Jiao et al., 2020; Wang et al., 2020b).

Most of the studies have been focused on PFCAs and PFSAAs (e.g. (Felizeter et al., 2012; Felizeter et al., 2014; Krippner et al., 2014; Wen et al., 2014; Zhang et al., 2019c)) but enrichment in plants was also investigated for other PFASs like diPAPs, FTOHs, fluorotelomer sulfonic acids, perfluoroalkyl phosphinic acids or perfluoro alkyl ethers (Bizkarguenaga et al., 2016; Lin et al., 2020b; Yoo et al., 2011; Zhang et al., 2021; Zhou et al., 2020). The uptake of PFASs in plants depends on several parameters, e.g. carbon chain length, functional group, plant species, lipid and protein content, soil and water characteristics, transpiration streams, etc. (Brandsma et al., 2019).

Bioaccumulation factor (BAF, ratio of contaminant concentration in plant to growth matrix) is commonly used to characterize the uptake and translocation efficiency of organic compounds in plants (Jiao et al., 2020).

PFAS bioaccumulation factors (BAF) for 37 agricultural plant species were reviewed by Lesmeister et al. (2021). The review compiles soil-to-plant BAFs for 45 PFASs from 24 studies. Most studies suggest that BAFs depend on the hydrophobicity of the PFASs. The BAFs were higher for vegetative plant parts than for reproductive and storage organs. In hydroponic studies (plants grown in nutrient solution instead of soil) the root -BAFs either increased with increasing chain length or showed a u-shaped dependency with minima for C6 or C7 PFAAs. The root-BAFs of C2 and C3 PFCAs were one or two orders of magnitude higher than for all other investigated PFCAs. Contrary to the observations in hydroponic

studies, root-BAFs based on soil concentrations show only very low or no chain length dependency or they decreased with increasing chain length. The BAF for other vegetative compartments and reproductive organs decreased with increasing chain length. This was also true if root-BAFs did not show this correlation and was independent of the type of study (culture in hydroponic solutions or soil). Combining all shoot-BAFs per single PFCA (C4-C14) and PFSA (C4-C10), median log BAFs decreased by $-0.25(\pm 0.029)$ and $-0.24(\pm 0.013)$ per CF_2 group increase (note: experimental conditions in the studies were quite heterogeneous in terms of plant species, plant parts, soils, PFASs etc.). Lesmeister et al. (2021) also investigated the effect of functional groups on BAFs. Compared to the chain length, functional head groups have lesser impact on the transfer. The presence of precursor can complicate the calculation of BAFs for individual compounds as it often is unclear if precursors have been transformed in the soil or in the plant after uptake.

The observations from Lesmeister et al. (2021) are similar to the ones reported in other reviews (Costello and Lee, 2020; Ghisi et al., 2019; Mei et al., 2021; Wang et al., 2020b). For example, Mei et al. (2021) also identified a significant and positive correlation for PFASs between the root concentration factor (RCF) and hydrophobicity ($\log K_{ow}$) under hydroponic conditions, whereas for PFCAs u-shaped relationships between the RCF and chain length were occasionally observed. Soil cultural experiments show no significant correlation between RCFs and hydrophobicity ($\log K_{ow}$) of PFASs. The translocation factor (ratio of concentration in aboveground tissues to that in roots) decreases with increasing chain length, regardless of whether plants were grown hydroponically or in soil. PFASs with a small molecular size and low hydrophobicity may be preferentially translocated. Furthermore, the translocation potential of branched isomers could be higher than those of linear isomers due to the higher hydrophilicity of branches isomers.

Similarly, Li et al. (2022b) recently compared the bioaccumulation pattern of PFASs among different plant species (e.g. cereals, vegetables and fruits) growing on contaminated soil. Among different kinds of vegetables, the BAFs for PFBA and PFOA in leafy vegetables were the highest, followed by fruit vegetables and root vegetables (see monitoring section B.4.2.6). BAFs for PFBA and PFHpA in cabbage were the highest, while high BAFs for PFPeA, PFHxA, and PFOA were found in sponge gourd, sweet pepper, and zucchini, respectively.

Based on the large variety in chemical structure and physico-chemical properties of the different PFASs their uptake, distribution and accumulation in plants varies widely. For instance, at the tissue level, PFOA and PFOS are transported from the nutrient solution to the plant root cortex via both apoplastic and symplastic route (Li et al., 2022b). At the cellular level, PFOA and PFOS were accumulated in cell walls, various root cell organelles (e.g. Golgi apparatus, cytoplasm, cell nucleus, and chondriosome), and intercellular space in the cortex (Li et al., 2022b). Generally, the accumulated short-chain PFASs (e.g. PFBA, PFPeA, PFHxA, PFBS) were more concentrated in the vegetative compartments than in the storage organs with $\text{TF}_{\text{shoot/root}}$ higher than unity (Lechner and Knapp, 2011). The root may be the main organ for bioaccumulation of other PFASs with $\text{TF}_{\text{shoot/root}}$ lower than unity (Costello and Lee, 2020). Further information on the translocation and bioaccumulation principles of PFASs in plants can be found from Zhou et al. (2021).

Recent research on exposure routes, bioaccumulation and toxic effects of PFASs on plants shows that bioaccumulation of PFASs in plants from contaminated sites varied extremely (review by Li et al. (2022b)). The reported log BAF values in the review by Li et al. (2022b) range in general between 0 and 1 indicating potential to transfer from soil to plant. High accumulation of some PFASs is indicated also by the study by Blaine et al. (2013), where the accumulation of PFCAs (C5-C10) and PFSAs (C4, C6, C7, C8, C10) was investigated in lettuce and tomato grown on biosolid-amended soils. The reported BAFs (lettuce, municipal soil) in this study ranged between 0.19 – 28.4 and BAFs (lettuce, industrially impacted soil) between 0.52 – 56.8 ($\text{C}_{10} \text{ PFDS} < \text{LOQ}$). The greatest accumulation was seen for C4 PFCA. Another study with plants from biosolid-amended fields reports the highest accumulation factor among all measured PFASs (PFCAs, PFSAs, FTOHs) for PFHxA, with a

grass/soil accumulation factor of 3.8 (Yoo et al., 2011). Accumulation potential decreased logarithmically with increasing chain length.

Furthermore, root and leaf BCFs have been studied for several perfluoroalkyl carboxylic acids (PFCAs) and perfluoroalkane sulfonic acids (PFSA) in two aquatic plant species, including one submerged species (*Echinodorus horemanii*) and one free-floating species (*Eichhornia crassipes*) (Pi et al., 2017). Long-chain perfluorotetradecanoic acid (PFTeDA, 12 C) and per-fluorotridecanoic acid (PFTrDA, 13C) exhibited whole-plant BCFs of 865 and 1 280 L/kg, respectively, while lower BCF values were observed for PFASs with the perfluoroalkyl chain length below 9.

The enrichment of HFPO-DA (substance of the group of perfluoro alkyl ethers) in plants has also been discussed in the support document for identification of HFPO-DA as a SVHC (ECHA, 2019d). It was summarized that HFPO-DA may enrich more strongly in plants than PFOA and may be more comparable to short-chain PFCAs. Due to the uptake observed in vegetables and fruits, consumption of these by humans and wildlife may contribute to the total exposure to HFPO-DA. The distribution of five selected PFAS-ether (HFPO-DA, ADONA, PFMOPrA, PFMOBA, F-53B) in longhair sedge was investigated by Zhang et al. (2021). All PFAS-ether were taken up by plant roots and translocated to shoot. The highest translocation factor was observed for HFPO-DA. Only F-53B had a translocation factor <1. Which was explained by the relatively higher hydrophobicity and lipophilicity compared to the other PFAS-ether.

A recent work on temporal trends of TFA describes for the first time the concentrations and temporal trends of TFA in biota by analyzing archived leaf samples of various tree species from the German Environmental Specimen Bank (observation period: 1989–2020). It is shown that due to its physicochemical properties, TFA can be efficiently taken up and accumulated by vascular plants. A statistically significant positive trend in the TFA concentration within the study period was found for most species/sites, which is likely the result of both bioaccumulation as well as increasing emissions of gaseous TFA precursors over the last three decades (UBA, 2021b).

The environmentally relevant concentrations of PFASs rarely lead to obvious phenotypic/physiological damages in plants, but markedly perturb some biological activities at biochemical and molecular scales (review by Li et al. (2022b)). PFAS exposure induces the over-generated reactive oxygen species and further damages plant cell structure and organelle functions. A number of biochemical activities in plant cells are perturbed, such as photosynthesis, gene expression, protein synthesis, carbon and nitrogen metabolisms.

Conclusion: Studies on accumulation of PFASs in plants are lacking for the majority of PFASs. However, several studies provide evidence that plants accumulate many PFASs to levels which exceed the expected levels based on equilibrium partitioning. Laboratory tests and field data indicate that short-chain PFASs accumulate in above-ground plant parts, while long-chain PFASs accumulate in roots and show lower translocation factors to the above-ground plant parts. This is influenced by the higher water solubility, lower molecular size and lower hydrophobicity of the short-chain PFASs. The transfer rates of PFASs decrease from roots to leaves to fruits, due to natural barriers within the plants. Most of the laboratory studies focused on PFCAs and PFSA but enrichment in plants was also investigated for other PFASs like diPAPs, FTOHs, fluorotelomer sulfonic acids, perfluoroalkyl phosphinic acids or perfluoro alkyl ethers. The reviewed laboratory studies suggest that bioaccumulation factors (BAFs) depend on the hydrophobicity of the PFASs and are higher for vegetative plant parts than for reproductive and storage organs. Root-BAFs either increase with increasing chain length or show a u-shaped dependency with minima for C6 or C7 PFAAs. Based on the various chemical structures and associated physico-chemical properties of different PFASs, their accumulation behaviour varies considerably. Particularly 6:2 Cl-PFESA has been shown to accumulate in plants but studies on accumulation of PFASs in plants are generally lacking for the majority of subgroups. In summary, although it is

challenging to make a direct comparison among studies in the scientific literature due to differences in sampling and reporting, laboratory and field data indicate PFAS have the property to enrich in plants, but it remains unclear if all substances/subgroups may have this property as data are lacking for the majority of PFASs.

With regard to the measured levels of PFASs in plants it can be concluded that plants are widely exposed to PFASs. The exposures lead to enrichment and high concentrations of certain PFASs in different parts of the plants. Consumption of PFASs-contaminated agricultural and other plant products represents an efficient pathway for the trophic transfer of PFASs along food webs. Removal from the environment, decontamination and purification.

B.4.5. Removal from the environment, decontamination and purification

Clean-up of sites facing a PFAS contamination and remediation of historically contaminated sites can in certain cases mitigate the impact of these pollutions. A general description of these approaches, summary of case studies and their costs is provided in Annex E. Below, a high-level description of possible treatment approaches is provided.

The point of treatment of a PFAS contamination can be selected based on economic considerations. The investment in Euros spent per mass unit of PFAS removed is largest in the source area (see No. 1 in Figure B.66). The absolute PFAS mass removed is greater in the source area when comparing to groundwater extraction and subsequent treatment. Also, PFAS mass removed in the source area will not be available to support plume growth in groundwater. The point of treatment can also be based to protect a sensitive receptor such as a drinking water (domestic No. 9, commercial, or public No. 10). Here an end-of-pipe technology would treat the PFAS-impacted and extracted groundwater to acceptable levels prior to use or distribution. Hydraulic control of a site could be critical to prevent contaminants to extend beyond the property boundary (No. 4). A series of extraction wells or a drainage wall/trench near the property boundary would ensure that PFAS-impacted groundwater does not extend beyond the property boundary by groundwater flow. The extraction well gallery or drainage would need to be installed perpendicular (as far as possible) to the groundwater flow direction and be long enough to cover the plume width. In most, if not all, cases, remediation of an entire PFAS-plume in groundwater is economically not viable since PFAS plumes are extremely large and, in comparison to other contaminants such as hydrocarbons or chlorinated solvents, they are a concern at very low concentrations.

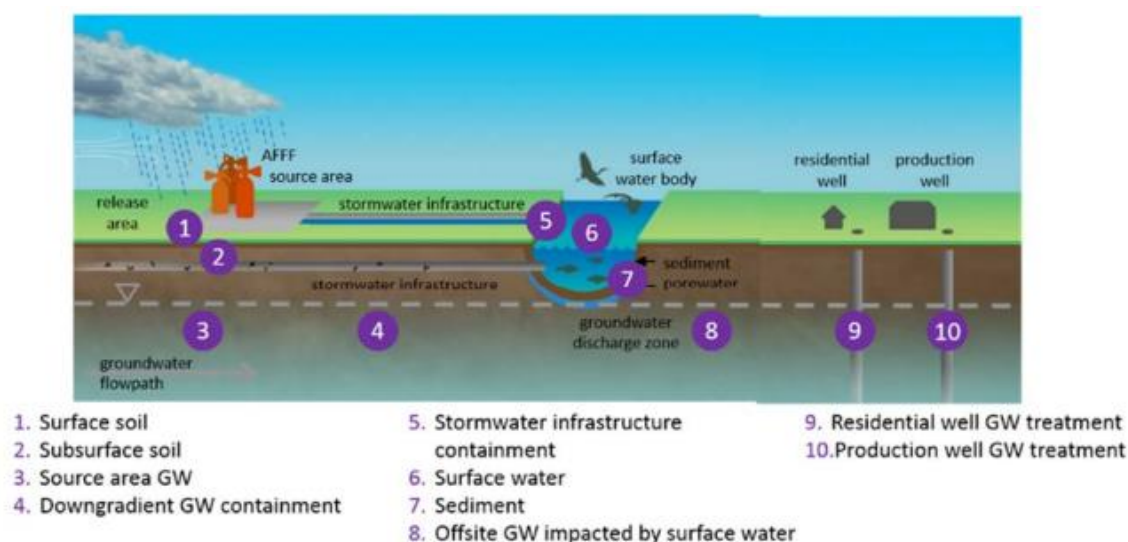


Figure B.66. Affected areas in contamination cases. Figure copied from Wood (2020a).

B.4.5.1. Source area treatment

Unsaturated and saturated soils are typically treated/remediated by means of excavation and disposal/incineration. Here the largest PFAS mass is typically removed from the subsurface in a short amount of time with high effectivity, efficiency and potentially long-lasting reduced environmental impact (depending on the end disposal route, e.g. if the leachate from the landfill is correctly collected and treated or if the incineration uses temperatures high enough to reliably destroy PFAS).

B.4.5.2. Hydraulic site control

To eliminate off-site migration of PFAS-contaminated groundwater, impacted groundwater is removed at the site boundary through one or more extraction wells or a drainage structure. The extraction process eliminates or greatly reduces the mass flux across the property line. While the hydraulic containment system is not able to recover PFAS-impacted groundwater that has already migrated to off-site areas, it can greatly reduce the potential impact on receptors that could be downgradient, including neighbouring properties or sensitive points of use such as private or public drinking water wells or agricultural use wells or surface water structures.

B.4.5.3. “End-of-pipe” treatment

In the event that PFAS-contaminated groundwater is removed for human use or consumption or for agricultural use, groundwater would need to be treated after extraction. Commercially available treatment technologies to recover PFAS from water include adsorption technologies such as granular activated carbon (GAC) or resins (regenerable and non-regenerable). Reverse osmosis can also be used to treat extracted groundwater.

Short-chain PFASs can be more resilient to some of these treatment technologies, so that more rigorous measures are required for effective treatment (e.g. a secondary treatment step using a resin that is optimised to retain the specific short-chain PFAS compounds, or higher temperature incineration). Different treatment options are discussed below.

B.4.5.4. Drinking water treatment

A recent review paper from Li et al. (2020b) on occurrence, impacts and treatment of shorter-chained PFCAs and PFSAAs concludes that:

- 1) shorter-chained PFCAs and PFSAAs are more widely detected, more persistent and mobile in aquatic systems, and thus may pose broader risks on the human and ecosystem health;
- 2) conventional adsorption, ion-exchange, and membrane filtration can remove short-chain PFASs, but are less effective than for the long-chain PFASs, and are challenged with poor material regeneration efficiency and disposal of process waste residual;
- 3) thermolysis and sonolysis can achieve complete mineralization, but come with a high process cost;
- 4) direct photolysis, oxidation/reduction, photocatalysis, and electrochemical reaction may degrade short-chain PFASs following similar degradation pathways as long-chain PFASs, but at a slower rate, and photocatalytic processes appear most promising.

Overall, this review reveals an urgent need for developing more cost-effective treatment technologies for shorter-chained and less adsorptive PFASs in drinking water.

There is ongoing research concerning treatment options, either removal or degradation technics. For instance foam fractioning exploits the surfactant properties of some of the PFASs. Foam fractioning has been investigated for several PFCAs, PFSAAs, FTSAAs, FASAs, HFPO-DA, ADONA, PFECHS in a pilot-scale foam fractionation system which was used for a landfill leachate (Smith et al., 2022).

One research project investigated the PFCA decarboxylation in polar aprotic solvents. Results show that reactive perfluoroalkyl ion intermediates were produced that degraded to fluoride ions (78 to ~100%) within 24 hours under relatively mild conditions (80 bis 120 °C). It has to be noted though that the experiment was so far only conducted under Lab conditions with a pure PFCA solution and that during the treatment als TFA was formed (Trang et al., 2022).

B.4.5.5. Conventional water treatment

Conventional and advanced water treatment processes cannot remove PFCAs and PFSA (coagulation/flocculation/sedimentation, raw and settled water ozonation, BAC filtration, and disinfection by medium-pressure UV lamps and free chlorine) (Appleman et al., 2014; Eschauzier et al., 2012; Quinones and Snyder, 2009; Rahman et al., 2014; Shivakoti et al., 2010).

PFECAs have been detected downstream of a PFAS manufacture site where they could not be removed from drinking water by conventional and advanced water treatment processes (raw water, ozonation, coagulation/flocculation/sedimentation, settled water ozonation, biological activated carbon (BAC) filtration, and disinfection by medium-pressure UV lamps and free chlorine (Sun et al., 2016). No removal was either observed in a study by Hopkins et al. (2018) by conventional surface water treatment processes (coagulation, flocculation, sedimentation, filtration, disinfection with free chlorine), neither by several advanced water treatment processes, including raw and settled water ozonation, biofiltration, and disinfection with medium-pressure ultraviolet (UV) lamps.

There is little information on the occurrence of PFPAs in water and the effectiveness of water treatment process on their removal. C8-PFPA (1.1–25 ng/L) and C10-PFPA (8.2–23 ng/L) have been detected in tap water from Spain and C10-PFPA (10 ng/L) in one sample in Germany (Llorca et al., 2012a); which suggests that conventional water treatment processes are not able to remove PFPAs from water.

B.4.5.6. Water treatment with powdered activated carbon (PAC) filters

Longer chained PFCAs and longer chained PFSA can be removed with powdered activated carbon (PAC) filters, with higher removal efficiency for PFSA compared to PFCA analogues (Eschauzier et al., 2012; Rahman et al., 2014; Sun et al., 2016).

Sun et al. (2016) performed adsorption experiment with (PAC) in a batch reactor using water samples contaminated with PFECAs, downstream a fluorochemical plant. The PAC achieved a 95% removal for PFO4DA ($C_6HF_{11}O_6$), 54% for PFO3OA ($C_5HF_9O_5$) and less than 40% for PFMOAA ($C_3HF_5O_3$), PFMOPrA ($C_4HF_7O_3$), PFOMBA ($C_5HF_9O_3$), PFPrOPrA (GenX $C_6HF_{11}O_3$) and PFO2HxA ($C_4HF_7O_4$).

PFECAs exhibited adsorbabilities to PAC lower than those of PFCAs and PFSA of the same chain length (calculated as the sum of carbon, ether oxygen and sulphur atoms), (e.g. PFMOBA < PFHxA and GenX < PFOA), suggesting that the replacement of a CF₂ group with an ether oxygen atom decreases the affinity of PFASs for PAC (Sun et al., 2016).

SC-PFAAs (and C7-PFCA) cannot be effectively removed by granular activated carbon (GAC) or PAC filters (Eschauzier et al., 2012; Rahman et al., 2014; Zaggia et al., 2016).

As the decrease in chain length for PFAAs leads to an increase in water solubility and decrease in sorption potential (section B.4.2.1), it can be assumed that the more hydrophilic SC-PFAAs, including SC-PFESAs, SC-PFECAs and SC-PFPAs cannot be effectively removed from drinking water in routine applications by granular activated carbon (GAC) or powdered activated carbon (PAC) filtration. Less efficiency of removal is expected for PFAAs with carboxylic acids groups (PFCAs and PFECAs) compared to sulfonic acids groups (PFSA and PFESAs) or phosphonic groups (PFPAs) due to their lower sorption potential and higher water solubility (section 1.1.4.4. of the main report).

B.4.5.7. Water treatment with ion exchange resins

Longer chained PFAAs can be removed with ion exchange resins, higher removal efficiency is achieved for PFSA compared to PFCAs analogues (Appleman et al., 2014; Rahman et al., 2014). In a full-scale treatment plant, iron infused AIX resin that was designed for

arsenic removal (5-9 months old) was able to remove C4-PFSA (81%) and partially remove C7-PFCA (46%) and C8-PFCA (75%) but not C4-PFCA (Appleman et al., 2014).

Removal of C4-PFCA and C4-PFSA with GAC and PAC filters and anion exchange resins has also been reported in pilot-scale column experiments (Rahman et al., 2014; Zaggia et al., 2016), but with extremely premature breakthroughs (<3 months) that make these solutions not practicable for routine applications.

When selecting an ion exchange resin, regeneration issues (e.g. loss of saturation capacity after regeneration) can be as important as the removal capacities of the resin (Rahman et al., 2014; Zaggia et al., 2016).

High-pressure membranes (high pressure nanofiltration and reverse osmosis) have shown to be effective (>90% removal efficiency) removing PFAAs ($\geq$ C4 PFSA and $\geq$ C4 PFCA from water) in bench- (Appleman et al., 2013) and full-scale studies (Appleman et al., 2014; Thompson et al., 2011). High efficiency of removal could also be expected for PFECAs and PFESAs (Hopkins et al., 2018). The disposal of concentrate, which will contain elevated concentrations of PFASs, will need to be addressed.

To summarise, the properties of especially the most stable PFASs resulting from the degradation of other PFASs in the environment, are such that render water treatment very difficult hence increasing the technical demands (and costs) of the treatment of water obtained for drinking water, process water and household water uses. The increasing number of findings of PFASs in surface waters, groundwaters and drinking water (see section B.4.2.1.3) demonstrates the need for purification of drinking water. EurEau (2022) has also assessed the purification methods for water suppliers and concludes that PFASs should be managed at their source due to the challenges in the water supply.

B.4.5.8. Wastewater treatment

Several studies showed that conventional wastewater treatment has a limited efficiency in removing both, short-chain and long-chain PFCAs and PFSA from aqueous waste streams. Shorter-chained and longer-chained PFCAs and PFSA accumulate in sludge and are released to receiving waters via WWTP effluents (Arvaniti and Stasinakis, 2015; Bossi et al., 2008; Eriksson et al., 2017b).

Shorter-chained and longer-chained PFCAs are generally found in higher concentrations in the effluent water than the influent water (Bossi et al., 2008; Eriksson et al., 2017b); Sinclair and Kannan (2006), which indicates that they are hard to remove from water during wastewater treatment process and that precursor PFASs can degrade into PFCAs and PFSA during the wastewater treatment.

Several PFCAs precursors (FTSAs, FTCA/FTUCA, diPAP) were found in lower concentration in the effluent water than the influent water of three WWTP in Sweden (Eriksson et al., 2017b), which, together with the calculated increase in the daily discharge of PFCAs (effluent and sludge) compared with the daily incoming amount in the influent water indicates that PFCA precursors can potentially degraded to PFCAs during wastewater treatment process.

More than 75% of the PFASs detected in sludge from 3 WWTP in Sweden were precursor compounds and intermediates to PFAAs (FTSAs, FTCAs, FTUCAs, diPAP, monoPAP; (Eriksson et al., 2017b).

The formation of PFAAs from precursors in WWTP is dependent on process temperature and treatment type, with higher rates of formation in biological WWTP (during the aerobic biological step) at longer hydraulic retention times and higher temperatures (Guerra et al., 2014). Care should be taken when comparing concentration of PFASs measured in the waste streams between WWTPs, due to the effect of the treatment process and the specific

sampling strategies (e.g. sampling at high or low flow periods and seasonal effects (Guerra et al., 2014; Sinclair and Kannan, 2006).

PFPAs with short perfluoroalkyl chains ($\leq C6$) are expected to combine high water solubility and low sorption to organic matter, therefore there will be hardly removed from water in WWTP. However, sorption is expected increase with increasing chain length PFAAs (Wang et al., 2016b); see section 1.1.1.4. of the main report), with larger fraction of the shorter-chained PFPAs partitioning into the sludge.

The adsorption of shorter-chained PFAAs in sludge has been observed to increase with increasing chain length (increase in distribution coefficient between influent water and sludge; (Eriksson et al., 2017b) which can be explained by increasing hydrophobicity of the molecules (Zhang et al., 2013a). However, for shorter-chained PFAAs, the electrostatic interactions between the anionic functional group and the sludge are expected to play a more important role than hydrophobic interactions (Zhang et al., 2013a) .

Higher solid-liquid distribution coefficients have been observed in WWTPs for PFOS compared to PFOA (Eriksson et al., 2017b; Guerra et al., 2014) and laboratory incubation (Zhang et al., 2013a), which can be explained due to the stronger hydrophobic properties of the sulfonic analogues. The lower distribution coefficient of PFHxS compared to PFHxA in sludge from a WWTP observed by Eriksson et al. (2017b) could be due to the higher formation of PFHxA from precursors in the sludge.

Municipal WWTPs are not able to effectively remove shorter-chained or longer-chained PFAAs and the discharge of municipal sewage water is a significant source of PFAAs to the aquatic environment (Becker et al., 2008; Filipovic et al., 2015; Loos et al., 2013). In addition, the disposal of the sludge from industrial and municipal WWTPs can also be a significant source of PFAAs to the terrestrial environment (Eriksson et al., 2017b; Gomez-Canela et al., 2012; Washington et al., 2010).

B.4.5.9. Remediation of contaminated sites

Leaching of PFASs to groundwater from contaminated soils can be reduced by sorbent amendment using activated carbon (94 and 99.9% PFOS reduction), compost soil (29 and 34% PFOS reduction) and montmorillonite (28 and 40% PFOS reduction) (Hale et al., 2017). However, an assessment of the suitability of the method for field application with higher PFAS concentrations and different PFASs is still required.

B.5. Human health hazard assessment

The majority of available data on human health effects address the toxicity of PFAAs (mainly PFCAs and PFSAs; in particular PFOA and PFOS), while less or no data are available for other PFAS groups. For the vast majority of PFASs (estimated >99%), no data on repeated-dose toxicity, carcinogenicity, or reproductive toxicity is available.

Existing recent literature reviews and assessments were explored (ATSDR, 2021; EFSA, 2020; EPA-US, 2021b; Fenton et al., 2021; NTP, 2016a; PFAS-TOX-DATABASE, 2021; Rice et al., 2021; Zeng et al., 2021) to identify the main types of effects of PFASs. Besides literature reviews and assessment reports, also registration data from the ECHA dissemination site and IUCLID were screened and available information used for the assessment. In addition, information from literature searches was included (Embase, Medline, Web of Science, PubMed, Scifinder). The literature searches were performed in 2021 to identify published data with relevance to human health that has not been covered by recent reviews. Search terms were selected based on EFSA (2020). Table B.13 lists the PFASs for which data have been reported in one or more of these reviews, assessments, and studies.

Table B.13. Non-exhaustive list of PFASs in assessed literature and study reports and examples for polymeric PFASs.

PFAS group	No. of C	PFAS	Abbreviation	CAS No	EC No
PFCAs	Perfluoroalkyl carboxylic acids / carboxylates				
	C2	Trifluoroacetic acid	TFA	76-05-1 2923-18-4 (Na ⁺ salt)	200-929-3 220-879-6
	C4	Perfluorobutanoic acid, Perfluorobutyric acid	PFBA	375-22-4 10495-86-0 (NH ₄ ⁺ salt)	206-786-3 -
	C5	Perfluoropentanoic acid	PFPeA	2706-90-3	220-300-7
	C6	Perfluorohexanoic acid	PFHxA	307-24-4 2923-26-4 (Na ⁺ salt) 21615-47-4 (NH ₄ ⁺ salt)	206-196-6 220-881-7 244-479-6
	C7	Perfluoroheptanoic acid	PFHpA	375-85-9 20109-59-5 (Na ⁺ salt)	206-798-9 243-518-4
	C8	Perfluorooctanoic acid	PFOA APFO	335-67-1 3825-26-1 (NH ₄ ⁺ salt)	206-397-9 223-320-4
	C9	Perfluorononanoic acid	PFNA	375-95-1 4149-60-4 (NH ₄ ⁺ salt)	206-801-3 -

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

PFAS group	No. of C	PFAS	Abbreviation	CAS No	EC No
	C10	Perfluorodecanoic acid	PFDA	335-76-2 3108-42-7 (NH ₄ ⁺ salt)	206-400-3 221-470-5
	C11	Perfluoroundecanoic acid	PFUnDA	2058-94-8	218-165-4
	C12	Perfluorododecanoic acid	PFDoDA	307-55-1	206-203-2
	C13	Perfluorotridecanoic acid	PFTTrDA	72629-94-8	276-745-2
	C14	Perfluorotetradecanoic acid	PFTeDA	376-06-7	206-803-4
	C16	Perfluorohexadecanoic acid	PFHxDA	67905-19-5	267-638-1
	C18	Perfluorooctadecanoic acid	PFODA	16517-11-6	240-582-5
PFSAs	Perfluoroalkane sulfonic acids / sulfonates				
	C1	Trifluoromethanesulfonic acid	TFMS	1493-13-6 2926-27-4 (K ⁺ -salt)	216-087-5 608-334-4
	C4	Perfluorobutane sulfonic acid	PFBS	375-73-5 29420-49-3 (K ⁺ -salt)	206-793-1 249-616-3
	C5	Perfluoropentane sulfonic acid	PFPeS	2706-91-4	220-301-2
	C6	Perfluorohexane sulfonic acid	PFHxS	355-46-4 3871-99-6 (K ⁺ -salt)	206-587-1 223-393-2
	C7	Perfluoroheptane sulfonic acid	PFHpS	375-92-8	206-800-8
	C8	Perfluorooctane sulfonic acid	PFOS	1763-23-1 2795-39-3 (K ⁺ -salt)	217-179-8 220-527-1
	C9	Perfluorononane sulfonic acid	PFNS	68259-12-1	-
	C10	Perfluorodecane sulfonic acid	PFDS	335-77-3	206-401-9
PFSIAs	Perfluoroalkane sulfinic acids				
	C8	Perfluorooctane sulfinic acid	PFOSI	647-29-0	-
PFPIAs	Perfluoroalkyl phosphinic acids				
		C6/C8 Perfluoroalkyl phosphinic acids	C6/C8 PFPIA	610800-34-5	-
		C8/C8 Perfluoroalkyl phosphinic acids	C8/C8 PFPIA	40143-79-1	-
		C6/C12 Perfluoroalkyl phosphinic acids	C6/C12 PFPIA	1240600-	-

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

PFAS group	No. of C	PFAS	Abbreviation	CAS No	EC No
				41-2	
		C8/C10 Perfluoroalkyl phosphinic acids	C8/C10 PFPiA	500776-81-8	-
PFECAs		Perfluoroalkyl ether carboxylic acids			
		Hexafluoropropylene oxide dimer acid	HFPO-DA, GenX	13252-13-6 62037-80-3 (NH ₄ ⁺ salt)	236-236-8 -
		Dodecafluoro-3H-4,8-dioxanonoic acid	DONA ADONA	- 958445-44-8 (NH ₄ ⁺ salt)	- 480-310-4
		2,3,3,3-tetrafluoro-2-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]propionic acid	HFPO-TA	13252-14-7	236-237-3
		Hexafluoropropylene oxide tetramer acid	HFPO-tetramer acid	65294-16-8	-
		Ammonium difluoro[1,1,2,2-tetrafluoro-2-(pentafluoroethoxy)ethoxy]acetate	EEA-NH ₄	908020-52-0 (NH ₄ ⁺ salt)	-
		Potassium 2-(3-trifluoromethoxy-1,1,2,2,3,3-hexafluoropropoxy)-2,3,3,3-tetrafluoropropionate	mv31 K ⁺	496805-64-2 (K ⁺ salt)	-
		Ammonium difluoro{[2,2,4,5-tetrafluoro-5-(trifluoromethoxy)-1,3-dioxolan-4-yl]oxy}acetate	F-DIOX	1190931-27-1 (NH ₄ ⁺ salt)	-
		Perfluoro-2-methoxypropanoic acid	PFMOPrA	13140-29-9	-
		Perfluoro-4-methoxybutanoic acid	PFMOBA	863090-89-5	-
		2,2,3,3,4,4-Hexafluoro-4-(nonafluorobutoxy)butanoic acid	4:4 C8 PFECA	174767-06-7	-
		2,2,4,4,6,6,8,8,10,10,12,12,14,14,14-Pentadecafluoro-3,5,7,9,11,13-hexaoxatetradecanoic acid	C8 Po-PFECA	39492-92-7	-
PFESAs		Perfluoroalkyl ether sulfonic acids			
		1,1,2,2,3,3,4,4-Octafluoro-4-(1,1,2,2,3,3,4,4,4-nonafluorobutoxy)-1-butanefulfonic acid	4:4 C8 PFESA	1237850-23-5	-
		4:2 chlorinated polyfluorinated ether sulfonic acid (2-(4-Chloro-1,1,2,2,3,3,4,4-octafluorobutoxy)-1,1,2,2-tetrafluoroethanesulfonic acid)	4:2 Cl-PFESA	737728-96-0	-
		6:2 chlorinated polyfluorinated ether sulfonic acid	6:2 Cl-PFESA	756426-58-1	-

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

PFAS group	No. of C	PFAS	Abbreviation	CAS No	EC No
		(2-[(6-Chloro-1,1,2,2,3,3,4,4,5,5,6,6-dodecafluorohexyl)oxy]-1,1,2,2-tetrafluoroethanesulfonic acid)			
		8:2 chlorinated polyfluorinated ether sulfonic acid (2-[(8-Chloro-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-hexadecafluorooctyl)oxy]-1,1,2,2-tetrafluoroethanesulfonic acid)	8:2 Cl-PFESA; PFESA-BP2, Nafion Byproduct 2	763051-92-9	-
		Mixture of 6:2 Cl-PFESA and 8:2 Cl-PFESA	F-53B	73606-19-6	-
		Perfluoroethylcyclohexane sulfonate	PFECHS	646-83-3; 335-24-0 (K ⁺ salt); 67584-42-3 (isomer to K ⁺ salt); 1135308-34-7 (isomer to K ⁺ salt)	-
PASFs		Perfluoroalkane sulfonyl fluorides			
		Perfluorooctanesulfonyl fluoride	POSF	307-35-7	206-200-6
n:2 FTOHs		n:2 Fluorotelomer alcohols			
		6:2 Fluorotelomer alcohol	6:2 FTOH	647-42-7	211-477-1
		8:2 Fluorotelomer alcohol	8:2 FTOH	678-39-7	211-648-0
n:2 FTSAs		n:2 Fluorotelomer sulfonic acids			
		6:2 Fluorotelomer sulfonic acid Ammonium Perfluorohexylethylsulfonate	6:2 FTSA	27619-97-2 59587-39-2 (NH ₄ ⁺ salt)	248-580-6
		8:2 Fluorotelomer sulfonic acid	8:2 FTSA	39108-34-4	254-295-8
n:2 PAPs		n:2 Polyfluoroalkyl phosphoric acid esters (PAPs)			
		8:2 Fluorotelomer phosphate monoester	8:2 monoPAP	57678-03-2	-
		8:2 Fluorotelomer phosphate diester	8:2 diPAP	678-41-1	211-649-6
FASAs		Perfluoroalkane sulfonamides			
		Perfluorooctane sulfonamide	PFOSA, FOSA	754-91-6	212-046-0
		N-ethyl perfluorooctane sulfonamide	EtFOSA	4151-50-	223-980-

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

PFAS group	No. of C	PFAS	Abbreviation	CAS No	EC No
				2	3
		N-Methyl perfluorooctane sulfonamidoacetic acid	(N)MeFOSAA, Me-PFOSA-AcOH	2355-31-9	-
		N-Ethyl perfluorooctane sulfonamidoacetic acid	(N)EtFOSAA, Et-PFOSA-AcOH	2991-50-6	221-061-1
		N-ethyl perfluorooctanesulfonamidoethanol	EtFOSE	1691-99-2	216-887-4
SAmPAPs	Perfluoroalkane sulfonamidoethanol phosphate esters				
		Ammonium bis[2-[N-ethyl (heptadecafluorooctane) sulfonylamino]ethyl]phosphate	FC-807	30381-98-7	250-166-5
PFE alkanes	Perfluoroether alkanes				
		A 3:1 mixture of perfluoro(5,8,9,12-tetramethyl-4,7,10,13-tetraoxahexadecane) and perfluoro(5,6,9,12-tetramethyl-4,7,10,13-tetraoxahexadecane)	Hostinert 216	-	403-050-5 (3:1-mixture of 404-710-5 and 404-730-4)
PFE alkenes	Perfluoroether alkenes				
		1,1,2-Trifluoro-2-(trifluoromethoxy)ethene	PMVE	1187-93-5	214-703-7
		1,1,1,2,2,3,3-heptafluoro-3-[(trifluorovinyl)oxy]propane perfluoropropylvinylether	PPVE	1623-05-8	216-600-2
		1,1,2-Trifluoro-2-(pentafluoroethoxy)ethene	PEVE	10493-43-3	234-018-7
		1,1,2,2,3,3-hexafluoro-1-trifluoromethoxy-3-trifluorovinylxyloxypropane	Mv31	40573-09-9	442-390-9
		1-[difluoro(trifluoromethoxy)methoxy]-1,2,2-trifluoroethylene	Move3	700874-87-9	-
		Hexafluoropropylene	HFO-1216	116-15-4	204-127-4
Other PFEAS	Other ether-based PFASs				
		2,2,3,3,5,5,6,6-octafluoro-4-(trifluoromethyl)morpholine	FC-3284; PF-5052	382-28-5	206-841-1
		1-[3-[4-((heptadecafluorononyl)oxy)-benzamido]propyl]-N,N,N-trimethylammonium iodide	PF-310	59493-72-0	407-400-8
		1-[2-(2,4-Dichlorophenyl)-3-(1,1,2,2-tetrafluoroethoxy)propyl]-1H-1,2,4-triazole	Tetraconazole	112281-77-3	407-760-6
		reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine	FC-████	██████-61-2	473-390-7

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

PFAS group	No. of C	PFAS	Abbreviation	CAS No	EC No
		and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine			
		1-[3,5-dichloro-2-fluoro-4-(1,1,2,3,3,3-hexafluoropropoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	Noviflumuron	121451-02-3	-
		2,3,3,4,4-pentafluoro-2,5-bis(1,1,1,2,3,3,3-heptafluoropropan-2-yl)-5-methoxytetrahydrofuran	-	957209-18-6	-
HFCs	Hydrofluorocarbons				
	C2	Pentafluoroethane	HFC-125	354-33-6	206-557-8
		1,1,1,2-Tetrafluoroethane	HFC-134a; Norflurane	811-97-2	212-377-0
		1,1,1,2,3,3,3-heptafluoropropane	HFC-227ea	431-89-0	207-079-2
		1,1,1,3,3,3-hexafluoropropane	HFC-236fa	690-39-1	425-320-1
		1,1,1,2,3,3-hexafluoropropane	HFC-236ea	431-63-0	207-076-6
		reaction mass of (R, R)-1,1,1,2,2,3,4,5,5,5-decafluoropentane and (S, S)-1,1,1,2,2,3,4,5,5,5-decafluoropentane	HFC-4310mee	142347-07-7; 138495-42-8	420-640-8; -
		1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorohexane	HFC-5213	355-37-3	206-581-9
		1,1,1-trifluoroethane	HFC-143a	420-46-2	206-996-5
		1,1,1,3,3-pentafluoropropane	HFC-245fa	460-73-1	419-170-6
		1,1,1,3,3-pentafluorobutane	HFC-365mfc	406-58-6	430-250-1
		1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorooctane	HFC-7613; C6-ethane	80793-17-5	-
		1,1,2,2,3,3,4-heptafluorocyclopentane	HFCPA; ZEORORA	15290-77-4	430-710-1
HFEs	Hydrofluoroethers				
		1,1,1,2,2,3,3,4,4-Nonfluoro-4-methoxybutane - 2-[difluoro(methoxy)methyl]-1,1,1,2,3,3,3-heptafluoropropane (1:1)	HFE-7100	-	422-270-2
		1-ethoxy-1,1,2,2,3,3,4,4,4-nonafluorobutane; reaction mass of: 1-ethoxy-1,1,2,3,3,3-hexafluoro-2-(trifluoromethyl)propane	HFE-7200	-	425-340-0
		1,1,1,2,2,3,4,5,5,5-Decafluoro-3-methoxy-4-(trifluoromethyl)pentane	HFE-7300	132182-92-4	459-520-5
		3-Ethoxyperfluoro(2-methyl)hexane	HFE-7500	297730-93-9	435-790-1
		3-(Difluoromethoxy)-1,1,2,2-tetrafluoropropane	HFE-356pcf3	35042-99-0	-

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

PFAS group	No. of C	PFAS	Abbreviation	CAS No	EC No
			Sevoflurane	28523-86-6	-
HFOs		Hydrofluoroolefins			
		2,3,3,3-Tetrafluoro-1-propene	HFO-1234yf	754-12-1	468-710-7
		3,3,3-trifluoropropene	HFO-1243zf	677-21-4	211-637-0
		(1E)-1,3,3,3-Tetrafluoro-1-propene	HFO-1234ze(E)	1645-83-6	471-480-0
		(2Z)-1,1,1,4,4,4-Hexafluoro-2-butene	HFO-1336mzz(Z)	692-49-9	-
		(2E)-1,1,1,4,4,4-Hexafluoro-2-butene	HFO-1336mzz(E)	66711-86-2	-
		1,1-difluoroethene	HFO-1132a; Vinylidenfluoride	75-38-7	200-867-7
TFA PRECURSOR					
		2,2,2-Trifluoroethanol	-	75-89-8	200-913-6
Oligomeric and polymeric PFASs					
		Polychlorotrifluoroethylene	PCTFE	9002-83-9	-
		Polytetrafluoroethylene	PTFE	9002-84-0	-
		Polyvinylidene fluoride	PVDF	24937-79-9	-
		Perfluoropolyether	PFPE	69991-67-9	-
		fluorotelomer-based acrylate polymer	-	-	-
		fluorotelomer-based urethane polymer	-	-	-

i.p. = in particular

From these reviews, assessments, and experimental data (peer-reviewed publications as well as study reports from industry), it can be inferred that exposure to PFASs can result in various health effects. The strength of evidence is not the same for all effects and all PFASs, given that not all endpoints and all PFASs have been studied extensively. EFSA (2018) and EFSA (2020) reviewed the epidemiological evidence for association between PFAS exposure and adverse effects in humans. Most of the available information covers PFOS and PFOA, but information was also available for other PFASs, in particular for PFCAs and PFSAAs. Based on human data, EFSA concluded that there is sufficient evidence for an association between serum levels of at least PFOS and PFOA and a reduction in antibody response after vaccination, increased serum cholesterol, increased serum alanine transferase (ALT) and reduced birth weight. There was also some evidence to suggest associations with increased propensity of infections. For other outcomes investigated, there was insufficient evidence to conclude such associations. EFSA selected effects on the immune system as the critical effect in both experimental animals and humans, and derived the TWI for four PFASs based on a human study (EFSA, 2020).

For PFOS, PFOA, PFNA, PFDA, and PFHpA and their salts, sufficient data for harmonised classifications for carcinogenicity (Carc. 2, except PFHpA), reproductive toxicity (Repr. 1B), effects on or via lactation (Lact., except PFHpA) and STOT RE 1 (except for PFDA) are available, see Table B.2. A harmonised classification has recently also been agreed on by RAC for 6:2 FTOH (STOT RE 2), which awaits official publication (ECHA, 2021b).

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Despite a lack of harmonised classification, available studies indicate similar concerns for some other PFASs. Of note, HFPO-DA, POSF, 6:2 FTSA and 8:2 FTSA have self-classifications for STOT RE, and POSF as well for reproductive toxicity. Of further note, and supporting evidence for similarities in the toxicity profile, is that several other PFAAs and PFAA precursors have self-classifications for Carc., Repr., Lact. and STOT RE (see Table B.2 and Table B.3).

A summary of the human health concerns from the available information is presented in the sections below. The Dossier Submitters applied a qualitative approach for the description of human health concerns with focus on endpoints considered most relevant for long-term exposure: repeated-dose toxicity (with targets most consistently affected by PFASs in experimental animals: liver, kidney, thyroid, immune system, and serum lipids), carcinogenicity, and toxicity to reproduction. The endpoints acute toxicity, irritation, corrosiveness, and sensitisation are not considered relevant for the human health risk assessment of this restriction proposal for PFASs. Mutagenic effects are reported only for a minority of PFASs; and hence, this endpoint is also not considered further for the PFAS hazard assessment. An update of epidemiological data not included in the EFSA 2020 scientific opinion is presented in B.5.3. The following sections only include statements for substances which were screened to date.

B.5.1. Toxicokinetics/ADME (absorption, metabolism, distribution and elimination)

B.5.1.1. Toxicokinetics/ADME of non-polymeric PFASs

The current state of knowledge on toxicokinetics of numerous and structurally diverse PFASs relies on studies with considerable heterogeneity. Existing data have recently been thoroughly reviewed for PFCAs and PFSA, and some precursors (ATSDR, 2021; EFSA, 2020; Fenton et al., 2021; Pizzurro et al., 2019), and for PFECAs (Rice et al., 2021) and is summarised below. Also, updated literature searches for these compounds as well as for PFASs not included in the scopes of these reviews have been performed and additional ADME data has been identified. Inter-species differences in toxicokinetics, in particular tissue distribution and elimination, should be taken into account when extrapolating animal data to human health (Pizzurro et al., 2019).

B.5.1.1.1. Absorption

EFSA (2020) and ATSDR (2021) have concluded that based on both experimental animal studies and human studies a range of PFASs and in particular PFCAs and PFSA are readily absorbed upon oral exposure. PFASs are also absorbed via inhalation and dermal contact, but no quantitative estimates are currently available (ATSDR, 2021).

Experimental animals

Data on absorption after oral exposure in rats, mice and monkeys are available for several PFASs, e.g. PFCAs (PFBA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTeDA), for some PFSA (PFBS, PFHxS, PFOS), for two PFECAs (HFPO-DA, ADONA). Fractional absorption ranges from >50% for PFBS to >95% for PFHxS, PFOA, PFBA, PFNA, PFDA, PFUnDA, and PFDoDA (ATSDR, 2021). PFPA and PFPIA are also absorbed into the bloodstream of rats, even high molecular weight compounds such as C6/C12 PFPIA and C8/C10 PFPIA (1002 amu) (D'Eon and Mabury, 2010; Joudan et al., 2017). Absorption half-lives were 2.7 ± 0.5 h for C6/C8 PFPIA, 2.1 ± 1.2 h for C8 PFPA, and 1.3 ± 0.4 h for C8/C8 PFPIA (Joudan et al., 2017). The fluorotelomer alcohol 8:2 FTOH is rapidly absorbed at rates of 27-57% in rats (EFSA, 2020). Also for Noviflumuron (a complex ether-based PFAS) high absorption rates of 74-93% of the orally administered dose have been reported in rats (TERC, 2003).

PFASs can also be absorbed via inhalation (evidence for PFOA in rats) or dermal contact (evidence for PFBA, PFOA, and PFOS in rabbits and rodents), but no quantitative estimates on the fractional absorption in animals were identified (ATSDR, 2021; Weatherly et al., 2021).

Humans

EFSA (2020) concluded that based on observations of elevated levels of PFCAs and PFSA in humans exposed to contaminated water the gastrointestinal absorption of these PFASs occurs to a significant degree. For example, adults exposed to specific PFASs via contaminated drinking water in Italy and Sweden had elevated serum concentrations of PFOA, PFOS and PFHxA when compared to the general population (Ingelido et al., 2018; Shi et al., 2016). Furthermore, elevated concentrations of 6:2 Cl-PFESA and 8:2 Cl-PFESA were observed in high fish consumers from China, indicating high oral absorption also of these two replacement PFASs (Shi et al., 2016), demonstrating similarities to already restricted PFASs such as PFOA and PFOS. Data on blood concentrations of a range of PFASs are described in detail in section B.9.21.

Absorption by inhalation and dermal contact is also based on indirect evidence. For example, in adults occupationally exposed to PFASs during fluorochemical production (primarily exposure via inhalation), elevated blood concentrations were observed, with

median PFOA, PFOS and PFHxS concentrations in the range 500 – 7 000 ng/mL (Fromme et al., 2009; Olsen, 2015). Also, studies on professional ski waxers reported elevated blood concentrations of a range of PFCAs (Freberg et al., 2010; Nilsson et al., 2013b; Nilsson et al., 2010b), probably because of inhalation of very high levels of PFASs measured in air in waxing cabins (Nilsson et al., 2010a).

Fluorinated gases are absorbed via inhalation at low rates. For HFCs, HFC-134a, HFC-143a, HFC-152a, HFC-145fa (Ernstgård et al., 2009; Ernstgård et al., 2012a; Gunnare et al., 2006; Gunnare et al., 2007) absorption rates from these studies have been summarised to be <4% (Ernstgård et al., 2012b).

B.5.1.1.2. Distribution

As concluded by EFSA (2020) and ATSDR (2021), and based on data from both animal and human studies, PFCAs and PFASs are distributed widely in the body and the highest concentrations have been observed in the protein-rich tissues liver, kidneys, and blood. Similar distribution patterns have been reported for some other PFASs, while different patterns have also been shown for certain PFASs.

PFAS protein binding in different animal species is detailed in B.4.2.9. PFCAs and PFASs bind in particular to serum albumin and some intracellular proteins including liver fatty acid binding protein (L-FABP) with implications for blood and tissue distribution.

Experimental animals

For ADONA (Rice et al., 2021), PFPAs and PFPIAs (D'Eon and Mabury, 2010; Joudan et al., 2017), wide distribution to protein-rich tissues have been observed, similar to the distribution of PFCAs and PFASs (ATSDR, 2021; EFSA, 2020). 8:2 FTOH distributes rapidly to blood and tissues in rats with highest levels of 8:2 FTOH in fat, liver, thyroid and adrenals (EFSA, 2020; Fasano et al., 2006). Noviflumuron (a complex ether-based PFAS) is distributed to organs in the order of fat >> adrenal = skin > ovaries followed by spleen and liver (TERC, 2004). For Noviflumuron, there was only limited transplacental transfer in rats (TERC, 2005).

6:2 FTSA, but not 6:2 FTCA, was detected at high levels in serum and liver following repeated-dose exposure (Sheng et al., 2017), whereas 6:2 Cl-PFESA has been shown to distribute to serum, gut (Pan et al., 2019b) and liver (Pan et al., 2021). Similarly, sodium p-perfluorooctanesulfonate (OBS) distribute to mouse liver, but also to the gut (colon, ileum). At the highest dose, OBS was also detected in serum, kidney and faeces (Wang et al., 2019a).

In addition to organ distribution, PFCAs and PFASs can be distributed to breast milk and cross the placenta and can thus be transferred from the dams to the foetus, resulting in maternal excretion of these compounds (see B.5.1.1.4) and exposure of the foetus/infant (ATSDR, 2021; Bartels et al., 2020; EFSA, 2020).

Humans

In humans, very few studies on organ distribution have been published, likely because of limited sample availability. Levels of PFASs measured in human organs and other human samples relevant for distribution are presented in section B.9.22 on human biomonitoring and Appendix B.5.1.1.2..

In three studies of PFASs in human liver tissues, PFOS was the most abundant PFAS at mean levels ranging from 14 – 27 ng/g (Karrman et al., 2010; Maestri et al., 2006; Olsen et al., 2003). PFBA detected at high levels in lung autopsy tissue in Spain by Perez et al. (2013) (median value of 807 ng/g lung tissue). Abraham et al. (2021) questioned PFBA accumulation in lung tissue as they found low or non-detectable levels in lung autopsy

samples from France. This is more in line with what is expected based on low bioaccumulation potential and currently estimated short biological half-life of PFBA (Chang et al., 2008).

A study by Wang et al. (2018a) demonstrated that several PFASs can cross the cerebrospinal fluid barrier. Detectable levels were observed in more than half of the cerebrospinal fluid samples for PFOA, PFNA, PFDA, PFHxS, PFOS and 6:2 Cl-PFESA. These compounds were also the most prominent compounds in the serum samples. This study supports a previous study (Fujii et al., 2015) that show the presence of PFASs in cerebrospinal fluid, but at significantly lower concentrations than in serum presumably due to the blood brain barrier in adults.

PFASs can cross the blood-follicle barrier and the resulting concentration in follicular fluid indicates exposure to maturing oocytes that grow in the ovarian follicle. The median blood-follicle transfer efficiencies (ratio of follicular fluid:serum) of PFAAs measured in four different studies ranged from 0.47 (PFDoDA) to 1.04 (PFHxS) (Hallberg et al., 2021; Heffernan et al., 2018; Kang et al., 2020; McCoy et al., 2017). The follicle transfer efficiencies for Cl-PFESAs have been reported to be 0.73, 0.75 and 0.91 for 4:2 Cl-PFESA, 6:2 Cl-PFESA and 8:2 Cl-PFESA, respectively, demonstrating similar properties for replacement PFASs as for already restricted PFASs such as PFOS and PFOA (Kang et al., 2020). Other investigated PFASs, e.g. 4:4 C8 PFESA, 4:4 C8 PFECA, C8 Polyether PFECA as well as 6:2 Cl-PFESA and PFECHS also had blood-follicle transfer efficiencies in the range from 0.72 to 0.94 (Hallberg et al., 2021; Kang et al., 2020). Strong correlations between PFASs in serum/plasma and follicular fluid indicate that serum/plasma is a good proxy for determining the oocyte exposure levels.

PFCAs and PFSAAs as well as replacement PFASs such as 6:2 Cl-PFESA and 8:2 Cl-PFESA, can readily cross the placenta and thus be transferred to the foetus (see section B.9.21 on human biomonitoring). A recent study on human embryonic and foetal organs found that concentrations in embryo/foetal tissue were lower than maternal serum and similar to placenta levels. The concentration of the sum of five PFASs (PFOS, PFOA, PFNA, PFDA and PFUnDA) was highest in lung and liver tissue and lowest in CNS samples (Mamsen et al., 2019).

B.5.1.1.3. Metabolism

Several PFASs have been shown to be excreted untransformed, i.e. without forming any metabolites or conjugates while others are readily metabolised, often to arrowhead PFASs and will thus contribute to exposure to these compounds (ATSDR, 2021; EFSA, 2020).

Experimental animals

No metabolism has been observed or is expected for PFCAs and PFSAAs (ATSDR, 2021; EFSA, 2020). Similarly, no metabolism has been reported for PFPAs (Joudan et al., 2017) and 6:2 Cl-PFESA (Wang et al., 2013b), as well as for PFECAAs HFPO-DA, ADONA, and EEA (Rice et al., 2021). These substances are thus considered metabolically inert and stable end-stage products. In contrast, studies on experimental animals have demonstrated that other PFAS groups such as FTOHs, PAPs and FASAs are transformed to the arrowhead groups PFCAs and PFSAAs (EFSA, 2020). 6:2 FTOH is also shown to be metabolised in rats, the primary stable metabolite being 5:3 fluorotelomer carboxylic acid (5:3 FTCA), but also PFCAs, such as PFBA, PFPeA, PFHxA, and PFHpA (Kabadi et al., 2018; Kabadi et al., 2020; Ruan et al., 2014). In addition, fluoride appears to be released during the metabolism (Mukerji et al., 2015). 8:2 FTOH metabolises to glucuronide and glutathione conjugates of the parent compound, oxidised and reduced intermediates and PFOA, PFNA, PFHpA and PFHxA (EFSA, 2020). In rats, PFPiAs are extensively metabolised by cleavage of one C-P bond yielding the corresponding PFPa and 1H-perfluoroalkanes (Joudan et al., 2017).

In a mouse study with exposure to aqueous film-forming foam (AFFF) PFAS mixture of C6

and C7 perfluoroalkane sulfonates (PFASs) were enriched in mouse serum, suggesting *in vivo* transformation of sulfonamide precursors. Some substituted C8 PFASs [keto-perfluorooctane sulfonate (PFOS), hydrogen-PFOS, and unsaturated PFOS] appeared to be more bioaccumulative than linear PFOS or were formed *in vivo* from unidentified precursors. Sulfonimide dimers were detected in serum that may have been a minor component of the AFFF or formed via metabolism (McDonough et al., 2020a).

Some metabolism was reported for Noviflumuron in rats (>5% of administered dose): urinary metabolites included a glucuronide, sulphate conjugates of hexafluoroalkoxy-fluorodichloroaniline and a mercapturic acid conjugate of parent compound, but 84-100% was parent test material (TERC, 2003).

Exposure to HFO-1234yf led to low extent (<0.1% of dose received) of biotransformation in rabbits (Schuster et al., 2010). Urinary metabolites included N-acetyl-S-(3,3,3-trifluoro-2-hydroxypropyl)-L-cysteine (predominant metabolite), S-(3,3,3-Trifluoro-2-hydroxypropyl)mercaptolactic acid, 3,3,3-trifluoro-1,2-dihydroxypropane, 3,3,3-trifluoro-2-propanol, and inorganic fluoride (Schuster et al., 2010).

Humans

Similar to experimental animals, no metabolism has been observed for PFCAs and PFASs (EFSA, 2020), and this is likely also the case for other PFASs that are not metabolised in experimental animals. It is shown that humans are able to transform precursors to PFCAs and PFASs, similar to experimental animals (EFSA, 2020). For example, 8:2 FTOH is transformed to FTCAs and FTUCAs and further to PFOA and PFNA (EFSA, 2020; Nilsson et al., 2013a).

For HFCs, no urinary metabolites were detected after exposure to HFC-134a (Gunnare et al., 2006), HFC-143a (Gunnare et al., 2007), HFC152a (Ernstgård et al., 2012a), or HFC-245fa (Ernstgård et al., 2009), summarized by Ernstgård et al. (2012b).

B.5.1.1.4. Excretion

As summarised by EFSA (2020) and ATSDR (2021) a range of PFASs, and in particular PFCAs and PFASs, are eliminated both through urine and via faeces. In addition, excretion through transplacental transfer, menstruation and breastfeeding has been demonstrated. In humans, long elimination half-lives have been observed for several PFASs, while other PFASs are excreted faster and do thus have shorter elimination half-lives.

Experimental animals

Urine is the main excretion route for PFCAs with less than ten carbon atoms ($C < 10$) (EFSA, 2020), while for PFCAs with ten or more carbon atoms, biliary excretion and subsequent excretion via faeces is the main elimination route (EFSA, 2020). Elimination of PFCAs in rats is faster in females than in males (EFSA, 2020). PFASs (only data available for $C \leq 8$) are primarily eliminated in urine, and to a lesser extent in faeces (EFSA, 2020). In rats, 8:2 FTOH is mainly eliminated via faeces (70%), to a lesser extent through biliary excretion (20-45%), and by less than 4% via urine (EFSA, 2020). For Noviflumuron (complex ether-based PFAS), 63% of the dose was eliminated via faeces (cumulatively) in rats and 53-90% of the dose was recovered in the faeces within 72 h (TERC, 2002; TERC, 2004). Urine is considered a minor excretion route for Noviflumuron, as only 0.7-5.0% was recovered in the urine independent of the dose (TERC, 2002) and the total cumulative urinary elimination was about 12% of the dose (TERC, 2004). Breast milk also represents a significant route of excretion for Noviflumuron in rats (TERC, 2005).

For fluorinated gases, metabolites of HFO-1234yf were mostly excreted in urine within 12 h after the end of exposure in rabbits ($t_{1/2}$ of ca. 9.5 h) (Schuster et al., 2010).

Serum half-lives of several PFCAs and PFSA in experimental animals have been summarised by EFSA (2020), ATSDR (2021) and Fenton et al. (2021). In rats, serum half-lives from less than an hour or few hours for PFHxA and PFBS up to more than 100 days for PFDA and one of the isomers of PFOS (1m-PFOS) have been reported. In mice, half-lives between 3 h (PFBA, females) and 228 days (PFNA, males) have been reported (EFSA, 2020). In male rats, the blood half-life was 0.95 h for C8 PFPA and 2.8 h for C8/C8 PFPIA (Joudan et al., 2017). A recent study on CD-1 mice reported serum half-lives of PFBS of 5.8 (M) and 4.5 (F) h, respectively (Lau et al., 2020). Large sex differences in elimination half-lives have been observed in rats, while the differences are smaller in mice (ATSDR, 2021; EFSA, 2020; Fenton et al., 2021). The 6:2 FTOH metabolite, 5:3 FTCA is estimated to have plasma half-lives of 64 (m) – 67 (f) days in rats, and under conditions of repeated oral 6:2 FTOH exposure it would take approximately one year for the 5:3 FTCA to reach steady state (Kabadi et al., 2020). The half-life of 8:2 FTOH was 7 – 9 days in rats (EFSA, 2020; Fasano et al., 2006).

Humans

Detailed data on PFAS concentrations in urine, breast milk, placenta and cord blood have been summarised in section B.9.21 and Appendix B.5.1.1.2. Table B.91 to Table B.95.

In humans, short chain PFCAs, are mostly excreted in urine, whereas PFNA and longer chain PFASs are preferentially eliminated through the bile (EFSA, 2020). 6:2 Cl-PFESA and 8:2 Cl-PFESA have also been detected in urine, demonstrating urinary excretion (Shi et al., 2016). 6:2 Cl-PFESA was not detected in urine from USA (Calafat et al., 2019; Kato et al., 2018), likely due to low human exposure to these compounds.

Breast milk also represents a significant route of excretion for PFCAs, and PFSA (ATSDR, 2021; EFSA, 2020). Replacement PFASs such as 6:2 Cl-PFESA and 8:2 Cl-PFESA have also been detected in relatively high concentrations in breast milk in China, indicating similarities with restricted PFASs such as PFOS and PFOA (Awad et al., 2020; Jin et al., 2020a). In contrast, 6:2 Cl-PFESA and 8:2 Cl-PFESA were not detected in breast milk from Sweden and Czech Republic (Awad et al., 2020; Cerna et al., 2020), likely because of low human exposure to these compounds.

Other routes of elimination are transplacental transfer and blood loss during menstruation as summarised for PFCAs and PFSA by EFSA (2020) and ATSDR (2021). Median ratios between foetal:maternal blood are in the range of 0.36-0.74 for PFHxS, PFOS, PFOA, PFNA and 6:2 Cl-PFESA (Chen et al., 2017b; EFSA, 2020). The transfer rates probably depend on the structure of the compound, where longer fluoroalkyl chain length and a terminal sulfonate group are associated with a lower foetal:maternal blood ratio (EFSA, 2020). Transplacental transfer, menstruation and breastfeeding may at least partly explain gender differences in levels of PFASs between men and women (EFSA, 2020). For 6:2 Cl-PFESA and 8:2 Cl-PFESA transplacental transfer has also been demonstrated, and both compounds were detected both in placenta samples as well as in cord blood (Cai et al., 2020; Chen et al., 2017b; Gao et al., 2019; Lu et al., 2021). Again, this shows similarities between these replacement PFASs and the restricted PFASs such as PFOS and PFOA.

Total elimination half-lives of PFCAs and PFSA in humans range from a few days (PFBA) to several years (for example PFOS, PFOA and PFHxS) (ATSDR, 2021; EFSA, 2020; Fenton et al., 2021). In a study by Li et al. (2018c), marked sex differences in elimination half-lives were observed for PFHxS and PFOS, with more rapid elimination in women compared to men, while the difference between sexes was only marginal for PFOA (Li et al., 2018c). The long human elimination half-lives of long-chain PFASs are mainly attributed to active renal and intestinal reabsorption via organic anion transporters (OATs) (Ducatman et al., 2021; EFSA, 2020; Fenton et al., 2021). PFOA and PFOS have been shown to have a high affinity for human transport proteins such as OAT1, OAT3 and urate transporter URAT1 (EFSA, 2020), contributing to their long half-lives in humans.

Differences in renal reabsorption is considered a main reason for variability in the half-lives of PFASs between species. Serum albumin binding is also important for the long half-life of many PFASs as it limits renal excretion due to less free PFASs in the circulation (Fenton et al., 2021). In a study including individuals with high exposure to 6:2 Cl-PFESA, a median elimination half-life of 15.3 years was reported, again indicating similarities between these replacement PFASs and the restricted PFASs such as PFOS and PFOA (Shi et al., 2016). It may be suspected that PFPA and PFPIA have longer half-lives in humans than in rats, though predictions are complicated by the metabolism of PFPIAs (Joudan et al., 2017).

B.5.1.2. Toxicokinetics/ADME of polymeric PFASs

ADME properties of oligomeric and polymeric PFASs can vary widely. The chemical composition of the principal monomers as well as the identification of the oligomeric/polymeric substance on the basis of general chemical descriptors, such as relevant names and numbers (such as CAS- and/or EC-no., chemical name or trade names) alone are not sufficient for human health assessment. Oligomers/polymers can vary in terms of molecular weight distribution, physical state, and possible inclusion of co-monomers and others, but can carry the same name and/or CAS number. Also, additives and non-intentionally added substances (NIAS) can play a relevant role in the final oligomeric/polymeric product. For further details see ECETOC (2019) and the following box.

From ECETOC (2019):

"Structural and morphological descriptors and/or physical, and chemical properties

Depending on the type of polymer under investigation, relevant key parameters may be structural and/or morphological descriptors as well as physico-chemical and screening-level fate properties (no order of properties is inferred):

- *Structural descriptors include e.g. chemical formula, degree of substitution, tacticity, Mw, Mw distribution (polydispersity), number average molecular weight (NAMW), and RFG(s);*
- *Morphological descriptors include e.g. physical state at ambient temperature and pressure (solid, liquid), shape (e.g. spherical, fibre, tubular), physical form (e.g. amorphous, crystalline);*
- *Physico-chemical properties include e.g. water solubility, n-octanol/water partition coefficient (log Pow), acid dissociation constant (pKa), net charge (under conditions that are relevant for ecological and human health hazard assessment), vapour pressure, viscosity / melt-flow index / glass transition temperature, density, degradability."*

Only a few studies with toxicokinetic/ADME information are available for this diverse group of oligomeric/polymeric PFASs. No studies are available on toxicokinetics of polymeric PFASs. All available studies on toxicokinetics/ADME studied oligomeric PCTFE (oils and/or pure oligomers). Under the REACH regulation, oligomers are not defined and do not fall under the polymer definition according to REACH (Article 5(3)). Oligomers are composed of a small number of linked monomer units and thus differ from non-polymeric PFASs. Most publications on PCTFE oligomer ADME and toxicity provide insufficient information on the identification of the substance or study details and results investigated.

Some evidence for absorption of PCTFE oligomers was reported for experimental animals (rodents and rhesus monkey) into blood, liver, and kidney, via repeated exposure to vapour via inhalation (Kinkead et al., 1989; Kinkead et al., 1987), and after oral administration via the GI tract (DelRaso et al., 1991; Jones et al., 1991; Kinkead et al.,

1987). Absorption via the skin cannot be excluded, because small insignificant increases of plasma fluoride concentrations after dermal absorption of PCTFE oligomers were shown in rodent urine and plasma (Kinkead et al., 1987).

There is evidence of distribution of PCTFE oligomers, after repeated inhalation into various tissues, such as kidney, liver, lung, testes, brain and fat (Kinkead et al., 1989; Vinegar et al., 1992). After oral administration, concentrations of pure PCTFE tetramers in the liver of rats were significantly higher compared to PCTFE halocarbon oil and to pure PCTFE trimers (DelRaso et al., 1991). Furthermore, composition of the ratio percentage of trimer to tetramer present in PCTFE HC 3.1 oil-C6:C8 (55:45) was found to be altered when measured in the liver (32:68) (DelRaso et al., 1991).

Data on metabolism are scarce. PCTFE oligomers were reported to be metabolised to carboxylic acid derivatives in rats based on physiologically based modelling and measurements of decreasing trimer and tetramer concentrations in blood and liver and release of fluoride (Vinegar et al., 1992).

PCTFE oligomers and/or unbound fluoride ions were excreted in urine after exposure to PCTFE oligomers (halocarbon oils of different compositions) via inhalation, dermal contact and oral uptake (Kinkead et al., 1989; Kinkead et al., 1987; Vinegar et al., 1992).

Because of the lack of data, it is not possible to conclude on ADME characteristics of oligomeric or polymeric PFASs. However, considering the few available toxicity data (B.5.2.1) ADME characteristics that allow interactions with biota cannot be excluded for oligomeric/polymeric PFASs.

B.5.2. Evidence from experimental animal data

B.5.2.1. Repeated dose toxicity (experimental animal data)

With respect to the large array of potential health effects and the vast number of different PFASs, this section focuses on the most prominent adverse effects that occur most consistently across different groups of PFASs. These are effects on liver, kidney, thyroid, immune system, and serum lipids. Toxicity to reproduction is covered in a separate section (B.5.2.2).

For oligomeric/polymeric PFASs, only few experimental studies are available. Predominantly oligomeric PCTFE oils were studied, some of which show effects dependent on chain length and mixture-ratio of different chain lengths (DelRaso et al., 1991; Kinkead et al., 1991). However, differences of oligomer/polymer properties and lack of data do not allow an in-depth assessment of the human health hazards. Thus, the RDT effects in this section give only an exemplary insight into possible health impact of oligomeric/polymeric PFASs.

For side-chain fluorinated polymers (SCFPs) it is known that the PFAS moieties on the side chains can separate from the carbon backbone of at least some commercial SCFPs over time, and may further degrade to PFCAs and PFSA in the environment and biota (OECD, 2022). Since most PFCAs and PFSA were shown to cause adverse effects in humans and animals, it can be concluded that SCFPs contribute to adverse health effects, e.g. in organs such as liver, kidney, thyroid, immunological tissues after repeated exposure. No further toxicity data are available for SCFPs and will not be addressed in the following section on specific effects.

B.5.2.1.1. Liver effects in experimental animals

Various reports and reviews demonstrate that the liver is a sensitive and one of the most consistently affected targets of PFAS toxicity in experimental animals (ATSDR, 2021; EFSA, 2020; Fenton et al., 2021). A recent review (Fenton et al., 2021) summarised liver effects for humans and animal studies and concluded that the liver is a primary target organ of PFASs, in particular PFCAs with $C \geq 8$ and PFSA with $C \geq 6$. Effects on the liver include specific P450 (CYP) pathway induction, significantly increased liver weight, hepatic steatosis, apoptosis, hepatocellular adenomas and carcinomas, and disrupted fatty acid metabolism that can be peroxisome proliferator-activated receptor alpha (PPAR α)-dependent or -independent and present across species (Cui et al., 2009; Filgo et al., 2015; Huang et al., 2013; Hui et al., 2017; Li et al., 2017; Maestri et al., 2006; NTP, 2020; Perez et al., 2013; Wan et al., 2012; Xu et al., 2016; Xu et al., 2020b; Yao et al., 2016; Zhang et al., 2016b). This section summarises the evidence from animal experiments. Epidemiological evidence for liver toxicity was discussed by EFSA (2020) and an update to EFSA (2020) is provided in section B.5.3.1.3.

Non-polymeric PFASs

Among all studied non-polymeric PFASs, the most consistent effect in the available animal studies is a dose-dependent increase in liver weight, mostly accompanied with hepatocellular hypertrophy and increases in liver enzymes (ALT, AST, ALP) indicative for liver cell dysfunction, for example in rodent models repeatedly exposed to

- PFCAs, PFSA (numerous studies reviewed by (ATSDR, 2021; EFSA, 2020; NTP, 2019a; NTP, 2019b),
- TFA (BayerCropScience, 2007; Blake, 1970; Just et al., 1989),
- Perfluamine (Triskelion, 2019b),
- PFECAs
 - HFPO-DA (e.g. (Rushing et al., 2017; WIL, 2008a; WIL, 2008b; WIL, 2009)),
 - ADONA (e.g. (Gordon, 2011; NOTOX, 2007a)),

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

- Mv31 K⁺ salt (Aventis Pharma Deutschland GmbH, 2002),
 - F-DIOX (RTC, 2013),
- PFESAs
 - 6:2 Cl-PFESA (Zhang et al., 2018a),
 - PFESA-BP2 (Lang et al., 2020),
- PFE alkenes
 - PMVE (WIL, 2016),
 - Mv31 (NOTOX, 2007b),
- complex ether-based PFASs, e.g.
 - Tetraconazole (Huntingdon, N/A-b; Huntingdon, N/A-d),
 - Noviflumuron (Dow AgroSciences, 2002a),
- Fluorotelomers
 - 8:2 FTOH ((Ladics et al., 2008; Wang et al., 2019b), reviewed by EFSA (2020)),
 - EtFOSE ((Xie et al., 2009), reviewed by EFSA (2020)),
 - 6:2 FTSA (6: 2 fluorotelomer sulfonic acid (Sheng et al., 2017),
- HFCs
 - HFC-134a (ICI, 1979; Zeneca, 1993),
 - HFC-245fa (Frauenhofer Institut für Toxikologie und experim. Medizin, 2005),
 - HFC-365mfc (TNO, N/A),
 - HFC-4310mee (DuPont Haskell, 2007b; Haskell, 1996b),
 - HFC-52-13 (Hita, 1994), HFC-76-13 (Hita, 2007a),
 - HFCPA (Huntingdon, 1998a; Huntingdon, 1998c; Huntingdon, 1998d),
- HFOs
 - HFO-1234yf (Tveit et al., 2013),
 - HFO-1234ze(E) (TNO, 2006),
 - HFO-1336mzz(Z) (DuPont Haskell, 2014),
 - HFO-1132a (Litton Bionetics, 1984),
- HFEs
 - HFE-7100 (Huntingdon, 1995; Huntingdon, 1996a; Huntingdon, 1996b),
 - HFE-7200 (Huntingdon, 1997),
 - HFE-7300 (Charles River, 2019b; Hita, 2004),
 - HFE-7500 (3M, 1998),
 - HFE-356pcf3 (DuPont Haskell, 2009; DuPont Haskell, 2011).

Moreover, there are indications for hepatocellular necrosis from experimental rodent models after repeated exposure (28 or 90 days) for

- most PFCAs and PFASs, except PFBS and PFHxDA (ATSDR, 2021; EFSA, 2020),
- several PFECAs, e.g.
 - HFPO-DA (Blake et al., 2020; Caverly Rae et al., 2015; DuPont Haskell, 2008a; Haskell, 2010; MPI Research Inc., 2013; Sheng et al., 2018b; Wang et al., 2017a; WIL, 2008a; WIL, 2010a; WIL, 2011a),
 - HFPO-TA (Sheng et al., 2018b),
 - EEA-NH₄ (Hita, 2006),
 - F-DIOX (RTC, 2010; RTC, 2011; RTC, 2012),
- PFESAs, e.g.
 - 6:2 Cl-PFESA (Zhang et al., 2018a),
- complex ether-based PFASs, e.g.
 - Tetraconazole (Huntingdon, N/A-c),
 - Noviflumuron (Dow AgroSciences, 2002b),
- Fluorotelomers, e.g.
 - 6:2 FTOH (Hita, 2007b; Mukerji et al., 2015; Rice et al., 2020; Serex et al., 2014; WIL, 2005),
 - 8:2 FTOH (Ladics et al., 2008), and
 - 6:2 FTSA (Sheng et al., 2017), and
- HFE-7300 (Hita, 2004).

Examples of PFASs that did not induce hepatotoxicity in animal studies are several perfluoroether-alkenes and -alkanes as well as some complex perfluoroether alkyl substances. Within fluorinated gases, hydrofluoroethers generally show typical increased liver weight and hepatocellular hypertrophy, but most hydrofluorocarbons and hydrofluoroolefins only increased liver weights, mainly without histopathological changes, e.g. HFC-134a (ICI, 1979), HFC-52-13 (Hita, 1994), HFO-1234yf (Tveit et al., 2013). For PFASs of different groups (PFCAs, PFSA, PFECAs), it has been demonstrated that potency differences for liver effects are largely determined by kinetics (serum half-lives) (Gomis et al., 2018).

The mechanisms underlying PFAS-induced hepatotoxicity has been extensively studied. As reviewed by EFSA (2020), ATSDR (2021), and Fenton et al. (2021), several PFASs lead to a transcriptional activation of mouse and human PPAR α -related genes in liver in adult-exposed models. Additionally, activation of other nuclear receptors such as PPAR γ , constitutive androstane receptor (CAR), and pregnane X-receptor (PXR) has also been reported. These nuclear receptors regulate lipid and glucose metabolism and transport as well as inflammation and some nuclear receptors, including PPAR α , are considered more responsive in tissues of rodents than in humans (Fenton et al., 2021; Rosen et al., 2017; Wolf et al., 2012). Predictions of the binding mode of PFOS, PFOA and PFHxS to PPAR α , PPAR γ and ER α are available and show that hydrophobic interactions play a key role in the binding of these PFAAs (Jiang et al., 2015). However, ATSDR (2021) concluded that hepatic effects of PFCAs and PFSA in rodents likely result from a combination of PPAR α -dependent and independent changes, which is in line with a CLH RAC opinion for PFOA (ECHA, 2011), demonstrating that human relevance of such effects should be expected.

Oligomeric/polymeric PFASs

Predominantly oligomeric PFASs were studied within repeated dosed inhalation, and oral toxicity studies. For the oligomeric PCTFE (CAS-no. 9002-83-9), liver related effects were reported in rats exposed to various oligomer ratios:

- Pure PCTFE trimers (C6) and pure PCTFE tetramers (C8) (DelRaso et al., 1991; Kinkead et al., 1991)
- PCTFE Halocarbon (HC) oils (base oils) of different (trade) names:
 - o S-27 oil (C8 : C10 unknown ratio) (Kinkead et al., 1990a),
 - o Safetol®3.1/ MLO-87-124 (70% C6 : 30% C8) (Kinkead et al., 1989; Kinkead et al., 1990b),
 - o PCTFE 3.1 (55% C6 : 45% C8 and 95% C6 : 5% C8) (DelRaso et al., 1991),
 - o PCTFE 3.1 (C6 : C8, unknown ratio) ((Jones et al., 1991)
 - o PCTFE 3.1 (C6 : C8, unknown ratio with additives) (Mattie et al., 1993)
 - o PCTFE HC (70% C6 : 30% C8 with additives) (Vinegar et al., 1992)
 - o PCTFE HC (55% C6 : 45% C8 without additives) (Vinegar et al., 1992)
- pure PCTFE trimers (C6) and pure PCTFE tetramers (C8) (DelRaso et al., 1991; Kinkead et al., 1991).

On the basis of repeated dose oral toxicity studies with oligomeric PCTFE (DelRaso et al., 1991; Kinkead et al., 1991; Kinkead et al., 1989; Kinkead et al., 1990a; Kinkead et al., 1990b; Mattie et al., 1993), common hepatotoxic findings in rats were increased relative liver weights as well as hepatocellular cytomegaly. Effects observed in oral studies were similar to those reported for two repeated inhalation studies (Kinkead et al., 1990b; Vinegar et al., 1992). After oral administration (Mattie et al., 1993) and after inhalation (Kinkead et al., 1989) of oligomeric PCTFE oil, increases in liver enzymes (ALT, AST) indicative for liver cell dysfunction were observed in rats.

Additional liver effects in rats associated with oligomeric PCTFE, differing between studies of pure tri- or tetramers and of various oil compositions, were e.g. altered hepatocellular architecture, elevated serum liver-associated enzymes, hepatocytic eosinophilic granular cytoplasm, and loss of hepatocytic cytoplasmic basophilia (DelRaso et al., 1991; Kinkead

et al., 1991). Kinkead et al. (1990a) concluded on the basis of further observations that the liver was probably the primary target organ of oligomeric PCTFE. For PCTFE oligomers in rats, repeated orally administered tetramers were observed to be more hepatotoxic than trimers (Kinkead et al., 1991; Vinegar et al., 1992).

For polymeric PTFE, the only available information on repeated-dose toxicity was an older study from Zapp (1962). In this publication it was stated that a laboratory study with rats, fed with a diet of 25% finely ground PTFE resins (polymer composition and further key parameters unknown) for 90 days, showed no signs of toxic effects and no pathological changes detectable by gross or microscopic examination of the tissues. Also in a book by Sheftel (2000) that summarises data of indirect food additives and polymers, PTFE was reported to cause no effect on rats after ten months oral administration. However, insufficiently reported study details in both sources (e.g. polymer properties, study design) weaken the power of the available information.

For one perfluoropolyether (PFPE) surfactant, Johnston et al. (1996b) communicated concerns in a letter to the editor, indicating that - based on unpublished data - the oligomeric PFPE surfactant cannot be assumed biologically inert, because it caused an increase in liver weight in rats. The authors state that the used PFPE surfactant was similar to the ammonium carboxylate PFPE surfactant used by Johnston et al. (1996a) ($\text{CF}_3\text{O}(\text{CF}_2\text{CF}(\text{CF}_3)\text{O})_3\text{CF}_2\text{-COO-NH}_4^+$), with an average molecular weight of 740 g/mol. For further details on the PFPE substance, Johnston et al. (1996a) cited Chittofrati et al. (1989), who described the PFPE surfactant with the formula $\text{R}_f\text{-CF}_2\text{-COO-NH}_4^+$, with R_f described as $\text{CF}_3\text{-}[(\text{O-CF}_2\text{-CF}(\text{CF}_3))_n\text{-(O-CF}_2)_m]\text{-O-}$ and R_f having $n/m = 3 \div 4$ monomer units with a molecular weight of 710 g/mol.

There is indication for significantly increased hepatic peroxisomal β -oxidation after oral administration of oligomeric PCTFE oils to rats (DelRaso et al., 1991; Kinkead et al., 1991; Kinkead et al., 1990a; Mattie et al., 1993). In monkeys the increase in peroxisomal β -oxidation was not significant (Jones et al., 1991). This effect was not observed in rats following inhalation of PFPE fluorinated oil (KrytoxTM) (Kelly et al., 1993).

In summary, there are indications that oligomeric PFASs can cause adverse liver effects, which is generally in line with the typical effects observed for non-oligomeric/non-polymeric PFASs. Clarity on liver effects of the highly diverse group of oligomeric/polymeric PFASs cannot be given on the basis of available data.

B.5.2.1.2. Serum lipids in experimental animals

Regarding **non-polymeric PFASs**, most animal studies addressing serum cholesterol have been conducted at much higher PFAS exposure levels than human studies (EFSA, 2020; Fragki et al., 2021). In general, studies with experimental animals mainly measured serum total cholesterol, which is rather reduced in rodents than increased as observed in epidemiological studies. For instance, total serum cholesterol was reduced after repeated doses for 28 or 90 days in male rodents by PFASs: PFBS, PFHxS, and PFOS (NTP, 2019b); PFCAs: PFBA (Butenhoff et al., 2012a), PFHxA (Chengelis et al., 2009b), PFOA (e.g. (Loveless et al., 2006)), PFNA, PFDA (NTP, 2019a), PFDoDA (Kato et al., 2015), PFODA (Hirata-Koizumi et al., 2012). For PFECAs, HFPO-DA (Conley et al., 2021; Conley et al., 2019; DuPont Haskell, 2008b; Sheng et al., 2018b; WIL, 2009), EEA-NH4 (Hita, 2006), and F-DIOX (RTC, 2013) reduced total cholesterol.

However, some studies report increases in serum cholesterol in mice exposed to human relevant PFOA-levels in combination with high fat or westernised diet (Rebholz et al., 2016; Schlezinger et al., 2020), suggesting that both exposure concentration, diet and sex may influence the effect of PFASs on lipid metabolism. Increases of total cholesterol were reported for HFPO-DA (Blake et al., 2020) and F-DIOX (RTC, 2011).

An increase in total serum cholesterol was also reported for 6:2 Cl-PFESA (Zhang et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

2018a), Tetraconazole (Huntingdon, N/A-b; Huntingdon, N/A-f) and Noviflumoron (Dow AgroSciences, 2002a; Dow AgroSciences, 2002b; Dow AgroSciences, 2005b).

Two hydrofluoroethers (fluorinated gases) induced a decrease in total serum cholesterol in rats after repeated exposure to HFE-7100 for 28 days (Huntingdon, 1995) or HFE-7500 for 5 days (3M, 1998).

Animal studies show a clear association of PFASs with changes in lipid metabolism. However, because of significant species differences affecting both lipid metabolism and PFAS toxicokinetics (Fragki et al., 2021) and often large differences in exposure levels, the animal experiments have not been able to elucidate the causality of the PFAS – serum cholesterol association demonstrated in epidemiological studies.

Serum triglycerides are mostly reduced in experimental animals (rodents) after repeated exposure to

- PFCAs:
 - PFHxA (Klaunig et al., 2015),
 - PFOA (DeWitt et al., 2009; Loveless et al., 2006; Qazi et al., 2010; Wu et al., 2018; Xie et al., 2003),
 - PFNA (NTP, 2019a; Wang et al., 2015c),
 - PFDA (NTP, 2019a),
 - PFTeDA (Hirata-Koizumi et al., 2015),
 - PFODA (Hirata-Koizumi et al., 2012);
- PFASs:
 - PFBS (Bijland et al., 2011),
 - PFOS (Lai et al., 2018);
- PFECAs:
 - HFPO-DA (Blake et al., 2020; Conley et al., 2021; Conley et al., 2019; DuPont Haskell, 2008b),
 - HFPO-TA (Sheng et al., 2018b),
 - mv31 K⁺-salt (Aventis Pharma Deutschland GmbH, 2002),
 - F-DIOX (RTC, 2013);
- other ether PFASs:
 - PEVE (Haskell, 1997),
- and some HFCs/HFOs:
 - HFC-236fa (Haskell, 1996a),
 - HFO-1336mzz(Z) (DuPont Haskell, 2010a).

However, similar to cholesterol effects, also considerable increases in serum triglycerides are reported in some rodent studies for

- PFHpA (Anonymous, 2017),
- PFOA (Loveless et al., 2006; Minata et al., 2010),
- PFDoDA (Zhang et al., 2008),
- PFOS (Huck et al., 2018; Su et al., 2019),
- 6:2 Cl-PFESA (Zhang et al., 2018a),
- HFPO-DA (Conley et al., 2021),
- F-DIOX (RTC, 2011), or
- HFCPA (Huntingdon, 1998c; Huntingdon, 1998d).

Regarding **oligomeric/polymeric PFASs**, serum triglycerides were increased after repeated oral exposure to oligomeric PCTFE oil (unknown ratio) in rhesus monkeys (Jones et al., 1991).

Serum bile acids are consistently increased in experimental animals after repeated exposure to some non-polymeric PFASs, e.g. PFCAs (NTP, 2019a) or PFSAAs (NTP, 2019b). EFSA (2020) concluded that such an increase in serum bile acids indicates cholestasis. Increased serum bilirubin as another indicator for cholestasis was also evident for some PFCAs (NTP, 2019a) and PFSAAs (NTP, 2019b).

B.5.2.1.3. Kidney effects in experimental animals

Non-polymeric PFASs

In experimental animal models (mainly in rats, sometimes mice), kidney weights relative to body mass were increased for some PFAAs, PFECAs, perfluoroether alkenes, complex ether-based PFASs, and a variety of fluorinated gases (HFCs including HFOs, and HFEs), underlining the variety of chemical structures of PFASs that can induce changes on kidney physiology. Epidemiological evidence for effects on the kidney are summarised by EFSA (2020) and updated in B.5.3.1.4.

Among substances that induced increases in relative kidney weights in rodents are

- PFCAs:
 - PFHxA (Chengelis et al., 2009b; Loveless et al., 2009; NTP, 2019a),
 - PFOA (Butenhoff et al., 2004; Cui et al., 2009; Griffith and Long, 1980; Loveless et al., 2006; Loveless et al., 2008; NTP, 2019a),
 - PFNA (NTP, 2019a),
 - PFDA (Frawley et al., 2018; NTP, 2019a),
 - PFDoDA (Kato et al., 2015),
- PFSAAs:
 - PFBS (NTP, 2019b);
- PFECAs:
 - HFPO-DA (Blake et al., 2020; Caverly Rae et al., 2015; DuPont Haskell, 2008b; MPI Research Inc., 2013; WIL, 2008b; WIL, 2009; WIL, 2010a; WIL, 2010b),
 - EEA-NH4 (Hita, 2006; WIL, 2011b),
 - F-DIOX (RTC, 2011; RTC, 2013);
- PFE alkenes:
 - PMVE (DuPont Haskell, 2007a; WIL, 2016),
 - PEVE (Haskell, 1997);
- other ether-based PFAS:
 - Tetraconazole (Huntingdon, N/A-b; Huntingdon, N/A-d; Huntingdon, N/A-e; Huntingdon, N/A-f),
 - Noviflumuron (Dow AgroSciences, 2002a; Dow AgroSciences, 2002b; Dow AgroSciences, 2005a; Dow AgroSciences, 2005b);
- FTOHs:
 - 6:2 FTOH (Hita, 2007b; Kirkpatrick, 2005; Mukerji et al., 2015; Rice et al., 2020; Serex et al., 2014; WIL, 2005)
- HFCs:
 - HFC-134a (ICI, 1979),
 - HFC-236fa (Haskell, 1996a),
 - HFC-365mfc (TNO, N/A),
 - HFC-76-13 (Hita, 2007a),
 - HFCPA (ZEORORA) (Huntingdon, 1998a);
- HFEs:
 - HFE-7100 (Huntingdon, 1996b),
 - HFE, 7200 (Mitsubishi, 1996),

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

- HFE-7300 (Hita, 2004), and
- HFE-365pcf3 (DuPont Haskell, 2009; DuPont Haskell, 2011).

For several of these substances, increased kidney weights were accompanied by histopathological changes in the kidneys. For example, minor microscopic findings, tubular epithelial hypertrophy or degeneration were found for

- PFCA
 - PFHxA (Klaunig et al., 2015; WIL, 2005);
- PFSA
 - PFBS (Lieder et al., 2009);
- PFECAs:
 - HFPO-DA (Caverly Rae et al., 2015; Haskell, 2010; MPI Research Inc., 2013; WIL, 2010a; WIL, 2010b),
 - ADONA (Charles River, 2007a),
 - EEA-NH4 (Hita, 2006),
 - F-DIOX (Toxicology Centre S.p.A., 2011);
- PFE alkenes:
 - PMVE (DuPont Haskell, 2007a),
 - PPVE (Charles River, 2017),
 - PEVE (Haskell, 1997);
- other ether-based PFASs:
 - Tetraconazole (Huntingdon, N/A-e)
 - Noviflumuron (Dow AgroSciences, 2005b);
- fluorotelomer alcohols
 - 6:2 FTOH (Kirkpatrick, 2005; Rice et al., 2020; Serex et al., 2014; WIL, 2005)
- HFCs:
 - HFC-245fa (Frauenhofer Institut für Toxikologie und experim. Medizin, 2005),
 - HFC-76-13 (Hita, 2007a),
- HFOs:
 - HFO-1216 (Haskell, 1989),
- HFEs:
 - HFE-7300 (Hita, 2004),
 - HFE-356pcf3 (DuPont Haskell, 2011),
 - Sevoflurane (Gonsowski et al., 1994a; Gonsowski et al., 1994b).

For some substances from different PFAS categories, necrotic effects were reported (PFHxA, HFPO-DA, ADONA, PEVE, HFE-7300, Sevoflurane, HFO-1216). For some other PFASs, including PFOA, PFOS, PFHxS, PFDA, PFOA, PFBA, and PFDoDA, animal studies did not indicate impaired renal function or morphological damage (ATSDR, 2021).

Oligomeric/polymeric PFASs

Kidney effects of oligomeric/polymeric PFASs were studied in repeated dose inhalation and oral toxicity studies.

For the PCTFE oligomers, kidney related effects, such as increase of relative kidney weights, were reported in rats exposed to various compositions of the fluoropolymer:

- PCTFE Halocarbon (HC) oils (base oils) of different trade names:
 - 27-S oil with C8-C10 chain length (Kinkead et al., 1990a),
 - Safetol®3.1/ MLO-87-124 (70% C6 : 30% C8) (Kinkead et al., 1989; Kinkead et al., 1990b),
 - PCTFE 3.1 (C6 : C8, unknown ratio) ((Jones et al., 1991)
 - PCTFE 3.1 (C6 : C8, unknown ratio with additives) (Mattie et al., 1993)
- pure PCTFE tetramers (DelRaso et al., 1991; Kinkead et al., 1991).

Significant increases in blood urea nitrogen (BUN) in rats were reported either after

inhalation of PCTFE oligomers (3.1 oil) (Kinkead et al., 1989; Kinkead et al., 1990b) or after oral administration of PCTFE pure trimers or PCTFE pure tetramers (Kinkead et al., 1991). Comparable effects were reported for PCTFE oils, such as 3.1 oil or HC 27-S oil (Kinkead et al., 1990a; Kinkead et al., 1990b). Moreover, Jones et al. (1991) observed significantly increased BUN in all treated rhesus monkeys (15-day, oral) exposed to 725 mg/kg bw/d PCTFE oligomers (HC 3.1 oil).

For perfluoropolyethers (PFPEs), one study reported histologic alterations, but no further effects on kidney: In a limit test with rats exposed to 1 000 mg/kg bw/d of polymeric PFPE Fomblin HC/25 product (Mn = 3 200, content of low molecular weight <1 000 less than 0.1%), compared to controls, three of five males (but not the females) showed significantly increased (localised) basophilia (Malinverno et al., 1996). The lower sensitivity of female rats compared to male rats is also known from the non-polymeric PFAS PFOA related to lower serum levels of PFOA in female rats (EFSA, 2020).

In summary, there are indications that low molecular weight oligomeric/polymeric PFASs (oligomeric PCTFE and polymeric PFPE Fomblin HC/25) can cause kidney effects, which is generally in line with the effects observed for non-polymeric PFASs. Clarity on kidney effects of oligomeric/polymeric PFASs cannot be given on the basis of available data.

B.5.2.1.4. Thyroid effects in experimental animals

Non-polymeric PFASs

In experimental animal models, several PFASs can increase thyroid weight, induce follicular hypertrophy and decrease serum T3 and T4, but only some PFASs induce all of these effects combined in rats (PFBA, PFOA, PFNA, PFDA, PFHxDA, PFHxS, (e.g., Butenhoff et al., 2012a; Hirata-Koizumi et al., 2015; MPI Research Inc., 2013; NTP, 2019a; NTP, 2019b; Ramhoj et al., 2018; Ramhoj et al., 2020)).

For several other PFASs (especially PFAAs, including some PFEASs), an indication for thyroid effects is available. Thyroid hormones were reduced without changes in thyroid weight or histopathological changes in rats (and one mouse study for PFHpA) after repeated exposure to:

- PFCA:
 - PFHxA (NTP, 2019a),
 - PFHpA (Anonymous, 2017);
- PFSA:
 - PFBS (Feng et al., 2017; NTP, 2019b),
 - PFOS (NTP, 2019b);
- PFECA:
 - HFPO-DA (Conley et al., 2021; Conley et al., 2019);
- PFESA:
 - 6:2 Cl-PFESA (Hong et al., 2020);
- HFEs:
 - HFE-7300 (Charles River, 2019b).

In contrast, for TFA and HFCs or HFOs there are almost no indications for thyroid effects, which may partially be explained by the limited available data.

The US EPA used perturbation of thyroid hormone levels as the critical effect to derive a subchronic and chronic reference dose for PFBS. It was acknowledged that there is uncertainty with regard to the potential for adverse developmental effects because of the lack of studies investigating neurodevelopmental effects. Nevertheless, taking all available data together, the US EPA concluded that the evidence in animals for thyroid effects supports a hazard (EPA-US, 2021a).

With respect to the mode of action, PFASs can interfere with thyroid metabolism on several levels in thyroid hormone biogenesis, distribution and receptor binding (EFSA, 2020; Köhrle, 2008). On the level of biogenesis, PFASs can potentially disturb sodium iodide symporters, haemoprotein thyroperoxidase, iodinases, or deiodinases (EFSA, 2020). On the level of distribution, there is evidence for competitive binding of PFAS to thyroid hormone binding proteins (transthyretin and thyroxine-binding globulin), but at lower affinities than thyroid hormones (Behnisch et al., 2021; Berg et al., 2015; EFSA, 2020; Fenton et al., 2021; Ren et al., 2016; Weiss et al., 2009; Zhang et al., 2016a). Binding of PFCAs and PFASs to thyroid receptors was shown for PFBA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTTrDA, PFTeDA, PFBS, PFHxS and PFOS, but not for FTOH (8:2) (Ren et al., 2015). Coperchini et al. (2021) concluded in their review that available evidence, mainly provided by *in vitro* studies and in animal models, supports a thyroid-disrupting effect of the exposure to both old- and new-generation PFASs, while stating that epidemiological data provided contrasting results.

Regarding **oligomeric/polymeric PFASs**, no studies observing thyroid parameters are known.

B.5.2.1.5. Immune effects in experimental animals

Strong evidence demonstrates that exposure to several **non-polymeric** PFASs modifies the immune response, with inhibition/suppression of the immune response as most consistent immunotoxic effect relevant for human health (DeWitt et al., 2019; Fenton et al., 2021; NTP, 2016b; Zeng et al., 2021). In the most recent EFSA opinion on PFASs (EFSA, 2020), effects on the immune system were considered the most critical effects and the risk assessment was based on reduction in vaccine antibody response in children allowing to derive a tolerable weekly intake (TWI) of 4.4 ng/kg bw per week for the sum of four PFASs (PFOS, PFHxS, PFNA, and PFOA). Recent epidemiological literature not included in EFSA (2020) is summarised in section B.5.3.1.1.

In support of the epidemiological evidence, immunotoxic effects have been observed in animal studies for a variety of different PFASs. The following effects have been reported for PFASs across many PFAS subgroups, such as PFAAs, PFEASs, and some fluorinated gases. Reduction of lymphoid organ weights was observed for, e.g. PFHxA (Loveless et al., 2009), PFOA, PFNA, PFDA (NTP, 2019a), F-DIOX (RTC, 2011), CAS No. 524709-77-1 (Non-Clinical Safety, 2017). Changes in lymphocyte counts or proliferation were observed for, e.g.:

- TFA (BayerCropScience, 2014),
- PFOA and PFOS (Vetvicka and Vetvickova, 2013),
- PFDoDA (Kato et al., 2015),
- HFPO-DA (WIL, 2008a),
- F-DIOX (RTC, 2013),
- PMVE (DuPont Haskell, 2007a),
- Tetraconazole (Huntingdon, N/A-b),
- HFC-236fa (Haskell, 1996a),
- HFC-365mfc (Huntingdon, N/A-a),
- HFO-1216 (Triskelion, 2019a).

Whereas most immunotoxic effects are reported in response to higher PFAS doses, reductions in T-cell-dependent antibody responses (TDAR) are observed also at non-toxic doses of PFOA and PFOS in mice (DeWitt et al., 2009; DeWitt et al., 2008; DeWitt et al., 2016; Dong et al., 2011; Dong et al., 2009; EFSA, 2020; Peden-Adams et al., 2008; Zheng et al., 2009). The TDAR is a measure of functional immune response and has only been performed for a few PFASs. Serum antibody levels were reduced after exposure to PFOA (e.g., DeWitt et al., 2009; DeWitt et al., 2008; DeWitt et al., 2016), PFOS (e.g., Dong et al., 2009; Peden-Adams et al., 2008; Suo et al., 2017; Zheng et al., 2009; Zheng et al., 2011), and histological alterations in immune organs were observed after exposure to, e.g.

PFHxA (WIL, 2005), PFOS (Wang et al., 2011a), F-DIOX (RTC, 2011), PMVE (WIL, 2016). The most common immunotoxic observations in animal studies are effects on spleen weight followed by thymus weight (reduction in most cases). A recent study in mice exposed to three different perfluoroalkylether carboxylic acids (PFECAs) demonstrated that perfluoro-2-methoxypropanoic acid (PFMOPrA) induced changes in splenic cellularity and perfluoro-4-methoxybutanoic acid (PFMOBA) decreased numbers of B and natural killer (NK) cells (Woodlief et al., 2021). Significant changes in NK cell cytotoxicity or T cell-dependent antibody responses were not observed in this study (Woodlief et al., 2021).

While the immunotoxic effects of some PFASs are well established, the mechanisms leading to the effects are still unclear (ATSDR, 2021; Beans, 2021; EFSA, 2020).

For **oligomeric/polymeric PFASs**, immunotoxic effects were shown in terms of decreased absolute spleen weight of rats after inhalation of aerosolised oligomeric PCTFE oil (Kinkead et al., 1989). After oral administration of oligomeric PCTFE oil, absolute thymus weight was significantly increased in rats (Kinkead et al., 1990a).

As detailed in section B.5.1.1, PFAS surfactants may increase the intestinal permeability, as demonstrated in vitro for PFOS, which may contribute to effects on the human immune system (Groh et al., 2017).

B.5.2.1.6. Other effects (experimental animal data)

Non-polymeric PFASs

For a specific group of compounds, the n:2 fluorotelomer alcohols, another adverse effect finding has been consistently reported in the performed animal studies. Adverse effects on teeth and bone, consistent with fluoride toxicosis, have been seen with increasing doses of 6:2 FTOH (Hita, 2007b; Kirkpatrick, 2005; Mukerji et al., 2015; Rice et al., 2020; Serex et al., 2014; WIL, 2005). Likewise, Serex et al. (2014) report that similar effects have been seen for 8:2 FTOH exposed animals. The observed effects include: discolouration of the incisors, irregular ameloblast alignment and pigmentation, missing/broken/misaligned incisors, degeneration and atrophy of ameloblastic epithelium, accentuation of the normal laminar pattern of dentin and an increase in incomplete decalcification of enamel. Also incomplete decalcification of nasal bones and long bones (tibia and femur) has also been observed. The animal groups that show adverse effects on teeth and bone have been shown to have statistically significant increases in fluoride concentrations in serum and urine (Rice et al., 2020; Serex et al., 2014).

Oligomeric/Polymeric PFASs

In an older study, fluorocarbon vapour animal experiments with polymers of PTFE, PCTFE and PCTFE including plasticiser of unknown compositions (continuous inhalation exposure of mice to concentrations greater than 10 ppm; 1 h/d, 28 days and 1 h/d, 2 weeks) resulted in death (Hagemeyer and Stubblebine, 1954). Daily exposures appeared to have a cumulative effect, particularly in the region of 10 ppm. Autopsies showed inflammation and destruction of the tissues, oedema of the lungs, and enlargement of the heart. However, insufficiently reported study details (e.g. no information on control group, chemical/polymer characteristics, study design, etc.) weaken the power of the available information.

Moreover, significant loss of body weight below the initial weight (>10%, manifested at day 7) during a 14-day repeated oral exposure of adult rats with pure PCTFE tetramers as well as with oligomeric PCTFE oil (3.1 oil-C6:C8, composed of 55% trimer and 45% tetramer oligomers) was observed for example by DelRaso et al. (1991). Furthermore, compared to controls, significantly decreased body weights and body weight gains of adult rats exposed to PCTFE oligomers/polymers were reported for either the oral route (pure trimers, pure tetramers, oligomeric PCTFE oils) (DelRaso et al., 1991; Hagemeyer and

Stubblebine, 1954; Kinkead et al., 1991; Kinkead et al., 1989; Kinkead et al., 1990a; Kinkead et al., 1990b), or for the inhalational route of an oligomeric PCTFE oil (70% trimer: 30% tetramer) (Kinkead et al., 1989; Kinkead et al., 1990b). Also for polymeric PFPE surfactant, Johnston et al. (1996b) reported reduced body weights of rats, based on unpublished data. Affected body weights in adult rodents are also observed for non-polymeric PFASs, such as PFHxA, PFNA, PFOS (EFSA, 2020).

Furthermore, oral oligomeric PCTFE oil administration to rats led to significant changes in total protein, glucose and in serum albumin (Kinkead et al., 1990a; Mattie et al., 1993) as well as in erythroid parameters (Kinkead et al., 1989; Mattie et al., 1993), and in signs of neurotoxicity accompanied by increased brain weight (Kinkead et al., 1990a), were reported.

Oral, dermal and inhalation repeated dose toxicity studies with experimental animals were summarised in an evaluating report regarding fluoropolymers as cosmetic ingredients, focussing on PTFE (Johnson and Zhu, 2018), but also on PCTFE in earlier versions (Johnson, 2018a; Johnson, 2018b).

Krytox™ (PFPE base oil) inhalation resulted in mild effects (increased lung weight) at the highest tested concentration (1 000 mg/m³), but no liver effects (such as liver weight, liver enzyme, peroxisomal β -oxidation or histopathologic examination) in rats (DelRaso, 1996; Kelly et al., 1993).

Some additional data on other effects of oligomeric/polymeric PFASs on humans are addressed under B.5.4.

B.5.2.2. Toxicity to reproduction (experimental animal data)

In a recent review, Fenton and colleagues concluded on reproductive toxicity that exposure to PFASs has adverse effects on conception, pregnancy, and foetal development. The underlying birth weight data are largely supportive, while the literature on growth and obesity is inconclusive (Fenton et al., 2021).

B.5.2.2.1. Developmental effects in experimental animals

Adverse effects on reproduction in experimental animal models, such as total litter loss and perinatal/postnatal mortality, have been observed for a variety of **non-polymeric** PFASs with different chemical structures. (Total) Litter loss was observed in experimental animal models after exposure to

- TFA (Covance Laboratories, 2020a), as well as after exposure to
- PFCAs of various chain lengths:
 - PFBA (Das et al., 2008),
 - PFOA (Abbott et al., 2007),
 - PFNA (Das et al., 2015; Singh and Singh, 2019a; Wolf et al., 2010),
 - PFDA (Harris and Birnbaum, 1989),
 - PFODA (Hirata-Koizumi et al., 2012)
- PFECa
 - F-DIOX (RTC, 2011).

Neonatal/Postnatal mortality was observed in experimental animal models for exposures to

- some PFCAs and PFSA:
 - PFHxA (Iwai and Hoberman, 2014),
 - PFHpA (Anonymous, 2017),
 - PFOA (Abbott et al., 2007; Lau et al., 2006; Song et al., 2018a; Yahia et al., 2010),

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

- PFNA (Das et al., 2015; Wolf et al., 2010),
- PFOA (Hirata-Koizumi et al., 2012), and
- PFOS (Lau et al., 2003; Luebker et al., 2005a; Luebker et al., 2005b; Yahia et al., 2008). Furthermore,
- PFECAs:
 - HFPO-DA (Conley et al., 2021),
 - ADONA (Charles River, 2007b),
 - EEA-NH4 (WIL, 2011b).
- Complex ether-based PFAS
 - Noviflumuron also resulted in postnatal mortality (Dow AgroSciences, 2004).
- FTOHs
 - 6:2 FTOH has also been shown to increase pup mortality (Kirkpatrick, 2005; O'Connor et al., 2014; WIL, 2005).

Reduction of offspring body weight and/or reduced body weight gain is also one of the more consistent developmental effects throughout different PFAS groups in experimental animal models. It can be a secondary effect of maternal toxicity (or influenced by it), caused by prenatal exposure, or by exposure through lactation (also see B.5.1.1.2 and B.5.1.1.4). Reduced offspring body weight (gain) was detected for all of the above-mentioned substances (except PFBA) and in addition for

- PFUnDA (Takahashi et al., 2014),
- PFTeDA (Hirata-Koizumi et al., 2015),
- PFBS (Feng et al., 2017), and
- Perfluamine/PTPA (Charles River, 2019a).

A variety of fluorinated gases (HFCs and HFOs) also caused reduced pup body weight (gain):

- HFC-245fa (Frauenhofer Institut für Toxikologie und experim. Medizin, 2005),
- HFC-4310mee (Haskell, 1994),
- HFCPA (ZEORORA) (Huntingdon, 1998b),
- HFO-1336mzz(Z) (DuPont Haskell, 2010b; DuPont Haskell, 2014; WIL, 2014),
- HFO-1336mzz(E) (Triskelion, 2016),
- HFO-1216 (Triskelion, 2019a).

Decreased pup body weight was also seen after 6:2 FTOH and 8:2 FTOH exposure (Kirkpatrick, 2005; Mukerji et al., 2015; Mylchreest et al., 2005; O'Connor et al., 2014; WIL, 2005).

Other effects indicating toxicity to reproduction were only evident for single substances or single groups of PFASs. Those effects include the impaired development of mammary glands, which is to date only investigated for PFOA exposure (Macon et al., 2011; Tucker et al., 2015; White et al., 2011).

Delayed ossification during development occurred in several PFAS groups (various PFAAs, HFPO-DA, several fluorinated gases, 6:2 FTOH as well as 8:2 FTOH) in experimental animal models (e.g., Lau et al., 2006; Mylchreest et al., 2005; O'Connor et al., 2014; Tveit et al., 2013; WIL, 2010a). Delayed ossification is often a secondary effect due to reduced pup weight or maternal toxicity. Still, there is emerging evidence that bone mineralisation may be affected by PFASs also in human children (see B.5.3.4.1) (Cluett et al., 2019; Fenton et al., 2021). Some PFASs caused developmental malformations in offspring of experimental animal models: TFA (Covance Laboratories, 2020b), PFOA (Lau et al., 2006), and HFC-125. However, for the latter the effect was only found in few pups at higher concentrations ((Huntingdon, 1992)).

For **oligomeric/polymeric PFASs**, no studies observing developmental toxicity are known.

B.5.2.2.2. Fertility effects in experimental animals

Reduced weight of reproductive organs might further affect fertility and is a consistent effect across various **non-polymeric** PFASs and various PFAS classes:

- PFCAs
 - TFA (Covance Laboratories, 2020b),
 - PFNA (NTP, 2019a),
 - PFDA (NTP, 2019a),
 - PFDoDA (Chen et al., 2019b; Kato et al., 2015),
- PFSAs
 - PFBS (Feng et al., 2017),
 - PFOS (Lee et al., 2015),
- PFECAs
 - HFPO-DA (Conley et al., 2019; Haskell, 2010; WIL, 2008a; WIL, 2010a; WIL, 2010b),
 - EEA-NH4 (WIL, 2011b),
 - F-DIOX (RTC, 2011),
 - 6:2 Cl-PFESA (Zhou et al., 2018),
- Other ether-based PFASs
 - Move3 (Triskelion, 2017),
 - Noviflumuron (Dow AgroSciences, 2002a),
- HFCs
 - HFC-134a (ICI, 1979),
 - HFCPA (ZEORORA) (Huntingdon, 1998b),
- FTOHs
 - 6:2 FTOH (Mukerji et al., 2015; O'Connor et al., 2014), and
- the TFA-precursor 2,2,2-Trifluoroethanol (Wilkenfeld RM, 1981).

Several different PFASs from different PFAS groups impaired sperm quality in experimental animal models after exposure to PFNA (Singh and Singh, 2019a; Singh and Singh, 2019b), PFDA (NTP, 2019a), and PFDoDA (Kato et al., 2015), as well as PFOS (Zhang et al., 2019b). Moreover, sperm quality was diminished in animal experiments by 6:2 Cl-PFESA (Zhou et al., 2018) as well as the fluorinated gas HFC-245fa (Frauenhofer Institut für Toxikologie und experim. Medizin, 2005) and the TFA precursor 2,2,2-Trifluoroethanol (Wilkenfeld RM, 1981).

Furthermore, a reduction of sex hormones (estradiol and/or testosterone) was measured in parental animals after exposures to different PFAAs: PFNA (Feng et al., 2010; Feng et al., 2009; NTP, 2019a; Singh and Singh, 2019a), PFDA (NTP, 2019a), PFDoDA (Shi et al., 2009; Shi et al., 2007), and PFBS (Cao et al., 2020), PFOS (Zhang et al., 2020c). Impairment of oestrus cyclicity was observed in rodents after exposure to PFDoDA (Kato et al., 2015), PFBS (Feng et al., 2017)(also in pup oestrus cycle), PFOS (Du et al., 2019; NTP, 2019b), and HFPO-DA (WIL, 2008a) and 6:2 FTOH (Mukerji et al., 2015).

Reduced fertility indices were observed in experimental animal models for Noviflumuron (Dow AgroSciences, 2004), for the fluorinated gas HFC-4310mee (DuPont Haskell, 2007b), and the TFA precursor 2,2,2-Trifluoroethanol (Wilkenfeld RM, 1981). Infertility was associated with PFOA and PFHxS in humans (Fei et al., 2009; Fenton et al., 2021).

For **oligomeric/polymeric PFASs**, no studies observing fertility effects are known.

B.5.2.2.3. Effects on or via lactation in experimental animals

Reduced pup weight gain during the lactation period was observed after exposures to TFA

(Covance Laboratories, 2020a), PFHxA (Iwai and Hoberman, 2014), F-DIOX (RTC, 2012) and Noviflumuron (Dow AgroSciences, 2004). However, reduced pup weight during lactation can have multiple reasons and only cross-fostering experiments with lactation exposure excluding prenatal exposure can clearly indicate lactational effects. For example, PFOA induced impairment of mammary gland development only via lactation without prenatal exposure (EFSA, 2020; White et al., 2009). For Noviflumuron, data from a cross-fostering study “indicate that the exposure of the test material to foetuses through the placenta is limited and the majority of exposure occurs postnatally through nursing.” (TERC, 2005) (also see B.5.1.2).

B.5.2.3. Carcinogenicity (experimental animal data)

Several **non-polymeric** PFASs have recently been classified as possibly or probably carcinogenic to humans. The International Agency for Research on Cancer (IARC) classified PFOA as possibly carcinogenic (Group 2B; (IARC, 2017)) based on positive associations observed for cancers of the testis and kidney as well as increased incidences of testicular Leydig cell adenoma, hepatocellular adenoma, and pancreatic acinar cell adenoma in animal studies. The US EPA found that there is suggestive evidence that PFOA (EPA-US, 2016b), PFOS (EPA-US, 2016a), and HFPO-DA (EPA-US, 2018) may cause cancer. The EFSA ContamPanel concluded in 2018 that there is insufficient support for carcinogenicity of PFOS and PFOA in humans from epidemiological studies, but that both compounds induced tumours in rats (EFSA, 2018). According to the CLP Regulation in the EU, 17 PFASs currently exhibit a harmonised classification as carcinogenic (Carc. 2 or Carc. 1B; e.g. PFOA and its ammonium salt, PFNA and its sodium and ammonium salts, PFDA and its sodium and ammonium salts, PFOS and its ammonium, lithium and potassium salts, trifluralin). Additionally, amongst the PFASs registered in the EU, 82 PFASs are self-classified by registrants as Carc. 1A/B or Carc. 2.

For PFOA (3M, 1983; Biegel et al., 2001; Kamendulis et al., 2022; NTP, 2019a), PFOS (Butenhoff et al., 2012b), HFPO-DA (EPA-US, 2018; MPI Research Inc., 2013), Tetraconazole (Huntingdon, N/A-e), Noviflumuron (Dow AgroSciences, 2005b), and HFC-134a (Collins et al., 1995) there is evidence for carcinogenic effects from animal studies (e.g. Leydig cell adenoma, hepatocellular adenoma and carcinoma, pancreatic acinar cell adenoma and adenocarcinomas, follicular adenomas and carcinomas of the thyroid, renal tubule adenoma or carcinoma). For the observed carcinogenic effects, the available information is not sufficient to rule out human relevance of the underlying mode of action (ATSDR, 2021).

Regarding **polymeric** PTFE, several studies found carcinogenic effects (e.g. malignant sarcomas/fibrosarcomas) after subcutaneous implantation of PTFE implants in rodents (Bryson and Bischoff, 1969; IARC, 1999; Oppenheimer et al., 1955; Russell et al., 1959; Tomatis, 1963). Comparable number of tumours were seen in experimental animals with similarly sized implants of glass (IARC, 1999; Tomatis, 1963) and non-fluorinated polyethylene (Oppenheimer et al., 1955). Solid-state carcinogenesis (IARC, 1999) might therefore be an explanation for the carcinogenic effects of PTFE implants.

For the vast majority of PFASs, long-term toxicity or carcinogenicity studies as well as epidemiological studies informative on potential carcinogenic effects are not available and thus, human relevance of carcinogenicity of most PFASs is unclear.

B.5.3. Evidence from epidemiological data

In 2021, ATSDR published Toxicological Profile for Perfluoroalkyls (ATSDR, 2021) including literature published before September 2018.

In 2018 and 2020, EFSA published two opinions on PFASs in food including literature searched covering the time period between January 2008 and July 2019. In the EFSA opinion from 2020, 27 PFASs¹³ were included but only PFOS, PFHxS, PFOA and PFNA were included in the risk characterization (EFSA, 2018; EFSA, 2020).

For the present restriction dossier, a new literature search (Medline) was performed in August 2021 to identify papers published on PFASs not included in the EFSA opinions, as well as papers published after July 2019 for the 27 PFASs covered by EFSA.

This section focuses particularly on evaluating whether new studies strengthen or weaken the conclusions made by EFSA (2020) and if data on additional PFASs follow the same patterns. A narrative review of the new information is provided below (sections B.5.3.1 to B.5.3.5).

Several studies have measured PFASs that were not included in the final statistical analyses due to low detection frequencies (e.g. detected in less than 70% of the study population). This does not rule out possible associations between these PFASs and health outcomes. For the less studied PFASs, the evidence for exposure-health association is limited due to the small number of studies.

B.5.3.1. Epidemiological evidence for effects on organ function, energy metabolism and the immune system

B.5.3.1.1. Immune outcomes

Since effects of PFASs on the immune system were considered the most critical for the risk assessment by EFSA (2020), the literature search for the immune outcomes in humans was extended to cover the period until 25th January 2022. The outcomes have been categorised into vaccination responses, common infectious diseases, asthma- and allergy-related outcomes and autoimmune diseases.

Vaccination response

EFSA concluded in 2020 that PFOS and PFOA are associated with reduced antibody responses to vaccination. Given the lower concentrations of other PFASs, the evidence for associations for these were weaker (EFSA, 2020). Further, ATSDR (2021) stated that PFOA, PFOS, PFHxS and PFDA are inversely related to vaccination responses, and reported also some limited evidence for similar associations for PFNA, PFUnDa and PFDoDa.

The new literature search identified three studies published between July 2019 and January 25th 2022. No studies on additional PFASs than the 27 included in EFSA (2020) were identified in the new literature search.

In a study based on a subset of data from a randomised controlled trial of early measles vaccination conducted in Guinea-Bissau (Timmermann et al., 2020), children's (n = 237) PFOS and PFDA levels at inclusion (4-7 months of age) were associated with lower measles antibody concentrations at 9-months among the children who had received a measles vaccine. Furthermore, there was a trend towards reduced pre-vaccination measles antibody levels with elevated PFAS levels (PFHxS, PFOA, PFNA, PFUnDa) indicated by

¹³ The PFASs included in EFSA (2020): PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDa, PFDoDa, PFTrDA, PFTeDA, PFPeDA, PFHxDA, PFODA, PFBS, PFHxS, PFHpS, PFOS, PFDS, PFOSI, 8:2 FTOH, 8:2 monoPAP, 8:2 diPAP, FOSA, EtFOSA, EtFOSE, FC-807.

sensitivity analysis where the most influential PFAS observations were removed.

In another prospective study from the Faroe Islands (Shih et al., 2021), the association between several PFASs (PFOS, PFOA, PFHxS, PFNA, PFDA) at birth, 7, 14, 22 and 28 years of age and serum antibody levels in adults vaccinated at age 28 against hepatitis type A and B, diphtheria and tetanus (n=172-399) were evaluated. Inverse, but not statistically significant, trends were observed between PFOA at ages 14 and 28 years and hepatitis type A antibody levels, as well as PFOA at 22 and 28 years and hepatitis type B antibody levels. No inverse associations of PFAS exposure were found with diphtheria and tetanus antibody concentrations.

In a cross-sectional study in vaccinated Greenlandic children (7 – 12 years of age), serum levels of PFHxS and PFOS was associated with lower diphtheria antibody levels in children with known vaccination record (n = 169). No similar associations were observed for tetanus antibody levels (Timmermann et al., 2022). No associations were observed for PFHpS, PFOA, PFNA, PFDA and PFUnDA.

All three studies reported inverse trends between levels of PFASs and vaccine antibody levels, hence supporting the conclusions of ATSDR and EFSA.

Common infectious diseases

EFSA concluded that there is some evidence to suggest that exposures to PFASs are associated with increased propensity of infections but that more studies with objective measures of infections (not self-reports) are needed (EFSA, 2020).

Twelve studies were identified in the new literature search. Of these studies, five examined the effect of prenatal PFAS exposure and health outcome in children, two examined childhood exposure and outcome in children/adolescents (prospective design), and five were cross-sectional studies in adults. With the exception of Zeng et al. that included 6:2 Cl-PFESA and 8:2 Cl-PFESA (Zeng et al., 2020), no data on additional PFASs than the ones included in EFSA (2020) were identified.

With regard to upper respiratory tract infections (URTI) (Dalsager et al., 2021; Kvaem et al., 2020; Wang et al., 2022) and gastric infections (Dalsager et al., 2021; Timmermann et al., 2020; Wang et al., 2022), there are inconsistent findings. When it comes to lower respiratory tract infections (LRTI), however, four of six prospective studies reported positive associations between either prenatal or childhood exposure to PFASs and LRTI (PFOS, PFHxS, PFHpS, PFOA, PFNA, PFDA, PFHpA and/or PFDoDA) (Ait Bamai et al., 2020; Dalsager et al., 2021; Impinen et al., 2019; Kvaem et al., 2020). A positive association was also reported for PFBS and respiratory tract infections, including both URTI and LRTI (Huang et al., 2020). Furthermore, two of the three prospective studies examining groups of infectious diseases as the outcome reported positive associations between either prenatal or childhood exposure to PFASs and infections (Timmermann et al., 2020): Fever, diarrhea, coughing or vomiting; (Dalsager et al., 2021): URTI, LRTI, GI or other infections). In the cross-sectional study on groups of outcomes, Bulka et al. (2021) reported on a positive association between PFAS exposure (PFOS, PFHxS, PFOA, PFNA) and pathogen burden (sum of seropositivity: cytomegalovirus, Epstein Barr virus, hepatitis C and E, herpes simplex 1 and 2, HIV, *T. gondii*, and *Toxocara* spp). The association between PFOS, PFOA, PFBA, 6:2 Cl-PFESA, 8:2 Cl-PFESA and the antibody levels of hepatitis B virus (HBsAb) were investigated in a cross-sectional study on Chinese adults. Lower serum HBsAb levels were observed for an increase in linear PFOS, 6:2 Cl-PFESA, 8:2 Cl-PFESA and PFBA. The association seemed to be stronger for 6:2 Cl-PFESA than for PFOS. Furthermore, cross-sectional studies in adults on COVID-19 infections reported positive associations with several PFASs (Grandjean et al., 2020; Ji et al., 2021; Nielsen and Joud, 2021).

Overall, the new studies strengthen the evidence for an association between PFASs and

common infectious diseases, and particularly with respect to lower respiratory tract infections.

Asthma and allergies

In a prospective study no associations between prenatal exposure to PFASs and doctor-diagnosed asthma were observed, whereas in another prospective study an association between PFNA and self-reported **asthma** (not doctor-diagnosed) was reported (Beck et al., 2019; Zeng et al., 2019b). Two cross-sectional studies were identified, one reported an increased risk of asthma in young children with exposure to PFOS and PFOA (Jackson-Browne et al., 2020), whereas no statistically significant associations were found in a study in adolescents (Gaylord et al., 2019).

There is little evidence for an effect of tested PFASs on **lung function** in humans. Three prospective studies have investigated the effect of prenatal PFAS exposures on lung function in childhood (4-12 years of age) (Agier et al., 2019; Kung et al., 2021; Manzano-Salgado et al., 2019), whereas one study has investigated the effect of exposure at age 10 years and lung function at the age of 16 years (Kvalem et al., 2020). No statistically significant findings were reported except an inverse association between prenatal exposure to PFOA and forced vital capacity (FVC) at age 4 years (Manzano-Salgado et al., 2019). With regard to cross-sectional studies in children and/or young adults, no statistically significant associations have been observed (Agier et al., 2019; Gaylord et al., 2019; Impinen et al., 2018; Kung et al., 2021; Kvalem et al., 2020).

Regarding **atopic dermatitis** in relation to PFAS exposure, no statistically significant associations were observed in a cross-sectional study including children (Kvalem et al., 2020). In studies with a prospective design, however, prenatal (Ait Bamai et al., 2020; Impinen et al., 2019; Lowe et al., 2019; Manzano-Salgado et al., 2019) or childhood (Kvalem et al., 2020) exposure to some PFASs (PFHxS, PFOS, PFHxA, PFOA, PFUnDA, PFTrDA, PFDoDA and/or N-MeFOSAA) have been associated with a reduced risk of atopic dermatitis, while one study observed a positive association with prenatal PFOA exposure (Wen et al., 2019). Most of the associations with atopic dermatitis are seen in relation to exposure to PFCAs. One study on total IgE levels were identified. Using piecewise linear regression, inverse relations were observed between PFASs (PFOS, PFOA, PFNA, PFDA) and total IgE below the turning point and positive relations above the turning point (Zeng et al. 2019).

As concluded by EFSA, there are no or inconsistent associations between prenatal and postnatal PFAS exposure and asthma in children and young adults. Furthermore, there is little evidence for an effect of PFAS exposure on lung function. With regard to allergy-related outcomes, there is increasing evidence for an inverse association between PFASs and atopic dermatitis, whereas no conclusion can be drawn with regard to the effect of PFAS exposures on rhinitis, urticaria, serum IgE or skin prick tests due to few studies and inconsistent findings. No data on additional PFASs than the 27 included in EFSA (2020) were identified.

Autoimmunity

According to EFSA (2018) and ATSDR (2021), there is some suggestive association between serum PFOA and an increased risk of ulcerative colitis, but not for other autoimmune diseases. No studies on autoimmune diseases were retrieved from the new literature search.

B.5.3.1.2. Thyroid function and disease

EFSA (2018) and EFSA (2020) concluded that the available evidence was insufficient to suggest that exposures to PFASs are associated with thyroid disease or changes in thyroid hormones. The vast majority of the reviewed studies were cross-sectional.

The updated literature search identified 14 studies. Several of the recent studies investigated PFAS mixture effects. Six publications used data from birth cohort studies and examined prospective associations between PFASs measured in maternal blood sampled in pregnancy and thyroid hormones measured in neonatal cord-blood. Of these, five also reported cross-sectional associations with maternal thyroid function and/or disease (Itoh et al., 2019; Lebeaux et al., 2020; Liang et al., 2020; Preston et al., 2020b; Preston et al., 2018; Xiao et al., 2020). Two studies reported cross-sectional associations where PFASs and thyroid function markers were measured in neonatal cord-blood (Guo et al., 2021) or in child blood at age 2, 4 and 6 years (Kim et al., 2020a).

Six studies reported associations between PFASs and thyroid hormones in adult populations, one was prospective (Blake et al., 2018), one a case-control study (Li et al., 2021d), and four were cross-sectional (Aimuzi et al., 2020; Gallo et al., 2022; Inoue et al., 2019; Sarzo et al., 2021).

Overall, the results from prospective studies indicated positive associations between prenatal PFAS mixtures and single PFASs (elaborated below) with T3 and fT3, inverse associations with T4 and/or fT4, and null associations with TSH. However, it is noted that the results were not consistent between the studies regarding which of the PFASs that contributed to the thyroid hormone associations, sex-differences, and/or maternal thyroid antibody status. For example, in Preston et al. (2020b) higher concentrations of PFAS mixtures (BKMR and WQS) showed that PFHxS and N-MeFOSAA contributed most to lower T4, and associations were predominantly found in male neonates, whereas Liang et al. (2020) showed that PFNA, PFDA and PFUnDA contributed most to the PFAS mixture (BKMR) association with higher T3, while Itoh et al. (2019) and Lebeaux et al. (2020) found that PFOA, PFOS and PFHxS contributed most to lower cord fT4 but was only found in mothers with higher TPO antibody levels.

For the studies in adults, some associations between individual PFASs and PFAS mixtures and thyroid function were indicated, while the two cross-sectional studies in neonates showed inconsistent associations. Overall, the new studies strengthen the concern that PFAS exposures might be associated with thyroid disease or changes in thyroid hormones.

B.5.3.1.3. Liver effect and metabolic outcomes

Liver enzymes and liver disease

EFSA (2020) concluded that “epidemiological studies provide evidence for an association between exposure to PFASs and increased serum levels of the liver enzyme alanine transferase (ALT). The magnitude of the associations was small, however, and few studies found associations with ALT outside the reference range. There were no associations with liver disease.”

Two cross-sectional (Attanasio, 2019; Jin et al., 2020d) and two prospective studies (Mora et al., 2018; Stratakis et al., 2020) were identified in the new literature search. A cross-sectional analysis of NHANES data (2013-2016) reported sex-differences for the associations between PFOA and PFNA and the liver enzymes ALT and aspartate aminotransferase (AST) in adolescents aged 12 – 19 years, with positive associations in females and inverse associations in males (Attanasio, 2019). Also, PFHxS was inversely associated with AST in males, but not in females. PFOA, PFNA, PFOS and PFHxS were positively associated with bilirubin levels in both male and female adolescents (Attanasio, 2019).

A prospective study in the US project Viva cohort examined associations between prenatal PFASs exposure and ALT levels in children (mean age 7.7 years). This study also reported sex differences and showed that in girls, prenatal exposures to N-MeFOSAA and N-EtFOSAA were associated with lower ALT. The other PFASs showed similar tendency (Mora et al., 2018). These two studies suggest that prenatal and early life exposures to PFASs may

show sex and developmental stage dependencies.

A study by Jin et al. (2020d) in children and adolescents with physician-diagnosed non-alcoholic fatty liver disease (NAFLD), reported associations between alterations in key amino-acids and lipids pathways underlying NAFLD pathophysiology and exposure to PFOA, PFOS, PFHxS and a mixture of PFAS.

In a subcohort from the Human Early-Life Exposome (HELIX) project, Stratakis et al. (2020) evaluated whether prenatal exposure to PFASs in 1 105 mothers and their children was associated with established serum biomarkers of liver injury and alterations in serum metabolome in children. Higher exposure to PFAS mixture (PFOS, PFOA, PFNA, PFHxS, and PFUnDA) during pregnancy was associated with higher liver enzyme levels of ALT, AST, and gamma-glutamyltransferase (GGT) in child serum. They also found significant perturbations in amino acid and glycerophospholipid metabolism associated with prenatal PFAS exposure.

Furthermore, a systematic review and meta-analysis of 24 human epidemiological studies and 85 rodent studies provide new evidence for a causal association between PFASs exposure and liver disease (Costello et al., 2022). Meta-analyses of the human studies revealed that exposure to PFOA, PFOS, and PFNA were associated with higher ALT levels. PFOA exposure was also associated with higher aspartate aminotransferase and gamma-glutamyl transferase levels in humans. In rodents, PFAS exposures consistently resulted in higher ALT levels and steatosis. Thus, the results for associations between PFASs and markers of liver function in observational human studies strengthen the evidence for PFASs hepatotoxicity from rodent studies.

The results from the new studies are in line with the findings in EFSA (2020) and strengthen the evidence for an association between exposure to PFASs and increased levels of the liver enzymes, mainly alanine transferase (ALT).

Blood lipids

In 2018, EFSA concluded that human epidemiological studies provided strong support for associations between exposure to PFOS and PFOA and increased serum levels of total cholesterol (TC) and LDL cholesterol (LDL-C). Evidence for a similar association for PFNA were reported by EFSA in 2020. However, there is uncertainty connected to the causality of this association because of potential confounding caused by common mechanisms of reabsorption of bile acids and PFASs in the small intestine (enterohepatic circulation) (EFSA 2020). Reabsorbed bile acids are negatively correlated with serum cholesterol, meaning that individuals with low enterohepatic circulation (e.g. by natural individual variability) can have low levels of PFASs and low levels of cholesterol, which leads to a significant but possibly not causal correlation (EFSA, 2020).

In the new literature search, one prospective birth cohort study and 15 cross-sectional studies were identified of which one had both a cross-sectional and prospective design (Liu et al., 2020b). Three of the studies (Cong et al., 2021; Han et al., 2021a; Yu et al., 2021c) included 6:2 CI-PFESA and 8:2 CI-PFESA that were not covered by EFSA.

A study in the Odense Child cohort examined PFASs in maternal pregnancy serum (PFOS, PFOA, PFHxS, PFNA and PFDA) and repeated lipid measurements in infancy (up to 18 months). The results showed that PFNA and PFDA were positively associated a higher TC (Jensen et al., 2020b).

Liu et al. (2020b) performed a 2-year follow-up study in adults investigating the effect of plasma PFASs (PFOS, PFOA, PFHxS, PFNA, PFDA) at baseline with lipoprotein and apolipoprotein subspecies both at baseline and at 2 years. At baseline, elevated plasma PFOA concentrations were significantly associated with higher apoB and apoC-III concentrations. PFASs were not associated with TC or triglycerides (TG). PFAS levels were

primarily associated with lipids or apolipoprotein concentrations in intermediate-to-low density lipoprotein (IDL+LDL) and HDL-C that contain apoC-III. Similar patterns of associations were observed at the two-year follow-up.

Several cross-sectional studies examined associations between PFASs and blood lipids in adolescents or adults. Positive association for PFASs (PFOA, PFOS, PFHxS, PFNA, PFDA, PFUnDA and/or 6:2 Cl-PFESA) with TC and/or LDL-C were reported in six studies (Averina et al., 2021; Canova et al., 2020; Cong et al., 2021; Han et al., 2021a; Lin et al., 2020a; Lin et al., 2020c). One study reported a positive association between PFOA and small dense LDL particles (Liou and Kaptoge, 2020). Two studies reported no associations between the PFASs and TC or LDL-C (Chen et al., 2020b; Menzel et al., 2021).

The majority of the studies on high-density lipoprotein cholesterol (HDL-C) and TG observed null associations with PFASs. However, positive and inverse associations were also reported (Canova et al., 2020; Chen et al., 2020b; Cong et al., 2021; Han et al., 2021a; Lin et al., 2020a; Lin et al., 2020c; Ye et al., 2021; Yu et al., 2021c; Zare Jeddi et al., 2021). This is in line with the previously described variability in these associations as described by EFSA (EFSA, 2018; EFSA, 2020).

Two studies examined PFAS lipid associations in pregnant women (Dalla Zuanna et al., 2021; Yang et al., 2021). In a cross-sectional study by Dalla Zuanna et al. (2021) plasma levels of TC, HDL-C and LDL-C were reported to increase throughout the trimesters. PFOA was inversely associated with TC, whereas both PFOA and PFHxS were inversely associated with LDL-C. All the three PFASs were positively associated with HDL-C. In a cohort of pregnant women in China, Yang et al. (2021) reported positive associations between PFHxS level and TC, LDL and LDL-C, as well as between PFUnDA level and HDL-C. Inverse associations were reported for PFDA and LDL-C, and for PFOA and the LDL-C/HDL-C ratio. No associations were reported for PFOS, PFNA, PFHpS and the sum of PFASs and the blood lipids. Of note, serum cholesterol is normally elevated during pregnancy.

In a cross-sectional study in Taiwanese children using lipidomics, 13 PFASs were analysed (Lee et al., 2021). PFTrDA and PFDA exposures were associated with serum lipid profiles, while PFOS exposure showed a borderline significant association. When examining the associations of exposure to each of these PFASs with each lipid, several lipids were identified associated with the levels of the PFASs.

In the cross-sectional Fit Futures study, the effect of serum PFASs in adolescents on dyslipidemia (defined as: TC $\geq$ 5.17 mmol/L and/or LDL-C $\geq$ 3.36 mmol/L and/or apolipoprotein B $\geq$ 1.10 g/L) was examined. The highest vs. lowest quartiles of total PFAS (Σ PFAS), PFNA and PFDA concentrations were positively associated with the risk of dyslipidemia (Averina et al., 2021).

In line with the findings in EFSA (2020), the review of new studies supports the association in non-pregnant adults between PFASs and total cholesterol, LDL cholesterol and inconsistency in the associations with HDL cholesterol and triglycerides. More data on PFASs other than PFOS and PFOA indicate similar associations also for PFHxS, PFNA, PFDA and PFUnDA, 6:2 Cl-PFESA and 8:2 Cl-PFESA.

Diabetes

In the EFSA Opinion on PFOS and PFOA (EFSA, 2018), 15 studies were reviewed on the associations between PFOS and/or PFOA and glucose homeostasis or diagnosis of diabetes. Overall, the results did not indicate adverse effects on glucose homeostasis or increased risk of diabetes. In EFSA (2020), eight studies were reviewed on associations between PFASs other than PFOS and PFOA, and diabetes (or metabolic syndrome), and the results were not consistent. EFSA (2020) thus concluded on insufficient evidence for associations between PFASs and diabetes.

The new literature search identified 11 studies published after July 2019 reporting on associations between PFASs and risk of diabetes, and one study published before 2019 addressing PFASs not discussed by EFSA in 2020.

Of the four prospective studies on **gestational diabetes**, three studies observed a statistically significant association with PFAS exposure (Rahman et al., 2019; Xu et al., 2020a; Yu et al., 2021a). The PFASs that were positively associated with gestational diabetes were PFOS, PFNA and PFHpA in Yu et al. (2021a) and PFNA, PFOA, PFHpA, PFDoDA in Rahman et al. (2019), and PFBS and PFDoA in Xu et al. (2020a). In the fourth study by Zhang et al. (2015), no associations were observed between N-ETFOSAA, N-MeFOSAA, PFDA, and PFOSA and gestational diabetes.

Two cross-sectional studies on gestational diabetes reported positive associations with PFAS exposure (Preston et al., 2020a; Ren et al., 2020). Preston et al. (2020a) reported a positive association between PFOS and MeFOSAA and biological markers linked to gestational diabetes. Ren et al. (2020) reported positive associations between PFOS, PFNA, PFDA, PFUnDA and PFDoA with glucose levels in pregnant women, linked to the risk of gestational diabetes.

Regarding **diabetes type 2**, a prospective adult cohort study which included six PFASs (PFOS, PFOA, PFHxS, N-EtFOSAA, N-MeFOSAA), found that PFOA was significantly associated with an increased risk of diabetes and that PFOS and N-EtFOSAA were associated with microvascular disease (Cardenas et al., 2019).

The four case-control studies on diabetes type 2 in adults showed inconsistent findings with positive, no or inverse associations between PFASs and diabetes type 2 (Charles et al., 2020; Duan et al., 2021; Han et al., 2021a; Schillemans et al., 2021).

Positive associations between PFAS exposure and diabetes were reported in two cross-sectional studies (Duan et al., 2020; Zeeshan et al., 2021). Zeeshan et al. reported positive associations between branched PFOS, linear PFOS, branched PFHxS, linear PFHxS, PFOA, PFHpS, PFNA, PFDA, PFUnDA, PFTTrDA and total PFAS and diabetes type 2. Duan et al. reported that PFHxA, PFOA, PFNA, PFHxS, Σ PFCAs C2-C3 (sum ultrashort-chain perfluoroalkyl carboxylic acids, i.e. 2-3 carbon atoms), Σ PFCAs C4-C7 (sum short chain PFCAs i.e., 4-7 carbon atoms), Σ PFCAs C8-C12 (sum long chain PFCAs, i.e., 8-12 carbon atoms), Σ PFCAs (sum all PFCAs), and Σ PFASs (sum all PFASs) were positively associated with glycemic biomarkers linked to increased risk of diabetes (Duan et al., 2020).

In line with the findings in EFSA (2020), the review of new studies shows inconsistent results with positive, no- or inverse associations between PFASs and diabetes type 2. However, there are new studies suggesting a positive association between several PFASs and gestational diabetes.

Obesity

EFSA (2020) concluded that “there is insufficient evidence for associations between PFASs and obesity”.

The literature review in 2021, identified 11 studies published after July 2019 reporting associations between PFASs and obesity, and one prospective cohort with repeated measures of both PFASs and outcome (Blake et al., 2018) reporting PFASs (Me-PFOSA and Et-PFOSA) not included in EFSA 2020. Five of these were studies in adults (Blake et al., 2018; Chen et al., 2020b; Ding et al., 2021; Mitro et al., 2020a; Mitro et al., 2020b) and seven in children and adolescents. Of the studies in children, those with PFASs assessed during pregnancy (Jensen et al., 2020a; Martinsson et al., 2020; Starling et al., 2019) are described in section B.5.3.2.2.

In adults, positive associations between PFAS and obesity were reported for PFOS (Chen

et al., 2020b; Ding et al., 2021; Mitro et al., 2020b), PFOA (Chen et al., 2020b; Ding et al., 2021; Mitro et al., 2020a; Mitro et al., 2020b)), PFHxS (Averina et al., 2021; Chen et al., 2020b), PFHpS (Averina et al., 2021), N-EtFOSAA (Ding et al., 2021), and N-MeFOSAA (Ding et al., 2021). In the study by Blake et al. (2018) none of the investigated PFASs (PFOA, PFOS, PFOSA, PFNA, PFHxS, PFDeA, Me-PFOSA and Et-PFOSA) were associated with obesity.

In children and/or adolescents, inverse associations between PFAS and obesity were reported for PFOS (Thomsen et al., 2021) and PFOA (Pinney et al., 2019), PFNA (Domazet et al., 2020), PFHxS (Domazet et al., 2020), and PFDA (Domazet et al., 2020; Thomsen et al., 2021).

The review of new studies suggests differences in associations between PFASs and obesity in adults and children/adolescents. Whereas the majority of the new studies report positive associations between PFAS exposures and obesity in adults, inverse associations were reported for children/adolescents. Overall, some associations between PFASs and obesity are indicated, but the evidence is still insufficient with regard to a link between PFASs and obesity.

Metabolic syndrome

EFSA (2020) concluded that “there is insufficient evidence for associations between exposure to PFASs and metabolic syndrome” (EFSA, 2020). Three cross-sectional studies in adults were identified in the new literature search.

Ye et al. (2021) measured a total of 20 PFASs. Positive associations were found for total PFOS, branched PFOS, linear PFOA and perfluoro-6-methylheptanoic acid (6 m-PFOA), PFNA and PFDA, while null association was observed for linear isomers of PFOS, PFHxS, PFDoA, PFTTrDA and PFUnDA. Yu et al. (2021c) quantified 32 PFASs in serum from Chinese adults. They found significantly positive associations for 6:2 Cl-PFESA, 8:2 Cl-PFESA and PFOS with metabolic syndrome. In addition, they found statistically significant positive associations between the PFAS mixture and metabolic syndrome when holding all PFAS at the 55th percentile or above compared to the median concentrations. There were no associations between PFOA, PFBA, PFHxS, PFHpA, PFNA, PFDA, PFUnDA, PFDoDA or PFTTrDA with metabolic syndrome. Zare Jeddi et al. (2021) examined the associations between serum PFAS levels and the prevalence of metabolic syndrome among highly exposed young adult (ages 20 – 39) residents in the Veneto Region (North-Eastern Italy). PFOA, PFHxS, and PFNA were not associated with the risk of metabolic syndrome, whereas PFOS was associated with a lower risk of metabolic syndrome.

One of the new studies included 6:2 Cl-PFESA and 8:2 Cl-PFESA, in which positive associations with metabolic syndrome were reported. However, due to the few additional studies and inconsistent findings, these studies do not strengthen the evidence for an association between PFASs and metabolic syndrome. Of note, different criteria were used for the identification of metabolic syndrome.

B.5.3.1.4. Kidney function and uric acid

EFSA (2020) summarised that there was insufficient evidence for associations between exposure to PFASs and kidney function and furthermore that “although several studies show association between PFASs and glomerular filtration rate, there is insufficient evidence to conclude that the associations are causal, due to plausible confounding and reverse causality”.

The literature search conducted in 2021 identified seven studies published after July 2019, and one study (Blake et al., 2018) including PFASs (Me-PFOSA and Et-PFOSA) not evaluated by EFSA (2020).

Three cross-sectional studies reported positive associations between several PFASs (PFOS, PFOA, PFNA, PFHxS) and two markers of reduced kidney function; increased serum uric acid/hyperuricemia (Scinicariello et al., 2020; Zeng et al., 2019a) and reduced estimated glomerular filtration rate (eGFR) (Moon, 2021). However, in the cross-sectional study by Arrebola et al. (2019), no associations were reported between PFASs (PFHxS, PFOA, PFOS, PFNA, PFDA and MeFOSAA) and serum uric acid levels in the study population.

Associations with markers of reduced kidney function were reported in a randomised control trial and a prospective study. In the randomised controlled trial (Blake et al., 2018), that included lifestyle interventions, it was found that plasma PFAS concentrations (PFOS and PFOA) during follow-up were inversely associated with eGFR. According to the prospective cohort study with repeated measures by Lin et al. (2021), serum PFNA, PFHxS, and PFDA were inversely associated with eGFR. In contrast, the PFOS precursor Me-PFOA was associated with an increase in eGFR.

Two cross-sectional studies reported positive association with urge urinary incontinence (Cui et al., 2021) and risk of kidney stones (Blake et al., 2018).

The review of new studies strengthens the support for associations between PFASs and outcomes related to reduced kidney function. However, as pointed out by EFSA (2020) and ATSDR (2021) confounding and reverse causation is plausible and thus a causal association between PFAS exposures and kidney function is uncertain.

B.5.3.1.5. Cardiovascular disease and mortality

EFSA (2018) concluded on no clear association between PFOS/PFOA and cardiovascular disease and in 2020 EFSA concluded that there was not sufficient evidence for other PFASs.

The new literature search identified eight studies examining associations between PFAS and cardiovascular outcomes published after July 2019, and one study from before July 2019 including other PFASs.

A cross-sectional study with 10 859 participants from NHANES observed positive associations were between N-EtFOSAA and $\Sigma 12$ PFASs and total cardiovascular disease, and between N-MeFOSAA and congestive heart failure (Huang et al., 2018).

In a prospective study, prenatal exposure to PFOA was positively associated with cardiometabolic risk score in children at age 12 (Li et al., 2021b). In another prospective study, PFOS and N-EtFOSAA were positively associated with risk of any microvascular disease (Cardenas et al., 2019).

Studies on blood pressure and/or hypertension observed positive associations with several PFASs; PFOS (Averina et al., 2021; Liao et al., 2020; Pitter et al., 2020b), PFOA (Averina et al., 2021; Liao et al., 2020; Mitro et al., 2020a; Pitter et al., 2020b), PFNA (Liao et al., 2020; Pitter et al., 2020b), PFHxS (Averina et al., 2021; Pitter et al., 2020b), and $\Sigma 18$ PFAS (Averina et al., 2021).

The results from the new literature search strengthen the evidence for an association between PFASs and increased risk of cardiovascular diseases.

B.5.3.2. Reproductive outcomes (epidemiological evidence)

B.5.3.2.1. Fertility, pregnancy and sex hormones outcomes

EFSA (2018) and EFSA (2020) concluded that “the available evidence is insufficient to suggest that pre- or postnatal exposures to PFASs are associated with effects on male fertility”. Concerning female fertility, EFSA (2018) and EFSA (2020) concluded that “there is insufficient evidence that exposure to PFOS or PFOA is related to menstrual cycle length,

menopause or puberty development” and that “there are no consistent associations between pre- or postnatal exposures to PFASs and female reproduction outcomes or puberty”. Furthermore, EFSA (2020) concluded “that there is insufficient evidence that exposure to PFOS/PFOA or other PFASs may adversely affect fecundity”.

Male and female fertility

The updated search identified seven studies on fertility or fertility-related parameters in adults or adolescents.

A cross-sectional study with couples undergoing *in vitro* fertilization (IVF) treatment suggested that both male and female exposure to several PFASs (PFOS, PFHxS, PFNA, PFDA, PFOSA, and PFHpA) were negatively associated with one of more intermediate IVF outcomes, i.e. the numbers of retrieved oocytes, mature oocytes, 2 PN zygotes and good-quality embryos (Ma et al., 2021). Furthermore, male exposure to PFNA and PFDA concentrations were associated with reduced sperm concentration and PFOSA was associated with reduced sperm count. None of the maternal or paternal PFAS concentrations were associated with IVF clinical outcomes.

Three cross-sectional studies on **male fertility** conducted in China were identified. The first (Luo et al., 2021) assessed associations of 24 PFASs, including seven branched PFOS isomers, two branched PFOA isomers, 8:2 Cl PFESA and 6:2 Cl-PFESA with male reproductive hormones. Hormones measured in serum included total testosterone (TT), oestradiol (E2), follicular stimulating hormone (FSH), luteinizing hormone (LH) and insulin like factor 3 (INSL3), and sex hormone binding globulin (SHBG). The results showed that in the young men PFAS mixture was significantly associated with reduced levels of E2, which was accompanied by inverse association with E2/TT ratio; and PFUnDA was identified as the main contributor. However, the overall associations between PFAS mixture and other reproductive hormones were generally non-significant (Luo et al., 2021). The second study (Pan et al., 2019a) investigated associations between PFAS measured in matched semen and serum samples with markers of semen quality. The results showed an adverse association between serum 6:2 Cl-PFESA and semen quality (Pan et al., 2019a). The third study (Cui et al., 2020) used the same study population as Pan et al. (2019a) and reported inverse associations between plasma concentrations of PFOA, PFNA, PFOS, and 6:2 Cl-PFESA) with total testosterone and indicated inverse associations also for other reproductive hormones (Cui et al., 2020).

In **females**, two prospective studies examined associations between PFASs and menopause/hormone levels during the menopausal transition, and both used data from the US Study of Women’s Health Across the Nation (SWAN). In the first paper, 1 120 women with 17-years follow up (5 466 person-years), all PFAS concentrations (linear PFOS, sum of branched PFOS isomers, linear PFOA, and PFNA) were classified into four PFASs clusters (low, low-medium, medium-high, and high) using k-means clustering to account for PFASs mixtures. Compared with the low exposure cluster, women in the high cluster had significantly increased risk, i.e. equivalent to 2 years earlier median time to natural menopause (Ding et al., 2020). In the second paper, associations between serum concentrations of 11 PFASs at baseline (1999-2000) and longitudinal serum concentrations of follicle-stimulating hormone (FSH), oestradiol, testosterone, and sex hormone-binding globulin (SHBG) at baseline and through 2015-2016 were examined in 1 371 women. PFOA and PFOS were positively associated with FSH, while PFNA and PFOA were inversely associated with oestradiol (Harlow et al., 2021). The results from both papers thus indicate that PFASs (linear PFOS, sum of branched PFOS isomers, linear PFOA, PFNA, PFHxS) are associated with earlier time of menopause and linear-PFOA, linear-PFOS, sum of branched PFOS isomers, total PFOS and N-EtFOSAA are positively associated with FSH, and PFNA and PFOA are associated with lower oestradiol-2 concentrations. The magnitude of the increase in TSH and decrease in oestradiol-2 was estimated to correspond to 2.5 and 4 years of aging (earlier age at menopause), respectively.

A prospective study in the UK ALSPAC cohort observed no associations between a range of prenatal PFAS exposures, including PFOS, PFOA, PFHxS, and PFNA, and Anti-Müllerian hormone, a marker of ovarian reserve in female offspring at 15 years of age (Donley et al., 2019).

A nested case control study within the Ronneby cohort in Sweden examined high/low exposure to PFASs through contaminated drinking water and polycystic ovarian syndrome (PCOS), uterine leiomyoma, and endometriosis. Ronneby is an ecological cohort where one third of all inhabitants in Ronneby municipality were exposed to high PFASs (mainly PFHxS and PFOS) through contaminated drinking water between 1985 and 2013. Exposure to high levels of PFASs in drinking water was associated with increased risk of PCOS and possibly uterine leiomyoma, but not with endometriosis (Hammarstrand et al., 2021).

The review of new studies provides limited suggestive evidence for an association between PFASs and adverse effects on male and female fertility.

Sex hormones and related outcomes in infants

In the updated literature search, two prospective investigations of PFASs and anogenital distance (AGD), one cross-sectional study on concentrations of oestrogens in cord blood, and one prospective study of serum hormones and hormone precursors in infants were identified.

In a study from the Faroe Islands maternal exposure to PFOA, PFOS, PFNA and PFDA, but not PFHxS, were significantly associated with longer AGD in male infants (n = 232) (Christensen et al., 2021). A study within the Canadian MIREC cohort did not find any clear evidence that maternal plasma concentrations of PFOS, PFOA or PFHxS were associated with infant AGD in either male (n = 205) or female (n = 196) infants (Arbuckle et al., 2020).

In infants with a mean age of 3.9 months in the Odense Birth cohort, there were no associations between five maternal PFASs (PFOS, PFOA, PFHxS, PFNA, PFDA) individually or combined with any of five sex hormones measured in boys (Jensen et al., 2020b). In girls, maternal PFDA concentration was associated with reduced dehydroepiandrosterone (DHEA). No associations were found for other PFASs or for the five PFASs combined.

A study from China (Liu et al., 2021a) reported significant cross-sectional associations between six PFASs (PFOA, PFDA, PFNA, PFOS, PFHxS, 6:2 Cl-PFESA) and three oestrogen concentrations (oestrone (E1), oestradiol (E2), oestriol (E3)) in newborn cord-blood. Results from analyses stratified by infant sex showed that in boys five PFASs (PFDA, PFNA, PFOS, PFHxS and 6:2 Cl-PFESA) were positively associated with oestrone, four PFAS (PFDA, PFNA, PFOS and 6:2 Cl-PFESA) were associated with oestradiol, and PFOA and PFDA were positively associated with oestriol (Liu et al., 2021a). The results in girls were less clear. Of the six PFASs, only PFNA was positively associated with oestrone, PFOA, PFDA and PFNA were positively associated with oestradiol, and no PFASs were associated with oestriol.

The review of new studies provide limited suggestive evidence for an association between PFASs and adverse effects on sex hormones and related outcomes in infants.

Timing of puberty

One new prospective study on pubertal timing was identified in the literature search. In the US Project Viva cohort, mid-childhood plasma PFASs were significantly associated with markers of delayed puberty (less pubertal development in early adolescence and older age at peak height velocity) in girls, but not in boys. In girls, the associations were significant for PFOA, PFOS, and PFDA, not significant for PFHxS and N-MeFOSAA, and borderline significant for an overall PFAS mixture (Carwile et al., 2021). The new study showed a consistent association between exposure to PFASs and delayed timing of puberty in girls

but no association with puberty in boys.

Miscarriage and preeclampsia

EFSA (2020) concluded that “there is limited evidence to suggest any association between PFASs and miscarriage”. Furthermore, EFSA concluded on insufficient evidence to suggest that PFASs are associated with pregnancy induced hypertension or preeclampsia (EFSA, 2018; EFSA, 2020).

The new search identified two studies that examined associations between PFAS exposure and the **risk of pregnancy loss**. A prospective study in China in women undergoing in vitro fertilisation-embryo transfer (IVF-ET) measured twelve PFASs measured in serum samples prior to IVF-ET treatment. There were no clear associations between the PFASs and early pregnancy loss (Wang et al., 2021b). A nested case control study within the Danish National Birth Cohort examined associations between plasma concentrations of seven PFASs in early pregnancy (mean gestational week 8) and miscarriage in gestational weeks 12-22. The results showed that PFOA, PFHpS and the PFAS mixture (weighted quantile sum, WQS) were associated with increased risk of miscarriage, particularly in parous women. The authors stated that larger studies among nulliparous women are needed to diminish the potential confounding by reproductive history (Liew et al., 2020).

In a case-control study in Sweden, serum samples collected early in pregnancy were obtained for 296 women diagnosed with preeclampsia (cases) and 580 healthy controls and analysed for PFOA, PFOS, PFNA and PFHxS. In the adjusted analyses, there were no associations between PFASs and preeclampsia (Rylander et al., 2020).

The review of new studies are in line with EFSA (2020) that the evidence for an association between PFASs and miscarriage and preeclampsia is still limited.

Preterm delivery

EFSA (2020) concluded that “the evidence for an association between PFASs and preterm delivery is limited”. In the Chinese Guangzhou Birth Cohort, both maternal serum 6:2 Cl-PFESA and PFOS were associated with significantly higher risk of preterm delivery (Chu et al., 2020). In contrast, in a nested case-control study in China there were no associations between maternal PFASs concentrations and spontaneous preterm delivery. However, PFOS and 6:2 Cl-PFESA were both positively associated with one of three markers of inflammation measured in the same blood samples as PFAS (Liu et al., 2020c).

The review of new studies are in line with EFSA (2020) that the evidence for an association between PFASs and preterm delivery is still limited.

B.5.3.2.2. Developmental outcomes

EFSA (2018) and EFSA (2020) concluded that there “may well be a causal association between PFOS and PFOA and birth weight” but that for PFASs, which were found in lower concentrations than PFOS and PFOA, the reported associations were inconsistent.

Birth weight

Seven new birth cohort studies published after July 2019 have continued to report associations for maternal PFOS and PFOA with reduced birth weight, birth length and/or foetal growth restriction (Chen et al., 2021a; Chu et al., 2020; Kashino et al., 2020; Souza et al., 2020; Wikstrom et al., 2020; Xiao et al., 2020). A study from the Swedish Ronneby cohort published after the search has also been reviewed (Engström et al., 2022). This is an ecological cohort where one third of all inhabitants in Ronneby municipality were exposed to high PFASs (mainly PFHxS and PFOS) through contaminated drinking water between 1985 and 2013. Engström et al. (2022) compared infants with mothers exposed

to PFASs contaminated drinking water (high exposure) and infants born to mothers not exposed to contaminated drinking water (low exposure) to infants born to mother in another county (referents). High exposure to PFASs was associated with infant birthweight in a sex-specific manner and was inversely associated with birthweight in boys, and positively associated with birthweight in girls. Other studies have also reported inverse associations with birth weight for PFNA, PFDA, PFOSA, PFHxS and PFUnDA, but the results are not consistent across all studies. In the Chinese Guangzhou Birth Cohort, a study in 372 mother-child dyads showed that the PFOS alternatives 6:2 Cl-PFESA and 8:2 Cl-PFESA in maternal serum were inversely associated with birthweight with clinically relevant effect sizes (Chu et al., 2020).

Overall, the new literature on associations between PFASs and birth weight support the conclusion from EFSA (2020) that there may well be a causal association between PFOS and PFOA and birth weight and strengthen the concern that other PFASs exert similar effects.

Birth defects

With regard to birth defects, EFSA (2018) reviewed several studies from the C8 cohort in the US, conducted in residents exposed to PFAS contaminated drinking water. There were no consistent findings between prenatal PFAS exposures and birth defects.

The new literature search identified only one new study, which is a nested case-control study conducted in a cohort of 11 578 new-borns in Guangzhou, China (Ou et al., 2021). Prenatal maternal serum PFASs and cord-blood PFASs were compared between 158 cases (newborn with congenital heart defects) and 158 healthy controls. The results showed that gestational exposure to most PFASs, especially linear PFOS, 6 m-PFOS, PFDA, and PFDoA, were associated with increased risks for congenital heart defects.

Neurodevelopmental outcomes

EFSA (2020) concluded that “there is insufficient evidence to suggest that prenatal exposure to PFASs may adversely affect neurobehavioral development.”

With regard to neurodevelopmental outcomes including emotional behaviour problems, attention deficit/hyperactivity (ADHD), autism spectrum disorder (ASD) and cognition, the updated search identified eleven new studies, nine prospective (Harris et al., 2021; Jedynak et al., 2021; Oh et al., 2021a; Oh et al., 2021b; Skogheim et al., 2020; Vuong et al., 2021a; Vuong et al., 2019; Vuong et al., 2021b; Yu et al., 2021b) and two case-control studies (Skogheim et al., 2021).

A prospective study in US Project Viva, reported that prenatal PFOS, but not other PFASs, was associated with more child behaviour problems measured by parent and teacher assessment of children’s emotional behaviour problems at age 6 – 10 years (Harris et al., 2021). This study also reported cross-sectional associations for PFAS measured in the children, which showed that PFOA, PFOS, PFHxS, and PFDA were associated with parent rated behaviour problems, but not teacher rated problems, while PFNA was associated with both parent and teacher rated behaviour problems.

In a prospective study including 708 mother-child pairs from five European cohorts, there were no significant associations for five PFASs (PFHxS, PFOS, PFOA, PFNA, PFUnDA) measured in maternal blood with child emotional behaviour problems assessed between three and seven years of age (Jedynak et al., 2021).

Two prospective studies used data from the MARBELS cohort in the US. This cohort recruited mothers who previously had a child diagnosed with ASD and therefore had higher risk of having a child with delays or deficits in areas of development or behaviour. One study examined associations between prenatal PFAS exposures and children’s cognitive

development assessed at 6, 12, 24, and 36 months of age (Oh et al., 2021b). This study included 140 mother-child pair with neurocognitive data at all time points. Of six PFASs detected in more than 60% of the samples, PFOA was consistently associated with lower neurodevelopmental scores at 24 months, 36 months and in the repeated measure trajectory (Oh et al., 2021b). The other study examined associations between prenatal exposure to individual and combined PFASs and clinically confirmed ASD in children at 3 years of age and included 173 mother-child pairs. The results showed that PFOA, PFNA, and the PFAS mixture (principal component) were associated with increased ASD risk (Oh et al., 2021a).

Two studies used data from The Norwegian Mother, Father and Child Cohort study (MoBa). PFASs were measured in blood around gestation week 18. The first study included 944 mother-child pairs and investigated the prospective associations between prenatal exposure to PFASs and symptoms of ADHD and cognitive functioning in a subgroup of children aged three and a half years (Skogheim et al., 2020). The children underwent extensive clinical assessment. The results showed no associations with ADHD symptoms, language skills or estimated IQ. However, PFOS, PFOA, PFHxS, PFHpS were negatively associated with nonverbal working memory, and PFNA, PFDA, PFUnDA were positively associated with verbal working memory in boys (Skogheim et al., 2020). The second study is a nested case-control study which included 821 ADHD cases, 400 ASD cases, and 980 controls. Diagnoses were obtained by linkage to the Norwegian Patient Registry. PFASs included PFOA, PFNA, PFDA, PFUnDA, PFHxS, PFHpS and PFOS. The results showed that for some PFASs (PFDA, PFOS, PFUnDA), as well as the mixture of all PFASs, there were inverse associations with ASD and/or ADHD, while PFOA was associated with a non-linear increased odd of ASD and ADHD in children (Skogheim et al., 2021).

A study using data from the Shanghai Birth cohort examined the association between prenatal PFAS exposure measured in early pregnancy and foetal brain-derived neurotrophic factor (BDNF, an important factor in neurodevelopment) level in the umbilical cord blood (Yu et al., 2021b). Quantile-based g-computation was applied to explore the joint and independent effects of PFAS on BDNF level. The results showed that PFHxS exposure was significantly associated with an increased BDNF level. There was no association between the PFAS mixture and BDNF.

Shin et al. used data from CHARGE (Childhood Autism Risk from Genetics and Environment), a population-based case-control study comprising index children and their families, with a goal to identify causes and contributing factors for autism (Shin et al., 2020). The study included 450 mothers with blood sampled at the time of study enrolment (when the child was 2 – 5 years old) and 453 children who completed the study with a final diagnosis of ASD or typical development. The study lacked prenatal samples because of its case control design and therefore, both model-based reconstructed estimates during pregnancy and concurrent (post-diagnosis) measurements of nine PFAS concentrations were used as surrogate of in utero exposure. The analyses showed that modelled prenatal maternal PFHxS and PFOS exposure, but not other PFASs (PFOA, PFNA, PFDA, PFUA, PFDoDA, N-MeFOSAA and N-EtFOSAA), were associated with increased odds of child diagnosis of ASD.

Three prospective studies used data from the US HOME cohort. One study investigated prenatal and childhood PFAS and cognitive abilities at eight years and whether sex modifies these associations (Vuong et al., 2019). PFOS, PFOA, PFHxS and PFNA were quantified in maternal serum during gestation and in child serum at three and eight years. There were no adverse prospective associations between prenatal and childhood PFAS and cognitive function at eight years. Another study investigated prenatal PFAS and neurobehavior through eight years of age (Vuong et al., 2021a). PFOA, PFOS, PFHxS and PFNA were quantified in maternal serum during gestation. Prenatal PFOS and PFNA were consistently associated with measures related to hyperactive-impulsive type ADHD. PFHxS was associated with increased problems for both externalizing and internalizing behaviours, while PFOA was not associated with any outcome (Vuong et al., 2021a). The third study

(Vuong et al., 2021b) investigated childhood concentrations of PFOS, PFOA, PFHxS and PFNA measured at three and eight years and neurobehavioral domains in children at eight years. The results showed that childhood serum concentrations of PFAS at ages three and six years were not associated with externalizing or internalizing behaviours in children at age eight years. However, there was suggestive evidence that child sex modified the associations between childhood PFAS and neurobehavior, where higher concentrations of PFOA and PFNA were associated with more externalizing problems, internalizing problems, and behaviour symptoms in boys compared to girls. Furthermore, this study confirmed that the previously reported associations between prenatal PFAS concentrations and more externalizing and internalizing problems in children reported by Vuong et al. (2021a) remain even after taking childhood concentrations into account (Vuong et al., 2021b).

Overall, the new studies revealed some indication of adverse associations between prenatal PFAS exposures and neurodevelopment, and several studies reported sex differences. However, as for the studies reviewed by EFSA (2018) and EFSA (2020), the new studies reported inconsistent results with positive, no or inverse associations between PFASs and the outcomes. The most consistent associations were observed for prenatal PFOS and PFHxS exposure and child neurodevelopment.

Other developmental outcomes

EFSA (2020) concluded that “there is insufficient evidence to suggest that exposure to PFASs may adversely affect overweight”.

For other developmental outcomes including growth in infancy and childhood, overweight, and metabolic risk factors, the updated search identified one cross-sectional (Spratlen et al., 2020), one case-control study (Martinsson et al., 2020) and six prospective studies (Blomberg et al., 2021; Carwile et al., 2021; Jensen et al., 2020a; Mora et al., 2018; Shih et al., 2022; Starling et al., 2019; Tian et al., 2021).

In a longitudinal study, prenatal PFASs were associated with sex-specific and chemical specific differences in infant weight and adiposity up to 5 months of age (Starling et al., 2019). A study in the Odense Child cohort examined PFASs in maternal pregnancy serum (PFOS, PFOA, PFHxS, PFNA and PFDA) and repeated markers of adiposity and lipid metabolism in infancy (up to 18 months). The results showed that PFNA and PFDA were positively associated with several markers of adiposity and higher total cholesterol (Jensen et al., 2020a). In a case-control study by Martinsson et al. (2020), none of the PFASs investigated (PFOS, PFOA, PFHxS and PFNA) were associated with obesity at age 4 years.

A study within the Faroe Islands birth cohort reported consistent associations between PFASs concentrations in serum collected at age 18 months, 5 years, and 9 years with serum adipokine hormones measured in the serum at 9 years (Shih et al., 2022). PFOS, PFOA, PFHxS, PFNA and PFDA at 18 months, 5 years and 9 years were associated with leptin, leptin receptor, and resistin at age 9 years, and the results were also evident for a PFAS mixture.

Three prospective studies reported that prenatal PFAS exposure were associated with disrupted lipid metabolism in neonates/children, but the results were inconsistent between studies and between different PFASs (Blomberg et al., 2021; Mora et al., 2018; Tian et al., 2021). Tian et al. (2021) included Bayesian Kernel Machine Regression (BKMR) models, which showed that the mixture of eight PFASs (PFHxS, PFOS, PFOA, PFNA, PFDA, PFUdA, PFDoA, PFTTrDA) were inversely associated with all lipid concentrations, i.e., total cholesterol, triglycerides, HDL-C, and LDL-C. PFASs were among the pollutants suspected to have been released during the collapse of the World Trade Center on 9/11/2001. A cross-sectional study in pregnant women exposed to the World Trade Center disaster reported that several cord-blood PFASs were associated with higher cord-blood lipid levels, including evidence of a strong linear trend between triglycerides and both PFOA and PFHxS (Spratlen et al., 2020).

Overall, the new studies indicate associations between multiple prenatal PFASs and other developmental outcomes, including growth in infancy and childhood, overweight, and metabolic risk factors in children. However, the evidence is still limited.

B.5.3.3. Carcinogenicity (epidemiological evidence)

A number of studies on cancer incidence or cancer mortality and occupational or environmental exposure reviewed by EFSA (2018) provided insufficient support for carcinogenicity of PFOS and PFOA in humans. The studies reviewed by EFSA in 2020 did not change the previous conclusion for PFOS and PFOA. For other PFASs, limited information was identified (EFSA, 2020).

Six studies were identified in the new literature search, of which five included breast cancer (Cohn et al., 2020; Itoh et al., 2021; Mancini et al., 2020; Tsai et al., 2020), one also included ovarian, uterine and prostate cancer (Omoike et al., 2021), and one study included renal cell carcinoma (Shearer et al., 2021). A study published after the main search was also included because it was highly relevant for this narrative review (Li et al., 2022a).

Cohn et al. (2020) used prospective data from a US cohort and examined nested case-control associations between in utero PFAS concentrations and risk of breast cancer over 54 years follow-up. The results showed that high maternal N-EtFOSAA, a precursor of PFOS, in combination with high maternal total cholesterol predicted a 3.6-fold increased risk of breast cancer in daughters. Conversely, maternal PFOS was associated with decreased daughters' breast cancer risk. No associations were reported for PFHxS and PFOA and breast cancer.

A prospective nested case control within the French E3N cohort (Mancini et al., 2020) reported no association between PFOS and PFOA and overall risk of breast cancer. However, the results showed positive linear associations between PFOS and the risk of receptor-positive (ER+ and PR+ tumours). There was no association between PFOA and receptor-positive breast cancer risk.

In Taiwan, Tsai et al. (2020) enrolled 120 cases with breast cancer and 119 controls and found no significant associations between PFASs and breast cancer (Tsai et al., 2020). After stratifying for age, a positive association for PFOS were observed for the <50 years age group. After stratifying for the oestrogen receptor status and age group, PFHxS and PFOS concentrations were associated with higher risk of ER positive tumours in the <50 years age group, while PFNA and PFDA exposure was associated with lower risk of ER positive tumours in the <50 years age group.

In a Japanese case-control study, 20 included PFAS congeners (PFHxS, PFHpS, linear and five branched PFOS, linear and branched PFOA, linear and branched PFNA, linear and branched PFDA, linear and branched PFUnDA, linear and branched PFDoDA, linear and branched PFTTrDA) were all significantly inversely associated with risk of breast cancer (Itoh et al., 2021).

In a cross-sectional study within the US NHANES, Omoike et al. (2021) reported that PFOA, PFOS, PFHxS, and PFDA were associated with ovarian cancer (OR range: 1.01-1.03) and PFOA, PFOS, PFNA. PFHxS and PFDA were associated with breast cancer (OR range: 1.01-1.09). PFDA and PFNA were inversely associated with prostate cancer, and PFDA, PFNA and PFHxS were inversely associated with uterine cancer.

Shearer et al. (2021) used prospective population-based data in the US for nested case control study (324/324) examining the associations between seven PFASs (PFOA, PFOS, PFHxS, PFNA, N-EtFOSAA, N-MeFOSAA and PFDA) and risk of renal cell carcinoma (Shearer et al., 2021). The results showed a statistically significant positive exposure-response association between prediagnostic serum PFOA concentrations and subsequent risk of renal

cell carcinoma.

Cancer incidence in a Swedish cohort with high exposure to perfluoroalkyl substances in drinking water caused by use of firefighting foams at a nearby airport was reported (Li et al., 2022a). This prospective ecological study in the Swedish Ronneby cohort included more than 60 000 individuals who ever lived in the Ronneby municipality during the period of PFAS contamination (in particular PFHxS and PFOS) of drinking water between 1985 and 2013. The study population and study period was fully covered by the Swedish Cancer Register. The results showed that high PFASs exposure was not associated with an overall higher risk of cancer, but that the highly exposed group had moderately increased risk of kidney cancer (HR 1.27; 95% CI 0.85, 1.89) and bladder cancer (HR 1.32; 95% CI 1.01 – 1.72). The results for kidney cancer are in accordance with previous findings for PFASs exposure in the C8 study.

In summary, due to inconsistent findings, the new studies do not provide clear support for an association between PFASs and breast, ovarian and prostate cancer. However, two new prospective studies strengthen the evidence that PFOA and multiple PFASs exposure are associated with renal cell carcinoma and kidney cancer.

B.5.3.4. Other outcomes (epidemiological evidence)

B.5.3.4.1. Bone mineral density

There were two studies related to bone mineral density in EFSA (2018) and EFSA (2020), and EFSA concluded that there was insufficient evidence for associations between exposure to PFASs and low bone mineral density (BMD) or osteoporosis.

The updated search identified one new study which examined associations between PFASs and BMD (Hu et al., 2019). In this randomised intervention study with four energy restricted diets assessing long-term weight loss in healthy overweight or obese individuals, cross-sectional and prospective associations between five PFASs (PFOS, PFOA, PFHxS, PFNA and PFDA) and BMD at six bone sites at baseline and after two years in participants aged 30-70 years were examined. A BMI related genetic risk score was calculated on the basis of 97 single nucleotide polymorphisms (SNPs). In cross-sectional analyses, inverse associations were observed between baseline PFOS and PFOA concentrations and BMD at all bone sites, and inverse associations were also indicated for the other PFASs. In prospective analyses, baseline concentrations of PFOS, PFNA and PFDA were associated with a faster decline in BMD at some bone sites, and PFOA concentration was associated with a faster decline in BMD at one bone site. These associations were independent of weight changes during the trial (Hu et al., 2019). PFASs-related declines in BMD were influenced by genetic predisposition to obesity.

More studies are needed to determine potential associations between PFAS exposures and accelerated bone loss.

B.5.3.5. General conclusion from new epidemiological data

Immune outcomes were chosen as the critical effect for risk assessment of PFASs in the EFSA 2020 Opinion (EFSA, 2020) and inverse relation between PFASs and vaccination response was also concluded by ATSDR (2021). The new studies identified in the literature search strengthen the evidence for an association between exposure to several PFASs, in particular PFOS, PFOA, PFHxS, PFNA, PFUnDA, and PFDA, and reduced vaccine responses in children. The adversity of the immunosuppressive effects of PFASs is further supported by increasing evidence for an association also with increased propensity of lower respiratory tract infections (LRTI) and possibly also other infectious diseases. The evidence for associations with asthma- and allergy-related outcomes (hypersensitivity) remain weak, but there is increasing evidence for an inverse association between PFASs and atopic dermatitis.

Liver toxicity and metabolic disruption are also outcomes of concern in relation to PFAS exposures. The evidence is still considered strong for a positive association between PFASs and plasma levels of the liver enzyme ALT, which is a marker of liver toxicity and fatty liver diseases. Furthermore, the new publications support the association between PFOS and PFOA and increased total and LDL-cholesterol in adults. Similar associations are suggested also for PFHxS, PFNA, PFDA and PFUnDA, 6:2 Cl-PFESA and 8:2 Cl-PFESA. However, the potential contribution of confounding due to similar intestinal reuptake mechanisms for PFASs and bile acids is still not clear. In the EFSA 2020 opinion, no clear association between PFOS or PFOA and **cardiovascular disease** was found (EFSA, 2020). However, recent studies strengthen the evidence for a positive association.

The review of new studies provides limited suggestive evidence for associations between PFASs and adverse effects on **reproduction and development**, including male and female fertility, miscarriage and preeclampsia, delayed timing of puberty, adverse effects on sex hormones and related outcomes in infants. The evidence for an association between PFASs and preterm delivery is still limited, however, the new literature supports the conclusion from EFSA (2020) that there may well be a causal association between PFOS and PFOA and birth weight and strengthen the concern that other PFASs exert similar effects. Overall, the new studies revealed some adverse associations between prenatal PFAS exposures and **neurodevelopment**, and several studies reported sex differences. However, as for the studies reviewed by EFSA (2018) and EFSA (2020), the new studies reported inconsistent results.

Regarding **cancer risk**, two new prospective studies strengthen the evidence that PFOA and multiple PFAS exposures are associated with renal cell carcinoma and kidney cancer. However, the new studies do not provide clear support for an association between PFASs and breast, ovarian and prostate cancer. With respect to **other organ toxicities**, the recent publications strengthen the concern that PFAS exposures might be associated with thyroid disease or changes in thyroid hormones, whereas potential associations with accelerated bone loss are still unclear. New studies strengthen the support for positive associations between PFASs and outcomes related to reduced kidney function, but confounding and reverse causation is plausible and thus a causal association between PFAS exposures and kidney function is uncertain.

B.5.4. Human data on oligomeric/polymeric PFASs

Inhalation of aerosolized waterproofing agents, sealants and ski waxes containing polymeric PFASs as well as inhalation of pyrolysis products of fluoropolymers (e.g. during manufacture or use) is reported to cause respiratory illness, such as acute chemical pneumonitis, reactive airway dysfunction syndrome, pulmonary oedema, occasionally accompanied by non-specific systemic symptoms, such as fever, chills, malaise, arthralgias, and nausea (influenza-like syndrome, polymer fume fever) in humans (Greenberg and Vearrier, 2015; Hays and Spiller, 2014). These effects are of unclear etiology but demonstrate a toxicological relevance of polymeric PFASs and their degradation products in acute inhalation exposure scenarios. For example, reduced lung function after occupational exposure of professional ski waxers, can be explained by particle exposure (Dahlqvist et al., 1992) or by exposure to degradation products from ski waxes, e.g. PFCAs (Freberg et al., 2010; Freberg et al., 2016; Nilsson et al., 2013b). Case studies of accidents with acute excessive inhalation exposure to fluoropolymers report severe symptoms of pulmonary oedema and polymer fume fever, e.g. after occupational inhalation of fumes from heated PTFE in a plastic factory (Lee et al., 1997) or after smoking ski wax-contaminated cigarettes (Strøm and Alexandersen, 1990). Occupational long-term exposure (for 28 years) to PTFE spraying can cause granulomatous lung lesions such as pneumoconiosis (Lee et al., 2018a). The authors conclude, such lesions appear to be caused not by the degradation products of PTFE from high temperatures but by spraying the particles of PTFE. Scanning electron microscopic (SEM) features of the lesion revealing fluorine elements show multiple round to oval granular material measuring 2 – 6 µm. Further results in comparison with standard PTFE and PTFE spray solution as used in the factory showed the presence of PTFE in the lung tissue. The particles found in the personal samples measured 1 – 22 µm by SEM, but particles smaller than 1 µm were also found. Choi et al. (2014) also report three cases of small airway-centered granulomatous lesions in workers employed at facilities that apply coatings to pans and other utensils. The workers were repeatedly exposed (inhalational PTFE exposure was between 7 and 20 years) to PTFE particles that were probably generated by the drying process when PTFE coatings are dried in a convection oven at high temperatures (380–420 °C).

PTFE is self-classified as STOT RE 1 (respiratory system/inhalation) by one notifier¹⁴. Moreover, when polymeric PFASs, such as PTFE and PCTFE are heated to very high temperatures above thermal stability, they may emit toxic decomposition products, such as tetrafluoroethylene (TFE), which itself is not in the scope of the proposed restriction (Huber et al., 2009). TFE is self-classified as STOT RE 2 (kidney) by one notifier and has a harmonised classification as Carc. 1B¹⁵ and was reported to be probably carcinogenic to humans (IARC, 2014).

¹⁴ <https://echa.europa.eu/de/information-on-chemicals/cl-inventory-database/-/discli/details/70383>, date of access: 2022-06-02.

¹⁵ <https://echa.europa.eu/de/substance-information/-/substanceinfo/100.003.752>, date of access: 2022-06-02.

B.5.5. Combined toxicity

Due to their persistence, mobility, bioaccumulation potential and thus tendency for long-range transport, PFASs are ubiquitously dispersed in the environment. Therefore, many different PFASs are co-occurring in the environment, drinking water, and food, resulting in a combined exposure to multiple PFASs that, based on the available data on some groups of PFASs, show similarity of effects. Accordingly, an assessment of hazards and risks taking into account such combined exposure would reflect exposure conditions more realistically than single compound assessments.

A precise modelling of combined effects of all PFASs in the scope of this restriction proposal is realistically not achievable because of lack of data on toxicokinetics, toxicodynamics, slope of dose response curves as well as limited knowledge of the mode-of action (Borgert et al., 2004). For most PFASs, no data on effects are available. However, the lack of data should not preclude to consider the risks and hazards from combined exposure to different PFASs because of the following:

First, it has been demonstrated in multiple studies that concentration addition may give a realistic worst-case estimation of combined toxicities for risk assessment procedures even if similarity of components is unknown (Backhaus et al., 2000; Martin et al., 2021). Therefore, Backhaus and Faust (2012) suggested to apply concentration addition as a precautionous first tier, irrespective of the modes/mechanisms of action of the mixture components. Dose-addition has also been adopted as the default assessment approach in EFSA's "Guidance on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals" (EFSA, 2019a). In recent studies, it has been demonstrated that cytotoxicity results of mixtures of PFASs were approximately additive (Hoover et al., 2019) or even more than additive (Ojo et al., 2021). Given similar effect patterns for many PFASs in animal studies, such as effects on liver, thyroid hormone system, and immune system, additive effects may be considered as realistic worst-case estimation.

Second, a common mode of action is not a prerequisite for grouping chemicals for a combined exposure assessment and thus evidence for the same target organ is considered sufficient (EFSA, 2019a). It has been demonstrated in vitro that very diverse chemical classes with different molecular mechanisms can act in a concentration additive manner if triggering a similar adverse outcome (Stalter et al., 2020).

Third, even low or insignificantly toxic concentrations of the individual components can add up to observable combined effects (Altenburger et al., 2013). This something-from-"nothing" phenomenon has been first observed for endocrine disrupting compounds (Silva et al., 2002) but applies also to other mechanisms of action (Versieren et al., 2016).

Combined exposure to multiple PFASs is documented in an increasing number of epidemiological studies, many of which demonstrate an association between increased exposure to PFAS mixtures and increased incidences of various health outcomes, such as immunotoxicity, metabolic effects, developmental toxicity, thyroid hormone effects, and others (see B.5.3). As concluded by Rosato et al. (2022), specific guidelines and tools for the assessment of mixture observational studies are warranted.

In vivo studies on effects of PFAS mixtures are scarce. Recently Marques et al. (2021) demonstrated cumulative mixture effects of PFOA, PFOS, and PFHxS on metabolic endpoints in mice. Combined effects of various PFASs have been suggested before for the endpoint immunotoxicity (McDonough et al., 2020b).

For liver effects, a risk assessment of mixtures of 16 PFASs has been applied by Bil et al. (2021) by use of a relative potency approach (RIVM et al., 2018). In this study, the authors derived relative potency factors (RPFs) for 14 PFAAs and 2 PFAA precursors taking into account potency for liver effects relative to PFOA. Based on the RPFs and the combined

PFAS exposure in two separate exposure scenarios (drinking water ingestion and fish consumption), total PFOA equivalents did not exceed the drinking water limit for PFOA in The Netherlands of 87.5 ng/L, whereas the total PFOA equivalents resulting from fish consumption did exceed the fish consumption limit for PFOA in the Netherlands of 1.5 ng/g wet weight. This example demonstrates the high relevance of combined exposure assessments of PFASs. It can be expected that more limit values are exceeded in other exposure scenarios and when other endpoints are considered, in particular when more PFASs are taken into account.

In an earlier study, a cumulative health risk assessment of 17 PFASs has been applied by use of the Hazard Index (HI) approach (Borg et al., 2013). The risk characterization showed a concern for hepatotoxicity and reproductive toxicity in a subpopulation eating PFOS-contaminated fish, illustrating that high local exposure may be of concern. For the occupationally exposed (e.g. ski waxers) there was concern for hepatotoxicity by PFOA and all congeners in combination as well as for reproductive toxicity by all congeners in combination.

The immense number of PFASs in addition to the fact that appropriate toxicological data are not available for the vast majority of them, renders approaches for combined risk assessments unattainable for all the PFASs within the scope of this restriction proposal. Additionally, a large fraction of total organic fluorine from various exposure scenarios cannot be accounted for by commonly analysed PFASs indicating the co-occurrence of unidentified PFASs (Borg and Ivarsson, 2017). In conclusion, it is emphasized that combined exposure to different PFASs affecting the same target organs may result in combined additive effects, rendering exceedance of effect thresholds or limit values more likely than single compound assessments.

B.5.6. Derivation of DNEL(s)/DMEL(s)

Derivation of DNELs/DMELs is not considered relevant for this dossier since PFASs should be treated as non-threshold substances for the purposes of risk assessment. Any release of PFASs to the environment (see B.9) can be regarded as an unacceptable risk to the environment and human health (similar to PBT/vPvB substances under the REACH regulation). Since the non-threshold approach requires minimisation of exposures/releases, there is no need to compare in quantitative way exposure levels with effect thresholds (i.e. DNEL or DMEL values) (Wilkenfeld RM, 1981).

Moreover, given the large number of substances covered, which are to a large extent still insufficiently researched in terms of human toxicity, it is considered impossible to establish a safe level for individual PFASs, let alone for the group in total. There is increasing evidence that effects of well-studied PFASs occur at lower levels than previously anticipated (e.g., EFSA, 2020), and that exposure to these few PFASs already exceeds existing limit values. Hence, any additional exposure to other PFASs will result in more severe effects and/or a larger part of the population exceeding the limit values. Exposure therefore needs to be minimised, as per non-threshold approach.

B.6. Human health hazard assessment of physicochemical properties

Not relevant for this proposal.

B.7. Environmental hazard assessment

B.7.1. Ecotoxicity

B.7.1.1. Notes on the procedure

PFASs represent one of the most rapidly increasing study fields in ecotoxicology, contributing with several hundred new scientific publications in each of the recent years. To get an overview over the scientific literature, investigating ecotoxicological effects of PFASs, an initial literature search was performed by using the search term PFAS* and effect* in isi web of knowledge¹⁶ in early 2021. The initial search was restricted to review papers. Further refinement of the search results was performed by screening titles and abstract. The initial literature search resulted in a list of 76 papers. After screening the titles for relevance, 20 papers remained. Two of these were only available in Chinese and were excluded. The remaining 18 review papers were downloaded in full text and their relevance for the present review work was assessed. Not all of the 18 review papers were considered useful and those are consequently not mentioned in this chapter. The collection of studies from the initial search was complemented non-systematically by other studies that came up during the process of writing.

The PFASTox Database¹⁷ was used to get an overview over the ecotoxicological threshold values which are being reported by scientific literature. Functional details, as well as information on quality assurance for the data compiled in that database are provided by Pelch et al. (2019). All entries for *in vitro* and *in vivo* studies except those of the effect category “endocrine disruption” (those are already included in section B.7.5) were downloaded as a study list generated from the database. The full study list was filtered to exclude entries with a focus on human health (e.g. studies with human cell lines, rats or mice). The effects of PFASs on human health are assessed in section B.5. The abstract entries of all references in the filtered study list were screened for threshold values which were then collected in a separate table (see Table B.14).

In a review paper from Ankley et al. (2021), Ankley and colleagues summarized the information on ecological effects of PFASs from the US EPAs ECOTOX Knowledgebase¹⁸ according to environmental compartments as well as different species with environmental relevance. The main findings from that compilation will be presented below together with complementary data from other studies not mentioned in the review from Ankley and colleagues.

B.7.1.2. Aquatic invertebrates

According to Ankley et al. (2021), crustaceans are often the most sensitive aquatic invertebrates to be affected by PFASs. Furthermore, they observed, that “toxicity in the same PFAS class tends to increase with increased fluorocarbon chain length”. Other authors observed a similar pattern in their investigation of the effects of PFBA, PFHxA and PFOA on *Daphnia magna* (Barmentlo et al., 2015). Ankley et al. (2021) found, that toxicity values (e.g. EC_x) from chronic exposure were mostly within the same order of magnitude as values from acute exposure for the same species. Effects on the development of invertebrates occur at lower levels concentrations than effects on growth and reproduction.

Studies with saltwater organisms are rare, compared to studies with freshwater organisms. Ankley et al. (2021) concluded that “marine invertebrates tend to show a higher sensitivity to PFOA and PFOS” compared to freshwater species. However, they highlighted that the data at hand is limited, and that the conclusion is subject to a high degree of uncertainty.

¹⁶ www.isiwebknowledge.com, date of access: 2022-12-01.

¹⁷ <https://pfastoxdatabase.org/>, date of access: 2021-10-07.

¹⁸ <https://www.epa.gov/chemical-research/ecotoxicology-database>, date of access: 2022-12-01.

In contrast, Mhadhbi et al. (2012) reported in their study on the effects of PFOA and PFOS on marine species from different trophic levels that effects occurred in marine species at higher concentrations compared to freshwater species suggesting that marine species are less sensitive.

B.7.1.3. Terrestrial invertebrates

Ankley et al. (2021) observed that ecotoxicological studies on the effects of PFASs with terrestrial invertebrates are scarce, compared to the number of studies with aquatic invertebrates. Thus, firm conclusions regarding the differences of the ecotoxicological effects of different PFAS groups in terrestrial invertebrates are not possible. The same applies for interspecies differences. However, Ankley and colleagues concluded that developmental toxicity in terrestrial invertebrates increases with carbon chain length within the same PFAS group. Additionally, they observed a trend regarding the toxicity of different PFAS groups which they described as perfluoroalkane sulfonamides (FASAs) > Perfluoroalkane sulfonic acids (PFSAs) > Perfluoroalkylcarboxylic acids (PFCAs) > fluorotelomer alcohols (FTOHs).

Ankley and colleagues suggested a few different mechanisms through which PFASs exert their toxic effects in invertebrates (terrestrial as well as aquatic): oxidative stress which affects the antioxidative defense systems; genotoxic effects such as DNA strand breaks, chromosomal breaks or apoptosis; neurotoxic effects expressed e.g. via altered brain morphology; metabolic effects e.g. fat accumulation due to alternations of different regulating pathways (e.g. interaction with peroxisome proliferator-activated receptors (PPARs)); effects on the immune system via adversely affecting immune-related cell viability.

B.7.1.4. Fish

Most of the available literature (90%), that was evaluated by Ankley and colleagues regarding the effects of PFASs on fish, focuses on PFCAs and PFSAs. Similar to aquatic invertebrates, most studies were performed with freshwater species (95% of the evaluated studies) while studies investigating the effects of PFAS on marine fish are rare (5%). Regarding acute toxicity, Ankley and colleagues observed a lower acute toxicity of PFASs compared to invertebrates. Based on the order of magnitude of ecotoxicological threshold values in Cyprinids, C4 PFAAs appear to be less acutely and chronically toxic than PFAAs with chain lengths > C6. Additionally, Ankley and colleagues concluded that “within the same chain length (C8), sulfonates are typically more toxic than carboxylates”. Similar results, regarding the relation of toxicity and chain length as well as a higher toxicity for sulfonic PFAAs were also reported in an earlier study by Ulhaq et al. (2013). They investigated the effects of 7 PFAAs (TFA, PFBA, PFOA, PFNA, PFDA, PFBS, PFOS) on zebrafish. Rericha et al. (2021) investigated behavioral effects of 58 different PFASs on early life stage zebrafish as means to assess their developmental toxicity. They observed that at least 2 substances each from the groups of PFCAs, PFSAs, phosphate ethers and phosphinic acids “induced larval behavior effects”. Regarding chain lengths of the investigated compounds they reported, that “PFCAs and PFSAs associated with abnormal larval behavior had 3–17 and 3–8 continuously fluorinated carbons (CFCs), respectively”. PFASs with unsaturated C-F chains did not cause behavioral effects in this study. Mortality was also not observed within the tests performed by Rericha and colleagues. PFOA and PFNA were the only two of the 58 PFASs tested, that caused morphological effects.

In relation to chronic effects, Ankley and colleagues concluded, that NOEC or LOEC values for effects on reproduction were lower than values for effects on growth (based on data for PFOA and PFOS from studies with Cyprinids only). Regarding the mechanisms of toxicity, it was concluded, that “different PFAS have been shown to elicit oxidative stress and apoptosis in fish both in vitro and in vivo”. Other than that, Ankley and colleagues mentioned that different PFASs act toxic via an activation of nuclear receptors involved in lipid metabolism e.g. PPARs which is associated with an increased liver lipid content and

steatosis (fatty liver) in mammals, but hepatic effects from PFOS exposure have also been observed in zebrafish.

B.7.1.5. Amphibians

According to Ankley et al. (2021), studies investigating effects of PFASs on amphibians are only available for 9 different PFASs (PFOA, PFNA, PFDA, PFUnA, PFOS, PFHxS, 6:2 FTS, 10:2 FTCA, 10:2 FTUCA) and the majority of the studies investigated the effects of PFOS and PFOA. Similar to other species, toxicity of PFASs towards amphibians is influenced by the carbon chain length, as well as the functional group of the individual PFAS. However, the data at hand was not sufficient to derive trends. Ankley and colleagues describe that effects from PFASs on growth and development in early live stages have been reported for several species.

B.7.1.6. Birds

From the limited data available (acute and chronic toxicity on birds has only been investigated for PFOS, PFBS, PFHxS and PFOA) Ankley and colleagues concluded that results from acute toxicity studies with birds are comparable to those from studies with rodents: PFASs with C8 carbon chains are more toxic, than short-chain PFASs, and sulfonates are more toxic than carboxylates with the same chain length. Results from different studies with PFOS indicate that bird species show different sensitivities to the same substance, but results are within the same order of magnitude. In two recent studies, Dennis and colleagues investigated the liver and eggs of northern bobwhite quail (*Colinus virginianus*) individuals that were chronically exposed to PFASs (PFHxA, PFOS, or PFHxS or a mixture of PFHxA and PFOS or PFHxS and PFOS) (Dennis et al., 2022; Dennis et al., 2021). From the residue values from the most sensitive subgroup, they derived chronic toxicity values and found them to be lower than similar values reported for birds from earlier studies. The reported values are in the <50 ng/g ww range. Additionally, Dennis and colleagues observed that “PFOS and PFHxS were more bioaccumulative than PFHxA in avian tissues, but PFHxA was more toxic to reproducing birds than either PFOS or a PFOS:PFHxS mixture”.

B.7.1.7. Reptiles

Ankley et al. (2021) compiled 5 studies that investigated the effects of PFASs (namely PFOS and PFHxS) in reptiles. Effects from those studies encompass decreased growth of juveniles and decreased egg viability.

B.7.1.8. Other species

Laboratory experiments with other species (i.e. species not commonly used for ecotoxicological tests) examined the effects of PFASs on different endpoints, including immunological, neurological, and histopathological endpoints. Ankley et al. (2021) collated studies with polar bears, sled dogs, marine mammals, which in total investigated the effects of 9 PFCAs, 3 PFSA, 3 FTOHs, and 3 “novel” PFASs (HFPO-DA, ADONA and 6:2 Cl-PFESA (major component of F-53B)). On the basis of this data, Ankley and colleagues concluded that “PFOS followed by PFOA has the greatest amount of toxicological data”. Regarding the toxicity of different PFAS groups, the data from other species shows similar patterns as the data from e.g. fish: PFCAs with chain lengths ≤ C6 appear to be less toxic than PFCAs with chain lengths from C8 – C12 (while PFTTrDA (C14-PFCA) again was considered less toxic). Within the group of sulfonic acids, Ankley and colleagues also observed a trend in toxicity according to chain length: PFOS (C8; most toxic) < PFHxS (C6) < PFBS (C4; least toxic). Data for 6:2 FTOH and 8:2 FTOH suggests, that these compounds exert “less toxicity than other C6 PFAS compounds”

Interspecies differences, e.g. regarding sensitivity, are difficult to evaluate in this context

due to limited data. Ankley and colleagues made an attempt considering only data for PFOS and concluded “Based on body weight/body weight gain effects, there were no discernible differences between species exposed to PFOS during gestation. Even when reproductive effects such as pup viability and/or weight gain are considered, PFOS effect levels between species were typically 10-fold or less based on dose”.

A review by Krafft and Riess (2015) observed that PFAAs with shorter chain lengths exert a lower toxicity, which concurs with observations from the studies mentioned previously. Additionally, they mentioned that “PFAS exposure has been consistently associated with lipid and carbohydrate metabolism disorders”, based on studies with exposed humans, which is in line with the observations from Ankley et al. (2021) regarding metabolism disorders in mammals. Accordingly, Krafft and Riess (2015) stated, that, concerning the toxicity of PFAAs, “the liver has been identified as a specific target organ.” but confined that these findings are “highly dependent on PFAS, dose, species, strain and gender”. Furthermore, Krafft and colleagues described effects of PFASs on the immune system as well as developmental effects e.g. a reduced antibody response and IgM antibody production in mice exposed to PFOS or PFOA, or developmental toxicity observed in adult rodents exposed in utero to PFOS, PFHxS or PFOA. Similar effects have been reported in the review from Ankley and colleagues for various species (see above).

Several of the studies, compiled by Ankley and colleagues, measured tissue concentrations of PFASs in different wild living animals that were exposed to PFASs (and other contaminants) in the field. Subsequently, these studies tried to link the measured tissue concentrations to adverse effects. The findings of Ankley and colleagues regarding the effects of PFASs in wild living animals, as well as complementary results from other studies, are discussed in more detail in chapter B.7.2.

B.7.1.9. Plants

As reviewed by Li et al. (2022b) occurrence of PFASs rarely lead to obvious phenotypic/physiological damages in plants, but markedly perturb some biological activities at biochemical and molecular scales. According to Li et al. (2022b) PFAS exposure induces the over-generated reactive oxygen species and further damages plant cell structure and organelle functions. A number of biochemical activities in plant cells are perturbed, such as photosynthesis, gene expression, protein synthesis, carbon and nitrogen metabolisms.

B.7.1.10. PFASTox Database

The filtered study list from the PFASTox database (see “Notes on the procedure” at the beginning of this chapter) comprised 167 entries. Only 23 entries reported threshold values in the abstract. These are listed in Table B.14. Several studies reported threshold values for more than one PFAS thus the table contains more than 23 entries.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.14. Ecotoxicological threshold values for different PFASs from scientific literature recorded in the PFASTox database. Additional information (Endpoint, species/cell line) are included to allow for a superficial classification of the threshold values.

Substance	Study type	Effect value	Effect	Endpoint	Species/Cell line	Reference
PFHxS	in vivo	2 µM	morphometric effects in the larvae, specifically increased length and yolk sac area	LOEC	<i>Danio rerio</i>	(Annunziato et al., 2019)
6:2 FTOH*	in vivo	2 µM	Behavioral endpoints: distance traveled & mean velocity	LOEC	<i>Danio rerio</i>	(Annunziato et al., 2019)
PFHxA	in vivo	0.2 µM	reduction in the overall length and yolk sac size (however not observed at higher doses)	LOEC	<i>Danio rerio</i>	(Annunziato et al., 2019)
6:2 Cl-PFESA	in ovo	150 ng/g (egg w)	lower heart rate	LOEC	Chicken (<i>Gallus gallus domesticus</i>)	(Briels et al., 2018)
6:2 Cl-PFESA	in ovo	1 500 ng/g (egg w)	enlarged liver (8%)	LOEC	Chicken (<i>Gallus gallus domesticus</i>)	(Briels et al., 2018)
PFHxS	in ovo	38 000 ng/g (egg w)	decreased tarsus length and embryo mass	LOEC	Chicken (<i>Gallus gallus domesticus</i>)	(Cassone et al., 2012)
PFOS	in vivo	1.4 µM (95% CI, Range 1.1-1.6 µM)	mortality	LC50	Nematode (<i>Caenorhabditis elegans</i>)	(Chen et al., 2018a)
PFBS	in vivo	794 µM (95% CI, Range 624-1 009 µM)	mortality	LC50	Nematode (<i>Caenorhabditis elegans</i>)	(Chen et al., 2018a)
PFDA	in vitro	7.8 µM	oocyte viability	LC50	Oocyte cells from pigs	(Domínguez et al., 2019)
PFDA	in vitro	3.8 µM	maturation	IM50	Oocyte cells from pigs	(Domínguez et al., 2019)
PFDODA, PFNA, PFOA	in vitro	107-647 µM	cytotoxicity	EC50	human placental choriocarcinoma cell line JEG-3	(Gorrochategui et al., 2014)
PFOS, PFOA, PFBS	in vitro	57 – 80 µM	aromatase inhibition	IC50	human placental choriocarcinoma cell line JEG-3	(Gorrochategui et al., 2014)
PFDODA	in vivo	1.2 mg/L	level of dopamine was upregulated significantly	LOEC	<i>Danio rerio</i>	(Guo et al., 2018)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Study type	Effect value	Effect	Endpoint	Species/Cell line	Reference
PFNA	in vitro	10 µg/L	negative effect on blastocyst formation	LOEC	Oocyte cells from cows	(Hallberg et al., 2019)
PFNA	in vitro	0.1 µg/L	lipid droplet distribution significantly altered	LOEC	Oocyte cells from cows	(Hallberg et al., 2019)
PFBS, PFHxS, PFNA, PFHpA	in vivo	100 000 µg/kg dw	increased mortality	LOEC	<i>Eisenia fetida</i>	(Karnjanapiboonwong et al., 2018)
PFNA, PFHpA	in vivo	100 000 µg/kg dw	significant weight loss	LOEC	<i>Eisenia fetida</i>	(Karnjanapiboonwong et al., 2018)
PFOS	in vivo	33 µg/L (95% CI, Range 29 – 37 µg/L)	genotoxicity (DNA strand breaks and fragmentation, chromosomal breaks and apoptosis)	EC50	Marine mussel (<i>Perna viridis</i>)	(Liu et al., 2014)
PFOA	in vivo	594 µg/L (95% CI, Range 341- 1 063 µg/L)	genotoxicity (DNA strand breaks and fragmentation, chromosomal breaks and apoptosis)	EC50	Marine mussel (<i>Perna viridis</i>)	(Liu et al., 2014)
PFNA	in vivo	195 µg/L (95% CI, Range 144 – 265 µg/L)	genotoxicity (DNA strand breaks and fragmentation, chromosomal breaks and apoptosis)	EC50	Marine mussel (<i>Perna viridis</i>)	(Liu et al., 2014)
PFDA	in vivo	78 µg/L (95% CI, Range 73- 84 µg/L)	genotoxicity (DNA strand breaks and fragmentation, chromosomal breaks and apoptosis)	EC50	Marine mussel (<i>Perna viridis</i>)	(Liu et al., 2014)
PFOS, PFOA, PFBS	in vivo	10 µg/L	reduced growth	LOEC (only one concentration tested)	<i>Chironomus riparius</i>	(Marziali et al., 2019)
PFOS	in vivo	29.8+/- 4.1 µM	behavior: prolonged backward swimming (indicating modified cellular cadmium conductance)	EC50	<i>Paramecium caudatum</i>	(Matsubara et al., 2006)
PFOA	in vivo	424.1+/- 124.0 µM	behavior: prolonged backward swimming (indicating modified cellular cadmium conductance)	EC50	<i>Paramecium caudatum</i>	(Matsubara et al., 2006)
FOSAPrTMA	in vivo	19.1+/-	behavior: shortened backward swimming	EC50	<i>Paramecium caudatum</i>	(Matsubara et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Study type	Effect value	Effect	Endpoint	Species/Cell line	Reference
		17.3 µM	(indicating modified cellular cadmium conductance)			(2006)
PFNA	in vivo	98.7+/- 20.1 µM	behavior: prolonged backward swimming (indicating modified cellular cadmium conductance)	EC50	<i>Paramecium caudatum</i>	(Matsubara et al., 2006)
PFDA	in vivo	60.4+/- 10.1 µM	behavior: prolonged backward swimming (indicating modified cellular cadmium conductance)	EC50	<i>Paramecium caudatum</i>	(Matsubara et al., 2006)
6:2 CI-PFESA	in vivo	6 mg/L	decreased survival	LOEC	<i>Danio rerio</i>	(Shi et al., 2017)
6:2 CI-PFESA	in vivo	5 µg/L	decreased liver triglyceride levels	LOEC	<i>Danio rerio</i>	(Shi et al., 2019a)
PFNA	in vitro	4.8 µM	inhibition of p-glycoprotein (p-gp) cellular efflux transporter	IC50	gill cells from marine mussel (<i>Mytilus californianus</i>)	(Stevenson et al., 2006)
PFDA	in vitro	7.1 µM	inhibition of p-glycoprotein (p-gp) cellular efflux transporter	IC50	gill cells from marine mussel (<i>Mytilus californianus</i>)	(Stevenson et al., 2006)
TFA	in vivo	700 mg/L (95% CI, Range 460- 1 000 mg/L)	sublethal endpoints (edema, malformations, non-hatched eggs, lack of circulation, reduced pigmentation, spinal curvature)	EC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFBA	in vivo	2 200 mg/L (95% CI, Range 1 200- 2 200 mg/L)	sublethal endpoints (edema, malformations, non-hatched eggs, lack of circulation, reduced pigmentation, spinal curvature)	EC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFOA	in vivo	350 mg/L (95% CI, Range 290- 430 mg/L)	sublethal endpoints (edema, malformations, non-hatched eggs, lack of circulation, reduced pigmentation, spinal curvature)	EC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFNA	in vivo	16 mg/L (95% CI, Range 7.7- 450 mg/L)	sublethal endpoints (edema, malformations, non-hatched eggs, lack of circulation, reduced pigmentation, spinal curvature)	EC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFDA	in vivo	5.0 mg/L (95% CI, Range 3.8-	sublethal endpoints (edema, malformations, non-hatched eggs, lack of circulation, reduced pigmentation, spinal	EC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Study type	Effect value	Effect	Endpoint	Species/Cell line	Reference
		6.6 mg/L)	curvature)			
PFBS	in vivo	450 mg/L (95% CI, Range 350- 600 mg/L)	sublethal endpoints (edema, malformations, non-hatched eggs, lack of circulation, reduced pigmentation, spinal curvature)	EC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFOS	in vivo	1.5 mg/L (95% CI, Range 1.1.- 1.9 mg/L)	sublethal endpoints (edema, malformations, non-hatched eggs, lack of circulation, reduced pigmentation, spinal curvature)	EC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
TFA, PFBA	in vivo	>3 000 mg/L	mortality	LC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFOA	in vivo	430 mg/L (95% CI, Range 290- 710 mg/L)	mortality	LC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFNA	in vivo	>10 mg/L	mortality	LC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFDA	in vivo	8.4 mg/L (95% CI, Range 5.3- 15 mg/L)	mortality	LC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFBS	in vivo	1 500 mg/L (95% CI, Range 1 100- 1 900 mg/L)	mortality	LC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
PFOS	in vivo	<10 mg/L	mortality	LC50	<i>Danio rerio</i>	(Ulhaq et al., 2013)
6:2 CI-PFESA	in vivo	15.5 mg/L	mortality	LC50	<i>Danio rerio</i>	(Wang et al., 2013b)
TFA	in vivo	70 mg/L	mortality	LC50	<i>Brachionus calyciflorus</i>	(Wang et al., 2014a)
PFPrA	in vivo	80 mg/L	mortality	LC50	<i>Brachionus calyciflorus</i>	(Wang et al., 2014a)
PFBA	in vivo	110 mg/L	mortality	LC50	<i>Brachionus calyciflorus</i>	(Wang et al., 2014a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Study type	Effect value	Effect	Endpoint	Species/Cell line	Reference
PFPeA	in vivo	130 mg/L	mortality	LC50	<i>Brachionus calyciflorus</i>	(Wang et al., 2014a)
PFHxA	in vivo	140 mg/L	mortality	LC50	<i>Brachionus calyciflorus</i>	(Wang et al., 2014a)
PFDODA	in vivo	1.2 mg/L, 1.2 mg/L and 6 mg/L respectively	upregulated gene expression levels of thyrotropin-releasing hormone (trh), corticotrophin-releasing hormone (crh) and iodothyronine deiodinases (dio2)	LOEC	<i>Danio rerio</i>	(Zhang et al., 2018b)
PFDODA	in vivo	1.2 mg/L and 6 mg/L respectively	downregulated gene expression levels of thyroglobulin (tg) and thyroid receptor (trbeta)	LOEC	<i>Danio rerio</i>	(Zhang et al., 2018b)

*6:2 FTOH has recently been classified via decision of ECHAs Risk Assessment Committee (RAC) as a substance that is very toxic to aquatic life with long lasting effects (Aquatic Chronic 1; H410, M=1) (ECHA News:

https://echa.europa.eu/documents/10162/2082415/news_annex_rac_seac_dec_2021_en.pdf/92b14f83-580d-323a-486a-32fade778505?t=1639041622096; RAC protocol: https://echa.europa.eu/documents/10162/17090/rac59_final+minutes_en.pdf/2f350729-0880-57da-9a1e-b812d24df808?t=1639990293786)

Ecotoxicological threshold values reported in the PFASTox Database differ over several orders of magnitude (ng-scale to mg-scale). A comparison, or averaging of the different values is not feasible due to the large differences between the different studies (e.g. test-design, sensitivity of species, reporting of results). The key message of this compilation-exercise is, that some of the concentration values at which certain PFASs cause ecotoxicological effects (mostly organ specific effects) are within the same order of magnitude at which PFASs have been detected in the environment (see chapter B.4.2). The significance of this comparison is of course very limited as it ignores e.g. inter-species differences regarding the sensitivity to PFAS-mediated effects as well as differences between laboratory conditions (under which the above values were derived) and real-world conditions. Still, it underlines the need to minimize emissions of PFASs to the environment. This is without prejudice to the assumption that PFASs are regarded as non-threshold substances from a regulatory perspective, due to their very high persistence.

Additionally, this compilation highlights the large knowledge gap which exists around the study of environmental effects of PFASs. The PFASTox Database, at the time of access, contains information for 29 out of potentially >10 000 individual PFASs. This shows, that the investigation of potential adverse effects of PFASs in the environment has not even begun to comprehensively assess this large class of substances despite severe efforts that have been put into this area of research over the past decades.

B.7.1.11. Conclusions

Despite the growing amount of studies investigating the ecotoxicity of PFASs, the available data on adverse effects of PFASs in the environment is limited to a small number of substances. Moreover, most studies investigate the aquatic toxicity of PFASs, leaving a huge gap of knowledge regarding the toxicity towards terrestrial organisms. Additionally, conventional ecotoxicological tests may not be suitable to detect long term effects from exposure to PFASs. PFASs can remain in the environment for long time periods (decades-centuries or even longer) due to their high persistence but ecotoxicological test systems usually cover only time spans of a few days – weeks.

Yet, for a small subset of PFASs, there is information available that suggests that these substances cause adverse effects in the environment. Some of the PFASs (especially PFOA and PFOS) have been investigated thoroughly and suggestions for possible mechanisms of action have been made. Based mostly on information for PFOS and PFOA, there is “ample basis to suspect that at least a subset of PFASs can be considered persistent, bioaccumulative, and/or toxic” as Ankley and colleagues phrased it in their review paper on the ecological risks of PFASs (Ankley et al., 2021). PFASs may also cause adverse effects, that are relevant for whole populations if they affect endpoints such as reproduction or survival of offspring. Two trends regarding the toxicity of PFASs could be derived from the currently data available:

1. Toxicity in the same PFAS class tends to increase with increased C-chain length.
2. PFASs are usually more toxic than PFCAs with the same chain length (C8) (Ankley et al., 2021).

However, interactions of substances with the environment are complex and depend on various factors. For example, the environmental behaviour and fate of PFASs depend both on the inherent physicochemical properties for each respective PFAS and their degradation products, the physico-chemical conditions of the abiotic environmental compartments that act as recipient systems (e.g. organic carbon content of sediments, or temperature, salinity, concentration of oxidants in seawater), and the physiological status and conditions of the recipient organisms which may take up and accumulate the given PFAS.

Considering that PFASs are very persistent and mobile, organisms living in different environmental compartments are continuously exposed to PFASs. Without reliable data that is suitable to detect also long-term effects of PFASs (inter-generational effects after inter-generational exposure), it is not possible to demonstrate safe use of PFASs. This warrants for a restriction of the use of PFASs to minimize emissions to the environment. At the time notable

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

effects from PFASs exposure occur in the environment it will be difficult, if not impossible, to remove the contamination. Thus, there is a threat of irreversible damage.

B.7.2. Effects on wildlife

B.7.2.1. Notes on the procedure

The basis for the following paragraphs is the chapter “Field-based effects studies in wildlife” in the review paper on ecological risks of PFASs from Ankley et al. (2021). The main findings from this chapter were summarized according to different animal groups (avian species, mammals, reptiles, fish and invertebrates). These findings were complemented by results from other studies that were compiled in the PFASTox database, see chapter B.7.1 for more details. The study list from that database was filtered for studies that investigated effects on wildlife and are not included in the review by Ankley and colleagues.

B.7.2.2. PFASs effects on wildlife

Several studies investigated tissue concentrations of PFASs in wild living animals that were exposed to PFASs (and other contaminants) in the field. Subsequently, these studies assessed the link of the measured tissue concentrations to adverse effects or endpoints related to impairments (e.g. oxidative stress) – in distinction to the studies compiled in chapter B.7.1 where “wildlife” species were subject to ecotoxicological tests under laboratory conditions. Ankley et al. (2021) stated in their review on ecological risks of PFASs that these types of studies are of special interest due to the fact that “field studies can provide a critical perspective on whether actual exposures in free-living organisms can reach levels that cause observable adverse effects”. However, they highlighted also limitations regarding the toxicity data from field studies, as it is “possible that other unidentified factors contribute to observed effects, and that any effects observed are influenced by the choice of endpoint” (Ankley et al., 2021). Thus, establishing links between contaminant exposure and health outcome is a difficult task (Rodríguez-Estival and Mateo, 2019).

The studies evaluated for this report reported various endpoints associated with PFAS exposure in the field. These endpoints comprise changes in brain chemistry (e.g. brain hormone levels), oxidative stress (e.g. induction of antioxidant enzymes), reproduction (e.g. eggshell thinning), changes in metabolism (e.g. PPARα and cyp4a), reduced biomass, endocrine activity (e.g. changes in hormone levels), or changes in immunologic parameters (e.g. a decreased antibody response).

Ankley et al. (2021) based their review on PFAS effects on wildlife on 39 studies that assessed avian species (19), mammals (11), reptiles (3), fish (2) and invertebrates (2). The PFASTox database yielded 8 complementing studies, 5 on avian species, 2 on mammals and 1 on fish.

B.7.2.3. Avian species

The endpoints from field studies with avian species, compiled by Ankley et al. (2021), comprise measures of oxidative stress and reproduction. They focused their evaluation on reproduction endpoints, presumably because this is a highly relevant endpoint to assess adverse effects on the population or ecosystem level. Two studies reported decreased hatching success for eggs of tree swallows (*Tachycineta bicolor*) from different regions in Minnesota. The effect was linked to PFOS concentrations in eggs of 150 ng/g ww and upwards. However, in a more recent study, where tree swallow eggs were sampled near an Air Force base in Michigan (coordinated by the same author), no impact on hatching was observed while concentration measurements in eggs resulted in concentrations >600 ng/g ww. According to Ankley et al. (2021), the authors of that study considered the effects from the earlier studies to be linked to the presence of co-contaminants. Two different studies, reviewed by Ankley et al. (2021), reported negative associations between PFAS contamination and reproductive endpoints. One study reported reduced eggshell thickness and hatching success for individuals of a population of Great tits (*Parus major*) that was nesting in a PFAS-contaminated environment (PFASs were also measured in the eggs) and the other linked concentrations of plasma PFDoA with a reduced hatching success in Arctic black-legged kittiwakes (*Rissa tridactyla*). However, Ankley and colleagues highlighted, that for these studies “mechanism-based quantitative linkages between exposure

and effect have not yet been established” (Ankley et al., 2021).

Additionally, Blévin et al. (2018) investigated the effects of environmental contaminants (organochlorines, PFASs and mercury) on the incubation temperature (relevant for breeding success) of wild breeding Arctic black-legged kittiwakes and found that PFAS body burdens were not related to the incubation temperature measured at the brood patches of the birds.

Costantini et al. (2019) observed protein oxidative damage as well as other oxidative status markers in male individuals of the Arctic black-legged kittiwakes with higher body burdens of long-chain PFCAs (C₁₁-C₁₃). Furthermore, they observed, that the “non-enzymatic antioxidant capacity (including antioxidants of protein origin) was significantly lower in those birds having higher plasma concentration of linear perfluorooctanesulfonic acid (PFOSlin)”. However, activity of glutathione peroxidase in erythrocytes could not be correlated to PFAS body burdens. The authors state, that more experimental work is needed “to demonstrate whether PFASs cause toxic effects on free-living vertebrates through increased oxidative stress”.

Miljeteig et al. (2012) did not find associations between PFAS levels in ivory gull (*Pagophila eburnea*) individuals and three endpoints (eggshell thickness, retinol (vitamin A) and alpha-tocopherol (vitamin E)) when they investigated effects of environmental contamination on the Arctic seabird.

Several PFASs (PFOS, PFNA, PFOSA, PFHxS and PFOA) were detected in the livers of wild common cormorants (*Phalacrocorax carbo*) from Lake Biwa, Japan (Nakayama et al., 2008). Subsequently they investigated the potential adverse effects of environmental contaminants through gene expression profiling. Nakayama et al. (2008) report that their results “suggest the induction of antioxidant enzymes in response to oxidative stress caused by PFCs and the suppression of molecular chaperones, leading to reduction in protein stability”. In addition, they aimed to identify possible combination effects of PFASs with dioxins and related compounds (DRCs) via multiple regression analysis and concluded that “the regression models suggested the potential of PFCs to enhance toxicities of DRCs”.

In a study to assess the correlation between thyroid hormone concentrations and plasma concentrations of halogenated organic contaminants in young individuals of two seabird species (*Rissa tridactyla* and *Fulmarus glacialis*), “Positive associations between total thyroxine (TT4) and PFCs (PFHpS, PFOS, PFNA)” were found (Nøst et al., 2012). The authors further qualified that “Although correlations do not implicate causal relationships per se, the correlations are of concern as disruption of TH homeostasis may cause developmental effects in young birds”.

B.7.2.4. Mammalian wildlife

Field-effect studies with mammals, included in the review from Ankley et al. (2021), “consistently show an association between PFAS exposure and alterations in biomarkers of exposure and effect.”. Ankley et al. (2021) indicated one study with polar bears, where changes in enzymes relevant for the neurotransmitter-system were significantly correlated with brain concentrations of PFOS and PFCAs. In a follow up study (Pedersen et al., 2016) investigated changes in the brain steroid concentrations of polar bears. Pedersen et al. (2016) report that ΣPFASs (PFBS, PFHxS, PFOS and PFDS) as well as ΣPFCAs (PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTTrDA, PFTeDA and PFPeDA) could be linked with increased testosterone concentrations in specific brain regions. However, that authors could not verify the exact mechanistic connection and suggested a “interference with de novo steroid synthesis” or a “disruption of peripheral steroidogenic tissues mainly in gonads and feedback mechanisms” as possible mechanistic explanations.

Kurtz et al. (2019), reviewed in Ankley et al. (2021), reported that ΣPFCAs (PFOA, PFNA, PFDA, PFUnA, PFDoA, PFTriA, PFTA) as well as ΣPFAAs (Ankley et al., 2021) ΣPFCAs + PFOS and PFOSA) positively correlated with PPARα mRNA and cytochrome P4504a (cyp4a) protein expression in the kidney of stranded marine mammals (cetaceans). Three studies mentioned in the review of Ankley and colleagues investigated links between environmental PFASs exposure and

immunologic parameters in marine mammals. Scotter et al. (2019) did not observe a relation between antibody prevalence and exposure to contaminants in their study with Atlantic walrus (*Odobenus rosmarus rosmarus*). Fair et al. (2013) detected significant positive associations between PFAS exposure and immunological parameters in bottlenose dolphins (*Tursiops truncatus*; absolute numbers of CD2+ T cells, CD4+ helper T cells, CD19+ immature B cells, CD21+ mature B cells, CD2/CD21 ratio, MHCII+ cells, B cell proliferation, serum IgG1, granulocytic, and monocytic phagocytosis). Kannan et al. (2006) found in their study that individuals of southern sea otters (*Enhydra lutris nereis*), that died of infectious diseases, had significantly higher concentrations of PFOS and PFOA compared to individuals that died of noninfectious causes.

Persson and Magnusson (2015) investigated liver concentrations of PFAAs (PFOA, PFNA, PFDA, PFUnA, PFDoA, PFTTrDA, PFBS, PFHxS, PFOS) in male individuals of wild American mink (*Neovison vison*) sampled in Sweden. The authors subsequently examined associations between contaminant-body-burdens and effects on the reproductive system and reported a negative association between anogenital distance - a potential marker for endocrine disruptor exposure (Foster, 2006; Mammadov et al., 2018) - and concentrations of PFOS, PFDA, PFUnDA as well as ΣPFAAs.

Soloff et al. (2017) evaluated PFAA concentrations in bottlenose dolphins (*Tursiops truncatus*) highly exposed via their environment and assessed the effects on the cellular immune system in an *ex vivo* flow cytometry-based assay. The authors report that "Baseline PFOS concentrations were associated with significantly increased CD4(+) and CD8(+) T cell proliferation". Together with further data from *in vitro* exposure Soloff and colleagues concluded that their results "suggest that PFOS directly dysregulates the dolphin cellular immune system and has implications for health hazards".

B.7.2.5. Reptiles

With regard to reptiles, Ankley et al. (2021) reviewed three studies that linked environmental PFAS exposure with reduced biomass (PFOS and PFNA for **male** individuals of *Malaclemys terrapin* and PFHxA for both sexes), adverse effects on uroporphyrin concentrations (PFOS; observed in *Caretta caretta*) as well as immunosuppression (PFOS; observed in four different turtle species).

B.7.2.6. Fish

Field-effect studies focusing on fish, that were discussed in the review by Ankley et al. (2021) reported ambiguous results regarding the effects of environmental PFAS exposure. A study from Bangma et al. (2018) with wild caught striped mullet (*Mugil cephalus*), described a positive connection between PFAS-liver-concentration and the number of eggs, which the authors assumed to be due to a higher food consumption. No other effects on reproduction endpoints were observed in this study. Oakes et al. (2010) observed liver effects in fishes (species not specified) shortly after AFFF contamination of the creek they inhabited, but the effects did not persist over time. A study from Guillette et al. (2020) with striped bass (*Morone saxatilis*) related serum concentrations of 23 different PFASs with endpoints relevant for the liver and immune-system.

In addition, a study from Houde et al. (2013) quantified twelve PFASs (PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTTrDA, PFTeDA, PFPeDa, PFHxS, PFOS, PFDS, PFECHS) in muscle, liver and plasma of northern pike (*Esox lucius*) environmentally exposed to contaminants via municipal wastewater effluents in St. Lawrence River, Canada. Next to significantly up regulated stress response genes (*MT*, *GST*, *SOD* and *CYP1A1*), the authors observed significant relationships between *VTG* gene expression in liver, *VTG*-plasma-activity and plasma concentrations of PFTTrDA, PFTeDA and PFDS.

B.7.2.7. Invertebrates

Ankley et al. (2021) included two field-effect studies with invertebrates in their review.

A study from Rusconi et al. (2015) reported that more sensitive taxa of invertebrates were found upstream of a wastewater influent from a fluorotelomer plant while downstream of the discharge point, these species were not present. Statistical analysis, however, did not result in significant differences between the two locations. Differences in the genetic diversity between the two locations were furthermore quantified for one species (*Hydropsyche modesta*) but could not be associated to the contamination.

Bakke et al. (2010) assessed training facilities for firefighting (former as well as active) in order to evaluate if these sites are affected by the discharge of PFAS-containing firefighting foams. Sampling of earthworms (*Eisenia fetida*) to assess the bioaccumulation of PFASs was part of the assessment. Adverse effects were not recorded during the assessment, however the authors of the study concluded: "Based upon predictions of no effect concentrations (PNEC) for 6:2 FTS, PFOS and PFOA in soils, soil organisms living within about 100 meters from these four sites may be at risk". However, the authors state with reservations that this assumption is based solely on PNEC values for only one species and that more information for a robust assessment is warranted (Amundsen et al., 2008).

B.7.2.8. Conclusion

A recent review paper from Ankley et al. (2021), as well as complementary studies, compiled in the PFASTox database, provide some evidence, that environmental exposure to PFASs is correlated to effects observed wildlife animals of different animal groups (avian species, mammals, reptiles, fish and invertebrates). Observable effects comprise various endpoints e.g. changes in brain chemistry or metabolism, oxidative stress, reproduction, reduced biomass, endocrine disruption, or changes in immunologic parameters. Due to the limitations of the studies, a clear link between PFASs measurements in the environment, or PFAS-body-burdens in the animals and the observed effects can rarely be established. Other factors such as co-contaminants, environmental conditions, age, or sex might have contributed to the effects. Complementary laboratory studies that can plausibly link effects in these species to PFAS exposure would be needed but are in most cases not available. Yet, the available studies provide evidence, that PFASs can cause adverse effects on wildlife species at currently relevant concentrations. Following a precautionary approach, this warrants for measures to minimize the emissions of PFASs into the environment. As emissions will continue, the pollution stock will increase over time due to the high persistence of PFASs (or their final degradation products) and adverse effects on population- or ecosystem-level will become more likely. At the time notable effects from PFASs exposure occur in the environment it will be difficult, if not impossible, to remove the contamination. Thus, there is a threat of irreversible damage.

B.7.3. Atmospheric compartment – global warming potential

Some PFASs are persistent and volatile and will partition to the atmosphere where they will stay for a very long time. These substances may have a considerable global warming potential which contributes to the greenhouse effect and global warming. In fact, some of the strongest greenhouse gases known are PFASs.

One of the most relevant subclasses of PFASs that contribute to global warming are the fluorinated gases, e.g. hydrofluorocarbons (HFCs) and hydrofluoroethers (HFEs). These are high-volume substances used as refrigerants, blowing agents, and solvents etc. with considerable emissions. Emitted substances evaporate and reside in the atmosphere (Oltersdorf et al., 2021). The demand for fluorinated gases is currently increasing.

In an expert insight paper by Sovacool et al. (2021) it is pointed out that fluorinated gases have been termed “supergreenhouse gases” given their severe and powerful impact on the climate. They are the most potent greenhouse gases known to modern science, with global warming potentials far greater than carbon dioxide, some up to almost 24 000 times more so. At the same time, they are also the fastest growing class of greenhouse gas emissions around the world, especially in developing countries. The global warming potential (GWP) of a substance depends, inter alia, on its lifetime in the atmosphere. Short-lived substances may therefore often have a lower GWP compared to long-lived substances if they otherwise are comparable in their contribution to radiative forcing. The Global Warming Potential over 100 years (GWP-100) is used for countries' greenhouse gas emission inventories reported to the UNFCCC. In this report the Dossier Submitters simply refer to GWP for GWP-100, unless otherwise stated. GWP is a relative measurement which measures the global warming potential of a substance relative to that of carbon dioxide (CO₂) with GWP = 1 by definition.

Radiative forcing is a term that is closely related to GWP, but unlike GWP, it does not have a time horizon. Radiative forcing describes how strongly the radiation balance of the atmosphere is influenced if the concentration of a given gas, chemical, or substance increases. Changes in the Earth's overall radiative forcing can be caused by changes in the concentration of greenhouse gases in the atmosphere, thus leading to global warming. Generally, the more fluorine atoms in a compound, the greater its GWP and radiative forcing (Sovacool et al., 2021).

Atmospheric lifetimes and global warming potential for fluorinated gases may be found in IPCC Assessment Reports. Emissions, up to 2020, are to be reported using the GWP - values from the IPCC fourth Assessment Report (Forster, 2007). Updated values from the IPCC fifth Assessment Report will be used for reporting under the Paris Agreement. A few examples are listed in Table B.15 below for comparison.

Table B.15. GWP-values (GWP-100) collected from the IPCC fourth Assessment Report.

Gas	Chemical formula	Lifetime (y)	GWP
Carbon dioxide	CO ₂		1
Methane	CH ₄	12	25
Nitrous oxide	N ₂ O	114	298
HFC-23	CHF ₃	270	14 800
HFC-32	CH ₂ F ₂	4.90	675
HFC-236fa	CF ₃ CH ₂ CF ₃	240	9 810
PFC-14	CF ₄	50 000	7 390
PFC-5-1-14	CF ₃ CF ₂ CF ₂ CF ₂ CF ₃	3 200	9 300
HFE-125	CHF ₂ OCF ₃	136	14 900
HFE-143a	CH ₃ OCF ₃	4.30	756
HFE-7100	CF ₃ CF ₂ CF ₂ CF ₂ OCH ₃	3.8	297

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

According to ECOS (2021) the latest generation of fluorinated gases (e.g. HFOs) were developed to replace earlier generations of gases that had high global warming potential. Although the HFOs often have low GWP, they may lead to formation of TFA during degradation in the atmosphere. The authors called for replacement of fluorinated gases with truly sustainable and futureproof alternatives, such as natural refrigerants.

Dudita and Kauffeld (2021) summarized the environmental impacts of HFO refrigerants and their alternatives, including their degradation products. The authors concluded that alternative refrigerants should be halogen-free, avoiding thus atmospheric TFA and HF formation. The study also looked into the refrigerants' indirect contribution to global warming through their manufacturing process and concluded that natural refrigerants (ammonia, CO₂ and hydrocarbons) have considerably lower CO₂ equivalent emissions during manufacture.

Cousins et al. (2020b) elaborate on the consequences of the high persistence of PFASs and points out that some PFASs, or their breakdown products, may have environmental effects in addition to the concerns usually considered under REACH, like e.g. high climate impact (e.g. in the case of perfluoroalkanes and perfluoro-tert-amines). In some cases, such PFASs are not covered by the F-gas regulation and its measures.

One example is perfluorotributylamine (N(C₄F₉)₃) which was studied by Tsai (2017). It was found that the substance has a very low solubility in water and relatively high vaporization from the water bodies, suggesting that perfluorotributylamine will sink into the atmosphere. The substance was reported to have an atmospheric lifetime of 500 years and a GWP = 7 100. Bernard et al. (2020) investigated the perfluorinated trialkylamines further and found the fully fluorinated triethyl and tripropyl analogues to have GWPs of 9 900 and 8 700, respectively.

The fluranes, e.g. sevoflurane, isoflurane, desflurane and enflurane, are perfluorinated alkyl ether substances with a considerable atmospheric lifetime and GWP, see Table B.16 with data collected from Hodnebrog et al. (2020). These substances are known for their anaesthetic effects. Two of them are listed in Annex II (reporting obligations only), of the F-gas regulation, while the other two are not included in the F-gas regulation.

Table B.16. GWP-values (GWP-100) for selected fluranes.

Gas	Chemical formula	Lifetime (y)	GWP
Sevoflurane, HFE-347mmz1	(CF ₃) ₂ CHOCH ₂ F	1.9	205
Isoflurane, HCFE-235da2	CHF ₂ OCHClCF ₃	3.5	565
Desflurane, HFE-236ea2	CHF ₂ OCHF ₂ CF ₃	14.1	2 720
Enflurane, HCFE-235ca2	CHF ₂ OCF ₂ CHFCI	4.4	686

The high climatic effect of fluoroform (HFC-23) is well known and measures to reduce the emissions of the substance has previously been introduced. Stanley et al. (2020) calculated that these measures should have seen global emissions drop by 87% between 2014 and 2017. Instead, atmospheric observations show that emissions of fluoroform (HFC-23) have increased and in 2018 were higher than at any point in history. The authors speculated that the magnitude of the discrepancy between reported emissions reductions and emissions inferred from the atmospheric data could result from developing countries have been unsuccessful in meeting their reported emissions reductions, or that there may be substantial unreported production of HCFC-22 at unknown locations which has been regarded as the main source of fluoroform (HFC-23) emissions. The discrepancy between the inventory-based emissions estimates of fluoroform (HFC-23) and the emissions based on atmospheric measurements is roughly equivalent to the total green-house gas emissions of Spain in 2017 (Stanley et al., 2020).

A literature survey on the emissions from incineration of fluoropolymer materials performed by the Norwegian Institute for Air Research (NILU) on behalf of the Norwegian Environment Agency disclosed information indicating that incineration of fluoropolymers leads to the formation of substances like CF₄ (PFC-14), CHF₃ (HFC-23), C₂F₆ (PFC-116), tetrafluoroethene (TFE) and

hexafluoropropene (HFP), some of which are potent greenhouse gases (Huber et al., 2009). The kind of compounds formed is strongly dependent on the incineration conditions like temperature, moisture, oxygen content, use of catalysts etc. The report concludes that incineration of fluoropolymer containing products has a great potential to contribute considerably to the total greenhouse gas emissions of Norway, but due to the lack of sound data on the fate of fluoropolymers in Norway as well as of the chemical reactions in the different types of waste incineration plants, no exact amounts can be given.

Stoiber et al. (2020) looked further into the disposal of products and materials containing PFASs and concluded that incineration of PFAS wastes can release toxic air pollutants and greenhouse gases, which may represent a cyclical problem as disposal of PFAS-containing wastes creates repeated cycles of contamination. Volatile PFASs may also be emitted into the air from landfills and wastewater treatment plants.

In the Chemicals Strategy for Sustainability the European Commission points out that in a safe and sustainable-by-design approach to chemicals, overall sustainability should be ensured by minimising the environmental footprint of chemicals in particular on **climate change**, resource use, ecosystems and biodiversity from a lifecycle perspective (EEB, 2020).

B.7.3.1. Legislation

Two legislative acts have already been adopted to control emissions from fluorinated greenhouse gases, including hydrofluorocarbons (HFCs), in the European Union: the F-gas Regulation and the MAC Directive.

B.7.3.1.1. F-gas Regulation

The current F-gas Regulation (Regulation (EU) No 517/2014), which applies since 1 January 2015, replaces the original F-gas Regulation adopted in 2006 (EC, 2014). The F-gas regulation has the following ambitions:

- **Limiting the total amount** of the most potent fluorinated greenhouse gases (called F-gases in the regulation) that can be produced and imported into the EU from 2015 onwards and phasing them down in steps to one-fifth of the level of 2014 in 2030. This will be the main driver of the move towards more climate-friendly technologies;
- **Banning the use** of F-gases (or F-gases with a GWP above a certain threshold) in many new types of equipment where less harmful alternatives are widely available, such as fridges in homes or supermarkets, air conditioning and foams and aerosols;
- **Preventing emissions** of F-gases from existing equipment by requiring leak checks, proper servicing and recovery of the gases at the end of the equipment's life.

Annex I of the regulation lists 27 specific fluorinated greenhouse gases (F-gases) for which the above regulations apply and for which the intentional release into the atmosphere shall be prohibited where the release is not technically necessary for the intended use. Annex II lists 43 additional fluorinated greenhouse gases (F-gases) that are subject to reporting obligations.

The basis for the F-gas regulation is the GWP of the substances in scope and their contribution to global warming, while other concerns are not taken into account, e.g. atmospheric degradation to TFA which precipitates and causes exposure to humans and the environment.

A discussion of degradation of some relevant fluorinated gases may be found in section B.4.1.3.2. The German Environment Agency recently published a comprehensive investigation of degradation of fluorinated gases: "Persistent degradation products of halogenated refrigerants and blowing agents in the environment: type, environmental concentrations, and fate with particular regard to new halogenated substitutes with low global warming potential" (UBA, 2021c).

The F-gas regulation is currently under revision and a proposal for a revised regulation was published in April 2022 (EC, 2022).

B.7.3.1.2. MAC Directive

The Mobile Air-Conditioning (MAC) Directive (Directive 2006/40/EC) covers the use of fluorinated gases with a GWP of more than 150 in passenger cars (vehicle category M1) and light commercial vehicles (category N1, class 1) (EC, 2006). The directive is enforced over three phases, and from 1 January 2017, the use of fluorinated greenhouse gases with a GWP higher than 150 in all new vehicles put on the EU market has been totally banned. introduced from 2011, and in all new cars and vans produced from 2017.

The traditionally used refrigerant in MAC systems, HFC-134a (CH_2FCF_3), has a GWP of 1 430 and has been phased out for use in air condition equipment in new cars in the EU. The Directive does not specify any particular refrigerant or system, leaving the technical choice on the car manufacturers.

The MAC Directive is limited to the use of fluorinated gases in air-conditioning systems in cars and vans, but not in buses, trains, ships etc. Air condition equipment is only one of several applications of fluorinated gases.

B.7.4. Microbiological activity in sewage treatment systems

Not specifically assessed. See section B.4.5 on the challenges to remove PFASs in STPs.

B.7.5. Endocrine activity and endocrine disruption

B.7.5.1. Notes of procedure

To obtain relevant literature that addresses the endocrine activity (EA) or endocrine disruption (ED) of PFASs in the environment an initial literature research for review papers was performed, using Scopus¹⁹ and PubMed²⁰. A first screening of the results showed that there were many overlaps between the results from the two different databases but the research in Scopus produced more relevant results. Thus, only references yielded from Scopus were screened thoroughly. In total 754 titles were screened. Twenty papers were selected for further reading after title screening. The results reported in the (mostly review) papers were collected in tabular form. In some cases, they were supplemented with more details from the primary references. Furthermore, the literature research was complemented by references compiled in the PFASTox database²¹. The database was filtered for *in-vitro* and animal studies on the endocrine system. PFASTox Database entries were extracted in tabular form and the most important results reported in abstracts were added to the tabular compilation of results. In case of ambiguities or insufficient description of results or methodologies the references were read in more detail. Lastly, it is important to note, that the EA or ED of PFAS which are already restricted (e.g. PFOS, PFOA, C9-C14 PFCAs) were not recorded in the tabular compilation unless for reasons of comparison or to describe trends.

B.7.5.2. Overview of results

The studies that were assessed in the course of this research reported EA/ED for 32 individual PFASs, and different mixtures of these substances. Considering the group of PFASs contains >10 000 individual substances this is a rather small dataset. From the present data no trends regarding chain length or functional groups that promote EA/ED could be derived. Thus, it is not possible to focus the assessment on a certain subset of PFASs. Most likely not all relevant studies describing EA or ED of PFASs in the environment were collected. Still, this shows that the overall data on endocrine effects of PFASs in the environment is scarce.

Four studies described adverse effects of different PFASs, evoked by an endocrine mode of action, which are considered relevant on population level (i.e. having the potential to negatively affect a whole population of animals e.g. through reduction of fecundity or fertility of individuals). In particular, 8:2 FTOH, PFBS, 6:2 Cl-PFESA and a PFAS mixture of PFOA, PFOS, PFBS and PFBA were found to cause adverse effects that can be considered relevant on the population level. In total 69 cases of EA/ED of 32 PFASs were recorded (*in silico* 1, *in vitro* 51, *in vivo* 17; incl. the 4 cases with effects relevant on population level). 11 cases with inconclusive results (*in vitro* 9, *in vivo* 2) and 12 cases of no EA/ED after exposure to PFASs were reported (*in vitro* 8, *in vivo* 4). A tabular overview of the EA/ED of each PFAS together with the respective study type and reference can be found in Table B.17.

A bias in the search results towards studies reporting EA/ED of PFASs has to be assumed due to the fact that the research was designed to discover studies describing such effects. Furthermore, the publication of negative results unfortunately is still not common practice in the scientific community which further strengthens the bias. Still the results of this research provide the insight, that some PFAS - with heterogenous structures and functional groups (e.g. carboxylic acids, sulfonic acids, telomer alcohols, ether, ester, sulfonamides, or cyclic PFAS) - show EA/ED in *in silico*, *in vitro* and *in vivo* tests and cause adverse effects through disruption of the hormone system - in some cases with the potential to negatively affect whole populations. Additionally, there is a very large group of PFASs for which no information regarding their EA/ED is available (as this research indicates). Some of these compounds, e.g. those with structural similarities to already known PFASs with properties causing EA/ED, might have the potential to cause adverse effects through interaction with the hormone system of organisms in the environment. To this

¹⁹ www.scopus.com, date of access: 2022-09-29.

²⁰ <https://pubmed.ncbi.nlm.nih.gov/>, date of access: 2022-09-29.

²¹ <https://pfastoxdatabase.org/>, date of access: 2022-09-29.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

moment it is however not possible to say with certainty which structural elements of PFASs are responsible for their EA/ED properties.

Table B.17. Overview over EA/ED of different PFASs.

Substance (CAS-, EC-No.)	Study Type	Endocrine activity/ Endocrine disruption	Reference
4:2 FTOH (2043-47-2, 218-050-9)	In vitro	+	(Rosenmai et al., 2016)
	In vitro	+	(Liu et al., 2007)
6:2 FTOH (647-42-7, 211-477-1)	In vitro	0	(Weiss et al., 2009)
	In vitro	+	(Rosenmai et al., 2016)
	In vitro	+	(Ishibashi et al., 2007)
	In vitro	+	(Liu et al., 2007)
	In vitro	+	(Liu et al., 2009)
	In vitro	+	(Maras et al., 2006)
	In vitro	+	(Benninghoff et al., 2011)
8:2 FTOH (678-39-7, 211-648-0)	In vitro	0	(Weiss et al., 2009)
	In vitro	+	(Rosenmai et al., 2016)
	In vitro	+	(Ishibashi et al., 2007)
	In vitro	+	(Maras et al., 2006)
	In vitro	+	(Benninghoff et al., 2011)
	In vivo	+	(Liu et al., 2010a)
8:2 FTOAcr (27905-45-9, 248-722-7)	In vitro	+	(Benninghoff et al., 2011)
8:2 monoPAP (57678-03-2, N.A.)	In vitro	+	(Rosenmai et al., 2016)
8:2 diPAP (678-41-1, 211-649-6)	In vitro	+	(Rosenmai et al., 2013)
	In vivo	-	(Rosenmai et al., 2016)
10:2 diPAP (1895-26-7, 217-585-5)	In vitro	-	(Rosenmai et al., 2016)
8:2 triPAP (N.A., N.A.)	In vitro	+	(Rosenmai et al., 2016)
PFBA (375-22-4, 206-786-3)	In vitro	0	(Weiss et al., 2009)
	In vitro	+	(Rosenmai et al., 2016)
	In vitro	+	(Behr et al., 2018)
	In vitro	0	(Vongphachan et al., 2011)
	In vitro	-	(Croce et al., 2019)
	In vitro	+	(Ishibashi et al., 2007)
	In vivo	+	(Godfrey et al., 2017)
	In vivo	+	(Godfrey et al., 2019)
PFPeA (2706-90-3, 220-300-7)	In vitro	+	(Rosenmai et al., 2016)
	In vitro	+	(Rosenmai et al., 2018)
	In vitro	-	(Wielogórska et al., 2015)
PFHxA (307-24-4, 206-196-6)	In vitro	+	(Weiss et al., 2009)
	In vitro	+	(Rosenmai et al., 2016)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance (CAS-, EC-No.)	Study Type	Endocrine activity/ Endocrine disruption	Reference
	In vitro	+	(Benninghoff et al., 2011)
	In vitro	+	(Vongphachan et al., 2011)
	In vitro	+	(Vongphachan et al., 2011)
	In vitro	-	(Wielogórska et al., 2015)
	In vitro	+	(Ishibashi et al., 2007)
	In vivo	-	(Cassone et al., 2012)
PFHpA (375-85-9, 206-798-9)	In vitro	+	(Weiss et al., 2009)
	In vitro	+	(Rosenmai et al., 2016)
	In vitro	+	(Benninghoff et al., 2011)
	In vitro	+	(Vongphachan et al., 2011)
	In vitro	+	(Ishibashi et al., 2007)
	In vitro	-	(Wielogórska et al., 2015)
PFBS (375-73-5, 206-793-1)	In vitro	+	(Weiss et al., 2009)
	In vitro	+	(Vongphachan et al., 2011)
	In vitro	+	(Behr et al., 2018)
	In vitro	-	(Croce et al., 2019)
	In vitro	+	(Ishibashi et al., 2011)
	In vivo	-	(Newsted et al., 2008)
	In vivo	+	(Chen et al., 2018b)
	In vivo	+	(Sant et al., 2019)
	In vivo	+	(Lou et al., 2013)
PFHxS (355-46-4, 206-587-1)	In vitro	+	(Weiss et al., 2009)
	In vitro	+	(Watkins et al., 2015)
	In vitro	+	(Vongphachan et al., 2011)
	In vitro	-	(Behr et al., 2018)
	In vitro	+	(Ishibashi et al., 2011)
	In vitro	-	(Wielogórska et al., 2015)
	In vivo	-	(Ramhoj et al., 2020)
	In vivo	+	(Cassone et al., 2012)
PFHpS (375-85-9, 206-798-9)	In vitro	0	(Vongphachan et al., 2011)
	In vivo	+	(Nøst et al., 2012)
PFDS (335-77-3, 206-401-9)	In vitro	+	(Benninghoff et al., 2011)
	In vivo	0	(Benninghoff et al., 2011)
HFPO-DA (13252-13-6, 236-236-8)	In vitro	+	(Li et al., 2019)
	In vitro	+	(Coperchini et al., 2020)
	In vivo	+	(Conley et al., 2019)
HFPO-TA (2641-34-1, 220-141-3)	In vitro	+	(Li et al., 2019)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance (CAS-, EC-No.)	Study Type	Endocrine activity/ Endocrine disruption	Reference
6:6 PFPIA (70609-44-8, N.A.)	In vivo	+	(Liu et al., 2019b)
6:8 PFPIA (610800-34-5, N.A.)	In vivo	+	(Liu et al., 2019b)
8:8 PFPIA (500776-69-2, N.A.)	In vivo	+	(Liu et al., 2019b)
	In vivo	+	(Kim et al., 2020b)
PFOSA (754-91-6, 212-046-0)	In vitro	+	(Wåggbø et al., 2012)
PFECHS (646-83-3, N.A.)	In vivo	+	(Houde et al., 2016)
6:2 FTUA (N.A., N.A.)	In vitro	+	(Weiss et al., 2009)
N-MeFOSE (24448-09-7, 246-262-1)	In vitro	0	(Weiss et al., 2009)
N-EtFOSE (1691-99-2, 216-887-4)	In vitro	0	(Weiss et al., 2009)
FOSA (754-91-6, 212-046-0)	In vitro	+	(Weiss et al., 2009)
	In vitro	+	(Rosenmai et al., 2018)
N-MeFOSA (31506-32-8, 250-665-8)	In vitro	0	(Weiss et al., 2009)
N-EtFOSA (4151-50-2, 223-980-3)	In vitro	0	(Weiss et al., 2009)
F-53B (Mixture of 6:2 CI-PFESA and 8:2 CI-PFESA) (73606-19-6, N.A.)	In silico	+	(Deng et al., 2018)
	In vitro	+	(Deng et al., 2018)
	In vivo	+	(Deng et al., 2018)
6:2 CI-PFESA (73606-19-6, N.A.)	In vitro	+	(Li et al., 2018a)
	In vivo	+	(Shi et al., 2018a)
	In vivo	0	(Zhou et al., 2018)
8:2 CI-PFESA (N.A., N.A.)	In vitro	+	(Li et al., 2018a)
PFAS mixture (PFOA, PFOS, PFBS, PFNA) (N.A., N.A.)	In vivo	+	(Lee et al., 2017)

+ = Activity/effects related to PFAS exposure

- = No activity/effects related to PFAS exposure

0 = inconclusive results

= Effects with presumed relevance on population level

B.7.5.3. Summary of main results from studies

A short summary and reference for each study which is mentioned in the following paragraphs can be found in Appendix B.7.5..

B.7.5.3.1. In silico

Two in silico studies show that different PFASs have the theoretical ability to interact with

receptors in the endocrine system of different species, or to bind to hormone transporting proteins and thus have the potential to interfere with hormone homeostasis.

B.7.5.3.2. In vitro

Different reporter gene assays show that PFASs can interact with hormone receptors from different cell systems incl. estrogen receptors (ER), androgen receptors (AR) or peroxisome proliferator-activated receptors (PPAR). Via these interactions PFASs can evoke (anti) estrogenic or (anti) androgenic activity and influence steroidogenesis. Examples for effects are an alternation of the receptor activity or an induction of VTG production or cell proliferation. Besides PPAR and relevant receptors from the hypothalamic–pituitary–gonadal (HPG) axis, PFASs have been shown to interact with the hypothalamic–pituitary–thyroid (HPT) axis too. *In vitro* binding to thyroxine transport proteins transthyretin (TTR) and thyroxine-binding-globulin (TBG) has been reported in different studies (see also B.5.2.1.4). Furthermore, some PFASs can alter the expression of thyroid-hormone responsive genes.

Some *in vitro* studies made an attempt at describing the relation between EA/ED of some PFASs and their structure (i.e. chain length or functional group). Binding to the human PPAR γ ligand binding domain was reported to increase with increasing chain length of PFCAs until a chain length of 11 carbon atoms. Similarly, PPAR α activity in HepG2 cells was observed to increase with chain length up until a chain length of C8. Interestingly, an *in vitro* study with Baikal seal (*Pusa sibirica*) PPAR α (BS PPAR α) made contradictory observations and reported that PFCAs with a chain length > C7 had a negative correlation between chain length and induction potency towards BS PPAR α . A test with HEK 293 cells found the activity of PFOA and substitutes towards the PPAR γ to increase in the order HFPO-DA < PFOA < HFPO-TA. A radioligand-binding assay testing for binding capacity to human TTR reported a maximum binding potency for PFCAs with a chain length of C8. The authors of this study suggested that the binding potency is directly linked to the number of fluorinated alkyl groups in the carbon-chain. Regarding the influence of functional groups on EA/ED, one *in vitro* study described the binding affinity towards PPAR to be stronger for PFASs, compared to their PFCA homologues. Another study however, reported that they found the transactivation potencies of PFCAs to be stronger than the ones of PFASs with similar chain length. TTR binding potency was observed to be stronger for PFASs than for PFCAs (at least for C4–C8 PFASs). Especially with regard to the interaction of PFAS with PPAR there is evidence suggesting a relationship between the chain length as well as the head group and the binding affinity of the compounds. Similar indications exist from one study investigating TTR binding potencies of different PFAS. But the results from different studies contradict each other and overall, there is not enough information to identify clear trends. Statements like “PFAS above/below a certain chain length or PFAS with/without a certain headgroup have a stronger/weaker endocrine activity” cannot be made on the basis of the data at hand.

B.7.5.3.3. In vivo

There is evidence for changes in the gene expression for genes regulated by hormones in fish and crustaceans after *in vivo* exposure to certain PFASs (e.g. *vtg*, a common indicator for an (anti)estrogenic MoA). Other *in vivo* studies report changes in the activity of enzymes that catalyze the biosynthesis of hormones in fish, or birds. Adverse effects observed in *in vivo* studies after exposure to certain PFASs include morphological changes in endocrine and other organs in fish, e.g. follicle cell degeneration and atrophy, or changes in swim bladder size (an indicator for disruption of HPT-axis as recently summarized by Dang et al. (2021), a decreased fecundity in fish, a reduced number of eggs spawned and other adverse effects on the F1 generation of exposed fish (e.g. changes in sex ratio, reduced spermiation) or reduced pipping success (pip = first crack in eggshell) and decreased tarsus length and embryo mass in birds exposed *in ovo*. All of the aforementioned adverse effects have the potential to negatively affect whole populations.

Additionally, several *in vivo* studies observed changes in hormone levels in different species after exposure to certain PFASs. Two studies with fish reported that changes in hormone levels were transferred to the F1 generation and adverse effects related to hormone level changes were

observed in F1 generation even though the F1 generation was not exposed. Such cross-generational effects in combination with the high persistence of PFASs (or their degradation products) can have severe impacts on whole wildlife populations and in the long run also disrupt networks of ecosystems. A positive relationship between changes in hormone levels and exposure to some PFASs was already observed in wildlife birds. Correlations do not necessarily show a causal relationship, but it still raises a concern about effects of certain PFASs on the endocrine system *in situ* (i.e. in the natural environment).

B.7.5.3.4. Conclusion

In summary, the *in silico*, *in vitro* and *in vivo* indications of interactions of some PFASs with the endocrine system of environmental species, adverse effects (some occurring cross-generational), and first observations of possible influences of PFAS body-burden on hormone levels in wildlife raise concerns about the presence of PFASs in the environment. The environmental presence of PFASs and their concentrations in wildlife will increase under continued use due to the high persistence of these substances or their final degradation products, increasing the probability for adverse and irreversible effects. At the time notable effects from PFASs exposure occur in the environment it will be difficult, if not impossible, to remove the contamination. Thus, there is a threat of irreversible damage.

B.7.6. Hazard and occurrence of fluoropolymers

Fluoropolymers are fluorinated polymers characterised by at most times fully-fluorinated carbon backbone (Buck et al., 2011). One example is polytetrafluoroethylene (PTFE). Other fluoropolymers are fluorinated ethylene propylene (FEP), perfluoroalkoxy alkanes (PFA), ethylene tetrafluoroethylene (ETFE), other tetrafluoroethylene-copolymers, polyvinylidene fluoride (PVDF), and fluoroelastomers (Gardiner, 2015).

Fluoropolymers are indirectly of concern because

- During their production and use monomers, oligomers smaller polymers and by-products are emitted into the environment
- During waste incineration at end of life, non-polymeric PFAS may be formed and emitted

PFCAs (including trifluoroacetic acid, TFA) and other fluorinated compounds are formed when fluoropolymers are incinerated. Today no safe option for end-of-life of fluoropolymers and articles containing fluoropolymers is known, recycling is not sufficiently possible (Drobný, 2008; Schlipf and Schwalm, 2014).

Fluoropolymers are produced with different production processes, leading to different products (e.g. granulate or powder) and are incorporated in different articles (e.g. cookware, membranes for clothing) (Lohmann et al., 2020). The same type of fluoropolymer (e.g. PTFE) can be produced by different production processes, using different building blocks or different manufacturing conditions (including different surfactants) in order to obtain specific properties suitable for different applications. From an environmental point of view the PFAS-based processing aids used in the production of fluoropolymers are of concern. They can be emitted to the environment during production of fluoropolymers, during the production of article containing fluoropolymers and during use and disposal of those articles. Processing aids are for example per- and polyfluoroalkylether carboxylic acids (PFECAs) like the ammonium salt of HFPO-DA (already identified as SVHC), cC604, is the ammonium salt of [perfluoro-{acetic acid}], 2-[(5-methoxy-1)], ammonium 4,8-dioxa-3H-perfluorononanoate (CAS 958445-44-8, ADONA) (Lohmann et al., 2020).

Certain types/forms of fluoropolymers can be produced without processing aid (emulsion polymerization is done with PFAS-based processing aids, suspension polymerization does not need PFAS-based processing aids). Further information can be found in Annex A section A.2.1.4.2.

Fluoropolymers themselves can pose an environmental hazard. Like for other polymers, fluoropolymer microplastics can be formed during their use phase or end-of-life phase. It is therefore important not only to look at the use phase but the whole life cycle of fluoropolymers. Monitoring data show that fluoropolymer microplastics are present in the environment. (see B.4.2.7.8).

Lohmann et al. (2020) state that fluoropolymers are extremely persistent under environmental conditions. The authors refer to Dams and Hintzer (2017). The Dossier Submitters are currently not aware of any study investigating the persistence of fluoropolymers under environmental conditions. Even though fluoropolymers are a large group of polymers with different properties, there are no indications that fluoropolymers will degrade in particular as one of their key properties are their thermal and weather stability for the uses as described (Dams and Hintzer, 2017). Therefore, persistence can be concluded.

B.7.6.1. Environmental hazard of fluoropolymers

Henry et al. (2018) argued that fluoropolymers are not toxic, based on a data set that was restricted only to a few fluoropolymer types typically >100 000 Da (Lohmann et al., 2020). Lohmann et al. have doubt concerning this assessment, because concentrations of leachable components were very low (1 ppm for PTFE fine particles) in the data set from Henry et al.

(2018), whereby leachable components are mainly processing aids. Other studies reported concentrations of 1–10 ppm in PTFE fine powder and much higher in PTFE aqueous dispersion (Wang et al., 2014c). Similar levels of PFAAs (0.3–24 ppm) were found in personal care articles that contained PTFE fine particles (assuming the cosmetics contained 1% PTFE, the range of leachables is 0.3–24 ppm; if the total organofluorine measurements represented PTFE fine powder, then the range of PFAA-leachables is 15 – 1 000 ppm) (Lohmann et al., 2020). One study analysed twenty targeted PFASs in fluoropolymer raw material and product samples made in China. The total concentration of PFASs except PFOA in the fluoropolymer product samples ranged from below the detection limit (0.1 ng/g; 0.0001 ppm) to 50.3 ng/g (0.0503 ppm). The total concentration of PFASs (except PFOA) in the fluoropolymer raw material samples ranged from < MDL (0.1 ng/g) to 8.3×10^5 ng/g (83 ppm). HFPO-TrA, HFPO-TeA and HFPO-DA, hexafluoropropylene oxide (HFPO, C₃F₆O) oligomers, were typical alternatives to PFOA in fluoropolymer manufacturing (Meng et al., 2021).

The following passages are similarly also addressed in the Microplastic restriction proposal (ECHA, 2019a) and a more detailed assessment can be found there. In this context RAC has agreed that although there are uncertainties in the understanding of the hazard and risk of microplastics, there is sufficient evidence to conclude that they constitute an intrinsic hazard because of their long-term persistence in the environment in combination with their particulate form and potential to cause adverse effects (ECHA, 2020).

According to the hazard assessment included in the Microplastic restriction proposal many studies in earlier years focused on ingestion of microplastics and their occurrence in the gut, rather than exploring adverse effects on organisms. Nevertheless, ingestion in laboratory studies has since been linked to a diverse range of sub-lethal endpoints, including reduced food intake, false satiation and reduced energy reserves, as well as mortality and sub-lethal 'apical effects', such as effects on growth rates or reproduction (summarized by Besseling et al. (2018)). Furthermore, in the microplastics dossier the following effects have been collected from publications: altered survival, feeding, growth, reproduction, moulting, behaviour, photosynthesis, oxidative stress, enzyme activity, gene expression, and nutrient cycling, as well as malformation, and inflammation.; all of which were considered by the authors to be relevant to population or community-level effects. Generally, it has to be noted that investigated effects were observed more in acute than chronic studies. Discussion about microplastics often addressed whether microplastics facilitate the uptake of organic pollutants such as POPs or metals. According to the microplastics Dossier current scientific consensus on this issue would suggest that ingestion of microplastics does not significantly enhance bioaccumulation of POPs relevant to other types of particulates present in the environment. Furthermore, fluoropolymer microplastics as vectors for organic pollutants may be even less relevant due to their minor adsorptive properties.

The bioaccumulation potential for polymers in general is poorly understood so far. Based on theoretical conclusions, nanoplastics as (bio)degradation products of microplastics may have a higher bioaccumulation potential and with that more likely evoke adverse effects. Cell membrane penetration cannot be excluded. Several studies have investigated adverse effects of microplastics in general. No negative effects on population level have been demonstrated so far but there is an emerging understanding of the potential effects of microplastics. More details on uptake and distribution are given in B.5.1.2.

B.7.6.2. Findings of fluoropolymers in the environment

There is a wealth of monitoring studies which investigated the occurrence of microplastics in the environment and biota. There are however to a lesser extent monitoring data which distinguish between different types of polymers.

PTFE microparticles have been found in fish and sediment (from remote Arctic Ocean). Bergmann et al. (2017) investigated microplastics in sediment samples from the Arctic. Samples were collected at 2 340 – 5 570 m water depth. Sampling took place in 2015. Analysis of microplastics took place with attenuated total reflection Fourier-transformed infrared (ATR-FTIR) spectroscopy

for particles >500 µm. For the small size fraction (<500 µm) organic material was removed before analysis with Fourier-transform infrared microscopy (µFTIR). Results from spectroscopy were compared to library material, automated in the case of small particles. 4 356 particles/kg sediment (overall mean number) have been found. Eighteen different types of polymers were identified, among them PTFE. In the larger size fraction all analysed particles were PTFE. For the smaller size fraction it was not possible to analyse for PTFE because “PTFE cannot be detected within the spectral region of 3 600–1 250 cm⁻¹ available for the particles <500 µm in µFTIR” (Bergmann et al., 2017). The occurrence of PTFE in all sediment samples is explained by the high density (2.10–2.30 g cm⁻³), which exceeds the density of seawater.

A density dependent distribution pattern between water and sediment were also observed in a study of small-scale Japanese rivers which investigated the abundance and distribution and characterised microplastics (Kabir et al., 2022). Polyvinyl chloride (PVC), polyethylene (PE), and polypropylene (PP) were the major polymers in this study. The polymers—polyvinyl chloride, polymethylmethacrylate, polyurethane, fluorinated ethylene propylene, and polybutylene in sediments were distinct from those detected in surface water, as were the predominance of large-size (1–5 mm) and fragment-shape microplastics. Fluorinated ethylene propylene (FEP) is a copolymer manufactured from hexafluoropropylene and tetrafluoroethylene. The authors conclude that it is theoretically obvious that MP particles of high-density (>1.0 g/cm³) polymers are prone to be settled easily in the freshwater environments and low-density particles float on the surface water or in the water column.

Kabir and coworkers also lists other studies which investigated microplastics qualitatively. Though there is a density dependent distribution pattern of polymers in the environment, in all listed studies the dominating polymers were not fluorinated. For instance, the polymers PE, PP, and PS made up >75% of all microplastics identified in the sediments in the rivers Rhine and Main in Germany (Klein et al., 2015). It should be noted that PE, PP, and PS, cover 55.7% of the European plastic demand, which is a reason for their large abundance (Plastics Europe, 2013).

Most common polymer types found in 106 fish from 22 species inhabiting three sites of the Han River, South Korea, were polypropylene (PP) (≥40%) and polyethylene (PE) (≥23%), followed by polytetrafluoroethylene (PTFE) (≥16%) at all sampling locations (Park et al., 2022). Omnivorous and insectivorous fish contained more Microplastics than carnivorous and herbivorous fish. In addition, studies investigating fish habitats showed that pelagic fish contained slightly higher levels of microplastics than demersal fish. Interestingly, it is essential to emphasize the detection of PTFE in fish because no PTFE was observed in water. This result was due to the high density of PTFE, and it was challenging to detect heavy plastic in water because the water sampling was conducted from the upper part of the river using a Manta net. The number of microplastics is corrected for the fish weight, the average number of Microplastics was 16.26 ± 12.51 Microplastics 100 g⁻¹ in the demersal fish; 17.69 ± 12.84 microplastics 100 g⁻¹ in the pelagic fish. In fact, the study found that the most common polymers in the fish were relatively light PP and PE. In contrast, sediment can be a sink for microplastics, especially high-density microplastics (Woodall et al., 2014). Therefore, demersal and benthic fishes may have been more exposed to high-density microplastics than pelagic species.

Capillo et al. (2020) analysed microplastics also in demersal fish from the Southern Tyrrhenian area (Central Mediterranean). Sampling took place in 2017. Selected particles were analysed with micro-Raman or ATR-FTIR spectroscopy. Five polymers were identified, among them PTFE. The major contaminant that affected examined individuals was represented by polytetrafluoroethylene (PTFE, 75%) in *Mullus barbatus barbatus* which is widely regarded as a bio-indicator species for its benthic behaviour, habitat and feeding modalities and its reduced mobility.

B.7.6.3. Conclusion

In conclusion, fluoropolymers are a group of materials with different properties, and for some of

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

the fluoropolymers persistence is well known. Other types of fluoropolymers would be expected to be persistent in the environment based on their chemical composition, see section B.4.1.2. Environmental exposure does take place as shown by monitoring data. Also, remote regions are already exposed, which confirms the persistent nature of the materials. The bioaccumulation potential is poorly understood so far. Based on theoretical conclusions nanoplastics formed due to weathering of microplastics may have a higher bioaccumulation potential and with that more likely evoke adverse effects. Cell membrane penetration cannot be excluded. Several studies have investigated several adverse effects of microplastics in general. No negative effects on population level have been demonstrated so far but there is an emerging understanding of the potential effects of microplastics.

B.8. PBT and vPvB assessment

See section 1.1.4. of the main report. No further assessment carried out.

B.9. Exposure assessment

In the exposure assessment both the environmental exposure and the human exposure is assessed. In section B.7 the environmental exposure is assessed. In section B.5 the human exposure is assessed.

Environmental emissions are described as service life emissions. Tonnage put on the market will lead to service life emissions, presented as [t]. (Next year, if for instance the same PFAS tonnage is put on the market, a similar service life emission is applicable). The emission value is generated e.g. by multiplying yearly tonnage put on the market by the default release factors (for instance an ECHA Environmental Release Category (ERC)). This is not an emission rate and is the emission over the whole service life.

Preferably industry specific emission factors were used and applied but this information was not always available. In case no industry specific information was available, ECHA generic ERC were applied. There are however no dedicated ERC for PFASs. Because of the lack of better alternatives, ERC for organic substances were applied.

Industry specific emission factors were used for PFASs manufacturing and the sectors food contact material and packaging (partly), metal plating and manufacturing of metal products, cosmetics, ski wax and HVACR. For medical devices consultant expertise was used.

For the other sectors, no industry specific information was available. For these sectors, default parameters for environmental release rates according to the REACH methodology described in the ECHA Guidance on information requirements and Chemical Safety Assessment, Chapter R.16 were used (ECHA, 2016a), see also Table B.18. The environmental release category (ERC) describes the broad conditions of use from the environmental perspective. In applying ECHA ERC, emissions from the lifestage (which can be several years) is allocated to the year of production. Waste stage emissions are also allocated to the same year, and the integrated emission over 20 years is taken for the emission from waste, see Guidance ECHA (2012a), p 46.

Uncertainties and limitation due to the use of ERC

- Correctness and completeness of the volumes of PFASs used for emission estimates are not fully known

Uncertainties and possible inaccuracies in the selection and application of ERC

- The wide range of substances. (If emission data from industry is lacking, ERCs have to be applied. The ERC for organic substances is used for emission estimation of a very broad group of vP PFAS substances with very different substance characteristics)
- The wide range of applications in the sectors
- The identification of relevant emissions during different life cycle stages of the substances
- Adding ERF for three compartments air, water, soil
- The emissions of polymeric PFASs in the use stage might be an overestimation due to lack of industry data and due to lack of specific ERCs for polymers. For high molecular, non-powdery PFASs the use of ERC may lead to an overestimation of emissions, whereas for micro-powder PFASs, the use of ERC may lead to an underestimation of emissions.

For the environmental impact assessment, the total release to the environment (one-compartment model) was used, based on the summation of the individual Emission Release Factors (ERF) to air, water and soil. The reasoning for assuming the environment as one compartment is that the overarching concern with PFASs in scope of this restriction proposal is persistence, which is independent of the compartment the PFASs are emitted to. Specific negative impacts may occur in connection to point sources due to high local concentrations.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

However, these are not included in the overall impact assessment. The ERF is derived from Chapter R.16 of the REACH guidance. In case the addition of the separate ERF to water, soil, and air exceeds 100%, a total emission to the environment of 100% is assumed.

The chosen approach therefore comes with considerable uncertainties. See Annex F (Uncertainties) for more details. In Table B.18 the methodology used to estimate emissions per sector is presented.

Table B.18. Methodology used to estimate emissions per sector.

Sector	REACH methodology	Other methodology
Manufacturing	No	Yes
TULAC	Yes	
Food contact material and packaging	Yes, partly	Yes, partly (Industry data for paper and board manufacturing)
Metal plating	No	Yes
Consumer mixtures	Yes	No
Cosmetics	No	Yes
Ski wax	Yes	Yes
HVACR	No	Yes
Medical devices	No	Yes
Transport	Yes	
Electronics and semiconductors	Yes	
Energy	Yes	
Construction	Yes	
Lubricants	Yes	
Petroleum and mining	Yes	
Waste	Yes	Adapted ERC for landfill and literature research

B.9.1. Introduction to hazard and risk

PFASs are non-threshold substances due to their properties that are similar to PBT/vPvB-. Emissions are a proxy for risk. Minimizing emissions is key to reduce risks in the long term. Therefore, a proper estimation of emissions is of importance. It is important to realise that because of the persistence properties of PFASs in the long term, the volumes put on the market will lead to environmental emissions (in or outside EEA).

In section B.9, data on emission of PFASs are provided and emission calculation/estimation will be described. The purpose is to provide:

- a. Estimates of the total amount of PFASs released to the environment in the EEA in the base year (i.e., the expected year of entering into force (EIF) of the restriction).
- b. Project total emissions for different timelines (20, 30 and 45 years after entry into force of the restriction).

Emissions are estimated for all investigated (use) sectors (see Table B.18), starting with emissions of PFASs during manufacturing and ending with emissions of PFASs in the waste stage.

Due to the combination of high persistence and broad use in articles across various sectors with wide variation in service-life duration and type of use PFASs emissions may last , many years following initial placing on the market, including the end-of-life stage. For many uses, significant volumes of PFASs enter the waste stage, due to a combination of the persistence of PFASs and low emissions during service-life of polymer containing articles. Waste emissions can for instance occur in waste transfer stations, landfills, waste-water treatment plants and waste incinerators. Additionally, also during recycling of materials, PFAS emissions are possible. -This is described in more detail in B.9.18.

Since sector specific emission factors often were not available to the Dossier Submitters, for most sectors, default Environmental Release Categories (ERC) from the ECHA guidance (ECHA, 2016a) were used to estimate emissions. OECD SPERCs, which are more sector specific compared to ERCs, have not been considered useful as not for all researched uses SPERCs are available and the status of SPERCs for sectors where they are available is often unclear. The quality of SPERCs is diverse (some are reviewed/evaluated, others not) and for several SPERCs, substance specific physico-chemical information is needed. In Table B.18 the methodology to estimate emissions is provided for each sector.

Yearly emissions in the EEA are considerably lower than yearly estimates of EEA PFAS production and use volumes. Some uses lead to direct emissions (like use of impregnation sprays) within the year of use of a product, whereas other uses lead to prolonged emissions stretching over several years (i.e., the use of coatings containing PFASs). The difference between estimates of PFAS volumes in production and use (Annex A) and emissions (part of this Annex B) is discussed in more detail in Annex F (Uncertainty).

Under real life conditions, emissions of PFASs do not only occur during current use and during the time periods addressed in the impact assessment. Several sectors have a long history of PFASs use, and PFASs may have been emitting for decades. Additionally, there is a significant technical stock of PFASs in articles (cars, fashion, etc.). As a consequence, PFASs have been accumulating in the environment for decades, leading to an environmental stock. Since there is insufficient data on the volume of PFASs used and emitted by sectors in the past, as well as on PFASs properties and fate of the individual PFASs, it is not possible to estimate the volume of this environmental stock therefore, the estimates of volumes and emission for the the base year of the assessment (2025, being the year in which the restriction is expected to enter into force). Implications will be further discussed in Annex E.2., and in section 2.4. of the main report.

In the impact assessment (Annex E.2.) the emissions to air, water and soil are considered together as emissions to the environment. Therefore a total environmental emission is also presented in the Annex.

B.9.2. PFASs manufacturing

B.9.2.1. Introduction

Initially, most PFASs were produced without consideration of the impact (Goldenman et al., 2019). This caused serious incidents in the past years at multiple PFASs manufacturing sites in Europe:

- 3M, Zwijndrecht, Belgium
- Chemours, Dordrecht, the Netherlands
- Solvay Miteni, Veneto, Italy
- Arkema/Daikin, Pierre-Bénite, France.

A description of PFASs manufacturing activities in the EU/EEA, the type of PFASs produced and the location of the different sites is presented in Annex A section A.2.1.

The production, import and export of PFASs used in the EEA has been evaluated. The methodology for estimating emissions consisted of two main elements:

- Review of relevant literature.
- Stakeholder surveys and interviews.

Information on emissions of PFASs to water, soil and air during production and processing activities was asked from stakeholders. Even though information was provided by some of the major producers and processors of PFASs present in the EEA, not all emissions were captured. For instance emission to soil was not presented although the situation at 3M Zwijndrecht suggest that PFAS soil emission for PFAS manufacturing cannot be neglected. In order to extrapolate, two values are needed. Firstly, the total volume of PFASs produced and processed per year. Secondly, an emission factor to predict the emissions to air and water of the aforementioned activities. (Emissions to soil were not applicable according to industry). The emission factor represents the percentage of PFASs which is released to the environment when a certain amount of PFASs is being manufactured or processed. The emission factors were derived from the information received from stakeholders on both volume and emissions. The following equation was used (Equation 1):

Equation 1. Calculation of emission factors

$EF_{comp} = E_{comp} / m \times 100,$		
Where:		
EF	emission factor of the produced/ processed PFASs	[%]
comp	receiving environmental compartment i.e.: water or air	[-]
E	Tonnes of PFASs emitted per year	[t/y]
m	Tonnes of PFASs produced/ processed per year	[t/y]

After deriving the emission factors to air and water for each individual company, an average emission factor to air and water was calculated. These average values were then applied to the

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

volume of produced/processed PFASs, which gave the results of the estimated PFASs annually released to the environment. The derived emission factors are shown in Table B.19.

Table B.19. Average emission factors to environmental compartments based on stakeholder information.

	PFAA and PFAA precursors + other PFASs		Fluorinated gases		Polymeric PFASs	
	Emission factor to water	Emission factor to air	Emission factor to water	Emission factor to air	Emission factor to water	Emission factor to air
Number of datapoints	5	5	6	6	7	6
Average emission factors [%]	0.04	0.06	0.00	2.06	0.01	0.02

B.9.2.2. Emissions

Some companies provided their annual production volume as a range. In this case, the average values were used for emission calculations, e.g. in case a manufacturer reported a production volume of 100 – 1 000 t/y, the average of 550 t was used. For some manufacturing sites (3M and Chemours), the information was cross checked with permit and enforcement data to get feeling with realistic numbers. Information on emissions resulting from PFASs manufacturing from literature was not used because it includes different year and types of PFASs. The investigation learned that there are about 20 PFASs production facilities in Europe (see Annex A section A.2.1.).

Table B.20 presents the estimated annual EEA emissions, split into PFAA and PFAA precursors (+ other PFASs), fluorinated gases, and polymeric PFASs to air and water.

Table B.20 Estimated annual EEA emissions of PFAA and PFAA precursors (+ other PFASs), fluorinated gases, polymeric PFASs and total PFASs from PFASs manufacturing.

	PFAA and PFAA precursors (+ other PFASs) (t/y)		fluorinated gases (t/y)		Polymeric PFASs (t/y)		Total PFASs (t/y)	
	low	high	low	high	low	high	low	high
<i>Volume</i>	<i>53 902</i>	<i>118 051</i>	<i>15 000</i>	<i>176 548</i>	<i>49 000</i>	<i>101 763</i>	117 902	396 362
Total emission	54	118	309	3 637	15	30	378	3 785
Emission to air	32	71	309	3 637	10	20	351	3 728
Emission to water	22	47	-	-	5	10	27	57

Emission of fluorinated gases to air by Chemours Dordrecht, The Netherlands, is approximately 70 t/y. However, efforts are made to drastically reduce emissions (blauw, 2021). Emissions of CF₄ to air by 3M Zwijndrecht, Belgium, is about 33 t/y (based on permit (p.51) (Provincie Antwerpen, 2018; Provincie Antwerpen, 2020). The total emission of fluorinated gases was 222 t

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

according to 3M²². Especially HFC-23 (not a PFAS) emissions were overseen. So in fluoropolymer production emissions of F-gases/fluorinated gases are of relevance.

Fluorinated gases, used to manufacture fluoropolymers and fluoroelastomers, have not been restricted by the provisions of the Montreal Protocol, because chemicals used as feedstock in the manufacture of other chemicals are excluded from the Montreal Protocol. Emissions of fluorinated gases used for fluoropolymer production seem to be significant. The emissions of PFAA and PFAA precursors (+ other PFASs) and polymeric PFASs to the environment are far lower than emissions of fluorinated gases (Rodriguez et al., 2021) (see Table B.20).

In the past (2013), Chemours Dordrecht in the Netherlands, the main production site in Europe for fluoropolymers such as Teflon™ and Viton™, was allowed to emit 7 t Hexafluoropropylene oxide dimer acid (HFPO-DA) per year. Currently, these numbers are lower²³. It is unknown if all permits for PFASs production sites in EEA have been updated to new, stricter, levels. Neither is known if enforcement takes place. Recently, potential illegal emissions of PFAA and PFAA precursors to water were reported²⁴.

The total emissions from PFAS manufacturing are estimated between 400 and 4 000 t/y (rounded numbers). The numbers are, order of magnitude, in line with site specific permit data (keeping in mind about 20 production facilities in EEA). It is important to note that indirect emissions to air, water and soil, from waste are not included in the total emissions. These emissions could be significant, see section 0. Emissions of PFASs from waste from Chemours in The Netherlands for instance was 13 times higher than via water. Total waste volume at this site is about 1 800 t/y (ILT, 2018; Tweede Kamer, 2019).

In the majority of cases, fluorinated polymer production requires not only fluorine-containing feedstock chemicals but also fluorinated production aids for polymers such as dispersion aids and polymerisation initiators. Production of such fluorinated production aids can also lead to emissions poly- and perfluorinated by-products, both highly volatile and water soluble (Hopkins et al., 2018; Lohmann et al., 2020).

Past emissions:

According to literature, production facilities of PFASs were responsible for >75% of total global perfluorocarboxylates (PFCA) emissions between 1950 and 2002 (Prevedouros et al., 2006).

Based on literature, emissions in the recent past likely have increased as can be seen in Figure B.67²⁵. This very likely is the result of increased production as is described in Appendix A.

²² <https://www.apache.be/nl/2021/06/15/3m-stootte-ongemerkt-gigantische-hoeveelheden-zwaar-broeikasgas-uit>, date of access: 2022-12-14.

²³

https://cms.dordrecht.nl/Inwoners/Overzicht_Inwoners/Dossier_Chemours_en_DuPont/Nieuws/Nieuwe_vergunningen_Chemours_gepubliceerd, date of access: 2022-12-14.

²⁴ <https://www.taylordailynews.net/chemical-company-3m-illegally-discharges-toxic-substance-fbsa-in-sche/>, date of access: 2022-12-14.

²⁵ <https://www.unep.org/explore-topics/chemicals-waste/what-we-do/policy-and-governance/global-chemicals-outlook>, date of access: 2022-12-14.

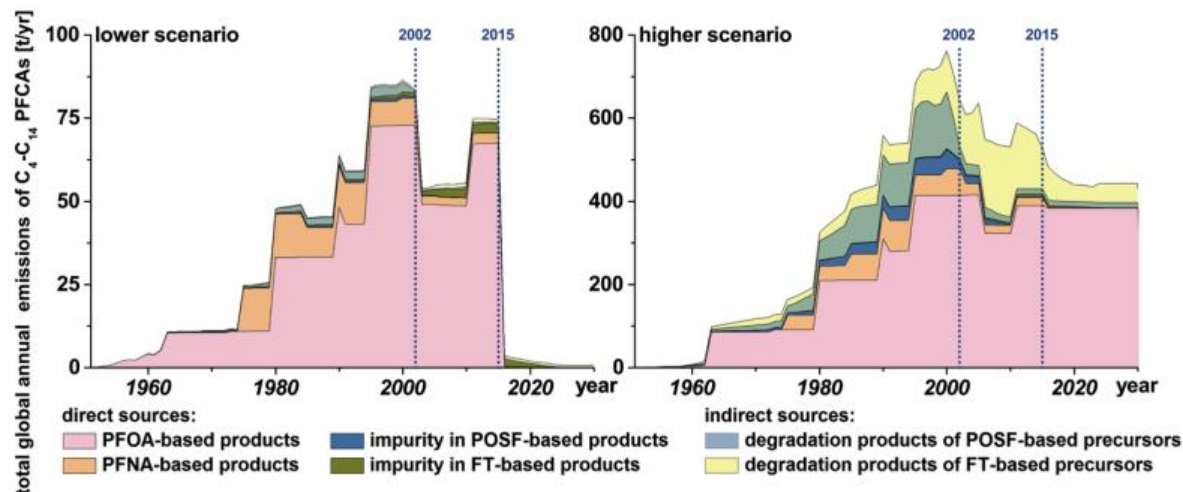


Figure B.67. Estimated annual emissions of PFOA from PFOA production sites (left) and fluoropolymer sites (right) in the United States, Western Europe and Japan (blue), as well as in China, Russia, Poland and India (orange) (OECD/UNEP, 2015).

According to the OECD/UNEP (2015), in 2015 there was an increase in the total global annual C₄-C₁₄ PFCA emissions between 1951 and 2002. This period was followed by a considerable decrease (approximately 40% reduction in emissions). Emissions continued to decrease in the US, Western Europe and Japan, while in the rest of the world an increase was observed. Although PFCA are only a fraction of the PFASs universe, these findings are in line with what the EU producers reported.

A total of 27 stakeholders provided information on past, current, and future emissions of PFASs. A summary is provided in

Table B.21. Stakeholders think both past and future emissions are lower than current emissions.

Table B.21. Comparison of past, current, and expected future emissions according to stakeholders.

Past emissions (compared to current status)			Future emissions (compared to current status)		
Higher	No change	Lower	Higher	No change	Lower
1	4	11	0	4	12

Notes: The values indicate the number of sites

Stakeholders think that, despite an increase in production, emissions of PFASs will remain the same or decrease because of the implementation of best available technologies.

B.9.2.3. Human exposure

It has been known for a long time that exposure to PFASs is of relevance and harmful, especially for higher exposed populations like factory workers and people living close to PFAS manufacturing sites. Greater plasma contamination levels have been detected in workers in the PFAS manufacturing Industry.

Recent studies demonstrate that the human population living close to a PFAS factory in

Zwijndrecht, Belgium is highly exposed to PFASs (ewg, N/T)²⁶. The water in the river Westerschelde contains levels of PFASs that are directly or indirectly linked to PFAS manufacturing. The Fishing industry is affected, and eating of fish from the Westerschelde is discouraged (RIVM, 2022).

In the Netherlands, citizens nearby a PFAS manufacturing facility are advised not to eat vegetables from gardens nearby the PFAS manufacturing plant (Générations Futures, 2022; RIVM, 2021). Since summer 2022, there are PFAS exposure issues (elevated concentrations in environment, breast milk, etc.) nearby a PFAS manufacturing plants in Lyon (France)²⁷.

Distance to a PFAS manufacturing facility is linked to the potential exposure level, as can be seen from Gebbink and van Leeuwen (2020). Exposure to PFASs via air decreases with distance from the manufacturing facility as indicated by D'Ambro et al. (2021).

B.9.2.4. PFAS processing

After PFAS manufacturing and before article production often processing of PFAS is required: drying, sintering, compounding, etc. There is no emission data from processors of PFASs, but there is evidence that the drying step (sintering) of fluoropolymers has led to substantial emissions of processing aids to air at sites that produce PTFE (West Virginia (US) and The Netherlands) (Lohmann et al., 2020).

²⁶ <https://vu.nl/en/news/2021/3m-pfas-plant-in-antwerpen-closed-down>, date of access: 2022-12-14.

²⁷ <https://www.euronews.com/next/2022/08/08/forever-chemicals-how-toxic-are-the-levels-of-pfas-found-in-french-tap-water-and-breast-milk>, date of access: 2022-12-16.

B.9.3. Textiles, upholstery, leather, apparel and carpets

B.9.3.1. Introduction

The use of PFASs in Textile, Upholstery, Leather, Apparel and Carpets (TULAC) is described in Annex A.

Total emissions of PFASs to the environment have been assessed. For this assessment a basic source-flow model has been developed to make use of the data from the market analysis and substance identification. One key caveat here is that on a more general level a very large number of substances have been identified as being in use or potentially in use (currently around 120 unique substances). Additionally, many of these unique substances appear in mixtures as combinations of substances, and furthermore in some mixtures it may be the case that specific substances are present as an impurity, rather than an intentional use. (Note that the data from stakeholders under the CfE does not always specify which substances are impurities and which are intentional uses). The quality of market data also varies significantly from substance to substance.

Therefore, the approach was not to estimate on a substance-by-substance basis, but by grouping. A key benefit of using grouping approaches is that impacts of varying specific data are lessened. The trade-off of this approach is that the estimates provided will have a higher uncertainty attached to them overall. However, this approach can still provide useful data to estimate the orders of magnitude for emissions when comparing PFAS groups and different sectors. Therefore, the emission characterisation was developed to answer three key questions:

- What is the magnitude of the estimated emissions by different PFAS groups for uses covering textiles? (assumed to cover the major TULAC categories)
- What are the key life-cycle stages for emissions?
- What are the key distributions amongst the environmental compartments (air, land, water) for emissions?

The estimates provided will help answer these questions and act as a guide as to the key groups and points of release (both in terms of life-cycle stage and receiving environment). The key caveat being that the estimates included in this section should be treated as indicative orders of magnitude and not definitive estimates to the nearest tonne.

One final additional caveat to include here, is that the European Commission conducted a study in 2019 – 2020 (Wood, 2020b) covering 'the use of PFAS and fluorine-free alternatives in textiles, upholstery, carpets, leather and apparel'. The Commission study also included an estimate of emissions for 15 non-polymeric PFASs (mostly longer chain $\geq C8$) as a life-cycle approach. It is not the intention of the current body of work to repeat the work already completed and presented within the Commission study. However, to maintain continuity the current approach does where possible aim to align the approach with the European Commission work, to allow some further comparisons to be made.

The low estimate calculates total PFAS usage per year in the EEA (including non-polymeric PFAS and fluoropolymers) as ~41 000 t/y. The high estimate, using the same approach, calculates total usage as ~143 000 t/y. As a means of comparison and reflection, the study commissioned by the European Commission in 2020 (Wood, 2020b) provides estimates of 45 000 – 80 000 t of PFAS used in TULAC (which also includes both polymeric and non-polymeric PFAS).

B.9.3.2. Emissions

In general, major life-cycle stages are broadly disaggregated into three stages:

- The TULAC production stage (including manufacture of components and mixtures, and textile treating).
- The use stage.
- The waste stage. Not described here, see 0.

For assumptions used, see Appendix B.9.3. Textiles, upholstery, leather, apparel and carpets.

B.9.3.2.1. Production stage

Based on the CfE, stakeholder interviews and literature review, the production stage covers three discrete sets of activities which have been managed separately for emission estimation:

- ▶ Manufacture of non-woven membranes (an example). This production process covers the manufacture of membranes and mesh, which can be carried out as cold or hot processes using physical manipulation of fluoropolymers (e.g. extrusion). Based on tonnage, PTFE is the dominant fluoropolymer in use. However, note the possible blending of fluoropolymers with fluoroelastomers (like FKM and FFKM) to attain the desired physical properties. The membranes produced by this process can be used as the final product (e.g. technical textiles such as filters) or as a component in other textiles (e.g. as an interliner).
- ▶ Manufacture of mixtures (formulations) for textile treatment. This production process covers the manufacture of commercial mixtures for textile treating. In this case the finalised mixture is a product in it's own right and the emissions associated with treating of textiles have been included as a separate activity. The production of these mixtures will use all forms of non-polymeric PFASs, fluoropolymers and other polymeric PFASs. Furthermore, the working concentrations within mixtures is likely to vary both by final application and by PFAS used. The process of blending and mixing liquid mixtures is carried out in process vessels in various but suitable processing conditions.
- ▶ Manufacture of components using processing aids. As a sub-activity to the above the CfE and discussions with industry stakeholders identified the use of non-polymeric PFASs as a processing aid in the manufacture of textiles. This could include the manufacture of fluoropolymer membranes (above) and non-fluorine based components for use in textile applications. The distinction made here is that the use of processing aids does not intentionally leave any fluoropolymers in the finished article. Whereas the first bullet point above used fluoropolymer as the raw material in the finished article.
- ▶ Textile treating. This activity covers the follow-on step from the manufacture of mixtures and includes the use of commercial mixtures to treat textiles as a finishing step for production of finished textile articles. This process is likely to vary on a site-by-site basis, but it is assumed that mixtures are applied by a general set of approaches covering dipping, spraying, brushing, and/or rolling. The activity may take place within a wider set of steps for textile finishing, or a separate activity applied to imported/pre-manufactured textiles.

B.9.3.2.2. Use stage

TULAC covers a very wide set of applications with the specific emissions varying on an application-by-application basis. Broadly the current approach identified the following major application types:

- Home textiles.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

- Consumer apparel (including clothing).
- Professional apparel (including PPE).
- Technical textiles.
- Medical textiles²⁸.
- Other textiles.

Furthermore, the study completed by the European Commission in 2020, aimed to provide a holistic approach to how emissions may occur across all these application types, based on setting (indoor/outdoor use) and frequency of cleaning (including laundry)/wetting (Wood, 2020b). The Commission study also made use of the ECHA R.16 Environmental exposure assessment guidance, including ERC default emission factors to guide estimates (ECHA, 2016a). To align continuity, the same approach has been adopted within the current study. Three overall release groups were identified:

- ▶ Release Group 1. (Indoors) treated textile or leather articles that are subject to frequent cleaning/washing and so have higher potential for release. Examples could include all types of clothing, PPE where visibility is an issue (i.e., High-Vis jackets), and medical textiles.
- ▶ Release Group 2. (Indoors) treated textile or leather articles that are subject to infrequent cleaning/washing. Examples could include carpets, rugs, and curtains.
- ▶ Release Group 3. (Outdoors) Other treated textile or leather articles, not included in group 1 or 2, that are used in situations where a low level of release could occur. Examples could include footwear, outdoor clothing, outdoor technical textiles, other textiles used outdoors.

Based on the three groups detailed above the major application types have been assigned as described in Table B.22.

Table B.22. Assigning major use applications to release groupings.

Major application type	Sub-uses	Release grouping
Home textiles	Carpets and rugs	Group 2
	Curtains	Group 2
	Upholstery	Group 2
Consumer apparel	Indoor and outdoor wear	Group 1
	Sports wear	Group 1
	Footwear	Group 3
Professional apparel	Professional sportswear	Group 1
	Footwear	Group 3
	PPE	Group 1
Technical textiles	Outdoor technical textiles	Group 3
	High performance membranes	Group 2
Medical textiles	Medical textiles	Group 1
Other	All other uses	Group 2 or 3

Note that where several of the major application types in Table B.22 cover more than one release group, it has been necessary to apply a split to the market data to apportion the quantity of PFAS used within the application type and its connected release grouping. Table B.23 provides details of how these splits have been applied.

²⁸ Note that medical devices can also include textiles in some cases. Medical devices are covered separately in B.9.10. To maintain clarity, medical textiles used in this section refers to any use of textiles in a medical setting, excluding use within or on the patient (i.e., implantable textiles like gauzes or applications used upon the body like bandages are included under medical devices). As examples of the textiles included within the current definition this could extend to articles such as mattress protectors upon hospital beds, curtains/drapes around the bed, and gowns / PPE used by medical professionals.

Table B.23. Market splits for situations where more than one release grouping exists. Assigning major use applications to release groupings.

Major application type	Release Group 1 indoor – frequent wetting as %	Release Group 2 indoor – infrequent wetting as %	Release Group 3 outdoor – assumed low release as %	Justification
Home textiles	0	100	0	All uses under this application are covered by Group 2 only.
Consumer apparel	40	0	60	This application includes clothing more generally. Based on the CfE, outdoor clothing such as 'raincoats' and hiking gear may be a more dominant use than items like sportswear.
Professional apparel	50	0	50	This group is likely to be highly diverse. In lieu of data assume equal splits.
Technical textiles	33.3	33.3	33.3	Very diverse application type. In lieu of data assume equal splits.
Medical textiles	100	0	0	This application appears under group 1 only.
Other textiles	0	50	50	In lieu of data split tonnages equally.

Table B.97 and Figure B.80 in Appendix B.9.3. provide a summary of all factors applied within the model and key assumptions which guide the flow of PFASs through various stages of products life-cycles.

ECHA ERCs were used to estimate emissions because more specific emissions factors could not be found. The overview of the estimated EEA yearly emissions for 2020 is shown in Table B.24. Most of the emissions go to air since PFAA precursors are volatile to a large extent, whereas the water soluble PFAAs occur at a lower degree in processing mixtures.

For non-polymeric PFASs the primary release point to environment (key life-cycle stages for emission) is either during the treatment of textiles with PFAS-based mixtures, or from the use stage for indoors textiles or leather articles subject that are subject to frequent cleaning/washing and so have higher potential for release.

Overall, the combined production of commercial mixtures and treating of textiles as a finishing step may be more emissive to the environment than the production of non-woven membranes.

Based on the existing quantity data of PFASs, the "low estimate" appears to be the more credible estimate of quantities of PFASs in the EU/EEA²⁹.

²⁹ Conclusive remarks on the provided quantity data of various PFASs reported in the study on TULAC carried out within the work on this dossier (see section G.2.3) were that based on existing quantity data of PFASs, "other sources of information" and comparative assumptions and calculations made by the consultant for "low estimate" and "high estimate", then the "low estimate" appears to be the more credible estimate of quantities of PFAS in the EU / EEA.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.24. Estimated annual EEA emissions of PFAA and PFAA precursors (+ other PFASs), fluorinated gases, polymeric PFASs and total PFASs in 2020 (baseline) in the TULAC sector.

	C2- C3 PFAS substances (t/y)		PFAA ≥C4 (t/y)		Sidechain fluorinated polymers (t/y)		Total PFAAs and PFAA precursors (t/y)		Fluoro polymers (t/y)		PFPE (t/y)		Total polymeric PFASs (t/y)		Total PFASs (t/y)	
	low	high	low	high	low	high	low	high	low	high	low	high	low	high	low	high
<i>Total volume</i>	2 150	10 300	3 512	8 612	2 430	14 236	8 092	33 148	32 305	107 861	786	1 683	33 091	109 544	41 183	142 692
Total emission	508	2 434	605	1 491	945	6 370	2 058	10 295	7 914	24 076	412	884	8 326	24 960	10 384	35 255

B.9.3.2.3. Past emissions

The previous section provided a set of emission estimates for PFASs used in TULAC for the year 2020 using a source-flow approach to provide a baseline. This section further provides additional estimates to map trends covering the backward-looking time-series (1990-2020). As part of the forward projections, assumptions around ongoing REACH restrictions have been implemented to best knowledge using a conservative approach as follows:

- ▶ C9-C14 non-polymeric PFASs that include PFAA precursors for the formation of side chain fluorinated polymers. In August 2021, a group restriction was included in Annex XVII, REACH on perfluorinated carboxyl acids (C9-C14 PFCAs) and those substances that may degrade to them. This means that they are restricted from 25 February 2023. C9-C14 PFCAs and their related substances in the following certain textiles shall not, from 4 July 2023, be used in, or placed on the market in:
 - textiles for oil- and water-repellency for the protection of workers from dangerous liquids that comprise risks to their health and safety;
 - the manufacture of polytetrafluoroethylene (PTFE) and polyvinylidene fluoride (PVDF) for the production of:
 - high performance, corrosion resistant gas filter membranes, water filter membranes and membranes for medical textiles;
 - industrial waste heat exchanger equipment;
 - industrial sealants capable of preventing leakage of volatile organic compounds and PM 2,5 particulates.

The projections in the August 2021 C9-C14 PFCA restriction report (which was finished before the publication of the restriction) assume a more conservative estimate with implementation by early 2022 at the latest and close of the transition window by the end of 2024, after which all use will cease. The market data from the CfE only, identifies two tonnes **of C9-C14 PFCAs** in TULAC in use for the 2020 baseline, and therefore it is possible that significant steps to transition or reduce impurities have already been taken.

As a general point regarding the development of emissions projections it is important to recognise that prediction of future usage rates and technologies are very challenging and cannot consider unpredicted sudden world events (with Covid-19 being a good example). Furthermore, the more forward in time the projection is the greater the uncertainty in future trends or events. Therefore, any estimate of usage (and associated emissions) as far forward as 2050 should be treated with a great deal of care and used only as indicative of possible usage rates and their associated emissions.

In the current context to help guide both the backward-looking estimates and the projections some common rules have had to be established, which are detailed below:

- ▶ Firstly, it is assumed that activity equals emissions. The source-flow model provides data as tonnages of PFASs (disaggregated between the different substance groups) for different application types (e.g. home textiles). It is assumed that where there is demand for PFAS in these applications that the emissions will be generated proportionate to the baseline. For example, if the demand for home textiles grows strongly in the next 30 years, it is assumed that the emissions of PFAS from that sector will also grow strongly and proportionate to demand. Therefore, growth rates in different application types can be used to provide proxies for emission trends.
- ▶ Secondly, based on the baseline emissions for those substance groupings and life-cycle stage combinations where there was no activity/emission it is assumed that this has always and will always be the case. For example, the manufacture of non-woven membranes utilises only fluoropolymers and side-chain fluorinated polymers

and no non-polymeric PFASs, and therefore it is assumed this has always and will always be the case.

- ▶ Where market trend data has not been identified a uniform growth rate of 2% per year is applied. The CfE and many stakeholder interviews demonstrated that the physical properties of PFASs are highly desirable within specific applications, and that therefore, as the economy of the EEA has grown since 1990 (and will continue to do so, see OECD (2015)), it can be assumed there will be increased demand for PFAS from 1990 (first year of the estimates) onwards.
- ▶ Changes in technology and processes have not been considered within the projections. It is possible that even under a business-as-usual scenario that the science will continue to evolve and new types of PFASs brought into commercial use. No effort has been made to consider these elements for the forward projections. The unpredictability of such developments is high. (In the automobile sector for instance the electrification has a disruptive effect).

Approach for backward looking time-series (1990-2020) – Assumptions and caveats

For the back-ward looking trends, Wang et al. (2014b) provides some useful steer based on a global level set of emission estimates for PFCAs. The authors comment that the usage and emission rates for PFCAs broadly go in three movements, which commences from 1951 – 2002, during which time the commercialisation of PFAS was completed and exponential growth in their use took hold³⁰. In the second movement from 2003 – 2015, mounting concerns around the longer chain PFASs, particularly PFOS saw a shift in production and use. Longer chain C8 PFASs such as PFOS were phased out by the major global producers of PFAS with a diversification towards shorter chain (C4 and C6) PFASs. This changes the emission profile, with emissions of PFOS in particular falling sharply from recognised point sources (particularly manufacture). In the third and final movement from 2016 – 2030 with the global level ban on PFOA and multiple regulatory restrictions covering not only the PFOA chemistry (C8 PFCA) and PFOS chemistry (C8 PFSA), but also the PFHxS chemistry (C6 PFSA) and longer chain C9-C14 PFCAs, there is a further diversification and move away from longer chain PFAS into other types of PFASs.

Table B.98 in the appendix provides some further details of the assumptions used to help map the back-ward looking (1990 – 2020) trends in usage of PFASs in specific application sectors. These growth trends in different application sectors drive the overall use of PFASs. Therefore, the average growth rate across all six major application sectors (home textiles, consumer apparel, professional apparel, technical textiles, medical textiles, and other textiles) has been derived and applied to the baseline market data from 2020 to map total usage rates from 1990 – 2020.

The same averaged growth rate has also been applied to the overall emissions from the 2020 baseline to derive annual total emission estimates from 1990-2020. As a caveat, it is recognised that based on the three release groupings from the previous section B.9.3.2, i.e.,

- Group 1 – Indoor use – frequent cleaning/wetting;
- Group 2 – Indoor use – infrequent cleaning/wetting; and
- Group 3 – Outdoor – low release,

that specific application types may be more emissive than others. Applying an averaged growth rate in the current approach will miss any nuance in the changing balance of PFAS-based substance used across the different application types. However, given the uncertainty in the overall emission estimates and variances in market data (and not least the assumptions in applied growth rates), these changes are likely to be within the overall uncertainty. Deriving and

³⁰ As a side note, "The Introduction to Fluoropolymers" (2nd Edition), authored by Ebnesajjad (2021), and published by Elsevier, comment that the first fluoropolymer, PTFE, was commercialised in 1947.

applying an averaged growth rate based on underlying changes at the application type level provides a transparent and simplified approach to provide emission estimates that can be used to understand what the future picture may look like.

The usage rates for PFASs are provided in Table B.25 while the results of the overall emission estimates as a time-series are provided in the sub-section that follows after the discussion on the 2020-2050 assumptions.

Table B.25. Assumed TULAC usage rates for PFASs 1990 – 2020 (using low estimate value as baseline). All values in tonnes.

PFASs groups	1990	1995	2000	2005	2010	2015	2020
Non-polymeric C2-C3 substances	1 173	1 297	1 435	1 588	1 757	1 943	2 150
Non-polymeric C4 Substances	8.8	9.7	10.7	12.4	14.7	16.5	17.0
Non-polymeric C5 substances	0.50	0.55	0.61	0.72	0.88	1.00	1.00
Non-polymeric C6 substances	1 506	1 666	1 843	2 170	2 661	3 104	3 399
Non-polymeric C9-C14 substances	1.1	1.2	1.3	1.5	1.6	1.8	2.0
Non-polymeric other substances	50	56	62	68	76	84	93
Fluoropolymers and other polymeric PFAS excl side chain fluorinated polymers	15 452	17 094	18 911	20 922	23 145	25 606	33 091
Side-chain fluorinated polymers	1 483	1 615	1 760	1 921	2 100	2 297	2 430
Overall total use	19 675	21 740	24 025	26 683	29 756	33 053	41 183

B.9.3.3. Human exposure

Exposure to PFASs in textiles may occur directly via dermal uptake and, particularly in children, via hand-to-mouth and object-to-mouth exposure (e.g. when sucking on clothes). However, these exposure routes have been estimated to be insignificant compared to other routes (EPA-DK, 2015a).

During the use stage, PFASs can be released from textiles through a number of mechanisms, such as evaporation of volatile PFAS residuals from the fabric, loss of particles and fiber fragments by abrasion, breaking of the carbon-oxygen bond of side-chain fluorinated polymers present in the fabric, and wash-out of water-soluble residuals, such as PFCAs (Xiong and Haddad, 2021).

Evaporated PFASs and PFASs in abraded particles and textile fibers can end up in indoor dust and air, which are known exposure routes to PFASs in humans (see B.9.21.4). In certain indoor environments with large quantities of textiles, such as furnishing, carpets and clothes, the levels of PFASs in air and dust may be elevated. For example, high levels of FTOHs have been reported in shops for outdoor wear and equipment (Langer et al., 2010; Schlummer et al., 2013). For the staff working in these shops, the exposure to PFOA from the indoor air (based on 5% conversion of FTOH to PFOA) was estimated to be of the same magnitude as the normal dietary intake of PFOA.

In a study of a Chinese textile manufacturing plant, the levels of FTOHs were reported to be 2-3 orders of magnitude higher than the levels measured in the shops mentioned above, indicating a potential of high exposure to textile workers (Heydebreck et al., 2016).

B.9.3.4. Summary

PFAS emissions occur during the production and use stage during the life cycle of TULAC products. These emissions were calculated using either default ERC information specified in the REACH methodology or with more specific emission data where available. Total emission was estimated between 10 000 and 35 000 t/y (rounded numbers).

B.9.4. Food contact materials and packaging

B.9.4.1. Introduction

Uses of PFASs in food (and feed) contact materials (FCM) and packaging are described in Annex A.

In the following section the emissions for three main food contact and packaging uses, listed below, are described under the manufacturing and service life stage.

- Packaging
 - Food (and feed) contact packaging
 - Generic packaging
 - Other packaging: Coating of beverage cans, ink and lacquer residues in labels and car wrapping.
- Consumer and industrial cookware
- Industrial food and feed production equipment

Waste stage emissions are covered elsewhere (see B.9.18). Understanding of waste management (recycling, landfill, incineration or composting) and the fate of PFASs sent to waste management is very important for understanding the potential for full life cycle emissions. This applies especially to this uses as (food) packaging material (paper as well as plastics) are recyclables with Extended Producer Responsibility regimes and are stimulated to be recycled.

B.9.4.2. Manufacturing stage emissions

Manufacturing stage emissions are described below and summarized in Table B.26.

B.9.4.2.1. A - Packaging manufacturing

A1) Food (and feed) contact packaging manufacturing

For packaging, emissions of PFASs are far more relevant in the manufacturing stage than in the use stage as the production process is a 'wet process' (i.e. for paper & board packaging, large quantities of cellulose pulp in water are moved through various stages of processing to get to the final product).

Limited specific emission data have been identified that enable a comprehensive estimation of the emissions of PFASs from the manufacturing of articles. However, some data were identified that allowed an estimation of emissions especially for the manufacture of Paper & Board (P&B) packaging. Information was based on US EPA data which was based on industry data .

Data on PFASs paper & board, was available in the US Inventory of Effective Food Contact Substance (FCS) Notifications (FDA-US, 2021). Specifically, some FCS notifications have an associated environmental assessment which may include estimates of PFAS releases from the paper-making process, i.e. product manufacture. These estimates have been used to derive emission estimates across the European Economic Area (EEA).

According to the REACH methodology the total emissions in the manufacturing phase to air, water and soil compartments is between 943 – 6 881 t/y. The calculations based on FCS results in emissions between 113.1 – 825.7 t/y. Since the FCS data are actual data from the paper and board manufacturing they are considered to be more accurate than the REACH data. The paper and board manufacturing emissions are based on USA FCS Notifications industry FDA data and are considered to be worst case scenario emissions (FDA-US, 2021). See appendix for more information on release factors and assumptions.

A2) Generic plastic packaging manufacturing

For plastic packaging, emissions, although largely unknown, also mainly occur in the manufacturing stage. PFASs in generic (thermoplastic) packaging have no function in the final article. It has been assumed that the proportion of non-paper and board packaging such as plastics containing PFASs is low to negligible, and that the plastics that do contain PFASs have it in low concentrations (BfR, 2020). Despite extensive stakeholder consultation and literature search, data collected on PFASs emission in generic plastic packaging were limited. Nevertheless, with the available data, emissions of PFASs from generic packaging manufacturing have been addressed in a qualitative manner.

For generic plastic packaging PFAS processing aids are a possible source of emission during manufacturing. An additional source could also be external lubrication of processing equipment where sometimes PFASs are also used.

Due to the absence of industry data it was not possible to provide an estimate of PFAS emissions from plastic packaging manufacturing. However as PFAS processing aid residues are estimated to be present in non neglectable tonnages (300 – 600 t, see Annex A.3.4.2.) and the production process is a 'wet' process where external (PFAS containing) lubrication is of relevance, emissions likely cannot be neglected.

A3) f-HDPE containers manufacturing

Based on US EPA data, it is seen that fluorinated high-density polyethylene (f-HDPE) containers and similar plastics (i.e., fluorinated polyolefins) can result in PFAS contamination of the product (being e.g. food)³¹.

Fluorination of plastic containers creates a barrier on the plastic's surface and increases packaging strength. According to the EDF investigation, the types of containers currently undergoing the fluorination process range from "*packaged food and consumer products to larger containers used by retailers such as restaurants to even larger drums used by manufacturers to store and transport fluids.*"

There is however no data on PFAS emissions from fluorination of HDPE containers. Potentially, emissions of fluorinated gases could occur but no data was available. Information what was available is mentioned below.

During the fluorination process, HDPE containers are subjected to fluorine elemental gas under elevated temperatures. The anticipated chemical reaction results in formation of partially fluorinated long chain polymers and possibly fully fluorinated short chain polymers. Similarly, when a mixture of fluorine and oxygen is used during fluorination, oxy-fluorinated polymers are formed. If short chain polyethylene compounds (either impurities/by-products in the manufacturing of HDPE containers or from the degradation of HDPE during fluorination) are present during fluorination, further chemical reaction could occur and transform the oxyfluorinated polymers into perfluorinated carboxylic acids. US EPA - EPA's Analytical Chemistry Branch PFAS Testing - Rinses from Selected Fluorinated and Non-Fluorinated HDPE Containers. Hundreds of million containers, articles, and plastic bottles are fluorinated each year³¹.

A4) Other uses: Coating of beverage cans, ink and lacquer residues in labels and car wrapping:

Industry specific data on PFASs used in beverage can coating manufacturing, ink and lacquer manufacturing, and car wrapping production were scarce. Emissions for manufacturing of PFAS coated cans, ink and lacquer residues and car wrapping were not available. During the extensive stakeholder consultation, data returns on this issue were very low and manufacturing stage

³¹ <https://www.foodpackagingforum.org/news/plastic-container-fluorine-treatments-create-pfas>, date of access: 2022-12-14.

emissions could not be calculated. Therefore ECHA ERC 10a (outdoor use) was applied.

B.9.4.2.2. B - Consumer and industrial cookware manufacturing:

The information was insufficient to allow a quantitative estimation of the emissions during the manufacture of consumer and industrial cookware in which fluoropolymers are used. Due to the absence of detailed manufacturing process information, even a default calculation using the REACH methodology was not enough to derive a quantitative estimate.

Emissions from manufacturing consumer and industrial cookware containing PFASs were estimated on a qualitative basis due to the absence of sufficient data for a quantitative analysis. Qualitative evidence was provided by stakeholders (CfE and 2nd stakeholder consultation) and was therefore used to estimate the emissions during normal operating conditions of manufacturing installations. Accidental emissions were not accounted for.

Fluoropolymer emissions from re-coating operations of cookware (mainly industrial cookware) could be significant because of the quantities of coatings removed, but data has not been received on the fate of this fluoropolymer. PFAS emissions from re-coating industrial cookware were estimated from data received during the stakeholder consultation. The wider question of emissions from disposal is described in B.9.18.

B.9.4.2.3. C - Industrial food and feed manufacturing:

For manufacturing of industrial food and feed equipment the production process is a 'dry' process and emissions during production are usually low. Analysis of the emissions from the manufacturing of PFAS (mainly fluoropolymers) for use in industrial food processing suggest emissions are lower than in 'wet processes' like the manufacturing of paper & board packaging. Although there are also indications that in the production of PFAS coated materials (PFAS) emissions cannot be neglected. See for instance the remarks from US EPA permit information (Super-Temp Wire & Cable Inc., 2014).

In PTFE paste extrusion lines, used for instance to coat cables and tubes used in a.o. electric equipment for food and feed production/preparation, emissions of particulate matter (PM), volatile organic compounds (VOCs), hazardous air contaminants (HACs), hazardous air pollutants (HAPs) and toxic thermal decomposition products are of relevance (Super-Temp Wire & Cable Inc., 2014).

Paste extrusion lines, printing lines, melt extrusion lines and fuse lines of fluoropolymers all have the potential to generate toxic thermal decomposition products. The carbonyl fluoride produced hydrolyses to hydrogen fluoride. Emissions of these toxic gases are not quantifiable as they are highly variable due to variations in oven temperature and line speed. However, permit data suggests that decomposition products can be minimised by maintaining oven temperatures below 540 °C.

Table B.26. Emissions of PFASs and methods used in the manufacturing stage.

Sub-use in Manufacturing stage	PFAS emission estimate (t/y)	PFAS Type ***	Estimation Scenario	Methodology	Other Details
A1) Food & Feed Packaging: Paper & Board	113 – 826	Telomers and polymers with side-chain telomers	Reasonable worst-case	Calculation based on FDA data. The FDA approach is preferred as it accounts for data from manufacturing	Based on data for large installations in the USA: A wet process with significant emissions

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Sub-use in Manufacturing stage	PFAS emission estimate (t/y)	PFAS Type ***	Estimation Scenario	Methodology	Other Details
				sites	
A2) Generic plastic packaging	No data	PPAs		No data	High tonnage (1 640 – 3 280 t) but no specific emission data for thermo plastic production. ERCs applied
A3) f-HDPE containers	No data	PFAA (precursors)			Important topic in USA
A4) Other uses	No data – likely low	Fluoropolymers		No data	
B) Consumer Cookware	Very low	Fluoropolymers including fluoropolymer PPA	Normal operating conditions	Estimation from stakeholder data	Qualitative assessment
C) Industrial food and feed production equipment	Very low	Fluoropolymers and PPAs	Normal operating conditions	Estimation from stakeholder data	Qualitative assessment
C2) Re-coating Industrial Cookware	0.4 – 1.2****	Fluoropolymers and PPAs	Realistic-case	Calculation from stakeholder data	Calculation is for PTFE only
TOTAL	113-827				Mainly caused by paper & board manufacturing

- * Standard REACH methodology (ECHA, 2016a).
- ** Based on 2% loss of fluoropolymer-coating during use. May be an under-estimate as can be seen in Figure B.70.
- *** Type of PFAS from which emissions originate using expert judgement. † May be an over-estimate.
- **** Emission to soil and water. Based on 90% disposal via waste.

B.9.4.2.4. Service life emissions

A - Packaging service life

Service life emissions of food contact material and (food/feed) packaging are of lesser relevance than manufacturing emissions. No industry specific emission factors were available.

Estimates presented here are derived using the first level (tier 1) methodology. This relies upon having tonnage data for the substance(s) of interest at the relevant point in the life cycle of that substance. Of the various ERCs defined the most appropriate were chosen, that being ERCs 10a and 11a. A description and justification behind the chosen ERCs are described in Appendix B.9.4. Food contact materials and packaging.

A1) Food (and feed) contact packaging service life

For emissions during the service-life of paper & board used in food and feed contact, the outdoor emissions of PFASs predicted from the REACH methodology are recommended to be used as a worst case scenario. In real world conditions it is unlikely food and feed packaging will be left outdoors and exposed to weathering during its service-life for any length of time. However for takeaway food, outdoor emissions could occur for example during transportation. In addition, paper & board packaging used for food and feed contact that has been discarded i.e. litter, will be exposed to weathering and therefore these emissions may be realised in part. A precautionary approach is recommended for instance to use the higher outdoor figures which could be seen as a worst-case scenario.

In Figure B.68 a tonnage and emission flow chart for paper & board packaging (the main packaging use where PFASs are applied) is plotted. Service lifes emissions as well as manufacturing stage emissions are covered. Values in the blue boxes represent tonnage flows of PFAS/year while values in the red boxes represent emissions of PFAS/year. As can be seen below in the red boxes the manufacturing emissions are by far the most relevant. More details on emission are presented in the Appendix. A distinction between indoor and outdoor emissions is made.

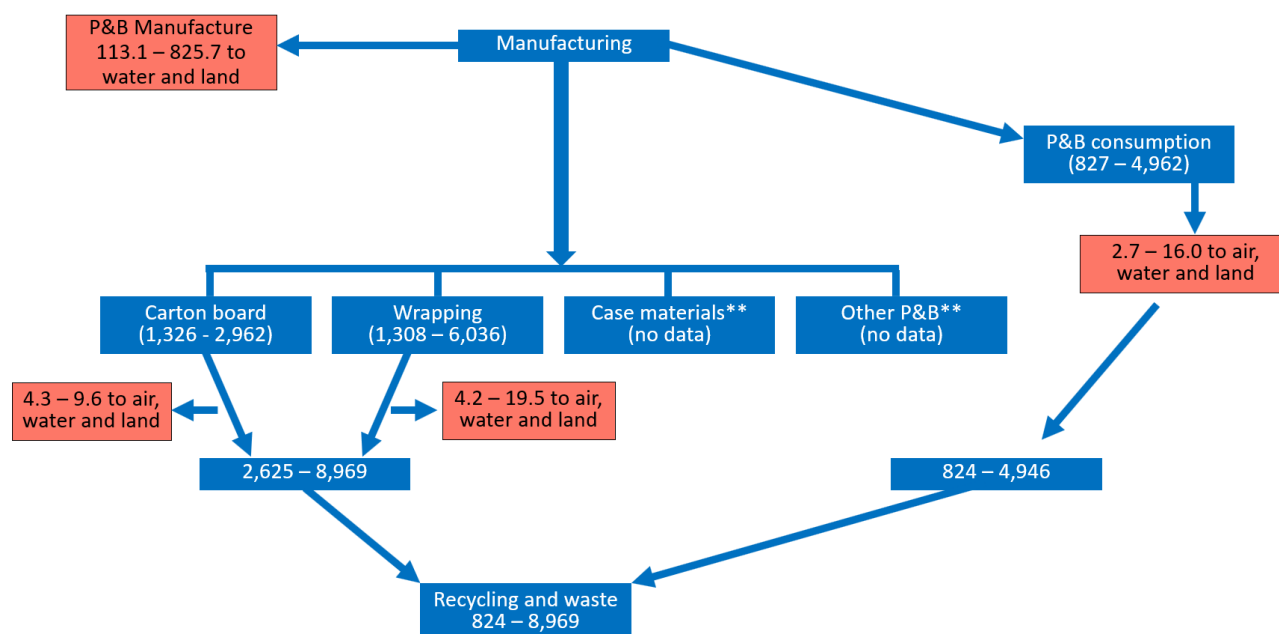


Figure B.68. Indicative PFAS tonnage flows (t/y) for paper & board packaging in service life and manufacturing stage. Values in blue boxes are tonnage flows of PFAS/year. Values in red boxes are emissions of PFAS/year. Left branch: detected (Table A.22. in Annex A), right branch: intentionally added (Table A.23. in Annex A): Giving similar results. EU-27 & NO & UK.

A2) Generic plastic packaging service life

Due to limited research on PFASs in plastic packing, data on service life emissions for PFASs in generic packaging were unavailable. A precautionary approach is used for the emission estimate i.e. to use the higher outdoor figures which could be seen as a worst-case scenario. Therefore for service life the 'standard REACH methodology', ERC 10a, has been used.

A3) Other uses: Coating of beverage cans, ink and lacquer residues in labels and car wrapping

Data on PFASs used in lacquers & ink, beverage can coating and car wrapping were scarce. During the extensive stakeholder consultation, data returns on this issue were very low. Nevertheless, on basis of available tonnage data (see Annex A, section A.3.4.2.), emissions of PFASs have been addressed in a qualitative manner. Service-life emissions as a result from these uses were calculated using the ERCs mentioned in Appendix B.9.4. Table B.99.

A4) f-HDPE

PFAS emission into the environment from fluorinated plastic like f-HDPE containers is likely to be low. However, PFAS migration from fluorination of HDPE containers into stored products might be a serious concern (EPA-US, 2021c).

B - Consumer and industrial cookware service life

B1) Consumer cookware

No publications have been identified that indicate the quantity of fluoropolymer lost during cookware use by consumers, although at the end of 2022 an article was published on micro plastics release from consumers cookware (Luo et al., 2022). However, numerous examples have been found online on consumer websites of pans that have clearly lost a significant part (2% or even 10% or more) of the fluoropolymer-coating during use, revealing the bare metal as shown in Figure B.70. An illustrative upper bound can be calculated assuming a 2% loss of

material per year for the consumer cookware sector, equivalent to an emission of 70 t/y (3 500 * 0,02).

The position of manufacturers is that consumers should purchase new kitchenware when the non-stick finish no longer performs as well as desired. This will likely correspond to only a small loss of material to consumers or the environment. No data sources have been identified that indicate the quantity of fluoropolymer lost during use by consumers.

B2) Industrial cookware

Given the criticality of the coating for industrial food production it seems unlikely that damage similar to that seen in the consumer cookware market would be tolerated. Emissions during service life (re-coating excluded) likely is very low.

In Figure B.69 a tonnage and emission flow chart for consumer cookware and industrial food & feed production equipment is plotted in which the service life as well as manufacturing stage emissions are covered.

Emissions in the use stage are expected to be low unless equipment is improperly used, for example scratched or overheated (Luo et al., 2022; Schlummer et al., 2015). Most polymeric PFASs in these articles enter the end-of-life stage where additional emissions might occur for instance from landfills or incineration.

During the preparation of the dossier, industrial re-coating of cookware has been seen as a potential emission source³². This use is not described in Annex A. Commercial bakeries use non-stick cookware and the coating is regularly replaced. In the case of non-stick baking pans after 12-24 months the old PTFE coating is removed and a new coating is applied. Comprehensive data on the quantities of fluoropolymers removed from industrial cookware for recycling purposes (which is then re-coated) have not been identified. However, for Sweden and Germany, information was available as shown in Table B.27 and has been extrapolated to the whole of EEA. Recoating is also done for cheese forms and likely other food contact items as well. Given the uncertainties with the tonnage and emission estimates, the values should be regarded as indicative only.

Table B.27. Quantities of PTFE in Industrial Cookware re-coating according to data.

Parameter	Quantity	Source
Pans re-coated in Sweden each year	20 000*	(RIVM, 2020) Stakeholder information
Pans re-coated in Germany each year	100 000*	
Total surface area of the Swedish + German yearly recoated pans	12 000 m ² (0.1 m ² /pan)	Stakeholder information
Density of PTFE	2.16 g/cm ³ = 2.16 t/m ³	(WSH, 2021)
Average coating thickness industrial cookware	35 – 100 µm	(PTFE Coatings, 2021) and stakeholder information
Population of Sweden + Germany	10.38+83.16= 93.54 million	(Statista, 2020)
Population of EEA (without UK)	454 million	(Eurostat, 2020)

Notes: *Assumed to be number of units stripped and re-coated per year.

³² Re-coaters advertised on Google for instance as seen here www.itn-coatings.com or https://hoffmann-germany.de/pages/wiederbeschichtungs_service, date of access: for both: 2022-12-14.

Each year in Sweden and Germany an estimated 0.42 – 1.2 m³ PTFE coating is replaced. Therefore 0.9 – 2.6 t of PTFE are removed from industrial bakeware annually in the two countries. Extrapolating to EEA via population figures leads to: $454/95.54 \times 0.9 = 4.3$ t up to $454/95.54 \times 2.6 = 12.4$ t removed volume fluoropolymer, which has to be split into emissions and waste. In case 10% of the re-coated tonnes are emitted, as realistic case, this leads to an emission of **0.4–1.24 t/y**. The other 90% is discarded as waste (where also emissions might occur). According to one stakeholder, the old coating is partially burnt out at 420 °C in a special circulating air oven. The resulting processed air is post-combusted at >1 000 °C. Closed-circuit gas scrubbing water is disposed of as hazardous waste. Sandblasting waste is said to be disposed of as hazardous waste. Other sources mentioned less rigorous destruction. Finally, not all hazardous waste is disposed as hazardous waste. Therefore, the recoating activity remains a potential source of emissions.

C - Industrial food and feed equipment service life

Industrial food and feed equipment consist of conveyor belts, O-rings, etc. used in factories which produce food or feed. Emissions of PFASs during the service-life of industrial food and feed equipment when used in the food industry are based solely on indoor use and represent a reasonable worst-case scenario, based on ERC 10a (indoor use). Emissions from the use of fluoropolymers in industrial food processing and the pharmaceutical sector³³ in the EU indicates a low emission of 0.2 t/y as can be seen in the red box on the right side of Figure B.69. As mentioned in Annex A, volumes for industrial food processing cannot be disaggregated from the pharmaceutical sector.

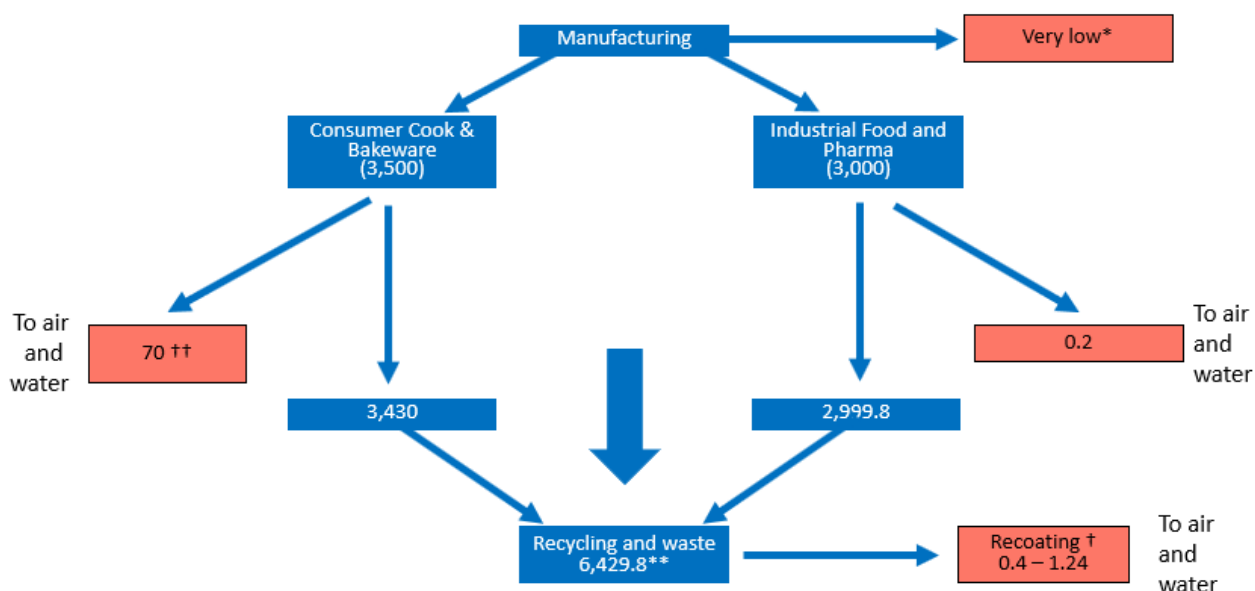


Figure B.69. Indicative PFAS (Fluoropolymers) tonnage flows (t/y) for both consumer cookware and industrial food products in 2015 (EU-28) in service life as well as manufacturing stage. Tonnages and emission are represented by the blue box and red box respectively.

Emission of fluoropolymers into the environment are represented by the red boxes shown in Figure B.69. Values in blue boxes are tonnage flows of PFASs from manufacturing through the

³³ The separate proportions going to food and pharmaceuticals has not been able to be disaggregated.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

service-life of products to waste/recycling.

Polymeric PFAS emissions for consumer as well as industrial use are expected to be low during (proper) use. For consumer as well as industrial cookware overheating of fluoropolymer coatings is not recommended due to the release/emission of fumes that may have detrimental health effects. Modern ovens, both for consumers and professionals, however, could easily exceed 300 °C posing a risk to fluoropolymer coating emission. For service life, the 'standard REACH methodology'/ERCs has been employed. Estimates presented here are derived using the first level (tier 1) methodology.

In Table B.28 the PFAS emissions from all distinguished sub-uses are summarised for the service-life stage.

Table B.28. Emissions of PFASs and methods used. Service life stage (proper use assumed).

Sub-use	PFAS emission estimate (t/y)	PFAS Type ***	Estimation Scenario	Methodology	Other Details
A1) Paper & Board FCM Packaging	3 – 20 (based on two different calculation methods)	Telomers and polymers with side-chain telomers	Worst-case	ERC REACH*	Based on outdoor emissions, ERC 10a
A2) Generic plastic packaging Lacquers and ink	5 – 11 2	PPAs (residues) Non polymeric	Worst case	ERC REACH	Based on outdoor emissions, ERC 10a
A3) Coated beverage cans	16	Fluoropolymers (PTFE wax)	Estimation	ERC REACH	Based on outdoor emissions, ERC 10a
A4) f-HDPE	No data, likely fluorinated gas	Fluoropolymers	-	-	Actual topic in the USA
A5) Other uses (Car wrapping)	13	Fluoropolymers	Worst case estimation	ERC REACH	Based on outdoor emissions, ERC 10a
B1) Consumer cookware	70**	Fluoropolymers	Reasonable worst-case	Own calculation assuming 2% loss per year, although sometimes 10% was seen (see Figure B.70)	Severe loss of polymer coating possible in case of low quality product and/or improper use
B2) Industrial cookware	Very low	Fluoropolymers	Reasonable worst case	No data	Based on industry quality standards

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Sub-use	PFAS emission estimate (t/y)	PFAS Type ***	Estimation Scenario	Methodology	Other Details
C) Industrial food and feed production equipment	0.2	Fluoropolymers	Worst-case	REACH	Based on indoor emissions, ERC 11a
TOTAL service life, excl. waste stage (rounded numbers)	109 – 132				

PFAS used in paper & board packaging are surfactants (telomers and polymers with telomeric side-chains/ side chain fluorinated polymers; PFAS used in consumer and industrial cookware are fluoropolymers.

- Standard REACH methodology (ECHA, 2016a).
- ** Based on 2% loss of fluoropolymer-coating during use. May be an under-estimate as can be seen in Figure B.70
- *** Type of PFAS from which emissions originate using expert judgement.

The emissions for food and feed contact material and packaging are further summarized in Table B.29. The main source of emission is attributed to the manufacturing of paper & board packaging.

Table B.29. Estimated annual EEA emissions in the FCM and packaging sector of PFAA and PFAA precursors, polymeric PFASs and total PFASs in 2020 (baseline) based on Table B.26 and Table B.28.

	Total PFAA and PFAA precursors (t/y)			Total polymeric PFASs (t/y)			Total PFAS (t/y)		
	low	mid-point	high	low	mid-point	high	low	mid-point	high
Total volume	3 267	6 305	9 342	15 330	17 880	20 430	18 597	24 185	29 772
Manufacturing stage emissions	113	470	826	0	0,5	1	113*	470	827*
Service life stage emissions	10	21	32	99	99	99	109	121	132
Total emission	123	491	858	99	100	100	222	591	959

*: Based on USA FCS Notifications industry FDA data. Cannot be fully disaggregated but mainly telomers and sidechain fluoropolymers.

B.9.4.3. Human exposure

The high price of fluoropolymers is mentioned by producers as a driver for minimising use and exposure. According to stakeholders, PFAS exposure to humans is very limited as (local) strict regulations and approval schemes are in place, although not always strictly enforced. On the other hand, available literature data suggest that diet is the major human exposure pathway for some PFASs (especially non polymeric PFASs), but that there is large variability in exposure levels across populations (De Silva et al., 2021). A possible source of fluoropolymer exposure

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

can be losses of fluoropolymer material from wear and tear of consumer cookware (Luo et al., 2022). These losses can be very high, particularly for low quality goods, see Figure B.70 shown below. According to a BfR FAQ of 2018 (BfR, 2018), PTFE minute particles, released from scratched coatings of coated cookware, ovenware and frying pans can be ingested. This is considered to not pose a risk to human health, since PTFE particles are excreted from the body unchanged. However, this applies only as long as the recommended conditions of use of fluoropolymers to protect human health are applied (e.g. no overheating).

In the use stage PFAS migration to food from paper and board contributes significantly to tolerable weekly intake (Lerch et al., 2022).

Additionally, it is stated that toxic vapours from fluorinated compounds and particles develop at temperatures above 360 °C which means an overheating of coated cooking, baking and frying utensils, especially when empty (BfR, 2018).



Figure B.70. Loss of PFAS coating during use.

FCM from paper and board (e.g. fast food packaging) can be a source of human exposure towards non-polymeric PFASs. However, with the exception of very specific exposure scenarios like very frequent consumption of microwave popcorn, the impact of FCM as a source of human exposure towards PFAS seems to be low compared to other sources such as food. EFSA (2020) concluded in their risk assessment of PFASs in food that exposure to residual PFASs in PTFE cookware was low in comparison to other sources (see also section B.9.21.1).

Moreover, fluorinated HDPE containers could lead to PFAS exposure of consumers when food is stored in these containers (Rand and Mabury, 2011) (Figure B.71). Fluorination of HDPE packaging is however commonly used in the US to treat polyethylene and polypropylene containers each year and if (illegally?) applied in Europe could be a source of human exposure towards non polymer PFAS³¹.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

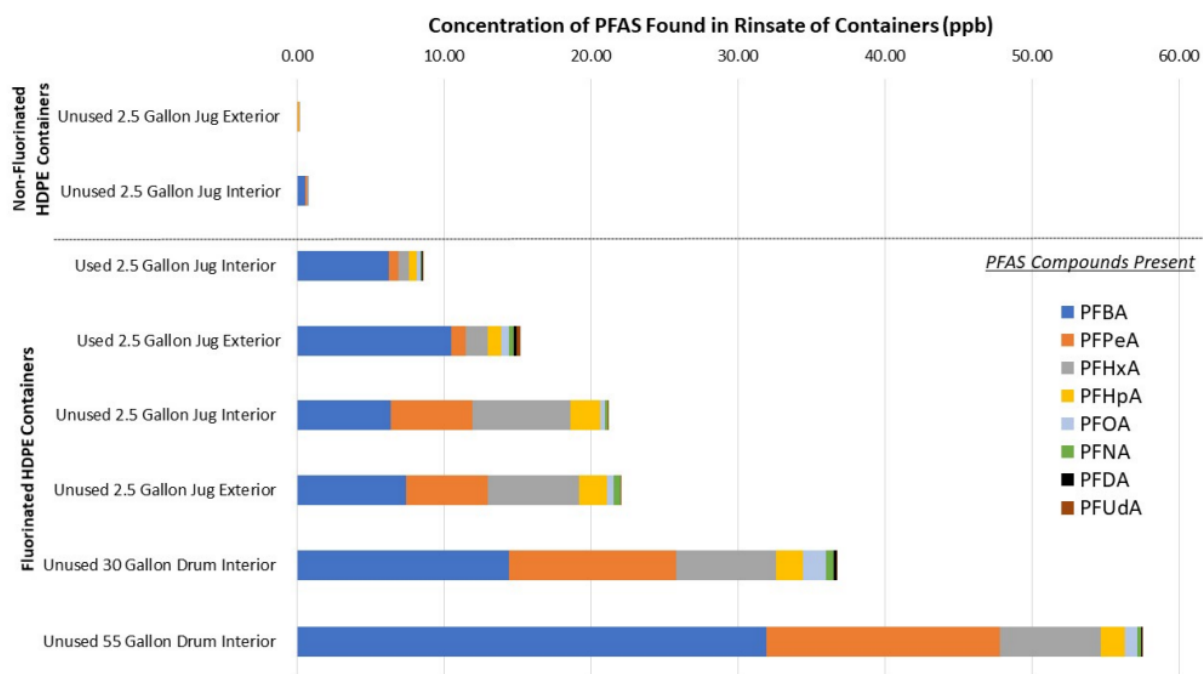


Figure B.71. Concentration PFAS found in rinsate of packaging containers (ppb). Source: EPA-US (2021c).

Fluorination of plastic is commonly used to treat hundreds of millions of polyethylene and polypropylene containers each year and could be a serious source of human exposure (especially if food is packed in such containers).

B.9.4.4. Summary

Emissions from the food contact and material sector were calculated for the manufacturing and service life stage using either default ERC information specified in the REACH methodology or with more specific emission data where available. Manufacturing stage emissions are of higher importance than service life emissions. Total emission of PFASs calculated for the manufacturing stage and service life stage together, amounted to **222 to 959 t/y**. This very likely is an underestimation as for instance in the manufacturing stage quite some emission values are lacking.

Human exposure to PFASs in food contact material may include lost material from consumer cookware from wear and tear, food packaging and storage of food in f-HDPE containers.

B.9.5. Metal plating and manufacturing of metal products

B.9.5.1. Introduction

The use of PFASs in this sector is described in Annex A.3.5.

B.9.5.2. Emissions

A distinction between emissions during metal plating and the manufacture of metal products is made.

B.9.5.2.1. Metal plating

Emissions of PFASs during metal plating processes originate e.g. from the rinsing steps between the electrolytes and from replacement of used solutions (UBA, 2017b). The galvanic bath is used for a couple of years. It is renewed e.g. when the emerging sludge may hamper the galvanic process. The galvanic solution without further treatment must be considered as process solution and becomes liquid waste. It is forbidden to dump the solution directly into a WWTP, not even if the solution is diluted. It has to be treated in a physical-chemical processing plant. In this plant metals are reclaimed and other substances are removed. PFAS can be removed via ion exchanger from the galvanic solution. But this technology is not state of the art yet and therefore it is not mandatory. Currently, the Reference Document on Best Available Techniques for the Surface Treatment of Metals and Plastics (STM-BREF) is revised. It is likely that this treatment step would become obligatory. According to the German central association for surface technology (Zentralverband Oberflächentechnik e.V., ZVO) in Germany 20% of the applied surfactant is lost by the plating processes itself over time, e.g. by trickling from treated devices (EPA-DK, 2011). For the lifetime of the surfactant in the galvanic bath no data are available. The Dossier Submitters assume that this share can be generalized across Europe.

Release of PFASs from metal/chrome plating processes into the environment is possible via air, wastewater and also via waste (e.g. metal hydroxide sludge, ion exchange resins). As already mentioned, ~20% of the applied surfactants are emitted into the environment. The following emission pathways for the fluorosurfactants were quantified: 50-85% via wastewater, 0.1-24% via waste (e.g. metal hydroxide sludge) and <0.1% via exhaust air (Hauser H., 2020). Waste related emissions are included B.9.18. Short-chain PFASs have a low adsorption potential and are difficult to remove during water treatment processes and will be released in receiving waters. PFASs with higher adsorption potential will be bound to the metal hydroxide sludge and removed via active carbon or ion exchangers (UBA, 2017b; UBA, 2022).

Based on information from the PFHxA dossier a current annual release of 6 t (central estimate, range 0.5-11.4 t/y) into the environment was estimated for 6:2 FTS in Europe during chrome plating. This central estimation was confirmed in the 2nd stakeholder consultation during preparation for this restriction dossier: A survey of suppliers of 6:2 FTS for surface treatment identified an emission of about 5 – 8 t/y.

Furthermore, one stakeholder noted an emission by wastewater of 25-50% of the applied 6:2 FTS during plastic etching. Another stakeholder described a carryover of <1% in the functional chrome plating process.

A further source of PFAS-emissions is de-chroming plating of defective batches and product carriers. Due to adsorption and desorption processes on plastic coated plating parts, PFASs can get to other partial streams of the electroplating plant and emitted via wastewater. Used process solutions from degreasing baths could also release PFASs. The degreasing solutions and their rinse waters are normally not specifically treated in order to remove PFASs (UBA, 2022). Due to the lack of information, a quantification of the PFAS release by dechroming is not possible.

Chromate solutions containing mist suppressing agents have a limited usage lifetime and have to be changed regularly. The used solutions are treated as chemical waste, where chromium is

isolated. The rest is disposed of with the risk of long-term leaching of PFAS to the groundwater or emission of PFAS-contaminated wastewater (NEA, 2017).

It is not possible to derive sufficiently representative numbers from the literature to calculate use quantities and emissions for the industry as a whole or for individual metal plating baths. Based on information from a stakeholder consultation the final article does not contain PFAS. In Table B.30 the overview of estimated PFAS emission is given.

Table B.30. Estimated annual EEA emission in the metal plating subsector.

Metal plating	6:2 FTS (PFHxA related substances) (t/y)		Total PFASs (t/y)	
	Low	High	Low	High
<i>Total volume</i>	2	57	2	57
Total emission	0.5	11.4	0.5	11.4

B.9.5.2.2. Manufacture of metal products

As stated in Annex A it is estimated that approximately 960 t/y of fluoropolymers are used in the production of metal products. Information on emission of PFASs during production and use of metal products is not available. Shares that are used for consumer uses like the production of cookware and bakeware and for industrial applications/coatings respectively are unknown. Information on emission of PFASs during production and use of metal products is not available (see Table B.31).

Table B.31. Estimated annual EEA emissions in the manufacturing of metal products.

Manufacture of metal products	Total PFASs (t/y)
<i>Total volume</i>	960
Total emission	No data

B.9.5.3. Human exposure

PFASs are used in metal plating processes as mist suppressant to decrease aerosol emissions (e.g. chromium) and reduce worker exposure. In the manufacturing of metal products PFAS are applied for various purposes (coating, corrosion inhibitor, cleaning, electrical insulation, etc. see Annex A.3.5.).

Stakeholders indicate that exposure levels of workers are low. Exposure to workers is suppressed with protective clothing, protective goggles, local exhaust, masks, etc. Exposure to consumers is low to negligible. E.g. PFAS are not present in the chromium-plated article as PFAS has no function in the final product.

B.9.5.4. Summary

Emissions from metal plating and manufacturing of metal products are estimated to be between **0.5 and 11.4 t/y** for 2020. This emission is solely linked to mist suppressants in the metal plating subsector. (Emissions from manufacture of metal products is unclear, so total emission for the sector is an underestimation).

As stated in Annex A.3.5., it is estimated that approximately 960 t/y of fluoropolymers are used in the manufacturing of metal products. Information on the concentration of PFASs per use, annual production tonnages, import volumes for metal plating/production of metal products is hardly available. The same applies for information on annual emissions/release and future

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)
emissions.

B.9.6. Consumer mixtures

B.9.6.1. Introduction

The use of PFASs in consumer mixtures is described in Annex A.

B.9.6.2. Emissions

In the CfE, one company estimated that up to 100% of PFASs used in cleaning products could potentially be emitted to the environment. This is in line with the respective ECHA standard exposure scenarios (ERC 8A and ERC 8D) for widespread use of non-reactive processing aids which are not included into or onto articles (ECHA, 2016a). So, based on data provided before, it must be assumed that 20 t PFASs/y is released into the environment by consumer mixtures in the EEA. For guitars strings alone, the yearly EEA tonnage is estimated at 3 t PFASs/y. The emission is estimated to be 3 t PFASs/y as well. These estimations are listed in Table B.32.

Table B.32. Estimated annual EEA emissions in the consumer mixtures sector of total PFASs in 2020 (baseline).

	Total PFASs (t/y)
<i>Total volume</i>	<i>21-30</i>
Cleaning agents, polishes, waxes emissions	20
Coated guitar strings emissions **	3*
Total emissions	23

*: Either fluoropolymers or a side-chain fluorinated polymer

**: The emission value is the same as the total volume. The reasoning is that, according to stakeholders, the coating is over time released to the hands, which after washing release to the water compartment.

B.9.6.3. Human exposure

Apart from direct exposure to PFAS due to application of cleaning agents, polishes, and waxes, indirect exposure via ingestion of house dust takes place for consumers. In general, a variety of PFAS can be found in dust in European households and offices, indicating that consumers are exposed to PFAS on a daily basis (Bohlin-Nizzetto et al., 2015; de la Torre et al., 2019; Eriksson and Kärrman, 2015; Harrad et al., 2019; Karásková et al., 2016; Padilla-Sánchez and Haug, 2016; Poothong et al., 2020; Weiss et al., 2021; Winkens et al., 2018). Cleaning agents, polishes, and waxes are one source of PFAS in dust. Other uses of PFASs, such as uses in textiles and in construction materials or articles containing PFASs, also contribute to the presence of PFASs in house dust. Further information on PFAS in house dust is provided in section B.9.21.4. PFAS concentrations can vary by several orders of magnitude, showcasing the effect of variable furnishing and consumer behaviour.

B.9.6.4. Summary

Limited information is available on the emission of PFASs from consumer mixtures. Up to 100% may be emitted, the emission estimate is therefore the same as the use estimate, which is **23 t/y**. PFASs from consumer mixtures may also gather in house dust, which leads to human exposure.

B.9.7. Cosmetics

B.9.7.1. Introduction

PFASs in cosmetic products is a research area which came into focus during the last decade.

Three different databases were consulted to get an overview of the identity and frequency of occurrence of PFASs in cosmetic products. About 170 unique PFAS ingredients potentially occurring in cosmetic products were identified within the cosmetic ingredient database (CosIng). Of these, 42 were present in products within three European cosmetic databases, among which polytetrafluoroethylene (PTFE; a PFAS polymer) and C9-15 fluoroalcohol phosphate were most frequent.

Based on measured PFAS concentrations, the share of products containing PFASs, sales data from Cosmetics Europe, as well as other parameters and assumptions, the total emission of PFASs from cosmetic products after use was estimated for the European Economic Area (EEA).

B.9.7.2. Emissions

Generally, four parameters have to be considered calculating a chemical's emission, in this case for PFASs (E_{PFAS} in kg/y) from products (see Equation):

- the concentration of a chemical in the products (C_{PFAS} in $\mu\text{g PFAS/g product}$),
- the total amount, or tonnage of the products sold per year ($A_{products}$ in t/y),
- the share of products containing the chemical ($f_{PFAS products}$), and
- the fraction of the chemical released from the product into a certain compartment ($f_{release}$) (e.g. wastewater or solid waste etc.).

$$E_{PFAS} \left[\frac{\text{kg}}{\text{year}} \right] = C_{PFAS} \left[\frac{\mu\text{g}}{\text{g}} \right] \times A_{products} \left[\frac{\text{t}}{\text{year}} \right] \times f_{PFAS products} \times f_{release} \times 10^{-3}$$

The factor 10^{-3} in the equation is a conversion factor from g/y to kg/y. The $f_{release}$ part can be neglected (i.e. set equal to one) in order to calculate the total emission or total content of PFASs in the products that can be emitted into the environment as a worst-case scenario.

All emission estimates are annual values for the EEA (not including Lichtenstein and Iceland), or correspondingly the EU27 and Norway. The total emissions are assumed to occur after product use only and to exclusively end up in wastewater or to solid waste. No other emissions were considered. The emissions to solid waste in all worst-case scenarios are equal to zero, as the entire emissions are assumed to go into wastewater. The total emissions in those worst-case scenarios are therefore equal to the emissions into wastewater. The concentrations of PFASs in the cosmetics products were derived using different analytical methods due to the complexities to characterize and quantify the large diversity of PFASs occurring in these products. These methods included measuring total fluorine (TF), the extractable organic fluorine (EOF) and individual PFASs (targeted analysis). The EEA emission estimates from cosmetic products were based on Total Fluorine (TF) and Extractable organic fluorine (EOF) concentrations. These were deemed as a more realistic concentration representation of emissions from listed ingredients. The emissions based on TF represents any kind of PFASs (low and high molecular weight PFASs, including polymers, non-polar and polar, as well as ionisable and non-ionisable PFASs), but can also represent inorganic fluorine if present in the product.

To avoid the potential for overestimating the PFAS content due to presence of inorganic fluorine, EOF was used to capture a wide range of organofluorines and removes inorganic fluorine. The EOF-based emission calculations are the best estimate for non-polymeric and polar (i.e., soluble in methanol) PFASs that are present in the cosmetic products. Targeted PFAS analysis, on the

other hand, is highly specific and sensitive, but does not capture PFASs not specifically included in the method. In the tables below fluorine content was converted to PFAS using a conversion factor of 1.7. Emissions are presented in Table B.33 below.

Table B.33. Total emissions of PFAS from use of cosmetic products/year , best case and worst scenario. A conversion factor of 1.7 (midpoint of 1.4-2) is used to make the tonnages and emissions based on PFAS content enabling comparison with other uses.

Emission (to wastewater*)	Total PFASs (kg/y)	
	Low	High
<i>Volume</i>	28	64 000
Total emission use phase (worst case)	15	64 000

*Emissions to solid waste is described in KEMI (2021b).

As Table B.34 demonstrates, skin care is the dominant cosmetic category in terms of use and emissions. For more details about the different categories, see KEMI (2021b).

Table B.34. Estimates for total emissions for the different cosmetic product categories in a best-, average- and worst-case scenario.

Product category	Emissions (kg PFASs/y)		
	TOTAL best case	TOTAL average case	TOTAL worst case
Skin Care	14	13 940	49 300
Toiletries	2	950	2 550
Hair Care	3	1 700	4 590
Perfumes and Fragrances	0	0	0
Decorative Cosmetics	10	2 040	6 970
Total emission (rounded)	29 (part to solid waste)	18 600 (part to solid waste)	64 000

The Skin Care product category contributed the most to the sum (PFCA) emission estimates, followed by Hair Care and Decorative cosmetics. More information on analytical challenges and emissions estimates can be found in the full report (KEMI, 2021b).

Emission estimates and other collected data in this study show, while subject to several uncertainties, that cosmetic products contribute to the occurrence of PFAS in the environment, both via wastewater and via solid waste. There may be environmental risks associated with PFAS in cosmetic products (Ahrens and Bundschuh, 2014). PFASs may be released to the environment from cosmetics during product manufacturing use and disposal. PFAS-containing cosmetics that are removed from the skin or body will enter wastewater streams or be directed to solid waste. It is unclear how these substances behave during wastewater treatment. However, wastewater treatment plants (WWTPs) have been identified as a significant source of PFASs releasing either to receiving water (via effluent outfalls), air (via off gassing from settling tanks), and fields (via application of sludge as fertilizer) (Ahrens et al., 2011; Lee et al., 2014; Yeung, 2017).

B.9.7.3. Human exposure

Food, dust, air, and drinking water are regarded as the major exposure pathways for known PFASs in the general population (Trudel et al., 2008; Vestergren et al., 2008). Dermal exposure to PFASs has so far been considered negligible, most likely due to a lack of data on occurrence

and dermal permeation of PFAS from cosmetic products (Winkens et al., 2017b). Given the large surface area of the skin ($\sim 22 \text{ m}^2$; Godin and Touitou (2007)) and the liberal application of some cosmetic products, dermal uptake may represent an important route of PFAS exposure particularly in children. Further investigation is needed.

B.9.7.4. Summary

Total emission of PFASs estimated in the EEA from cosmetic product use was based on parameters including measured PFAS concentrations (i.e TF, EOF, targeted PFAS analysis), the share of products containing PFASs, and sales data from Cosmetics Europe. Emissions were assumed to occur after product use only and to exclusively occur to wastewater and solid waste. As worst case scenario with emissions going 100% to waste water, the calculated total emissions of PFASs from use of cosmetic products is 64 000 kg PFAS/y and equal to the tonnage put on the market. Skin care products are the largest contributor to emissions.

Despite limited data, it is thought that dermal exposure to PFASs may represent a relevant uptake route. However further investigation is needed.

B.9.8. Ski wax

B.9.8.1. Introduction

PFASs commonly used in the production of gliders and other ski wax products can be released into the environment, as the wax containing PFASs will be worn off through abrasion against the snow, causing diffuse spreading of PFASs through the snow, water and sediment. During application, wax can be brushed off the ski, ending up on the ground. This may eventually end up on the snow if not correctly disposed of.

Direct human exposure to PFAS can occur when applying ski wax treatments, as the application often includes heating, melting, brushing and sanding of mixtures containing PFASs close to the airways, meaning users can be exposed to high concentrations of PFASs (Nilsson et al., 2010b).

B.9.8.2. Emissions

For this assessment, a basic source-flow model was developed. The development of this source-flow approach began with a consideration of the key life-cycle stages and the kinds of emissions that may occur at each life-cycle stage.

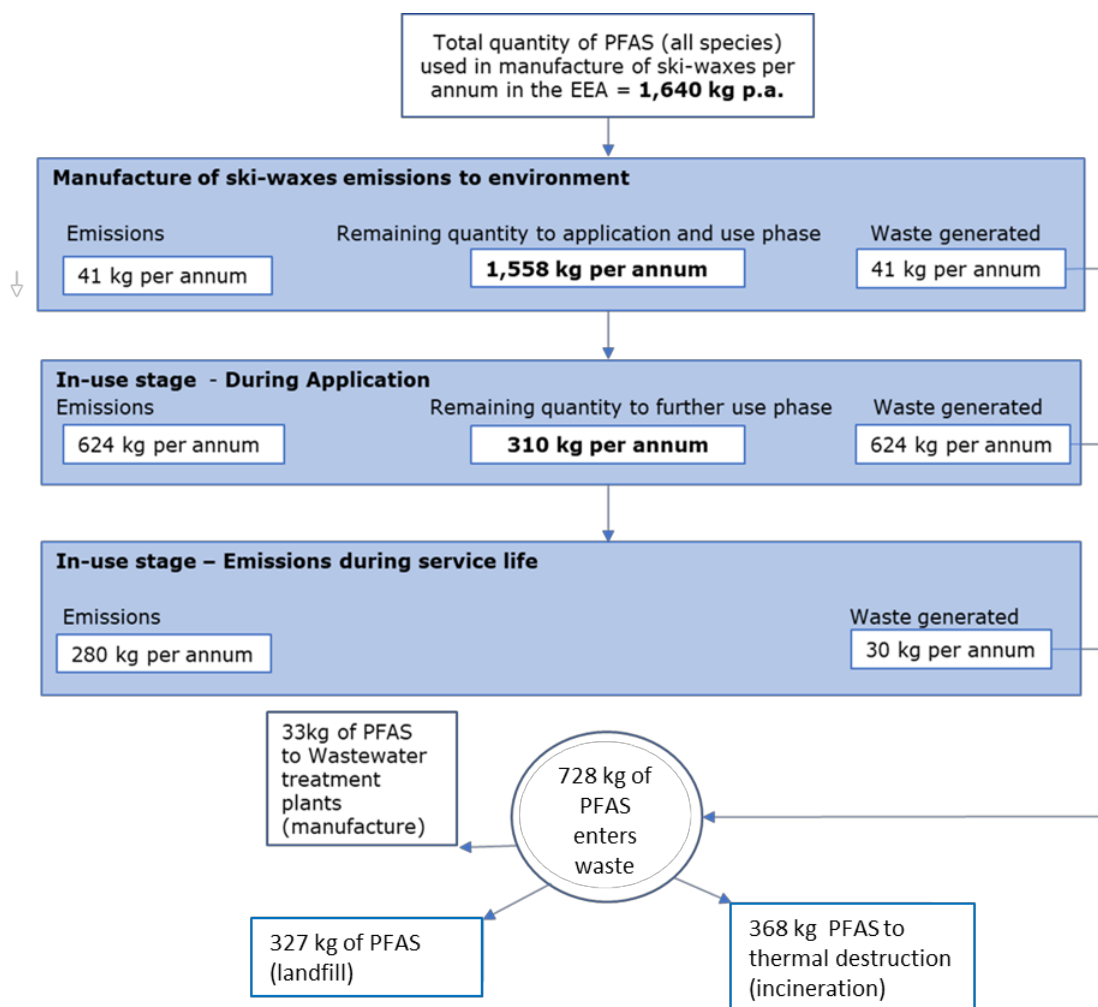
ERCs were only applied for the manufacturing stage. For other parts of the flow, an analysis for each step in the life-cycle was performed with a basis in what is known from practical experience and stakeholder information.

Four basic life-cycle stages are considered based on the likelihood for emissions to occur, or for material to flow through into the next life cycle stage (Figure B.72):

- **Formulation of the ski wax:** This includes consideration of the PFAS substances used within the ski wax. Note, that it was assumed that the life-cycle begins at this stage rather than the manufacture of the PFASs themselves.
- **Storage:** For other sectors beyond ski-waxes, storage can potentially be an important life-cycle stage for potential emissions. Therefore, for completeness 'storage' has been included within the current source-flow approach. However, during storage of ski waxes it is unlikely that leaks or spillages are to occur, which would directly contribute to environmental emissions. Therefore, emissions from this stage are assumed to be zero.
- **Use:** Active use of ski waxes is likely the most important life-cycle stage. To provide a higher level of disaggregation, this stage is split into two sub-components:
 - Emissions to the environment during the application of ski-wax to skis/snowboards etc.
 - Further emissions to the environment associated with the continued service life (i.e., during skiing).
- **Waste:** The waste cycle includes three key pathways, landfill of wastes and/or end of life product (i.e., any unused final quantities of wax discarded), thermal destruction (incineration), and wastewater treatment plants.

In Figure B.72 shown below, the PFAS quantities (material flow) and PFAS emissions are presented for the different life cycle stages.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)



All material not lost directly to the environment will enter the waste stage through three main pathways: Waste generated during manufacturing, excess wax discarded during application, and unused ski wax in service life (i.e. because of date expiration).

Figure B.72. Material flow diagram for PFASs (all species) in ski-waxes for the European Union.

Active use of ski waxes is likely the most important life-cycle stage. To provide a higher level of disaggregation this stage is split into two sub-components based on a basic source-flow model that has been developed to make use of the data from the market analysis and substance identification:

- Emissions may occur during the application of ski-wax to skis/snowboards. This is potentially the single biggest point of release in the life-cycle. Based on consultation with industry, the efficiency of applying ski-wax to skis/snowboards for instance is relatively poor. The average of the values provided suggests that 80% of ski-wax applied is lost during the application process. This can occur both indoors and outdoors over snow. Further feedback suggests a significant proportion of lost material may be recaptured and consigned to waste (e.g. via vacuuming). Therefore, it is assumed that 80% is initially lost, with 40% (half) recaptured and consigned to waste and 40% (half) truly lost to the environment, with an equal split between water and land. The remaining 20% is retained on the skis/snowboard. The application life-cycle stage is estimated to emit 624 kg of PFASs to the environment annually (equivalent to 38% of the total quantity of PFASs used in ski-waxes per year).
- Secondly, after application there may be further losses during service life (i.e., skiing). It is assumed that, worst case, 100% of the wax applied is lost during this stage through

erosion of the wax with further emissions to air, water, and soil during active skiing. This amounts to 280 kg lost directly to the environment per year. In lieu of better data it is assumed 10% (approximately 30 kg) of the wax purchased is not used and enters the waste cycle (this is where the ski-wax bars are worn particularly thin, or liquid products are residue amounts in containers).

- All material not lost directly to the environment during formulation or use will enter the waste stage through three main pathways (i.e., wastes generated during formulation; excess wax discarded during application; and unused ski wax which has expired).

Figure B.72 and Table B.35 provide the results of the emission estimates, which highlights the main receiving environments to be equally shared between surface water and soil. This is based on the use of the ERC emission factors. In practice it could be expected that the main receiving environment is snow itself, which in due course (i.e., spring melts) will lead to contamination of surface waters and soil. Figure B.72 also highlights that of the 1 640 kg of PFASs (within ski-wax) used per year a total of 945 kg is lost to the environment (58% of the total used), primarily during application, and 728 kg/y enter the waste stage (equivalent to 44% of total PFASs used).

Table B.35. Estimated annual EEA emission in the ski wax sector of total PFASs in 2020 (baseline).

Compartment	Total PFASs (t/y)
Total volume	1.6
Emission to soil	0.452
Emission to surface water	0.452
Emission to air	0.041
Total emission	0.945

It should be noted that ski waxes account for only a small share of total PFAS use. As a consequence, ski waxes are most likely not very significant in terms of total environmental PFAS exposure. However, environmental exposure does occur when waxes are released during skiing onto the track where people are skiing. Stakeholder consultation highlighted contrasting opinions with respect to the amount of ski wax released to the environment during skiing, ranging from 1-5% (depending on the contact area between the ski and the snow and on the snow conditions) to 100% of the wax. One interviewee claimed, without providing evidence, that given the very small amounts of PFAS in the waxes it should be considered that the amounts of PFAS found in snow could come from other sources like air, the ski clothes, lubricants used in lifts and vehicles, or fire-fighting foams³⁴. However, a scientific study examining the presence of PFASs in soil, earthworms (*Eisenia fetida*), and bank voles (*Myodes glareolus*) from a skiing area in Trondheim, Norway, found long chain PFCAs at high concentrations, compared to the reference area with no skiing activities which was dominated instead by short-chained PFCAs (Gronnestad et al., 2019). on an outdoor recreation area with significant cross-country ski activity, found evidence of high levels of both long and short chain PFASs in the snow at the starting line of a ski race, with the longer-chain analytes (C10-C14) predominating. Importantly, the 14 PFASs detected in the snow matched what has been found in ski wax. PFAS levels diminished at around 4 km from the starting line, but soil and groundwater were also found to be contaminated with PFASs. The authors conclude that ski wax use, from which fluorocarbons abrade onto snow during a ski race, was the main source of PFAS contamination at that specific sampling site. The soil was contaminated by the same four dominant PFASs that were present in the snow samples, although at a lower concentration. Groundwater contained only short chain PFAS at low concentrations (Carlson and Tupper, 2020).

³⁴ Interview with FIS.

B.9.8.3. Human exposure

Direct human exposure to PFASs can occur when applying ski wax treatments, as the application often includes heating, melting, brushing and sanding of mixtures containing PFAS close to the airways, meaning users can be exposed to high concentrations of PFASs. Prior to application, the sole of the skis is usually cleaned with a liquid non-fluorinated base cleaner and a cloth.

To provide context about the potential magnitude of human exposure to PFASs from ski waxes, the **magnitude of the use** should be considered. About 21 t of PFAS-based waxes are produced per year in the EEA³⁵ (see Annex A section A.3.8.2.). It is expected that a similar quantity of PFAS-based ski waxes is currently used in the EEA, because they are mostly produced and used in the EU (interviewees suggested the EU accounts for some 60% of the global production and 70% of the global market³⁶). PFAS-based ski wax may contain up to 100% PFAS, although the concentrations depend on the formulation. However as noted previously, the reported concentration data only looks at a subset of PFAS substances for which analytical methods and standards are available and does not quantify total PFAS content or allow differentiation between those substances present in ski wax (including as impurities) or those actively used/added. The following input was received from stakeholders regarding the **potential for human exposure** to PFASs from ski waxes:

No specific information was provided regarding PFAS exposure during **production of ski waxes**, although producers suggested that the main potential for exposure is during application of the wax to the ski.

Prior to **application of ski wax to the ski**, the sole of the skis is usually cleaned with a liquid non-fluorinated base cleaner and a cloth. The high-end ski wax is then placed on the sole of the ski as a powder, melted with an iron and distributed evenly on the ski sole. Upon cooling the wax becomes solid again and much of the wax is removed from the ski base by scraping, and brushing, leaving a thin layer of wax on the ski sole. This has led to several concerns:

- The range between melting point and boiling point of the compound is very narrow, so fumes can be released even when the boiling point is not reached. As a result PFAS has been found in the blood of people applying ski wax. It should be noted however that emissions of fumes from the application of fluorine-free alternatives may also have health concerns.
- A proportion of the wax applied will fall to the floor.
- Scraping and brushing can lead to formation of dust that could be inhaled.
- Professional ski technicians use protection equipment to shield themselves from potential exposure, including gas masks, fume hoods, gloves and protective clothing. However, this is not as common for non-professionals.
- Often, especially with non-professionals, the contained wax is disposed of in general waste or even in the snow/outside, but some ski wax producers and EEA countries (e.g. Norway) have recommendations in place for waste wax to be disposed of by waste handling companies (e.g. through incineration).

Another formulation of PFAS-containing ski wax is as a liquid with the fluorinated ingredients as a suspension. Applications of these will result in much lower exposure as they do not require melting with an iron or the same level of scraping and brushing. The waste generated is also considerably less. However, the performance of liquid wax during skiing does not match the best powder waxes.

Interviews with ski wax manufacturers seemed to suggest that at least professionals applying ski waxes are expected to use the high-end powder wax, but there may be others (notably athletes at lower or amateur level competitions) that use the same. There have been studies

³⁵ Interview with Rodewax.

³⁶ Interviews with Rodewax and Swix.

which document a direct correlation between years exposed as a ski waxer and concentration of several different perfluoroalkyl carboxylate (PFCA) compounds in blood, with one study showing that Swedish wax technicians' median blood level of PFOA is 112 ng/mL compared to 2.5 ng/mL in the general population (Freberg et al., 2010; Nilsson et al., 2010b).

Recently, one of the main producers of ski wax, Swix, had a campaign where anyone (at least in Norway) could deliver fluorine-based ski wax from any manufacturer to Swix for safe waste handling. The customer was even awarded a €50 certificate for shopping in the Swix online store³⁷.

Starting from the ski wax producers, the potential number of workers through the supply chain and users of PFAS-based ski waxes is estimated in the following.

- **Producers of ski waxes:** According to interviews with some of the main ski wax producers, around 100-200 people are employed by at least 20-25 ski wax producers (many of which are small companies) in the EEA³⁸. This includes the production of both PFAS-based and fluorine-free ski waxes. Considering that most producers offer both, it is not possible to distinguish workers relating to only PFAS-based ski waxes.
- **Wholesale, distribution and retail:** No information on the number of workers in wholesale, distribution and retail of ski waxes was available. However, these workers are very unlikely to be directly exposed to PFAS-based ski waxes, because the waxes are packed during these supply chain stages. Hence their numbers of employees are less important in the context of this proposed restriction.
- **Application of waxes to skis:**
 - The total number of people involved in the waxing of skis with PFAS-based ski waxes is highly uncertain, because at lower or amateur level skiing competitions skiers will likely manage their equipment themselves (or their parents will, in the case of junior competitors). In some cases sports shops offer to wax skis as a service, but it is assumed that a minor part of skis are prepared in this way.
 - For higher level competitions, the number of professionals involved in applying PFAS based ski waxes can be estimated to be around a few hundred based on interviews with ski wax manufacturers .
- **End-users (skiers):** Exposure of both workers and skiers is negligible during the use-stage. However, from each skier a small amount of wax is released to the environment during use. PFAS-based ski waxes are mostly used during competitions. Competition skiers are then estimated to be in the order of 7 million at all levels in the EEA (tourist skiers hardly use PFAS wax). However, such estimate is based on uncertain assumptions so it should be considered as a rough indication of the potential order of magnitude only.

B.9.8.4. Summary

PFAS emissions from ski wax were calculated for the manufacturing and use stages (during application and emission during service life). Total emissions were estimated to be 0.945 t/y for 2020. Around 58% of the the total quantity of PFASs used in the manufacture of ski waxes are emitted into the environment, while 44% goes to waste. Direct human exposure to PFAS can occur when applying ski wax treatments. A direct correlation between years exposed as a ski waxer and concentration of several different perfluoroalkyl carboxylate (PFCA) compounds in blood have been reported in literature. It is not clear how many people are actually involved in the waxing of skis with PFAS-based ski waxes. For higher level competitions this is estimated to be a few hundreds, while a higher number of active amateurs are usually waxing their own skis, with varying level of protective equipment.

³⁷ <https://www.swixsport.com/no/kampanjer/fluorfri/>, date of access: 2022-12-14.

³⁸ Interviews with Rodewax and Swix.

B.9.9. Applications of fluorinated gases

B.9.9.1. Introduction

The use of fluorinated gases in the HVACR sector is described in Annex A.

B.9.9.2. Emissions

Data on emissions of fluorinated gases from different applications have primarily been collected from the GHG Inventory data, estimated on the basis of UN methodology (EEA, 2022). It is to be noted that the GHG Inventory data include HFCs and PFCs, while HFOs, HFEs, fluoroketones etc. are not considered. The same methodology was used for use volume estimates and additional details on the information sources may be found in Section A.3.9.2. Based on market volumes, HFOs are increasing and currently constitute 24% of the market of fluorinated gases, the other subgroups are expected to be of limited volumes. Emissions can be assumed to follow a similar trend. Estimates for HFO emissions have been derived by combining market volumes from the F-gas report and implied emission factors (IEF) derived from the GHG Inventory based on data for market volumes and emissions for HFCs in similar applications. Stock emissions are to be understood as emissions from products and equipment currently in service life.

Appendix IV shows the estimated total emissions of fluorinated gases from the different sub-applications. The estimates are based on the GHG Inventory data and are limited to the substances reported there (HFCs and PFCs, which constitute the major part of the fluorinated gas uses and emissions). However, they do not include volumes of e.g. HFOs which is an emerging fluorinated gas subgroup. All emissions are to air. Emissions are disaggregated at the subapplication level and not on the substance level.

Appendix V compares the activity data and emission estimates for fluorinated gases in 2018. Emissions from manufacturing, as well as emissions from the use stage, are included. For comparative purposes, manufacturing and stock emissions as a proportion of the total emissions have been calculated and presented. These figures are calculated as follows: Tonnes of fluorinated gas emitted (single application)/Total tonnes fluorinated gas emitted (all applications) x 100.

From the GHG Inventory data it is apparent that the emissions during the manufacturing of products and equipment is generally low, between 0 – 3% of the fluorinated gases used for all activities other than foam blowing. By contrast emissions from stocks are significantly higher as would generally be expected and are in the range 0 – 13% for all activities other than aerosol use. Commercial and industrial refrigeration, mobile and stationary air conditioning accounting for 82% of the total emissions from stocks. Figure B.73 below shows the emissions of HFCs/PFCs from the different applications with basis in the GHG Inventory data.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

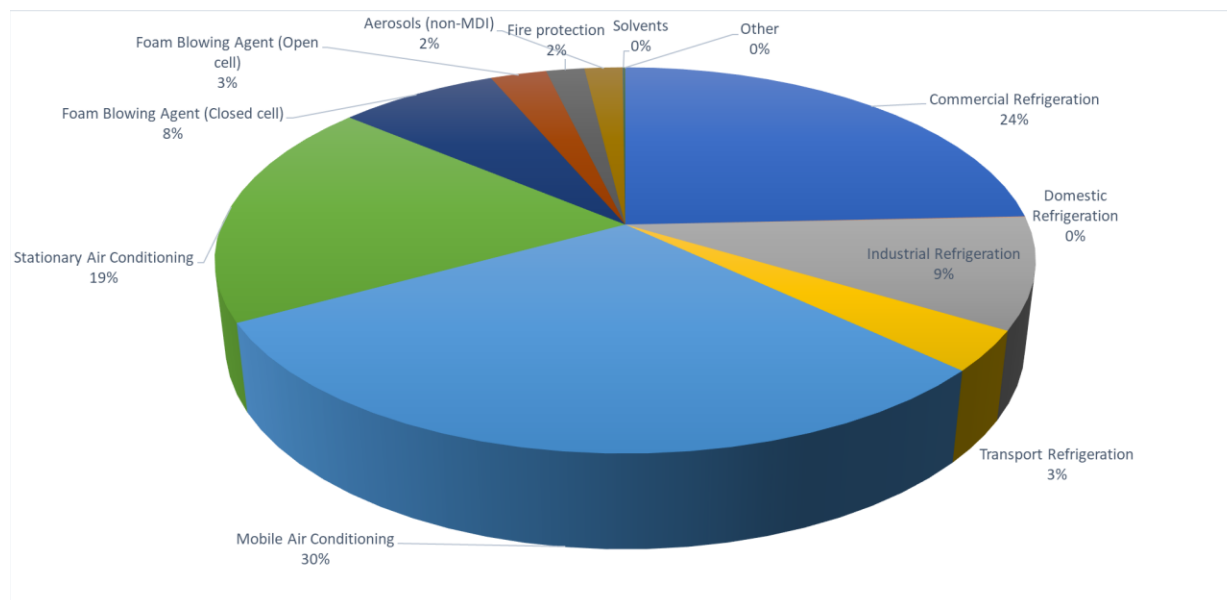


Figure B.73. Emissions of fluorinated gases from stocks 2018. Source EEA (2022).

For open cell foams, foam blowing agents are almost entirely released at initial use and therefore it is expected that after the initial use there would be very low emissions from stocks since there are very little if any left in the stocks. With regards to closed cell foam stakeholder discussions in this assessment indicate generally fluorinated gases remain locked up in the foam until decommissioning and losses from stocks would be of the order of 1% per year.

In total, the emissions of fluorinated gases in 2018 (HFOs excluded) from the different uses were as follows:

Manufacturing of products and equipment:	1 696 t/y
Stocks (i.e., service-life):	38 806 t/y

For comparison, Öko-Recherche developed an estimate on behalf of the German Environment Agency for the total fluorinated gas emissions (HFCs and HFOs) at ca. 60 000 t/y for 2020 (UBA, 2021c). The estimate was based on modelling with the AnaFgas model which projects the demand and emissions of fluorinated greenhouse gases in the EU in various scenarios. The model is based on market data and estimates of the annual sales of equipment containing these substances and the number of substances needed to manufacture and/or maintain appliances within the EU. Emissions from stationary air conditioning was estimated at 12 193 t/y in 2020 by UBA, which is higher than 7 458 t/y for stationary air conditioning and heat pumps that is estimated in the present assessment based on the GHG Inventory data (HFCs only, 2018).

Industry stakeholders have underlined the importance of hydrofluoroolefins (HFOs) and fluoroketone (FK) alternatives during the development of this dossier. Primarily this is because in several applications they can substitute the function provided by other fluorinated gases alone or in blends, whilst at the same time having significantly lower global warming potential (GWP). The GHG Inventory data contains emission estimates, but does not include HFOs and FKs. On the other hand, the F-gas report includes HFOs (no data on FKs), but emissions are not estimated. In the market section it was estimated that the HFOs/HCFs currently constitutes 24% of the market of fluorinated gases. The majority of HFOs/HCFs currently being used commercially as a single substance (rather than a blend) are in mobile air conditioning (MAC) systems for passenger cars and in light goods vehicles and commercial refrigeration, commercial air conditioning, heat pumps and process cooling.

Figure B.74 below shows the projected demand and emissions of fluorinated gases (HFCs and

HFOs) for various applications modelled with the AnaFgas model and as presented by Öko-Recherche (UBA, 2021c).

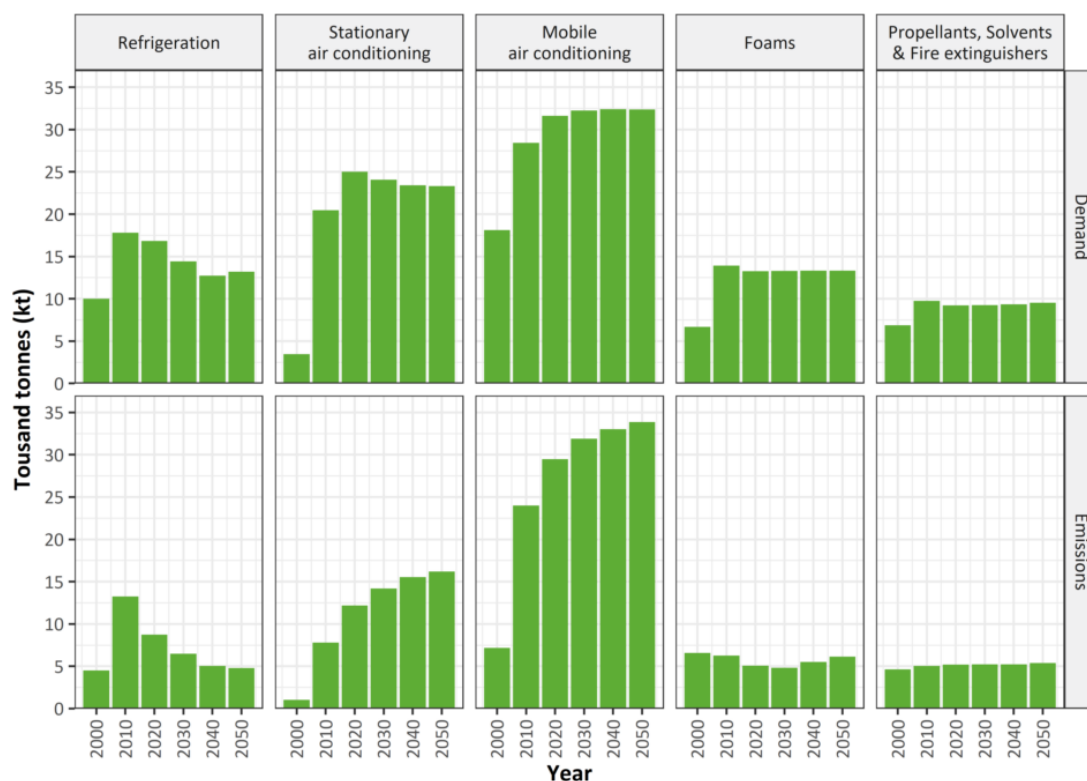


Figure B.74. Quantity of projected demand and emissions of sum HFCs/HCFCs and HFOs/HCFOs in Europe (EU-28) in metric kilotonnes (kt) in the years 2000 to 2050 in 10-year increments by sector, from UBA (2021c).

B.9.9.2.1. Estimated emissions from mobile air conditioning (MAC)

Emissions from mobile air conditioning have been looked at in more detail as this is a sector with large uses and emissions. A key change in the sector is the transition from HFC-134a as the main refrigerant to HFO-1234yf which is accompanied by a large reduction in climate impact as the GWP is much lower for the latter (GWP 1 430 vs. 4). As HFOs are not reported in the GHG Inventory, emissions from MAC are largely underestimated if HFOs (i.e. HFO-1234yf) are not taken into consideration.

The Dossier Submitters estimated overall emissions of fluorinated gases from MAC with basis in GHG Inventory data uses the annual emissions of HFCs and PFCs from MAC technical stocks as a starting point: 11 648 t, see Table B.36.

EC Directive 2006/40/EC on MAC required all new passenger cars (and light goods vehicles) from 1 January 2017 to be filled with a refrigerant with a global warming potential (GWP) no more than 150. As a result, almost 100% of new cars after this date use HFO-1234yf refrigerant instead of HFC-134a (EFCTC, 2022). However, the requirements in the MAC Directive were introduced gradually, so the change from HFC to HFOs had started even before 2017.

Data for 2017 – 2018 demonstrates that approximately 30 million new passenger cars are introduced in EU-28 each year, which equates to approximately 11% of the total number of

passenger cars of 271.5 million³⁹.

In 2018, due to the MAC Directive, one year of vehicles with HFO-refrigerants had been introduced on the market (= 11%), in addition to the fraction that had already entered the market due to the gradual phase-in of the MAC Directive requirements, assumed at 9%. Hence, a total of 11%+9%=20% of the vehicles in 2018 are estimated to contain HFO refrigerants.

While 20% of vehicles in the EU in 2018 used HFO-refrigerants, the remaining 80% used HFC-refrigerants, corresponding to emissions of 11 648 t according to the GHG Inventory and Table B.36 below. Assuming a similar emission rate, HFO emissions in 2018 would amount to 2 912 t. In total, fluorinated gas emissions from MAC in 2018 would then be 11 648 t (HFCs)+2 912 t (HFOs)=14 560 t (fluorinated gases).

The 30 million new passenger cars (=to 11% of the total number) put on the market each year, all with HFO-refrigerants, would then correspond to 1 602 t of HFO emissions with basis in 2018 numbers, see Table B.36.

Table B.36. Estimates of total emissions of fluorinated gases from MAC (2018), in tonnes per year.

	HFCs (t/y)	HFOs (t/y)	Fluorinated gases total (t/y)
Stocks total volume			493 173
Stocks total emission	11 648	2 912	14 560
New use total volume			30 671
New use total emission	0	1 602	1 602

The fraction of cars with HFO-refrigerant in the total technical stock of fluorinated gases in MAC will gradually increase with time until HFC refrigerants have been phased out in essentially all new vehicles.

Figure B.75 is copied from the EEA F-gas report in 2021 and provides information on the amounts of HFCs and HFOs imported in mobile air condition equipment since 2014. The figure below confirms that HFOs were gradually phased in before 2017. However, as explained previously, it is likely that the import of HFOs in vehicles is under-reported due to the high reporting threshold.

³⁹ <https://www.acea.be/statistics/tag/category/key-figures>, date of access: 2022-05-19.

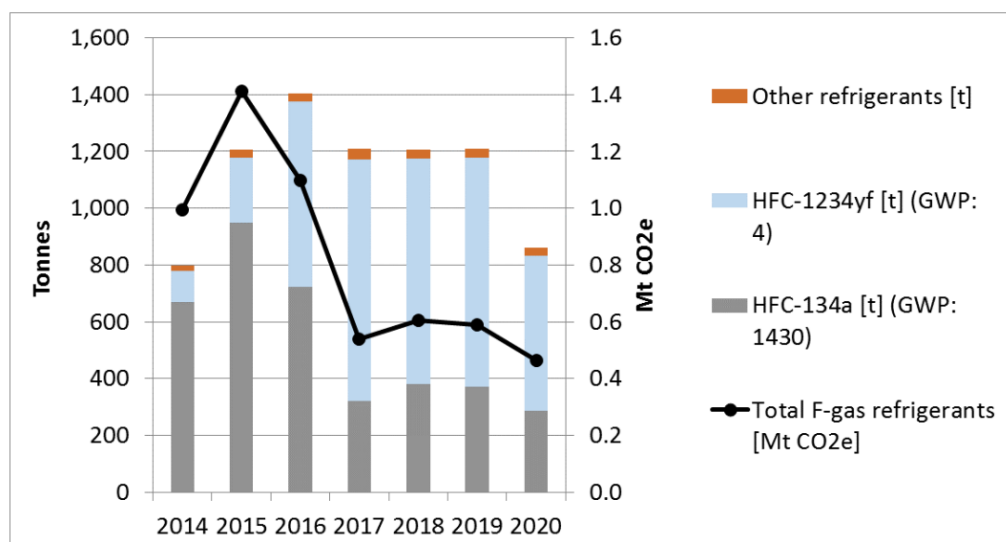


Figure B.75. EU imports of fluorinated-gases within air-conditioning equipment for vehicles EU-27 + UK, from EEA (2021).

An alternative approach to estimate emissions of fluorinated gases from MAC starts with the number of vehicles in the EU/EEA (243 million passenger cars, 34 million trucks and vans and 690.000 buses)³⁹ and the amount of fluorinated gases used in AC in each vehicle category (0.6 kg in cars, 1 kg in trucks/vans and 6 kg in buses). Furthermore, a leakage rate of 1.67-5%⁴⁰ is assumed. A total fluorinated gas emission from MAC could then be estimated at ca. 3 073 t/y – 9 200 t/y. This estimate is somewhat lower compared to the estimate derived from the GHG Inventory. Noting that in the GHG Inventory, an emission factor of 9.94 has been used, the difference is not dramatic.

For comparison, the estimate developed by Öko-Recherche for total emissions of fluorinated gases from MAC for 2020 was 29 466 t based on the AnaFgas model (UBA, 2021c). A 15% overall increase in emissions was estimated from 2020 to 2050.

The estimate of 14 560 t total emissions of fluorinated gases from MAC with a basis in GHG Inventory data is taken as the main estimate of fluorinated gases from mobile air conditioning in this assessment. Two alternative approaches to the same estimate were explored for comparison, one giving a lower and the other giving a higher emission volume from this sector.

The estimated total emissions of fluorinated gases from the different sub-applications are presented in Table B.37.

⁴⁰ 1.67% is based on stakeholder information. 5% represents ERC 9b Widespread use of functional fluid (outdoor).

Table B.37. Estimated total emissions of HFCs and PFCs from the different sub-applications (in t/y).

	Total fluorinated gases [t/y]		% HVACR emission from total all fluorinated gas applications (separate % for manufactured products and stocks)
		High	
Total, all applications	Manufactured Products	1 696	100
	Stocks	38 806	100
Commercial refrigeration	Manufactured products	121	7
	Stocks	9 426	24
Domestic refrigeration	Manufactured products	1	0
	Stocks	16	0
Industrial refrigeration	Manufactured products	77	5
	Stocks	3 603	9
Transport refrigeration	Manufactured products	29	2
	Stocks	1 312	3
Mobile air conditioning	Manufactured products	78	5
	Stocks	11 648	30
Stationary air conditioning	Manufactured products	47	3
	Stocks	7 411	19
Foam Blowing Agent (Closed cell)	Manufactured Products	1 272	75
	Stocks	2 914	8
Foam Blowing Agent (Open cell)	Manufactured Products	45	3
	Stocks	1 029	3
Fire suppressing Agents	Manufactured Products	1	0
	Stocks	702	2
Propellants (non-MDI)	Manufactured Products	2	0
	Stocks	699	2
Solvents	Manufactured Products	No data	No data
	Stocks	11	0
Cover gas	Manufactured Products	23	1
	Stocks	No data	No data
Other	Manufactured Products	0	0
	Stocks	35	0

B.9.9.3. Human exposure

Worker exposures to fluorinated gases in plants manufacturing equipment or putting the gases into a product should be small, given the need to use closed systems (mentioned by many respondents to the CfE). Outside of the manufacturing plant, however, there may be greater exposure of workers, for example during service and at sites reclaiming refrigeration equipment at the end of its service life and in case of accidental emissions.

B.9.9.4. Summary

Emissions of HFCs and PFCs from HVACR and other applications of fluorinated gases are estimated to be 1 696 t/y for manufactured products and 38 806 t/y for products and equipment in service. Emissions from the sector were estimated using GHG Inventory data and data from the F-gas report (i.e. data reported under the climate convention and F-gas regulation). HFOs represent an emerging subclass of fluorinated refrigerants that have increased from 6% to 24% of total volumes of fluorinated gases from 2016 to 2019. In mobile air conditioning (MAC) HFOs represent a considerable fraction of the refrigerants, and estimates based solely on HFC/PFC data will be an underestimate. The overall emissions of fluorinated gases in MAC was estimated at 14 560 t/y for 2018 (11 648 t/y HFC+2 912 t/y HFO), and the HFO/HFC ratio is gradually increasing as HFO-1234yf is introduced as a substitute for HFCs with higher GWP. Worker exposures to fluorinated gases in manufacturing sites is expected to be limited (e.g. due to closed systems), however for workers outside the manufacturing plant exposure is expected to be higher (e.g. during service and at sites reclaiming refrigeration equipment).

B.9.10. Medical devices

B.9.10.1. Introduction

Medical devices are regulated under EU Regulation 2017/745 and are, generally speaking, instruments, materials, reagents or other articles intended for diagnosis, prevention, monitoring or treatment of diseases in human beings (see for the full definition the EU Regulation). The use of PFASs in medical devices is described in Annex A.

B.9.10.2. Emission

Production of medical devices requires a high degree of cleanliness, purity, chemical stability and thermal resistance. PFAS are therefore already used in medical device production processes. Emissions from these processes are not taken into account here as information is lacking.

In Table B.38, an overview of PFAS volumes and estimated emissions is given for the medical sector. Fluoropolymers in medical applications generally have a low emission profile during use. The highest emissions are from the MDI propellant. Their arrowheads are mainly TFA and/or other PFAAs. 1,1-difluoroethane (HFC-152a) is an exemption: this substance is not in the chemical scope of the proposed PFASs restriction.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.38. Estimated annual EEA emissions in the medical devices sector of PFAA and PFAA precursors, fluorinated gases, polymeric PFASs and total PFASs in 2020 (baseline).

	PFAAs and PFAA precursors (t/y)		Fluorinated gases (t/y)		Fluoro polymers (t/y)		Total PFASs (t/y)	
	low	high	low	high	low	high	low	high
<i>Total volume for all medical use categories</i>	1 279	3 495	20 160	46 000	3 233	12 032	24 672	61 527
Emission	128	350	MDI: 144 Other: 1 000 TOTAL: 1 144	MDI: 5 400 Other: 2 000 TOTAL: 7 400	32	120	3 932	7 870 Median: 5 901

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Emission factors were based on consultant expertise, not on ERCs for this use:

- 90% for (MDI) propellants and 5% for non propellant use of fluorinated gases;
- 10% for non-polymer PFAS in industrial processes (heat transfer agents, specialty cleaners, and end-products) and
- 1% for PFAS polymers (by wear and tear). This is lower than ERC 11a but for wear and tear indoors in a medical setting 1% seems more realistic.

Regarding MDIs, a distinction should be made between MDI used by patients and the production stage. The emission factor of propellants by MDI use is high (70-100%) whereas the emission factor of propellants during production is much lower, probably <10%. Production phase emissions were not taken into account.

An uncertainty factor of at least 2 is applicable.

Not all MDIs are (completely) used before they are disposed of. According to a stakeholder, about 30% of fluorinated gases remain in the MDI after proper use. A stakeholder mentioned that unused propellant is captured and sent back to the original supplier of the propellant. The amount recycled at one EU site ranges from 30 to 40 t and the amount recycled at the other EU site ranges from 100 to 150 t. Another stakeholder mentioned that separate collection of MDIs was highly unsuccessful. If the return, recovery and/or destruction rates increase, the specific emission value might be reduced in future.

Polymeric PFASs emission in the use stage are likely very low, therefore these mostly reach the waste stage, which is described in section B.9.18.

B.9.10.3. Human exposure

In general, human exposure to emissions coming from medical devices is considered to be low. Some remarks made by stakeholders regarding exposure:

- It is unlikely that polymeric PFASs will be released from the devices during their lifetime because PFAS polymers tear and wear is limited during (human) lifetime.
- During normal use PTFE articles will not pose harm to human health and are not expected to deteriorate during their use. It is only during the waste stage where PFAS could be released to the environment.
- Regarding applications of PFAS fluids in medical devices, including solvent cleaning, carrier solvent and heat transfer, these products can be emitted to the air during use.
- When used in industrial applications like lubricant and coating deposition and precision cleaning, workers are typically exposed to solvent vapor during their shifts, which is why determining acceptable exposure limits is a critical factor in selecting process solvents.

For MDI use the exposure to fluorinated gases is high.

B.9.10.4. Summary

PFASs emission from medical devices was calculated using emission factors; emission from the use phase of medical devices only is estimated from 4 000 to 8 000 t/y (rounded numbers). The emission profile of medical devices is generally low, most notable is emission of fluorinated gases during the use stage of MDIs. MDIs causes significant human exposure to PFASs. Emissions from the manufacturing of medical devices have not been taken into account as information is lacking.

B.9.11. Transport

B.9.11.1. Introduction

The use of PFASs in the transport sector is described in Annex A.3.11.

B.9.11.2. Emissions

Information that can be used to estimate emissions in the transport sector was only available for fluorinated gases and polymeric PFASs. The emission of fluorinated gases is described in B.9.9.2.

B.9.11.2.1. Fluoropolymers (e.g. applied in coatings and finishes or sealing applications)

Since information was only available on volumes used in the automotive sector (Annex A. 3.11.) no estimates were made for the other sectors.

To estimate emissions of polymeric PFASs, it is assumed, that they can be released from transportation vehicles through wear processes, e.g. abrasion or erosion. The stronger the various effecting factors that are described below are, the higher the wear rates.

It is likely that indoors (e.g. in the passenger compartment) wear rates are lower than those outdoor and in parts that are subject to harsh conditions (e.g. in the engine bay area) wear rates are higher. However, because of a lack of data it is not possible to make a precise distinction between indoors and outdoors nor between different conditions. Therefore, it is assumed that emissions of FPs in automotive applications occur indoors and outdoors, each with a share of 50%.

Emissions were estimated based on ERC and the volume of polymeric PFASs in road transportation vehicles. In Annex A.3.11.2.4., the lower estimate for polymeric PFASs in cars is 0.35 kg (Améduri, 2020) and the higher estimate is 0.8 kg (stakeholder information). These estimates, together with information on the number of road transportation vehicles registered in the EU in 2019 (277 759 682 sum of all personal vehicles, trucks and busses) (ACEA, 2020), were used to estimate the total amount of polymeric PFASs emitted from road transportation vehicles. The average service life of road transportation vehicles is assumed to be 11.95 years (ACEA, 2021). Details on calculations of emissions are included in Appendix B.9.11. Total emission estimates are provided in Table B.39.

B.9.11.2.2. HVACR systems in transportation vehicles and HVACR-systems for transport refrigeration

Estimations on the emissions of fluorinated gases from HVACR systems in transportation vehicles and transport refrigeration are presented in section B.9.9.2.

Stakeholders did not provide information on emissions of fluorinated gases from HVACR-systems in ships trains and aircrafts.

Table B.39. Estimated annual EEA emissions in transportation products and articles of PFAA and PFAA precursors (+ other PFASs), fluorinated gases, polymeric PFASs and total PFASs in 2020 (baseline) (t/y).

	Total fluorinated gases (t/y)	Total polymeric PFASs (t/y)		Total PFASs (t/y)	
		Low	High	Low	High
Total volume	13 232	6 410	14 652	19 642	27 884
Total emission		269	609	269 + amount reported under section B.9.9.2	609 + amount reported under section B.9.9.2
Road transportation vehicles		269	609	269	609
HVACR-systems in transportation	See section B.9.9.2	See section B.9.9.2		See section B.9.9.2	See section B.9.9.2

It is important to note that the emissions presented in Table B.39 are very likely a significant underestimation as tonnages (and therefore also emissions) from PFAS use in ships, trains and aircrafts are missing due to a lack of information.

B.9.11.3. Human exposure

Polymeric PFASs which make up the greatest share of PFASs used in the transportation sector are considered to be stable up to 300 °C. Therefore, exposure of workers or consumers is assumed to be low during the service life of transportation vehicles. During production, or end of life, other conditions can apply that may lead to an exposure.

B.9.11.4. Summary

Emissions from the transportation sector were calculated using ERC. Total emissions of polymeric PFASs amount to between 269-609 t/y. Most emissions likely occur in the production stage or during end of life. Only qualitative information is available on exposure of workers and consumers. Stakeholders believe exposure is limited because of stability of PFASs up to 300 °C.

B.9.12. Electronics and semiconductors

B.9.12.1. Introduction

The use of PFASs in the Electronics and Semiconductors industries is described in Annex A. 3.12.

B.9.12.2. Emissions

Emissions were calculated for the different life-cycle stages. Because of uncertainties in the estimated volumes and many unspecified actual and patented uses, an emission calculation per substance is not possible. Instead, an approach was used with default emission factors corresponding to different emissions scenarios described by ECHA. Default release factors from the REACH environmental release categories (ERC) were used in the emission characterisation. Estimates of product service-life emission to the environment were derived using the latest version of the standard REACH methodology (ECHA, 2016a).

Emissions were calculated for combined values of soil, water and air.

The following life cycle stages are considered in the assessment:

- Production
The manufacturers included in this section are mainly companies that specialise in modifying or combining raw materials to create new products.
- Use
In this stage all PFASs that are produced in the production stage are assumed to enter the use stage, except for the solvents (non-ionic non-polymeric PFASs).

There are regulations for the collection and handling of e-Waste e.g. the WEEE directive and part of the used electronic devices is incinerated or exported to low-income countries. Waste stage emission are included in section 0.

For emission calculations, a distinction is made between polymeric PFASs and non-polymeric PFASs. Polymeric PFASs include fluoropolymers and perfluoropolyethers, and non-polymeric PFASs include side-chain fluorinated polymers and ionic and non-ionic PFASs. This is done because the various PFASs groups differ in their uses and emission pathways.

According to stakeholders, the following uses are most common:

1. Fluoropolymers are generally used in or on articles and form a solid matrix.
2. Perfluoropolyethers are usually applied as oils or waxes, meant to treat surfaces, but they can also contain one or more functional groups which make them able to bond to substrates or be useful as crosslinkers.
3. Side-chain fluorinated polymers are generally used in or on articles and form a solid matrix.
4. Non-polymeric PFASs are smaller molecules and are mostly used as processing aids, solvents, cleaning liquids, surfactants, coatings and heat transfer fluids.

Environmental release categories (ERC), that describe the use of PFASs most closely including release factors were assigned to the production and use stages. A detailed description on emission calculations using volumes in Annex A.3.12., ERC, release factors and calculation factors, as well as a justification for the choices made, is included in Appendix B.9.12. The emissions are summarised in Table B.40. The emissions in Table B.40 are rounded values as it is estimates based on stakeholder information. Therefore, values may slightly differ when calculating emissions from the use stage and production stage compared to the total emissions.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.40. Estimated annual EEA emissions in electronics and semiconductor sectors of PFAA and PFAA precursors, fluorinated gases, polymeric PFASs and total PFASs in 2020 (baseline).

	C2- C3 PFAS substances (t/y)		PFAA ≥C4 (t/y)		Side-chain fluorinated polymers (t/y)		PFAAs and PFAA precursors		Fluorinated gases (t/y)		Fluoro polymers (t/y)		PFPE (t/y)		Polymeric PFASs (t/y)		Total PFASs (t/y)	
	low	high	low	high	low	high	low	high	low	high	low	high	low	high	low	high	low	high
Total volume	159	221	671	1 315	11	13	841	1 549	140	140	1 551	4 063	9	552	1 560	4 615	2 541	6 304
Production stage	8	11	335	658	5	7	348	676	7	7	5	12	4	276	9	288	364	971
Use stage	0	0	0.3	1	0.005	0.007	0.3	1	0	0	2	4	0.004	0.3	2	4	2	5
Total emission	8	11	335	659	5	7	348	677	7	7	7	16	4	276	11	292	366	976

B.9.12.3. Human exposure

Stakeholders indicate that exposure levels of workers are low. Instructions on safe handling and minimisation of release are included in the technical data sheet and safety data sheets (SDS). Industrially, frequent handling of parts may cause skin exposure. According to industry, the use of filters, personal protective equipment, clean rooms and closed systems, as well as training, leakage tests, and frequent servicing, contribute to minimising exposure of workers.

Some stakeholders stated that their applications of PTFE cause no emissions, but rather serve to protect humans and environment from dangerous media. An example is the protection against acids in the semiconductor industry.

PFAS-based solvents are used to clean electronic components. This is commonly done in special sealed equipment where solvents can be recovered and reused. According to a stakeholder, exposure during the application of solvent is expected to be low, as the safety margin for PFASs solvents is higher than in non PFASs solvents. The stakeholder stated that it is important to establish acceptable exposure limits and set a standard for personal protection.

Stakeholders stated that in parts used in electronics devices, like gaskets, tubes and membranes, the fluoropolymers and elastomers are utilised in a bound state (and stable at up to 300 °C), and therefore human exposure is hardly possible.

According to industry, microelectromechanical systems device manufacturing is highly automated and takes place in a closed system in a clean room environment. It is designed in such a way that there is minimal potential for human contact. For some of the processes exhaust hoods are used, and equipment in the manufacturing process has internal cold trap filters that remove more than 99% from the exhaust stream.

The semiconductor industry has, according to industry, implemented stringent risk management measures and safety practices to prevent the release of chemicals during all stages of the manufacturing process. According to stakeholders there is no release to the workplace environment during normal production due to closed system manufacturing equipment, which is installed in a cleanroom environment. Automated chemical delivery systems create a barrier between workers and the manufacturing process and protect against chemical and physical hazards. The stakeholders also stated that emission of gaseous PFASs in the exhaust gas of the manufacturing equipment can be almost completely eliminated by incineration.

A lot of electronics are produced outside EEA. Certain regulations are in place to manage and minimise emissions/exposure, although the Industrial Emission Directive seems to be not applicable for this Industry. A stakeholder commented that relevant regulations include the General Product Safety Directive 2001/95/EC and the F-Gas Regulation (EU) No 517/2014. Additionally, standards such as ISO 9001, ISO 14001, ISO 45001 are used to minimize release and ensure safety. Lastly, it is important to notice, that multiple stakeholders stated that there is no release from multiple uses, but release may differ based on the use and knowledge on the material. A stakeholder mentioned that their supplier stated that no protective measures need to be taken when coated metal products and solid components made of fluoropolymers or fluoroelastomers are used as intended.

B.9.12.4. Summary

Emissions from the electronics and semiconductor sectors in the production and use stages were calculated using ERC. Total emissions of non-polymeric PFASs (including side-chain polymers) amount to between 300 and 700 t/y (rounded numbers), of polymeric PFASs to between 10 and 300 t/y (rounded numbers) and of fluorinated gases to 7 t/y. Almost all emissions occur in the production stage. Only qualitative information is available on exposure of workers and consumers. Stakeholders generally believe exposure is limited because of the use of closed systems, filters, PPE and training of workers.

B.9.13. Energy

B.9.13.1. Introduction

The use of PFASs in the energy industry is described in Annex A.3.13.

B.9.13.2. Emissions

Emissions were calculated for different stages in the life cycle of PFASs. Because uncertainties in the estimated volumes and many unspecified actual and patented uses, an accurate emission calculation per substance is not possible. Instead, an approach was used with default emission factors corresponding to different emissions scenarios described by REACH (ECHA, 2016a). Emissions are estimated based on combined values for soil, water and air. Each stage in the life cycle of a product has a different likelihood of emissions.

The following life-stages are considered in the assessment:

- Production
The industry that produces PFASs from raw materials is included in section B.9.2. The manufacturers included in this section are mainly companies that specialise in modifying or combining raw materials to create new products.
- Use (service life)
Most uses of PFASs in the energy sector are industrial or professional

There are Regulations for the collection and handling of e-waste e.g. the WEEE directive and the Battery directive. Waste stage emission are included in section B.9.18.

According to responses from stakeholders, the following applications are most common:

1. Fluoropolymers are generally used in or on articles and form a solid matrix.
2. Perfluoropolyethers are usually applied as oils or waxes meant to treat surfaces but they can also contain one or more functional groups which enable them to bond to substrates or be useful as crosslinkers
3. Side-chain fluorinated polymers are generally used in or on articles and form a solid matrix
4. The non-polymeric PFASs are smaller molecules and are used for applications such as cleaning agents for precision cleaning and insulation gas in switchgear in the energy sector.

Environmental release categories (ERC), that describe the use of PFASs most closely including release factors were assigned to the production and use stages. A detailed description on emission calculations using volumes in Annex A.3.13., ERC, release factors and calculation factors, as well as a justification for the choices made, is included in Appendix B.9.13.. The emissions are summarised in Table B.41.

The emissions in Table B.41 are rounded values as it are estimates based on stakeholder information. Therefore, values may slightly differ when calculating emissions from the use stage and production stage compared with the total emissions.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.41. Estimated annual EEA emissions in the energy sector of PFAA and PFAA precursors, fluorinated gases, polymeric PFASs and total PFASs in 2020 (baseline).

	C2- C3 PFAS substances (t/y)		PFAA ≥C4 (t/y)		Side-chain fluorinated polymers (t/y)		PFAAs and PFAA precursors (t/y)		Fluoropolymers (t/y)		PFPE (t/y)		Polymeric PFASs (t/y)		Total PFASs (t/y)	
	low	high	low	high	low	high	low	high	low	high	low	high	low	high	low	high
Total volume	233	233	20	20	40	41	293	294	2 590	2 917	2	3	2 592	2 920	2 884	3 214
Production stage	12	12	10	10	20	21	42	42	8	9	1	2	9	10	50	53
Use stage	0.00	0.00	0.01	0.01	0.02	0.02	0.03	0.03	2	3	0	0	3	3	3	3
Total emission	12	12	10	10	20	21	42	42	10	12	1	2	12	13	53	56

B.9.13.3. Human exposure

Stakeholders indicated that exposure levels of workers in the energy sector are low. Instructions on safe handling and minimisation of release are included in the technical data sheet and safety data sheets (SDS). Industrially, frequent handling of parts may cause skin exposure. In multiple cases, fluoropolymers and elastomers are utilised in a bound state (and stable at up to 300 °C) and do therefore barely contribute to human exposure. The use of filters, personal protective equipment, clean rooms and closed systems, as well as training, leakage tests, and frequent servicing, contribute to minimising exposure of workers.

Stakeholders stated that Proton Exchange Membrane (PEM) fuel cells and PEM electrolyser are usually operated at low temperature of 40-90 °C. Studies into these fuel cells are conducted at 200-400 °C and prove that e.g. Nafion ionomers will not degrade at operating temperatures. Additionally, stakeholders mentioned that they have no knowledge on human or environmental exposure during operation of gas diffusion layers in fuel cells or electrolyzers.

According to stakeholders, human exposure to PFASs in batteries can only occur during the manufacturing and recycling stages. No release of or exposure to PFASs is expected during use. One stakeholder commented that due to the presence of (other) hazardous substances (metal salts and oxides used for electrodes) in batteries, safety measures are in place, both for the environment as well as for workers. Since waste batteries are recycled in accordance with the Battery Directive 2006/66/EC PFASs are, according to stakeholders, not released into the environment.

For medium voltage switchgear, a stakeholder mentioned that PFAS insulation gases are always used in closed loop systems. Leakage rates are small (<0.1% annually, <5% over the full device lifetime; according to the standard IEC 62271-200) because of the use of leak-tight compartments (Dansk Standard (DS), 2021). The stakeholder further stated that human exposure is at 0.002 x the exposure limits when assuming a leakage rate of 1% per year (IEC 62271-4 ed.2) (Dansk Standard (DS), 2022). In high-voltage equipment, gas-insulated switchgear needs to be extremely gas-tight. In DIN EN IEC 62271-203 (and linked standards), requirements for emission reducing measures and designs for Switchgear technologies is described. According to stakeholders, the use of such standards, will ensure minimal human exposure to polymeric PFASs or lubricants containing PFASs, under normal conditions.

B.9.13.4. Summary

Emissions from the energy sector in the production and use stages were calculated using ERC. Total emissions of non-polymeric PFASs (including side-chain polymers) amount 42 t/y (rounded number) and total emissions of polymeric PFASs amount to 13 t/y (rounded number). Almost all emissions occur in the production stage. Only qualitative information is available on exposure of workers and consumers. Stakeholders generally believe exposure is limited because of the use of closed systems, filters, PPE and training of workers.

B.9.14. Construction products

B.9.14.1. Introduction

The use of PFASs in building materials/construction products is described in Annex A.3.14. For emission estimations, the PFASs used in construction products are divided into polymeric PFASs and non-polymeric PFASs

The polymeric PFASs that are included in the emissions estimate are:

- PTFE (polytetrafluoroethylene)
- ETFE (ethylene tetrafluoroethylene)
- PVDF (polyvinylidene fluoride)
- Other fluoropolymer substances (including the fluoroelastomers FKM, FFKM and THV)
- Side chain fluorinated polymers

The first three substances (fluoropolymers) account for 97% of the reported total usage of polymeric PFASs in the construction sector while the latter two covers 3% of the usage.

It should be noted that for the emission estimation, side-chain fluorinated polymers are considered to be PFAA precursors.

B.9.14.2. Emissions

The PFASs and uses identified and included in Annex A.3.14. broadly cover one of the following three major categories:

1. **Articles.** In many cases the articles produced (such as architectural membranes) are 100% fluoropolymer manufactured through extrusion as a hot or cold process. Extruded fluoropolymer can also be manipulated or woven to form meshes, tapes, or other thin film technologies for use across a very wide range of applications.
2. **Processing aids.** Non-polymeric PFASs are used as processing aid in the manufacturing of articles. PFASs are used as a processing aid (PA) in the production of these products but are not retained (intentionally) within the final products. Polymer processing aids (PPAs), used to produce thermoplastics, thermosetting plastics and elastomers, are included in the resin and therefore becomes a part of the final article.
3. **Construction mixtures.** This category covers blended liquid mixtures which are either 100% PFASs or more commonly where PFASs is added to tailor the physical properties of the mixture or the final article to which it is added. A good example here are paints, where PFASs can be added as a surfactant to aid spreading and levelling within specialised applications.

Four basic life-cycle stages are considered in which emissions may occur, or from which PFASs flow through into the next life cycle stage:

1. **Formulation (articles and commercial construction mixtures only).** This life-cycle stage covers the first step in the production of articles and commercial construction mixtures. Two different types are considered:
 - Type 1 which covers the extrusion and/or manipulation of fluoropolymers to form articles like meshes, membranes, tapes, thin films, or other solid forms for use in construction
 - Type 2 which covers the blending/mixing and formulation of commercial construction mixtures, and PFASs are used to achieve desired technical functions and physical properties.
2. **Processing aids.** This stage covers the use of PFASs based processing aids in the manufacture of articles. The processing aid is expected to be expended and is not included (intentionally) in the final article. Stakeholders state that capture systems are

in place to retain and re-use the processing aid as many times as possible and will after the final use be thermally destructed.

Those applications in which PPA are used and PFASs are intended to still be present in the final article, are covered in the formulation step under point 1.

3. **Application (commercial construction mixtures only)**. This stage covers the application of commercial construction mixtures. These applications can take place both indoors and outdoors. The mechanism of application for commercial construction mixtures can vary widely (e.g. by spray, roller, cloth, brush, 'dipping', etc.).
4. **Use stage (articles and commercial construction mixtures only)**. This stage covers the use service life. Again, these uses can be split between outdoor and indoor applications. Primary emission for outdoor applications is likely to be through a combination of weathering and abrasion depending on the specific application. This makes applying emission factors at a high-level (i.e., all indoor articles) challenging. For articles, this may include both use by professionals and DIY products used by consumers. It also means that use itself can be both within public buildings and domestic properties, which also affects the potential rates of emission, pathways, and exposure. No further efforts have been made to disaggregate between articles used in public and private buildings.

Emissions in the waste stage is included in section B.9.18.

Environmental release categories (ERC), that describe the use of PFASs most closely including release factors were assigned to each of the stages described above. A detailed description on emission calculations using volumes in Annex A.3.14., ERC and release factors, as well as a justification for the choices made, is included in Appendix B.9.14..

Estimated PFASs emissions from construction products, based on the source-flow model using the year 2020 as a baseline, are provided in Table B.107. In the table emissions from each life-cycle stage is shown for both construction articles and construction mixtures.

The source-flow model used for the emission estimations is based on a grouping approach rather than a substance-by-substance. The trade-off of using such an approach is that the estimates provided will have a higher uncertainty. However, this approach can still provide useful data to estimate the orders of magnitude for emissions when comparing PFAS groups, life-cycle stages, sub-uses and different sectors.

As can be seen in Table B.42, emissions are dominated by construction mixtures which is dominated by the life-cycle stage 'Application'. Furthermore, it can be seen that the use stage outdoors contributes more than indoor and that fluoropolymers contribute more than non-polymeric PFASs.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.42. Estimated annual EEA emissions in the construction sector of PFAA and PFAA precursors, polymeric PFASs and total PFASs in 2020 (baseline).

	Emission estimates	PFAA C2-C3 (t/y)		PFAA ≥C4 (t/y)		Side-chain fluorinated polymers (t/y)		PFAAs and PFAA precursors ^a (t/y)		Fluoropolymers (t/y)		Total PFASs (t/y)	
		low	high	low	high	low	high	low	high	low	high	low	high
Total volume								987	2 405	4 254	10 320	5 241	12 725
Articles	Formulation			4	11			4	11	8	20	12	30
	Processing aids ^b	0.04	0.1					0.04	0.1			0.04	0.1
	Use stage - outdoor			6	15			6	15	13	31	19	47
	Use stage - indoor			0.1	0.2			0.1	0.2	0.2	0.5	0.3	1
	Total	0.04	0.1	11	26			11	26	21	52	32	78
Mixtures	Formulation			5	11	0.3	1	5	12	77	193	82	205
	Application - outdoor			44	106	3	10	47	116	827	2 003	874	2 119
	Application - indoor			22	53	2	5	24	58	411	997	435	1 055
	Use stage - outdoor			1	3	0.1	0.3	2	4	27	65	28	69
	Use stage - indoor			0.02	0.1	0.002	0.005	0.02	0.1	0.4	1	0.4	1
	Total			72	174	5	16	77	190	1 343	3 259	1 420	3 449
Total articles and mixtures												1 451	3 527

^aThe volume of non-polymeric PFASs and the split between processing aids (C2-C3 PFAAs) and PFAAs ≥ 4 is estimated based on Glüge et al. (2020).

^bProcessing aids is here placed under C2-C3 PFAAs, however, they can also be PFAS-based solvents/functional fluids

B.9.14.3. Human exposure

The construction sector employs about 18 million people in the EU⁴¹. 16 companies provided data on the number of workers employed in the production and handling of well over 100 different PFAS-based construction products. In total, approximately 12 000 people work in these companies (rounded to closest 1 000).

Considering the uncertainty of the estimate of the overall market for PFASs in construction products and given that many of the stakeholders who provided their number of workers, did not specify the related tonnage of PFASs in construction products, extrapolation to the whole market was not possible. Given the diverse uses of PFASs in construction products, it can be assumed that the share of construction workers that handle PFAS-based products, at least occasionally, is significant.

Industrial exposure during production of articles could occur through inhalation of vapours or of dust generated during mechanical manipulation of materials. Stakeholders mentioned that many production plants make use of abatement equipment as well as personal protection equipment to reduce exposure to both vapours and dust. Some stakeholders stated that only trained professionals are handling installations and decommissioning of articles containing PFASs.

Stakeholders mentioned that the processes to produce processing aids are largely automated and take place in closed systems to capture and re-use PFASs as far as possible. There may be some exposure, particularly during maintenance, but overall exposure is expected to be low. It should be noted that there are several examples of environmental releases of PFASs from factories that use processing aids for the production of fluoropolymers (Lohmann et al., 2020).

The addition of PFASs to mixtures during blending and mixing takes place at higher temperatures during which vapours are generated. Stakeholders highlighted that fluoropolymer such as PTFE, ETFE and PVDF are highly stable and have a low vapour pressure. It should be noted that also non-polymeric PFASs and side-chain fluorinated polymers are used in paints and coatings.

The highest worker exposure will likely occur during the application stage of paints and coatings (and potentially adhesives). PFAS-based mixtures can be added as coatings/impregnation by spraying, rolling, or brushing onto finished articles, this may occur both indoors and outdoors.

B.9.14.3.1. Consumers use

For Do-It-Yourself (DIY) sealant and adhesive products, tapes, DIY durable water repellent, impregnation and aftermarket floor protection and paint exposure is possible. (Though, it is not clear to what extent paint used by consumers contain PFASs). However, there is no information on the number of consumers using these products. It is possible that PFAS-based mixtures are occasionally used in DIY adhesives and sealants, most likely in small quantities. This suggests that potential exposure is limited.

Products for DIY durable water repellent impregnation of stone, glass, tiles and aftermarket floor protection can contain between 0.5% and 2% PFASs (usually side chain fluorinated polymers). If applied as an aerosol spray, high exposure can occur, and cases of acute intoxication have been observed (both consumers and professional workers) (ECHA, 2017a).

Fluoropolymers (such as PTFE, ETFE, and PVDF) are largely stable from degradation, while non-polymeric PFASs may be bound within the matrix of the article. The greater potential for release and exposure may occur where articles are abraded during use (i.e., moving parts) or where maintenance involves cutting, which would generate dust.

Exposure to materials in buildings in which PFAS-based construction products are used is

⁴¹ https://ec.europa.eu/growth/sectors/construction_en, date of access: 2022-12-14.

possible. However, if undisturbed and not subject to direct weathering or washing, the potential release of PFASs is likely low.

B.9.14.4. Summary

Emissions from construction articles, processing aids and mixtures may occur during formulation (articles and commercial construction mixtures only) in the manufacturing of articles (of processing aids), in the application stage, (commercial construction mixtures only) and in the use stage (articles and commercial construction mixtures only).

Emissions were calculated using ERC. Total yearly EEA emissions of non-polymeric PFASs (including side-chain fluorinated polymers) amount to between 100 and 200 t/y (rounded number) and total yearly EEA emissions of polymeric PFASs amount to between 1 300 and 3 300 t/y (rounded number). Almost all emissions occur in the production stage. Only qualitative information is available on exposure of workers and consumers. Stakeholders generally believe exposure is limited because of the use of closed systems, abatement systems, personal protection equipment and handling only by trained employees. High exposure of consumers may take place using DIY products containing PFASs especially when applied as aerosol sprays.

B.9.15. Lubricants

B.9.15.1. Introduction

The use of PFASs in the lubricants industry is described in Annex A.3.15.

B.9.15.2. Emissions

Three basic life-cycle stages are considered in which emissions may occur, or from which PFASs flow through into the next life cycle stage:

1. **Formulation of lubricants** (including manufacture of sealed articles). This stage covers the formulation of lubricant products, and manufacture of articles containing lubricants. Lubricants include low viscosity lubricants (oils), greases or other mixtures (e.g. solid/dry-film lubricant which is a solvent containing a solid additive such as micro-powder PTFE). Stakeholders highlighted that 95-97% of all PFAS-based lubricants are used within sealed articles, where lubricants are added once (at point of manufacture). For the remaining 3-5% a total loss is assumed during use and there is a need for re-lubrication at later stages of use. The formulation stage will cover the emissions associated with formulating lubricants (blending/mixing) and losses during filling/injection of lubricants into the manufacture of sealed articles.
2. **Use emissions from sealed articles.** This life-cycle stage covers the release of PFASs from sealed articles during service life (e.g. leaks, faulty equipment, accidental releases). The applications in this life-cycle stage have been further disaggregated into:
 - Outdoor applications (automotive, aviation hydraulic systems and landing gears, industrial machinery used outdoor, diving equipment etc).
 - Indoor applications (ovens, belts and chains, gears, industrial machinery used indoors, automotive uses (e.g. inside a car).

It is assumed that any PFASs released outdoors end up directly in the environment, while PFASs released indoors more likely end up in wastewater systems.

3. **Use emissions from open applications.** This life-cycle stage covers the smaller set of applications identified previously (3-5% of total use). The applications from this life-cycle stage have been further disaggregated into:
 - Outdoor' applications (e.g. use of specialist dry-film lubrication for bike chains etc). Here it is assumed all PFASs are released into the environment.
 - Indoor applications (mould release agents, re-lubrication of belts and chains etc).

Besides the life-cycle stages mentioned above, emission of PFAS-based solvents for cleaning before lubrication is also included.

Environmental release categories (ERC), that describe the use of PFASs most closely including release factors were assigned to each of the stages described above. A detailed description on emission calculations using volumes in Annex A.3.15., ERC and release factors, as well as a justification for the choices made, is included in Appendix B.9.15..

Estimated PFASs emissions (t/y) from lubricants, based on the source-flow model using the year 2020 as a baseline, are provided in Table B.43. In the table, emissions from each life-cycle stage are shown. Emissions in the waste stage is included in section 0.

Table B.43. Estimated annual EEA emissions in the lubricants sector of PFAA and PFAA precursors, polymeric PFASs and total PFASs in 2020 (baseline).

Emission estimates	Fluorinated gases (solvents) ^b		Non-polymeric PFASs ^a (other additives than PTFE)		Fluoropolymers (micro-powder PTFE, solid additive)		PFPEs (base oil)		Total fluoropolymers and PFPEs		Total PFASs	
	low	high	low	high	low	high	low	high	low	high	low	high
Total volume	70	150	1	10	800	1 200	300	800	1 100	2 000	1 171	2 160
Formulation stage	1	2	0.02	0.2	19	29	7	19	26	48	27	50
Use stage - Sealed equipment - Outdoor application	1	2	0.03	0.3	22	33	8	22	30	54	31	57
Use stage - Sealed equipment -Indoor application	1	3	0.03	0.3	25	38	10	25	35	64	36	66
Use stage - open - outdoor application	0	0	0.01	0.1	11	16	4	11	15	27	15	27
Use stage - open - indoor application	0	0	0.02	0.2	13	19	5	13	17	32	17	32
Use of cleaning agents outdoor	18	38									18	38
Use of cleaning agents indoor	8	17									8	17
Total											152	287

^a Assumed to be PFAAs ≥ 4 ^b The use of PFAS-based solvents (functional fluids/fluorinated liquids) for industrial cleaning is described in Annex A.3.9. on Fluorinated gases.

The source-flow model used for the emission estimations is based on a grouping approach rather than a substance-by-substance. The trade-off of using such an approach is that the estimates provided will have a higher uncertainty. However, this approach can still provide useful data to estimate the orders of magnitude for emissions when comparing PFAS groups, life-cycle stages, sub-uses and different sectors.

B.9.15.3. Human exposure

B.9.15.3.1. Lubricant formulation/production

It is estimated by various stakeholders that fewer than 1 000 workers are involved in the formulation of PFAS containing lubricants in the EU/EEA. It is stated by stakeholders that worker exposure is very low due to strict controls, closed systems or encapsulation and low volatility of PTFE and PFPE. No exposure data were provided or identified. The same applies for formulation of lubricants containing PFAS-based solvents where some inhalation exposure cannot be excluded.

B.9.15.3.2. Immediate downstream users

The immediate downstream users are those typically incorporating the lubricants containing PFASs into parts/articles such as bearings. As indicated in section A.3.15, there are many different types of parts and equipment and an estimate of the number of workers exposed to PFASs from handling lubricants are not possible to make. Stakeholders estimate there are 10 000

– 100 000 workers. They stated that many processes have been or are being automated (estimated for applications covering 30 – 70% of the lubricant volume), which reduces worker exposure. Further, it is stated that many applications take place in clean rooms or under conditions that are similar to clean rooms. It is mentioned that the sector has a strong focus on occupational health and safety compliance.

In open applications (3-5% of the lubricants containing PFASs) there might be a higher potential for worker exposure than for the above-mentioned more automated processes.

B.9.15.3.3. Equipment end-users

Stakeholders believed that workers using equipment with lubricants containing PFASs are generally not exposed to PFASs, or the potential for exposure is very limited, due to the low potential for release.

B.9.15.3.4. Cleaning

PFAS-based solvents are used to clean mass-manufactured parts (such as electronic components). This is commonly done in specially sealed equipment in which solvents can be recovered and reused. For these types of applications, stakeholders argue that exposure is expected to be low.

Cleaning of articles that were previously lubricated with PFAS-based lubricants, using PFAS-based solvents (cleaning of parts/articles prior to adding lubricants, cleaning of production machinery or during maintenance of e.g. wind power installations) may take place during the entire lubricant life cycle. Worker exposure during these type of cleaning activities is possible and is likely to be relevant because the solvents are volatile and sometimes applied as aerosols. In addition, it is assumed that these activities might be less strictly controlled as they are only carried out occasionally and not always in industrial settings. It is therefore assumed that this could lead to inhalation as well as dermal exposures. No exposure data on this type of exposure were identified or received from stakeholders.

B.9.15.3.5. Note on professional uses

Most of the above-described worker exposure situations can be seen as industrial uses, but some of the re-lubrication ('open'/'total loss' applications) and some cleaning uses might be seen as professional uses. Further, some of the uses described below for consumers might also be relevant for some professionals (e.g. bike repair).

B.9.15.3.6. Consumer use of lubricants

Consumer exposure is expected by industry stakeholders to be very limited as consumers generally do not use this type of lubricants because of the expense. One exemption from this are speciality products for bicycle chains.

Consumer PTFE lubricants for bicycle lubrication is available on the web at a cost of DKK 70 (equalling around €9.4) for 400 mL. Other multiple purpose PTFE lubricants, which can be acquired via websites have also been identified. Some of these latter lubricants can be bought by consumers but might be intended for professional users.

While no evidence of widespread use of PFAS-based lubricants by consumers has been found, the price quoted above does not support the claim that PFAS-based lubricant is too expensive for consumers, considering more expensive fluorine-free lubricants are also being sold.

In any case, all industry stakeholders interviewed do not consider fluorinated lubricants for consumers use as critical or essential.

B.9.15.3.7. Consumer use of lubricated equipment

Similarly, as for worker end-users, industry stakeholders consider consumer exposure to PFAS-based lubricants in consumer articles (cars, household appliances, power tools etc.) to be very limited, due to the low potential for releases in these lifetime lubrication applications.

B.9.15.4. Summary

Emissions from lubricants may occur during formulation, use emissions of sealed articles, and use emissions from open applications. Emissions were calculated using ERC. Total emissions of non-polymeric PFASs amount to between 0.1 and 1 t/y (rounded numbers) and total emissions of polymeric PFASs amount to between 110 and 230 t/y (rounded number). Emission of fluorinated gases amount to between 30 and 60 t/y (rounded numbers). Only qualitative information is available on exposure of workers and consumers. Stakeholders generally believe exposure is limited because of the use of closed systems, abatement systems, personal protection equipment and handling only by trained employees.

B.9.16. Petroleum and mining

B.9.16.1. Introduction

The use of PFASs in the petroleum and mining sector is described in Annex A.3.16.

B.9.16.2. Emission

B.9.16.2.1. Emissions from tracers

Limited specific data have been obtained in the assessment on the precise release patterns of PFAS-based tracers (e.g. in which environmental compartment release will occur), or exactly how these substances will behave when released to the environment. It should be noted that the volume of emissions for these products estimated during formulation using the ECHA (2016a) guidance ERCs are broadly in line with an estimate provided by a supplier.

B.9.16.2.2. Emissions from anti-foaming agents

Very limited specific data have been obtained in the assessment on the precise release patterns of PFAS-based anti-foaming agents e.g. in which environmental compartments release will occur, or exactly how these substances will behave when released into the environment.

B.9.16.2.3. Emissions from fluoropolymers

An estimate has been made for the total sales and use of fluoropolymers in Europe for the 2020 baseline year for petroleum and mining sector (3 500- 7 500 t), however it has not been possible to differentiate between different types of fluoropolymers within this estimate. Therefore, the emissions estimate conducted takes a general approach in terms of fluoropolymers used in the petroleum and mining sector rather than attempting to disaggregate for different polymer types.

The estimate of emissions from this part of the life cycle only considers the 'new' usage of fluoropolymers in the baseline year. As noted by Lohmann et al. (2020), it is important to distinguish between fluoropolymer substances, fluoropolymer products, and fluoropolymers in finished articles, as there are many different processes of making fluoropolymer products (Lohmann et al., 2020). While it could be expected that fluoropolymer itself could be released to an extent at various stages of the product lifecycle (e.g. through abrasion of tubes, linings and joint sealants during use, release from end-of-life processes such as landfill, incineration, etc.), the availability of data to provide quantitative estimates of releases from these routes is currently lacking so this aspect has not been considered in the present study.

While it has been considered that fluoropolymers are distinct from other non-polymeric PFASs and should be separated from them for hazard assessment or regulatory purposes (Henry et al., 2018), the possible releases of 'leachable' non-polymeric PFASs (e.g. processing aids, synthesis by-products and oligomers) from the use of fluoropolymer in specific downstream uses need to be considered (Lohmann et al., 2020).

The level of residual monomeric PFASs in the fluoropolymer matrix is highly uncertain and limited specific data were available in this assessment. The ECHA ERCs for the formulation and use stages were applied to the total PFAS content estimated for the total fluoropolymer.

Broad 'high' and 'low' [residual concentration] scenarios were used to produce an estimate and wide range of total quantity of monomeric PFASs present in the fluoropolymer used in Europe were presented between these two scenarios, to illustrate this uncertainty.

The 'high' scenario was used by the ECHA (2015a) Annex XV restriction report on PFOA to derive estimates for the proportion of total fluoropolymer used containing different concentrations of

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

monomeric PFASs. The assumptions made and PFAS concentrations used in deriving an estimate for the residual PFASs content for the 'high' scenario are presented in Table B.44.

Table B.44. Content of monomeric PFASs in fluoropolymers "high" scenario.

PFAS concentration range (ppm)	PFAS concentration used (ppm)	ECHA (2014) PFOA Annex XV restriction scenario	Proportion of FP market applicable (2020) (%)
0		Worst case/Refined	67
20-50	35	Worst case/Refined	17
1 000-2 000	1 500	Refined	17

The 'low' scenario makes the broad assumption of 1ppm concentration for PFASs (unspecified) in all fluoropolymers. Using this approach, an estimate for the residual quantity of monomeric PFASs in the fluoropolymer is 4-8 kg (low scenario) and 900-1 900 kg (high scenario).

These estimates only consider the emissions from 'new' fluoropolymer being used in this sector each year. It has not been possible to estimate the tonnage of 'in-situ' fluoropolymer in this sector, which could act as a source of residual monomeric PFASs to the environment.

B.9.16.2.4. Emissions from non-polymer PFASs

An overview of the total emissions (baseline 2020) of non-polymeric -PFAS to the environment from the petroleum and mining industry in the EEA is provided in Table B.45. Emissions from waste are further described in section B.9.18.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.45. Estimated annual EEA emissions in the petroleum and mining industry of PFAA and PFAA precursors, polymeric PFASs and total PFASs in 2020 (baseline).

Group	PFAS compound	Quantity of product used (kg)	Quantity of PFAS (kg)	Emissions to air (kg)	Emissions to freshwater (of which transferred to waste) (kg)	Emissions to marine water (kg)	Emissions to land (kg)	Total Emissions (kg)	Total quantity entering waste (kg)
Water and gas tracers	Fluoro-alkane tracers + other PFAS-containing tracers	1 000	1 000	25-70	20-25 (20)	0-110	0-5	165-185	20-145 ^[1]
Drilling/ Production chemicals	Fluoro-siloxane antifoaming agents	170 000	3 400 – 8 500	85-635	70-210 (15-40)	20-760	0-45	170–1 650	70-360 ^[2]
Fluoro-polymers (all) Low scenario	Monomeric PFAS (not specified)	3 500 000 – 7 500 500	4-8	1-2	<1 (<1)	<1	<1	1-3	<1 (formulation) 1-3 (end of life)
Fluoro-polymers (all) High scenario	Monomeric PFAS (not specified)	3 500 000 – 7 500 500	900-1 900	270-580	3-6 (2-4)	20-40	20-45 (1-2)	310-670	3-6 (formulation) ³ 310-670 (end of life) ³

[1] ~20 kg from the formulation stage (freshwater and soil); 0-125 kg from the use stage (recaptured at surface)

[2] 70-170 kg from the formulation stage (water (before STP) and soil); 0-190 kg from the use stage (recaptured at surface)

[3] Calculated using the total calculated residual monomeric PFAS content of the fluoropolymer and the total emissions across all use stages

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

For tracer and anti-foam products, the levels of emissions estimated in Baseline year: **2020**

Notes on ranges of data: [1] Scenario 3; [2] Scenario 1; [3] Scenario 1 and 2;

For a full description of each scenario, see NEA (2021).

* Calculated using Environmental Release Category (ERC) emission scenario no.2 for 'formulation into a mixture' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 2.5% w.w to air; 2% w.w to wastewater and 0.01% w.w to soil.

Figure B.81 and Baseline year: **2020**

Notes on ranges of data: [1] Scenario 3; [2] Scenario 1; [3] Scenario 2 and 3;

For a full description of each scenario see NEA (2021).

* Calculated using Environmental Release Category (ERC) emission scenario no.2 for 'formulation into a mixture' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 2.5% w.w to air; 2% w.w to wastewater and 0.01% w.w to soil.

Figure B.82 are expected to be directly proportional to volumes of production and use of these products. Therefore, the pattern of emission levels (relative to the 2020 baseline) from 1990 to 2050 period, is expected to follow the same trend as presented in the baseline scenario for expected tonnage of sales and use for these products as presented in A.3.16.2.

B.9.16.2.5. Historic emissions

Backward looking (1990 – 2020)

For tracer and anti-foam products, the levels of emissions estimated are expected to be directly proportional to volumes of production and use of these products, therefore the pattern of emission levels (relative to the 2020 baseline) from 1990 to 2050 period, is expected to follow the same trend as presented in the baseline scenario for expected tonnage of sales and use for these products (see Annex A.3.16.2.).

In the case of fluoropolymers the emission levels of monomeric PFAS from fluoropolymer will be dependent on the overall residual levels present in the fluoropolymer material after manufacture. A general assumption has been made (based on the discussion in Lohmann et al. (2020), and informed by consultation with manufacturers and suppliers in the assessment) that a higher concentration of monomeric PFAS in fluoropolymer can be expected in the fluoropolymer used in previous years (e.g. pre-2020) compared to the 2020 baseline year.

For purposes of the 'high' scenario presented in this assessment, the quantities of monomeric PFASs in the 1990-2020 period have been based on the scenarios outlined in the ECHA (2015a) PFOA Annex XV restriction report. In this assessment, the 2020 baseline, has been based on the 'refined scenario'. It is assumed that the 'worst case' scenario presented in the ECHA (2015a) PFOA Annex XV restriction report applies in the period 1990-2000, with an assumed transition between the 'refined' and 'worst case' scenarios applying in 2010.

An overview of the assumed proportions of fluoropolymer containing different concentrations of residual PFASs for the period 1990 to 2020 (low scenario) is provided in Table B.46 below.

Table B.46. Concentrations of monomeric PFAS in fluoropolymer (high scenario), assumed for the period 1990-2020.

PFAS concentration range (ppm)	PFAS concentration used (ppm)	ECHA (2014) PFOA Annex XV restriction scenario	Proportion of market (1990) (%)	Proportion of market (2000) (%)	Proportion of market (2010) (%)	Proportion of market (2020) (%)
0	0	Worst case / Refined	67	67	67	67
20-50	35	Worst case / Refined	17	17	17	17
1 000-2 000	1500	Refined			8	17
1 000-50 000	25 500	Worst Case	17	17	8	

For purposes of the 'low' scenario presented in this assessment, the quantities of monomeric PFASs in the 1990-2020 are based on simple general assumption (based on the discussion in Lohmann et al. (2020) that all fluoropolymer pre-2000 will have a residual PFASs concentration of 10 ppm, and all fluoropolymer from 2020 will have a residual PFAS concentration of 1 ppm, with an assumed transition between these scenarios applying in 2010.

An overview of the assumed concentrations and proportions of PFASs in the fluoropolymer for the period 1990 to 2020 (low scenario) is provided in Table B.47 below.

Table B.47. Concentrations of non-polymeric PFASs in fluoropolymer (low scenario), assumed for the period 1990-2020.

PFAS concentration range (ppm)	Proportion of market (1990) (%)	Proportion of market (2000) (%)	Proportion of market (2010) (%)	Proportion of market (2020) (%)
1			50	100
10	100	100	50	

For fluoropolymers, the emissions of monomeric -PFASs will be dependent on the residual content of PFASs in the polymer matrix. The emission time series has been derived, based on scenarios of estimated PFAS concentrations on fluoropolymer in past and future years. In general, it is expected that pre-2000 fluoropolymer will have much higher concentrations than the 2020 baseline and concentrations would decline after the 2020 baseline. This explains that the projected emission of PFAS from use of fluoropolymers (high scenario) has been higher before 2000 than the projected emission of PFASs from antifoaming agents. However, projected emission of PFAS from use of fluoropolymers have decreased below the level of the antifoaming agents by 2020.

B.9.16.3. Human exposure

- It is not expected that direct exposure to consumers or the general public would occur. It is expected that direct exposure will only occur potentially for occupational workers across the supply chain. This could include: Workers involved in formulation of PFASs/fluoropolymers in products.

- b) Workers handling PFASs/fluoropolymer products on site.
- c) Workers involved in handling wastes containing PFASs on site.

Exposure to fluoropolymers and non-polymeric PFASs can occur at various points along the supply chain, but this is expected to be minimal due to the use of adequate PPE, closed equipment and ventilation. Both the landfilling and incineration of fluoropolymer could potentially lead to the release of PFASs to the environment (Lohmann et al., 2020).

It has not been possible to derive an estimate for the total number of workers impacted by the use of PFASs and/or fluoropolymers in these sectors, due to a lack of data and the relatively large number of steps and complexity in the supply chain.

B.9.16.4. Summary

Total emissions to the environment from tracer products amount is between 165–185 kg, total emissions from anti-foaming agents amount is between 170–1 650 kg, and total emissions from fluoropolymers amount between 310–670 kg for the high scenario and between 1–3 kg for the low scenario. Emissions from the petroleum and mining sector were calculated using ERC. However, for the use phase, the default values in the ECHA (2016a) Guidance have been adjusted to take into account the estimated distribution of use between onshore and offshore installations and the assumed impact this has on the emission pattern of chemicals at these facilities. This is a 90:10 split between offshore: onshore installations, assuming a 100% release to marine waters at offshore installations, and a 50% release to soil, 50% release to fresh water at onshore installations. Direct exposure to consumers or the general public is not expected to occur. It is expected that direct exposure will only occur potentially for occupational workers across the supply chain. Unfortunately, it has not been possible to derive an estimate for the total number of workers impacted by the use of PFASs and/or fluoropolymers in these sectors, due to a lack of data and the relatively large number of steps and complexity in the supply chain.

B.9.17. Active substances in Plant Protection Products (PPP), Biocidal Products (BP) and Medicinal Products (MP)

As the uses of active substances in Plant Protection Products (PPP), Biocidal Products (BP) and Medicinal Products (MP) are derogated from the restriction proposal without a time-limit, this sector has not been studied in detail. Specific information on emissions from these uses can therefore not be presented in this section.

B.9.18. Waste

B.9.18.1. Introduction

The waste stage is part of the life cycle of a substance as is, in a mixture or in an article. Therefore, its distribution via the supply chain including service-life of articles and waste stage as an emission source with its associated risks is taken into account in this Annex XV proposal. Understanding of waste management (recycling, landfill, incineration or composting) and the fate of PFASs in the waste stage, is important for understanding the potential for full life cycle emissions.

The waste stage, following use of substances, mixtures and articles, is included in the rules and guidelines for chemical safety assessment. This means also for the waste stage of substances registrants have the obligation to proof that risks are adequately controlled for human health and the environment (ECHA, 2008; ECHA, 2010).

PFAS emissions heavily depend on the physical state of the substance (gaseous, liquid or solid), its application (open or closed, process application, its presence as a constituent of another substance, or its presence in a mixture or article) and may arise during all the life cycle steps: production, application, use and end-of-life/waste stage. This is reflected in Figure A.1 in Annex A. Waste stage emissions may be of relevance for all uses where PFASs are still present in the products or articles at the end-of-life stage. So, the waste stage emissions would be typically relevant in case emissions during use represent only a fraction of the total PFASs content in the product or article.

In this section the end of life stage and emissions in this phase are described. For a number of PFAS uses, a significant percentage and tonnage of PFASs enter the waste stage. Waste operations (from collecting, bulking, sorting to composting/landfilling/incineration/recycling) could contribute significantly to the environmental releases of PFASs, and thus a qualitative or quantitative assessment is needed. In case of a (partial) restriction, for impact assessment purposes it is helpful to know if waste stage emissions are (partly) prevented. In the impact assessment (Annex E.2.) the waste stage emissions are not taken into account in the different use sectors, mainly because of the high (emission) uncertainty related to the routes of disposal and the final waste treatment method applied.

In Figure B.76 the emission routes from waste collection to final waste treatment are presented.

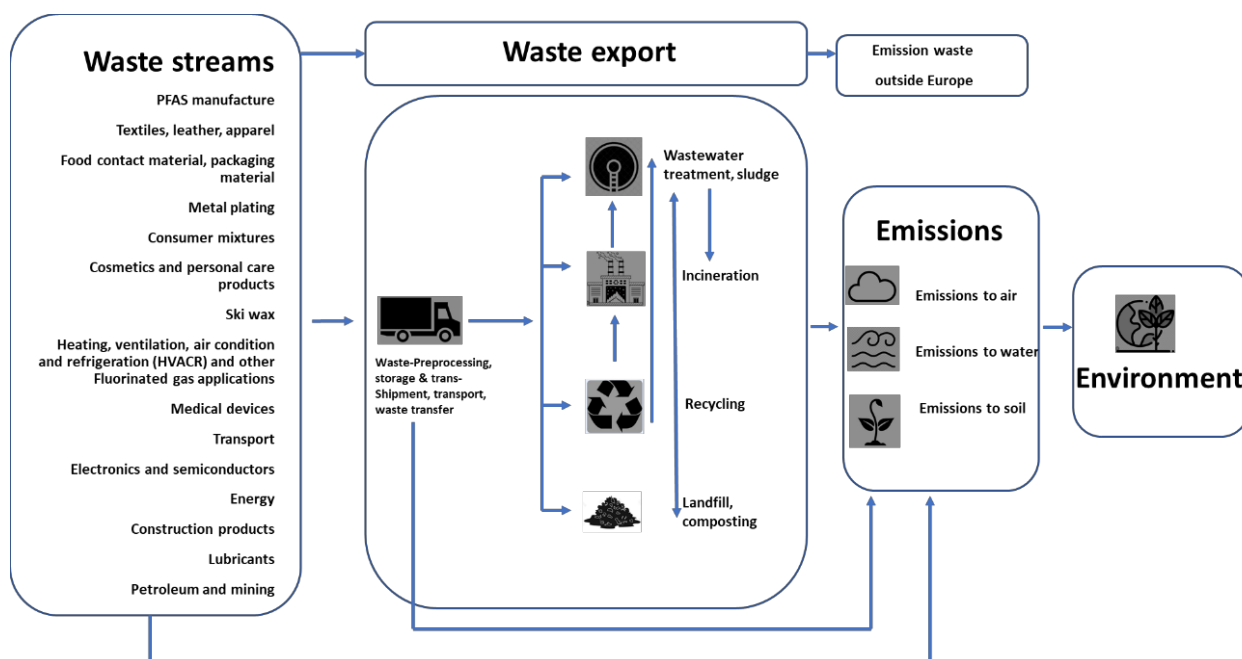


Figure B.76. Overview waste stage emissions.

Some waste treatment processes are interlinked, e.g. landfilling and waste water treatment. Emissions from waste treatment may affect different resources important to society (farmland, food, drinking water, etc.). A number of relations between PFAS emissions from waste (treatment) and affected resources is shown in Figure B.77.

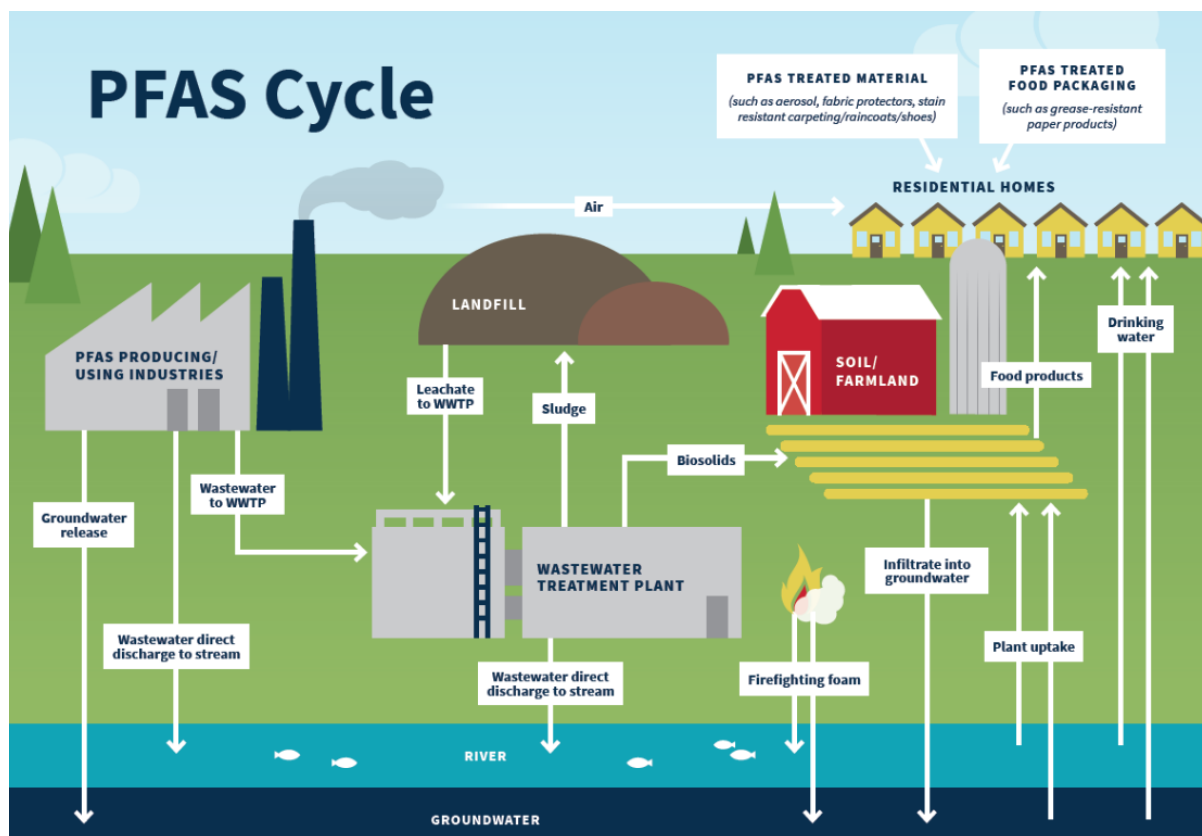


Figure B.77. Schematic overview of PFAS emissions with waste treatment facilities as important source(s). This overview is meant as an illustrative example that is non-exhaustive. Adopted from: Helmer et al. (2022).

B.9.18.2. Overview of waste stage emissions

The Dossier Submitters consider waste stage emissions for PFAS uses in the following sectors: TULAC, food contact material and packaging, construction products, transportation, medical applications, HVACR, electronics and semiconductor, and energy. These sectors are given a high priority for the assessment, based on anticipated waste volumes containing PFASs. In Table B.48 the groups of PFASs used in the various sectors, their presence in open or closed applications and high waste stage emission relevance is provided. The relevant uses in which high emissions are expected, are highlighted in green. The uses that are not highlighted are expected to contribute to emissions from waste to a lesser extent.

For fluorinated gases much remains unclear regarding potential emissions in the waste stage. A high tonnage enters the waste stage (see Table B.59) but it is unclear to the Dossier Submitters if destruction and recovery of fluorinated gases fully prevent emissions of fluorinated substances in these waste treatment processes as information is rare on this topic.

Table B.48. Groups of PFASs used in the various sectors, presence in open or closed applications and high waste stage emission relevance (light green).

PFAS use	Polymeric PFASs	Fluorinated gases	PFAA and PFAA precursors	Open application (emission mainly in use stage)	Articles (high relevance in waste stage and recycling if ticked)	Recycling
TULAC	x		x		x	x
Food contact materials and packaging	x		x		x	x
Metal plating and manufacturing of metal products	x		x	x		
Consumer mixtures			x	x		
Cosmetics				x		
Ski wax				x		
HVACR		x		x	x	
Medical applications	x	x	x	x	x	
Transportation	x				x	x
Electronics and semiconductor	x	x	x		x	x
Energy	x		x		x	
Construction products	x		x		x	x
Lubricants	x		x	x		
Petroleum & Mining				x		

B.9.18.2.1. Main shortcomings in linking waste stage emissions to use categories

Linking PFAS use categories (the uses presented in the table above) to potential waste stage emissions are associated with a number of uncertainties. There is no clear connection between PFAS use categories and EWC waste categories (Eurostat, 2010), and it is not always clear in which waste treatment operations (e.g. landfill, incineration, recycling) the PFASs containing articles are processed. Besides this, the effectiveness of waste treatment is not always clear and many uncertainties remain (e.g. EPA-US (2020)).

Furthermore, it is not fully clear where the main emissions during the waste stage occur. Not all emission routes are clear and very often only some (specific) PFASs are measured. In a recent study on leachate from landfills, 88% ± 4% of the extractable organofluorine substances were unknown (Bjorklund et al., 2021).

Ideally, PFAS emission factors per main disposal or recovery operation should be derived. This information is currently not available as for deriving a reliable emission factor, information on full PFAS input as well as full PFAS output with regard to the waste operation

is needed. This should be done for each waste category and treatment method. This often is not possible as i.e. PFAS output measurement (in leachate, flue gas, treated wastewater, etc.) are reported in literature but information on total PFAS input (i.e. to landfill or to incinerate) is generally not available or scarce.

B.9.18.2.2. Methods applied

Two methods were used to get an overview of waste stage emissions where possible: Literature study and using ECHA ERCs.

A literature study was conducted on yearly EEA PFAS waste stage emissions. The following main waste treatment options were analysed to try to get emission estimates (with all limitations):

- Landfilling
- Incineration
- Waste water treatment

PFAS emissions related to these main waste treatment methods are described with a brief overview of literature and the limitations encountered. For these three waste treatment methods a brief overview of conclusions from former PFAS restriction dossiers is included as well.

The three waste treatment methods that are covered are potentially important emission sources. Additional emissions can occur from sewage sludge applications and from waste transfer stations for instance.

In section B.9.18.2.10 the PFAS waste stage emissions for the relevant PFAS uses of Table B.59 are described.

B.9.18.2.3. Landfilling

Landfilling is a common waste treatment method for numerous waste streams. The intention of the European Commission is to lower the amount of waste being landfilled⁴².

Landfilling in general does not fully destruct PFAS in waste streams. The individual contribution of certain PFAS uses to PFAS landfill emissions is hard to determine. It can be assumed that waste streams containing high PFAS concentrations like some industrial waste will likely contribute more to PFAS emissions from the waste stage than waste streams with low PFAS concentrations (ITRC, 2021; Lin et al., 2022; Solo-Gabriele et al., 2020). Based on the data published from 10 countries (>250 landfills), C4-C7 PFCA are predominant in leachate, while FOTH is dominant in landfill air (Zhang et al., 2023).

The relevance of landfills for PFAS emissions has been shown in multiple studies. It was found that a waste water treatment plant (WWTP) receiving leachate from a landfill can have up to three-time higher PFAS concentration in the influent than a WWTP that does not receive leachate (Masoner et al., 2020). This indicates the risk of PFAS emissions from landfills. Recently, this was also seen in the Netherlands where landfill leachate appeared to be a major PFAS source in a study on PFAS in WWTPs (STOWA, 2021b). PFAS emissions to air are less well researched but could be of importance, especially for telomeric alcohols (Lin et al., 2022).

It has also been shown that the climate and the age of waste deposited on the landfill have an effect on the PFAS concentration in the leachate (Lang et al., 2017). It is assumed, that over time 100% of all containing PFASs or their degradation products will eventually end

⁴² https://environment.ec.europa.eu/topics/waste-and-recycling/landfill-waste_en, date of access: 2022-12-15.

up in the leachate or in the ground. Additionally, intentional and unintentional fires on landfills may release PFASs to air.

Based on an extensive literature review performed by the Dossier Submitters, an annual EEA emission of PFASs from landfill of 1-6 t/y was estimated.

Combining the concentration of PFASs in leachate (around 7 460 ng/L) with the leachate generation factor from Brennan et al. (2016) (0.2 – 1 m³ leachate generated per tonne of waste landfilled per year) and the total amount of landfilled waste in 2018 (838 861 071 t), the PFAS load generated in the EU from the waste landfilled per year can be calculated (Table B.49).

Table B.49. Calculated total PFAS annual loads based on the available Eurostat data (landfills).

PFAS Annual load min (t/y)	PFAS load mean max (t/y)	PFAS load median min (t/y)	PFAS load median max (t/y)
1.14	5.72	0.597	2.98

Research in Sweden showed that there likely are significant unknown PFASs present in leachate as “PFAS 11 analysis” could only explain 5-40% of Total Organic Fluorine (TOF) analysis (Avfall, 2021). Therefore total PFAS load could well be 2-20 times higher than targeted measurements of PFASs in samples.

In addition, PFASs continue to be released from landfills for many years, even after closure of a landfill (Propp et al., 2021).

Landfill mass balance

For landfill emissions there are numerous studies on PFAS leachate concentrations, however information on a mass balance is scarce. In the USA, in the PFAS Waste source testing report, an attempt was made to make a PFAS mass balance for landfilling by measuring PFASs in certain (not all) waste streams entering the landfill and PFAS leachate measurements (SANBORN, 2019).

To help evaluate what fractions of the PFAS compounds potentially leach from waste, versus what is sequestered (i.e., what is held on to) in the landfill a mass balance was derived. Information on PFAS load entering the landfill via waste, estimated via waste sampling, and PFAS load leaving the landfill, estimated with leachate sampling, was collected and analysed. A large PFAS mass imbalance was seen, see also Figure B.78. It was noticed that:

- A significant portion of PFASs is sequestered in the landfill for a long time. Longer chain PFASs are sequestered to a higher degree than short chain PFASs.
- PFAS emissions to air from the landfill were not considered but could be of relevance for volatile PFASs.

Exhibit ES-2 – Estimated Total PFAS Mass Flux In and Out of the Landfill

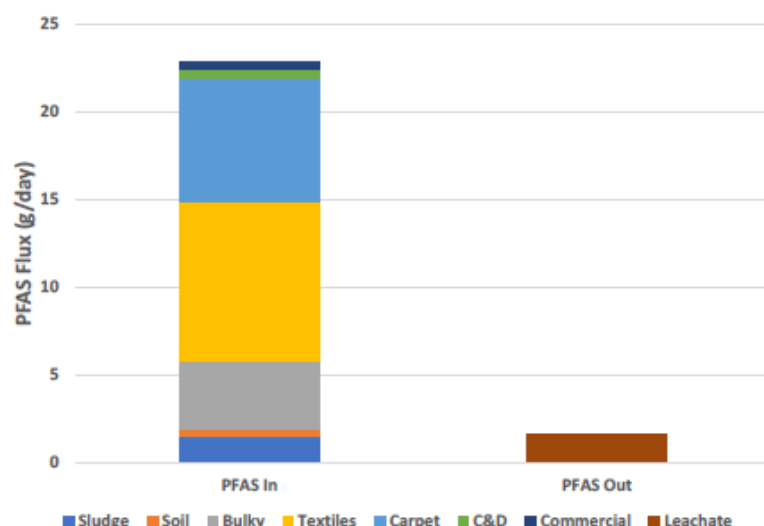


Figure B.78. PFAS mass imbalance landfill. Source: SANBORN (2019).

Because of sequestration and delay between PFASs entering the landfill and PFASs leaving the landfill via leachate (or air), a PFAS restriction will on the short term not lead to lower PFASs leachate concentrations. There will be a strong delay before lower PFASs loads entering the landfill will result in lower PFASs leachate concentrations. Even closed landfills continue to emit PFASs via leachate (and possibly via air) (Propp et al., 2021).

Landfilling in previous restriction dossiers

In the Annex XV dossiers for both PFOA and PFHxA, landfill has been mentioned as important sinks for these substances in specific product groups. The PFOA Annex XV report indicated that landfills may pose a potential source of PFASs in the environment through volatilization and through leaching to soil and groundwater (Bossi et al., 2008; Busch et al., 2010). The report further indicated that although untreated waste landfilling is not permitted since 2005, old landfills may still pose a problem and that the treatment of leachate is applied to most, but not to all landfills. A German case study indicated that more than 20% of active and non-active landfills are not treated at all.

Further uncertainty was recognized concerning the disposal of the sludge and filters applied in the treated landfills. The dossier recognized that emissions might be higher than expected due to degradation and indicated a potential lag in time due to persistency. No quantitative data on PFOA mass flows in landfills were provided.

The PFHxA annex XV report reported between 55 and 60% landfilling based on Eurostat data for 2018, but indicated considerable differences between the European member states. The report also indicated that no specific disposal data and recycling rates for paper and cardboard and for textiles were provided, which was considered essential for a proper evaluation.

Based on recent Eurostat data for emission calculation it was assumed that 38% of waste is landfilled. The DS is aware that this is a heavily simplified approach as landfill rates vary strongly among waste streams as well as among EEA countries and time.

B.9.18.2.4. Incineration

Waste incineration is a major waste treatment method in the EEA and its share in waste treatment methods has grown in recent years. In most European Member States, incineration is applied⁴³. The amount of waste incinerated in EU member states increased by 105% between 1995 and 2018⁴⁴. Currently a total of about 100 million tonnes of waste are incinerated in the EEA per year (Bjorklund et al., 2021). The main waste categories that are incinerated are industrial hazardous waste, healthcare waste and municipal waste. For municipal waste, 29% (2018) was incinerated with energy recovery⁴⁵.

PFASs are more difficult to break down than other halogenated organic chemicals such as PCB, due to PFAS fluorine's electronegativity and the chemical stability of fluorinated compounds (EPA-US, 2020).

Waste incineration can be divided into:

- Municipal waste incineration with and without energy recovery. (There are about 500 active municipal waste incinerators in the EEA).
- Hazardous waste incineration (including co-incineration in cement kilns). Hazardous waste incinerators have higher operating temperatures than municipal waste incinerators. There are over 100 installations in Europe.

Waste incineration is a high potential source of PFAS emissions as volumes of waste incinerated are increasingly large. The Dossier Submitters are of the opinion that incineration conditions (e.g. temperature) are not likely adequate to fully break down PFASs into non-hazardous fractions like HF, CO₂ and H₂O. Consequently, not properly controlled incineration may lead to air emissions and a solid ash fractions containing PFASs. Considering the broad application of PFASs the Dossier Submitters assume that most PFASs will end up in non-hazardous waste streams handled by municipal waste incinerators. Specific waste streams that are classified as hazardous (such as infectious medical waste and certain industrial waste) will partly end up in dedicated hazardous waste incinerators.

Limited PFAS releases from incineration plants are indicated in literature, and they depend on the type of material and type of incineration. Studies which take into account practical incineration conditions are scarce. Previous Annex XV dossiers concerning PFASs also indicate that there are still large uncertainties on the releases, as a full fluorine mass balance is lacking for incinerators.

In Table B.50 the degradation products from the incineration of PFASs found in literature are listed (García et al., 2007; Geertinger et al., 2019; Huber et al., 2009).

Table B.50. End products of the thermal degradation of reported PFAS compounds.

PFASs	End products
Fluoropolymers	CO ₂ , CF ₄ , C ₂ F ₆ , CHF ₃ , C ₃ F ₆ , CClF ₃ , C ₄ F ₈ , C ₂ Cl ₃ F ₃ , HF, trifluoroacetic acid and other perfluorinated gases
PFOS	CF ₄ , C ₂ F ₆ , CHF ₃ , C ₂ H ₂ F ₂ , HF
PTFE	CO ₂ , CO, CF ₄ , C ₂ F ₆ , C ₃ F ₆ , C ₂ F ₄ , and other fluorinated compounds

Based on waste incineration Best available techniques REference documents (BREF) municipal solid waste incineration plants are required to operate at 850 °C with a residence time of two seconds. These conditions may not be suitable for the destruction of PFAS-

⁴³ <https://www.cewep.eu/waste-to-energy-plants-in-europe-in-2019/>, date of access: 2022-12-14.

⁴⁴ https://ec.europa.eu/eurostat/statistics-explained/index.php?title=File:Municipal_waste_landfilled_incinerated_recycled_and_composted_EU_1995-2020.png, date of access: 2022-12-16.

⁴⁵ <https://www.cewep.eu/municipal-waste-treatment-2017/>, date of access: 2022-12-14.

containing waste. Incomplete destruction of PFASs during incineration can result in the formation of smaller PFASs or mixed halogenated organic byproducts. For complete destruction, without side products, temperatures above 1 400 °C are needed which can be reached in cement kilns (Winchell et al., 2021). It is not clear if PFAS containing waste is fully mineralized to CO₂, H₂O and HF in real life operational conditions in other incinerators than cement kilns. Waste incinerators cannot process a large intake of fluor containing waste as the HF that is formed can destroy critical parts of the incinerator.

Research states that temperatures need to be between 1 600 and 2 000 °C for full destruction. Hazardous waste incinerators (not many capacity available however in Europe) and cement kilns may therefore be better suited for (nearly) full PFAS destruction than municipal waste incinerators (Bolan et al., 2021).

Wang et al. (2015a) showed that the addition of calcium hydroxide can catalyse the defluorination process. At temperatures of 900 °C, this method showed high transformation rates, indicated by the formation of calcium fluoride.

Flue gas, bottomash and fly ash

Although PFASs can rarely be found in the flue gas and no quantitative data is available, some publications reported the occurrence of PFASs in the fly and bottom ash of representative waste incinerators, indicating that the PFASs are not fully destroyed. .

Additionally, one publication also analysed PFASs in fly ash (Sandblom, 2014), however no fly ash data was available for Europe. Abis et al. (2020) reported that 3% of the incinerated material becomes fly ash and BiPRO (2005) stated that 2.25% of the incinerated material becomes fly ash. Ultimately, the 3% from Abis et al. (2020) was chosen to reflect a worst case scenario. The data generated for fly ash should however be analysed with care, as the data is based on only one publication and data set.

From this data, an emission value can be calculated to compare the PFAS occurrence in bottomash to the landfill and WWTP data (Table B.51,

Table B.52, Table B.53). Three publications from Sweden and the Netherlands were identified resulting in the following mean and median values (Rijkswaterstaat, 2020; RWS, 2020; Sandblom, 2014; Wohlin, 2020):

Table B.51. Calculated mean and median concentrations in incineration bottom ash and fly ash for the PFAS groups (rounded). Data taken from three studies. n.A.: not analysed.

Substance	Mean (bottom ash) (pg/g)	Median (bottom ash) (pg/g)	Mean (fly ash) (pg/g)
ΣPFCA	811	43	8 981
ΣPFSA	312	0.00	1 805
ΣPFPA	n.A.	n.A.	n.A.
ΣPrecursors	578	0.00	n.A.
Total PFAS	1 701	43	10 786

Table B.52. Amount of bottom ash (rounded) from Blasenbauer et al. (2020) and incinerated waste in 2018 in Europe as well as the amount of fly ash generated from that waste. A generation factor of 3% for the fly ash was used from Abis et al. (2020).

Amount of bottom ash [t]	Amount of incinerated waste [t] 2018 [t]	Amount of generated fly ash [t]
15 323 000	144 077 000	4 322 000

With this data the amount of PFAS in bottom and fly ash can be calculated (Table B.53).

Table B.53. Calculated total PFAS amounts in incinerator bottom and fly ash.

Mean PFAS amount (bottom ash) [kg]	Median PFAS amount (bottom ash) [kg]	Mean PFAS amount (fly ash) [kg]
25.5	1.3	46.6

While most bottom and fly ash is landfilled in Europe it can also be used in pavement or highway foundation (Blasenbauer et al., 2020; ECHA, 2012a). Fly ash is often used in cement, concrete and gypsum as well as restoration and filling material in open cast mines, quarries and pits.

Most publications conclude that very low amounts of sampled PFASs can be found in the flue gas and that most sampled PFASs are destroyed >99%. Incineration studies monitor a limited number of (PFAS) compounds, leaving the question of unmonitored PFAS and Particles of Incomplete Combustion (PIC) unanswered (Stoiber et al., 2020). Most of these sources are based on laboratory studies and do not necessarily represent circumstances in reality. Neither are full fluorine mass balances provided to make clear where fluorine ends up.

Excessive operating temperatures could lead to sludge ash fusion and clinker forming. Very high operating temperatures will be prevented to extend refractory life and increase the time between costly maintenance shutdowns.

As recently stated in literature a major weakness in studies is that they do not mimic full-scale operational variations in thermal treatment systems. These variations are significantly different from those in lab scale systems. The lack of closed mass balances (>90% F accounted for) for nearly all experiments strongly implies that fluorinated products may escape thermal and post-treatment processes, elude detection, and be released to the environment.

US EPA recently stated that very little information is published on PFAS destruction. Fluorine chemistry is sufficiently different than chlorine chemistry. Chlorine chemistry cannot be extrapolated (Linak and Lee, N/T). US EPA also indicated that temperatures in incinerators are very heterogenous. Waste is heterogenous (composition, humidity, caloric value, etc.) and incineration conditions are heterogenous as well. Residence time, temperature, waste humidity and the presence of catalytic surfaces, often metals, are crucial variables. HF, just as HCL, is affecting the waste incinerator as it can be very aggressive for equipment. Waste incinerator operators and permit requirement will steer toward low HF emissions. (Sorbent injection is often used by operators to prevent damage caused by HF).

Collection of highly volatile PFASs is not a standard requirement for incinerators and limited information is available on PFASs in the scrubber systems of incinerators which could lead to a higher amount of PFASs in scrubber water. Winchell et al. (2021) mentioned that little is known about the fate of PFASs through incineration. PFASs in flue gas, ash, or water streams used for incinerator pollution control may be undetectable. Water used in the air pollution control systems contained PFASs and may mask the levels emitted by the furnace. The authors also noted that the inorganic fluoride content of the wet scrubber discharge water was over 10 000 times that of the influent flow plus the measured PFASs fed to the first fluidized bed furnace.

The impact from energy consumption associated with operating any incineration PFASs destruction technology is negligible compared to the reduction in greenhouse gas emissions due to the destruction of fluorocarbons (UNEP, 2018).

Incineration in previous dossiers

Incineration has been mentioned as important waste treatment option in both the PFOA and PFHxA Annex XV report.

For the PFOA restriction the dossier concluded that 'Although incineration might destroy PFOA, a final conclusion cannot be made since insufficient information is available on the behavior of PFOA and PFOA-related substances during the incineration process (see chapter B.4.4.4 in the corresponding dossier).'

The PFHxA Annex XV report also discusses incineration as a disposal route but potential releases from incineration are mentioned only qualitatively in the PFHxA Annex XV report.

The current restriction proposal on PFAS in AFFF remarks the following: Page 66. One of the measures to achieve minimized emissions is the safe disposal of PFAS-containing waste. The exposure assessment assumes incineration as disposal method to estimate the emissions to the environment from disposal. However, it is noted that the nature and quantities of emissions of PFASs or other fluorinated substances resulting from these disposal processes are not well known and further research should be carried out in real industrial conditions to ascertain their efficiency. Also, the impact on the emissions of greenhouse gases has not been calculated.

B.9.18.2.5. Waste water treatment

Waste water treatment from both domestic and industrial sources is known as an important source of PFAS release and has been discussed in previous restriction dossiers. Possible primary sources of PFASs are industry sectors producing or using PFASs (e.g. fluoropolymer production industry, the paper – and textile industry, the photo industry, electroplating companies) as well as landfills. Domestic sources such as households can be secondary PFAS sources (i.e. via toilet paper and personal care products discharge). Generally, PFASs are difficult to remove in Waste Water Treatment Plants (WWTPs) and often higher concentrations are observed in the effluent than in the influent. These increases in concentration in the effluent compared to the influent can be as high as 35 times and are attributed to the conversions of (unknown) PFAS precursors to stable PFAS end-products (STOWA, 2021a).

WWTP sludge can serve as a sink for PFASs and thus lead to PFASs emissions and pollution to agricultural soil in case the sludge is used as a fertilizer, which is common practice in some EU countries.

Most authors concluded that long-chain PFAS tend to accumulate more in the solid phase than in the liquid phase due to higher intermolecular interactions between the long PFAS chain and the solids (Coggan et al., 2019; Glimstedt, 2016).

Some publications also measured PFASs in the air above the water and around the waste water treatment plants. However, these emissions are assumed to be up to a factor 10 lower compared to the PFAS emissions from the effluent (Ahrens et al., 2011). The following mean and median concentrations were calculated (Table B.54, Table B.55, Table B.56)

Table B.54. Calculated mean and median concentrations in the influent/effluent water as well as sludge (WWTP) for the PFAS groups. Data taken from 7 studies.

Substance	Mean influent [ng/L]	Median influent [ng/L]	Mean effluent [ng/L]	Median effluent [ng/L]	Mean sludge [ng/g]	Median sludge [ng/g]
ΣPFCA	618	150	388	102	51	2
ΣPFSA	59	12	162	21	16	2
ΣPFPA	4	0.00	0.90	0.00	0.00	0.00
ΣPrecursors	116	8	17	2	47	35
Total PFAS	797	170	567.9	125	114	39

Table B.55. Reported influent, effluent and sludge data from Eurostat for 2016⁴⁶.

Influent [million m ³]	Effluent [million m ³]	Sludge production [t in d.s.]
14 299	16 944	6 577 000

Table B.56. Calculated total yearly PFAS load for selected EU-Member States based on the available Eurostat data (WWTP). All values in [kg].

Mean PFAS load influent	Median PFAS load influent	Mean PFAS load effluent	Median PFAS load effluent	Mean PFAS load sludge	Median PFAS load sludge
11 374	5 657	9 614	3 097	748	406

Recent, sampling based, research in the Netherlands estimated a yearly PFAS load in effluent of WWTPs of 65 – 180 kg PFAS/y for the whole of the Netherlands, while 15–45 kg PFAS/y leaves the treatment plants via sewage sludge (STOWA, 2021a). Given the order of magnitude, this is in line with the calculations above.

The effluent from the WWTP flows directly into European surface waters and as such the contained PFASs are directly emitted into the freshwater or marine aquatic environment. It is assumed that approximately 2/3 of the total load of PFASs contained in sewage sludge is not destroyed as it is either applied on land, composted or disposed of in a landfill. Only roughly a 1/3 of the sewage sludge is incinerated.

Waste water treatment in previous restriction dossiers

In the PFOA Annex XV report municipal wastewater treatment plants (WWTPs) were identified as important sources of PFOA and other PFASs, but the report also indicated that it was almost impossible to trace back the origin of PFOA and precursor emissions from municipal sewage treatment plants and to estimate the share in overall emissions from different industry sectors and consumer households. The report identified some important sources (textile- and photo industry, landfills and electroplating). The report further indicated that it is difficult to remove PFOA, that PFOA may be formed in the WWTP processes and that air emissions of PFAS may occur. PFOA concentrations in the effluent are often higher than in the influent. It was further indicated that PFOA may bind to sewage sludge and that it can be a potential PFOA source in the environment

⁴⁶

https://ec.europa.eu/eurostat/databrowser/view/TEN00030/default/table?lang=en&category=env.env_wat.env_nwat, date of access: 2022-12-19.

through the application of sludge for soil fertilization, which is still common in many European countries.

The PFHxA Annex XV dossier indicates that it is very difficult to remove PFHxA from the wastewater and thus WWTPs act as a source of PFHxA through their effluents and through the generation of sludge. Modelling results showed that 81% of the incoming PFHxA will be passed to the effluent, 12% to sludge and 8% to air. PFHxA is found by various studies in wastewater effluent and sludge, which confirms the model distribution. The aerial emissions may be related to volatile substances, such as 6:2 FTOH, which may be formed by the degradation of from side-chain fluorinated polymers. The behaviour of PFHxA in treatment plants is triggered by its low adsorption potential (see B.4.2.1) and the persistence. The PFHxS Annex XV dossier describes various industries that may be important sources for the WWTPs such as the chrome plating and pulp and paper mills. The dossier indicates that *'Emissions might be severely underestimated because potentially large direct emissions to the environment are possible from pulp and paper mill sludge that is produced during the treatment of wastewater derived from a paper mill.'*

B.9.18.2.6. Conclusion on PFAS emissions from landfilling, incineration and WWTPs

It has been shown that, keeping in mind all the uncertainties mentioned in B.9.18.2.1, WWTP via its effluent contributes the most to PFAS load to the environment with landfilling and incinerations contributing less. However, insufficient data was available for flue gas. Hence, an underestimation for waste incineration is likely. In the Table B.57 below the mean and median PFAS loads are presented.

Table B.57. PFAS emissions (rounded) in EEA for three main waste treatment methods based on literature research.

Waste treatment method	Mean PFAS load (t/y)	Median PFAS load (t/y)
Landfilling		
Leachate (water)	1.1-5.7	0.6-3.0
Air	No data	No data
Incineration		
Flue gas	No data	No data
Bottom ash	0.026	0.001
Fly ash	0.047	no data
Waste water treatment		
Effluent (water)	9.6	3.1
Sludge	0.75	0.4
Air	No data	No data

B.9.18.2.7. Sewage sludge

Sewage sludge is generated in WWTP by separating the undissolved particles from the water, which is done in lagoons or basins. As WWTP receives waters from urban and industrial sources they can contain PFASs originating from the production and use stage of the PFAS products (e.g. cosmetics, washing of textiles, etc.). Throughout the wastewater treatment, the PFASs also end up in the sludge, especially the longer-chain PFASs as the intermolecular interaction between the PFAS molecule and the surface of the particles is higher the longer the chain is (Glimstedt, 2016). After the treatment in the WWTP, sludge

from urban wastewater is recovered (agricultural use or compost and other uses) or disposed of (incinerated or disposed of otherwise). Within the EEA sewage sludge from urban wastewater treatment is disposed of or recovered (land application) in roughly equal proportions⁴⁶.

Most sewage sludge is generated in Western Europe. In Southern and Northern Europe more sewage sludge tends to be recovered, while more is disposed of in Western and Eastern Europe. Bianchini et al. (2016) reported, that due to the Landfill Directive (1999/31/EC) amounts of sewage sludge disposed of in landfills will rapidly decrease in upcoming years as Member States reduce the amount of biodegradable waste sent to landfills by 2016. Generally, the total sludge quantities fluctuate slightly but remain between 5,78 and 6,53 million tonnes dry substance (d.s.) since 2011. The PFAS load in sludge is estimated at 0.40 t in the EEA per year.

Treatment methods vary among the EU Member States and also develop differently. In Central Europe, it is to be expected that the agricultural use of sewage sludge will be further reduced or restricted by regulations. In The Netherlands and some Austrian federal states, land application is already prohibited. In Central Europe, it is to be expected that the agricultural use of sewage sludge will be further reduced or restricted by regulations. In Eastern Europe, an increasingly larger percentage of households connected to treatment plants can be expected. There, agricultural use of sludge is still considered the preferred disposal method. The use of alternatives such as co-incineration are expected, but the market implementation might be influenced by public concerns or possible administrative obstacles due to national legislation⁴⁷.

The reuse of biosolids as soil improver/fertilizer in arable crops represented the most used disposal/recovery option in some European countries. This has led to restrictions in the use of biosolids with Directive 86/278/EEC, however, an evaluation of the directive in 2014 has found shortcomings also with regards to contaminations such as PFASs. These are currently not regulated.

Currently Directive 86/278/EEC is under evaluation and PFASs are likely to be an important attention point⁴⁸. Examples in EEA (Rastatt, Germany) and the USA illustrate the need to be careful with land application of sludge and biosolids (Johnson, 2022; Treat, 2021).

France, Finland, Germany, Ireland, Italy and Spain currently have the highest share of biosolids recycled to land. Most countries in the EU have prohibited the use of untreated sludge on land, while some Member States (France, Ireland and the UK) permit the use of untreated sludge (Collivignarelli et al., 2019).

B.9.18.2.8. Waste transfer stations

Waste transfer stations are generally used to sort, crush and bulk waste in order to enable an efficient waste packing for further transport. During this process liquids are usually decanted into a separate container (JRC, 2019). During the sorting and crushing process liquids may be spilled from the waste and can end up in the leachate from the waste transfer station. It has been shown in literature, that the amount of PFASs in the leachate from waste transfer stations can reach levels of up to 46 µg/L (Wang et al., 2020a). This study was performed in China and may not be representative of the European waste transfer stations in Europe, however it indicates the risk arising from these transfer stations (RWS, 2020).

According to the European Waste Management Association (FEAD) there are 2 400 recycling and sorting centers in Europe (FEAD, 2021). It is unclear how many of these are

⁴⁷ <https://eu-recycling.com/Archive/22374>, date of access: 2022-12-19.

⁴⁸ https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12328-Sewage-sludge-use-in-farming-evaluation_en, date of access: 2022-12-19.

waste transfer stations. The actual number of waste transfer stations in Europe is unknown. Waste transfer stations might be an important source of PFAS contaminated surface runoff water as was indicated by RWS (2020).

Leachates from waste stored at waste incinerators maybe an important source of emissions also (Liu et al., 2021b).

B.9.18.2.9. Recycling

The aim of the restriction is to end all emissions of PFAS substances mentioned in the entry. As the dossier has demonstrated a concern resulting from PFAS exposure, there is a concern for recycled materials containing these substances as well. Therefore this restriction proposal also includes PFASs released during the recycling process and PFASs in recycled material and articles made from recycled materials.

The recycling market is a worldwide market. Materials can be exported outside EEA to be recycled/treated. Next to that, recycling is extending the lifetime of an article but in the end landfilling, incineration, composting or dumping/littering remain.

Recycling may appear for all types of PFASs that are applied in articles, but is expected to be high in textiles and paper, construction products, End-of-Life vehicles and electronics.

Especially for lacquers and ink, PFASs likely stays either in the recycled paper and/or is released to water in recycling facilities. For plastics, although much less studies are available, the same risk could be applicable as both paper and plastics are major recycling flows. From moulded fibre, elevated levels of PFASs have been reported (see Straková et al. (2021)). If such fibres are composted, all PFAS content will be released in the environment, leading to soil, water, and crop contamination⁴⁹. For paper and board for instance it is observed that increased recycling will lead to spread of PFASs throughout all the paper and board market, as cited for instance by (Lowe et al., 2021). The Single Use Plastic Directive could lead to more moulded fibre food packaging being used, most of which contains PFASs for water and grease resistance. This could (further) contaminate paper and board recycling streams.

Eurostat (2019) has provided 2019 recycling percentages for plastic packaging and E-waste with 42% and 41% respectively. Recycling of textiles is considered low by the European Commission⁵⁰.

Fluoropolymers are very broadly applied but recycling of fluoropolymers is hardly possible as they are often coated on other materials. It has for instance to be noted that, as also mentioned by stakeholders, the fluoropolymer-content of metal cook- and bakeware is <1% weight/weight and is only removable via sand blasting or burning of the non-stick coating. And this applies to very many other articles: Recycling of fluoropolymers is hardly possible/cost effective.

Currently, lithium-ion batteries (LIB) as well as solar panels are niche waste streams. This will quickly change as both categories experience tremendous growth⁵¹. PFAS emissions from improper waste treatment and accidental fires of these applications may become a potential risk. There are for instance a lot of fires at recyclers caused by Li-ion batteries. There will be (PFAS) emissions (Larsson et al., 2017).

For solar panels the fluoropolymer coatings in front and back sheets currently can hardly be recycled and end up in shredder fractions which can be applied in (road) foundations or

⁴⁹ <https://www.fidra.org.uk/news/pfas-in-compostable-packaging/>, date of access: 2022-12-14.

⁵⁰ The EC indicate that textile recycling is low: [Strategy for textiles \(europa.eu\)](https://ec.europa.eu/eurostat/tgm/table.do?tab=table&init=1&language=en&code=sdg_12_8_1)

⁵¹ <https://www.rystadenergy.com/news/reduce-reuse-solar-pv-recycling-market-to-be-worth-2-7-billion-by-2030>, date of access: 2022-12-14.

incineration (Späth et al., 2022).

Recollection of fluorinated gases from air conditioners and cooling equipment is crucial to prevent emissions in the waste stage. A crucial way to prevent the release of environmentally persistent fluorinated gases into the atmosphere is through collection and immediate destruction of the gases. Destruction methods for fluorinated gases require extreme conditions due to their chemical and physical inertness (Sheldon and Crimmin, 2022). In case recollection of fluorinated gases and/or destruction is not properly conducted, gas emission from waste treatment of cooling equipment can lead to serious PFAS emissions in the waste stage.

Recycling materials enter the production phase again. This is for instance an important factor in paper production where very often new and recycled material are mixed to produce paper. ECHA (2016a) R.16 guidance page 36) states that '*Where the process leading to the recovery of the substance is the same as the substance manufacturing (like e.g. for some metals), this last step in the waste operation (i.e. when recovery follows other waste treatments) may be already covered in the assessment of the manufacturing process. Other operations regularly carried out in the context of recycling/recovery (e.g. dismantling processes, milling and separation processes) may need a particular assessment.*'. For the release to water and air the default release factors in Table R.18-10: Defaults for the paper scenario in the R.18 Guidance may be used. Values provided in Table R18-30 for shredding may be used as well. For other recycling streams, such defaults are not provided.

Recycled products, although its lifecycle is extended, will finally be incinerated, landfilled or littered.

Recycling in previous restriction dossiers

Recycling was only mentioned qualitatively in the *PFOA restriction dossier*, which indicated that reuse and recycling should not be prohibited to facilitate the sustainable management of resources. Recycling of paper and cardboard was mentioned in the dossier, but could not be quantified because limited information was available. Recycling was not mentioned for the other product groups. Except for transferring PFOA to next generation products, emissions to air and water were also expected due to landfilling and incineration of waste.

According to the *PFHxA restriction dossier* there might be a recycling issue with regard to paper, textiles, semiconductors and building materials. Although textiles and paper and cardboard were considered very relevant sources of PFHxA in the PFHxA restriction dossier, releases from recycling of these materials (i.e. shredding, washing and pulping of wastepaper and cardboard prior to re-use) were not considered in the assessment as no data on PFHxA emissions from the process of wastepaper recycling were available to the Dossier Submitters.

B.9.18.2.10. Estimation of waste stage emissions based on ERC

Because of all uncertainty regarding waste stage emission as stated in literature, also emission calculation based on ECHA ERCs was applied.

To get an indication of the amounts of PFASs that are released from the waste stage ERCs for waste treatment were applied to the volumes of PFASs that enter the waste stage. It was assumed that 38% of waste containing PFASs is landfilled, 38% is recycled and 24% is incinerated. For paper uses, ECHA has different ERC (with higher emission percentages)

The volume of PFASs entering the waste stage based on Eurostat 2018 numbers. The

website in the footnote⁵² is a starting point for the estimations. ECHA is assuming a residence time of 20 years for waste in landfills.

For landfill emissions in Table B.58 ECHA R.18 Landfill ERC were used. This likely leads to an underestimation of life time PFAS landfill emissions as landfills have a longer lifetime than the default 20 year period. From Figure B.78 above it can be seen that an ERC of around 10% seems more likely. Taking into account that PFAS leachate emissions will continue for many years after closure of a landfill, the 10% could still be an underestimation of the PFAS landfill life-time emission factor (Propp et al., 2021)⁵³.

As explained in Figure B.78, and due to the persistence of PFASs, the fact that the applied ERC is for organic substances and not very persistent PFASs, and the fact that leachate will continue to emit many years after landfill closure, a worst case emission factor of 10% is applied as well in Table B.58. It should be noted that after 20 years (the residence time in landfills assumed via the ERC), PFASs will still be present in the landfill and for decades if not centuries. Part of the PFASs will be sequestered in the landfill but how much is unclear.

Table B.58. ECHA ERCs for the waste stage (ECHA, 2012a).

	Air	Water	Soil	Sludge	Remark
Incineration	0.0001	0.0001	0		
Landfill	0.0005	0.032	0.0016		
Recycling	0.025	0.0025	0		For paper recycling there are separate (much higher numbers)
Paper	0.15	0.9014	0.00144		
WWTP	0.001	0.09	0	0.91	

The PFAS load entering the waste stage is a starting point for the estimations and applying a generic division among the different waste treatment techniques (landfill, recycling and incineration) based on Eurostat 2018 numbers⁵².

Subsequently the standard ERC release factors from the ECHA guidance (ECHA, 2012a) for estimating the releases for landfilling, incineration and recycling are applied. ECHA is assuming a residence time of 20 years for waste in landfills.

⁵² https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Waste_statistics, date of access: 2022-12-23.

⁵³ <https://www.wastetodaymagazine.com/article/minnesota-pfas-groundwater-contamination-landfills/>, date of access: 2022-12-19.

Table B.59. Waste stage emissions based on ECHA ERCs. Air, water and soil emissions presented as environmental emissions.

Use	PFAS load (t) entering solid waste stage - midpoint unless stated others	TOTAL ENVIRONMENTAL COMPARTMENT life time emissions	TOTAL ENVIRONMENTAL COMPARTMENT life time emissions ERC 10% landfill (water)
Lubricants	1 447	34	71
TULAC	69 118	1 621	3 407
FCM and Packaging Paper and board packaging (midpoint)	4 897	115	241
Consumer bakeware & professional bakeware	6 429	151	317
Other uses (packaging, can's etc)	15 240	357	751
Consumer mixtures	0	0	0
Construction products	6 495	152	320
Cosmetics	0	0	0
Metal plating and manufacturing of metal products	954	22	47
Production	36 000*	540*	540
Ski wax	1	0.946	n.a.
Transportation (stock)	12 850	301	633
Transportation (new on market)	6 141	144	303
Petroleum & Mining	1	0	0
Medical applications	5 901	138	291
HVACR and	19 724	Unknown	unknown

Use	PFAS load (t) entering solid waste stage - midpoint unless stated others	TOTAL ENVIRONMENTAL COMPARTMENT life time emissions	TOTAL ENVIRONMENTAL COMPARTMENT life time emissions ERC 10% landfill (water)
other fluorinated gases applications			
Electronics and semiconductor	3 752	88	185
Energy	2 995	70	148
TOTAL		3 736	7 255

* Extrapolated based on Chemours, the Netherlands data.

Total waste stage emissions based on ERCs are (far) higher than the literature estimates and range between 4 000 and 7 000 t/y. However the emissions of fluorinated gases is not taken into account as there was no data available.

B.9.18.2.11. Summary

PFASs are used in thousands of applications. All these applications sooner or later reach an end of life stage: The waste stage. In final waste treatment, landfilling and incineration are the most important waste treatment methods. Recycling can extend the lifetime but in the end, for almost all substances, mixtures or articles, only emission in the use phase or during landfilling and incineration apply.

Landfilling of PFAS containing material leads to very slow release of PFASs. This can continue for decades or even longer after closure of the landfill. Landfills have more or less a symbiotic relationship with Waste Water Treatment Plants (WWTP) as landfills send leachate to WWTP and WWTP send sludge to landfills.

Waste water treatment plants (WWTP) are not capable of removing PFAS: In many cases even higher PFAS concentrations are measured in effluent compared to influent. Spreading of (WWTP) sludge is a high risk for PFAS spreading.

In waste incineration many remains unclear. Due to the fluorine electronegativity PFAS are even harder to breakdown via high temperature than other halogenated substances like PCB's. Incomplete destruction of PFAS compounds can result in the formation of smaller PFAS and/or products of incomplete combustion. The latter compounds have not been researched and could be a potential concern. No study has been found with a full fluorine mass balance. Scrubwater of incinerator flue gas cleaning systems is less well researched but could be a significant source of PFAS.

In recycling, PFAS cannot be removed. It will be present in the recycled articles such as paper or plastics.

Based on literature research the yearly emissions from landfilling, incineration and waste water treatment are 1-6 t/y. There are serious limitations in literature f.i. incomplete PFAS analysis and lack of closed fluorine mass balances. Therefore additional emission calculations have been also performed.

ERC calculations:

No specific emission factors for waste treatment methods have been found. In some cases like landfilling and incineration (some) PFAS *output* measurements are available, though often incomplete. But PFAS *input* to a landfill or incinerator is hardly ever clear. Therefore for additional emission estimates the Dossier Submitters had to rely on generic ECHA ERCs for organic substances.

Especially for food contact and packaging waste stage emissions seem to be significant. (Because ECHA has different ERCs for paper packaging). TULAC waste stage emissions are also relatively high due to the high tonnage entering the waste stage. Waste stage emissions in PFAS manufacturing could also be relevant as was shown for Chemours in the Netherlands (and 3M Zwijndrecht and Miteni in Italy). These are however limited examples whereas there are about 20 PFAS manufacturers in EEA.

In general waste stage emissions, using ERCs are not to be neglected and for landfilling will continue for a very long period. The risk that PFAS emissions in waste stage are (severely) underestimated is prominent because of the many uncertainties in PFAS waste treatment emissions (incomplete analysis, lack of mass balances, no clear picture on emission of fluorinated gases in HVACR treatment, etc.) and the application of an ERC for organic substances for a very persistent group of substances.

Based on ECHA ERCs the lifetime waste stage emissions (20 year) coming from yearly PFAS loads entering the waste stage, are between 4 000 and 7 000 t (rounded numbers). The fate of fluorinated gases, the PFAS group with the highest emission in manufacturing/ use phase, is unclear in waste stage. Fluorinated gases are recovered or destroyed but for the Dossier Submitters it remains unclear if and to what extent PFAS emissions (emission of fluorinated gases) are to be expected.

Because of societal stock and because PFAS use has increased over the last decades, the waste stage will remain an important source of PFAS emissions for many years to come, even in case of a swift full PFAS ban.

B.9.18.2.12. Human exposure

As a lot of waste streams contain (some) PFASs. Waste treatment can be a source of human and worker exposure. In waste collection until final waste treatment the most risk full phase regarding PFAS worker exposure likely is the waste pre-treatment and sorting phase where dust exposure is often prominent. In waste sorting higher levels of PFAS were found in waste recycling plant workers serum and urine compared with other job assignments, such as managers, suggesting that sorters may be directly exposed to PFAS. And in dust samples collected from e-waste areas in China PFAS concentration was 15 times higher than in clothing shops (Peng et al., 2022).

According to another study, waste workers are chronically exposed to PFAS released during the recycling/repurposing of materials at e-waste processing sites. Although the study was performed in China, exposure at EU (e-waste) recycling facilities likely is non-neglectable as well (Garg et al., 2020). Also in recycling/processing of construction materials including construction waste, (PFAS) dust exposure is a risk. As construction waste is a high volume, often dusty, waste stream, this could be of relevance for worker exposure (Chamberlain et al., 2022; Fernández et al., 2021).

Exposure during waste treatment can result in PFAS intake through inhalation, ingestion, and dermal routes (Tansel, 2022).

Not only waste sorters and waste recycling workers are exposed to PFAS, also people and communities around waste treatment sites are (disproportionately) affected. Studies from the U.S. and Europe reported that waste facilities such as incinerators and landfills are more frequently located in disadvantaged communities, causing pollution and health inequalities in addition to economic and social injustices (Stoiber et al., 2020). Risks to

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

occupational and public safety from waste are greater in low-income and middle-income countries. Export of PFAS containing waste (i.e. WEEE) to countries outside EEA could lead to serious (worker) exposure issues in the waste receiving countries, especially in case informal waste treatment methods like open burning etc. are applied (Cook and Velis, 2020).

B.9.19. Other sources (for example natural sources, unintentional releases)

Besides the manufacturing of PFASs, some PFASs may also be formed as a by-product of other manufacturing processes. A significant emission source of PFCs (specifically tetrafluoromethane and hexafluoroethane) is the aluminium and rare earth metal smelting industry (Kim et al., 2021)⁵⁴. In the primary production of aluminium, anode effects during the Hall-Heroult process result in the production of tetrafluoromethane and hexafluoroethane as by-products, which is generally emitted to air. Reduction in the emissions of these PFCs cannot be regulated through the EU REACH regulation, as it involves industrial emissions of by-products. Other regulatory actions are being applied to reduce these sources of PFCs to the environment, as these substances are also very long-lived greenhouse gases with a high global warming potential, giving these substances the potential of becoming a near-permanent legacy of the industrial era (Victor et al., 1997).

Another assumed source of a specific PFAS – trifluoroacetic acid (TFA) – that cannot be regulated, are natural processes under extreme conditions – like undersea hydrothermal vents (Solomon et al., 2016; UNEP, 2015). However, there is discussion on the relevance of natural sources of TFA in the environment, especially when it comes to the non-marine environments (Joudan et al., 2021; UNEP, 2015).

⁵⁴ <https://www.epa.gov/f-gas-partnership-programs/aluminum-industry>, date of access: 2022-12-19.

B.9.20. Overall environmental exposure assessment

Assuming a one-compartment model, all emissions to the environment can be considered as direct exposure to the environment. Although the type of exposure may differ, e.g. direct exposure by emissions of fluorinated gases and slow release from fluoropolymers over a long period of time, eventually the environment is exposed to all PFASs that are emitted. In Table B.60 total yearly EEA emissions to the environment are provided for the researched PFAS uses. Emissions from Plant Protection Products (PPP), Biocidal Products (BP) and Medicinal Products (MP) and emissions in the waste stage are not included mainly because of the high (emission) uncertainty related to the routes of disposal and the final waste treatment method applied.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.60. Summary of EEA yearly emissions of PFASs per use sector (waste stage and active ingredients from PPPs, MPs and BPs not included).

Application	PFAAs and PFAA precursors (t/y)			Fluorinated gases (t/y)			Polymeric PFASs (t/y)			Total PFASs (t/y)		
	low	mid	high	low	mid	high	low	mid	high	low	mid	high
Manufacture	54	86	118	309	1 973	3 637	15	23	30	378	2 082	3 785
TULAC ^b	2 058	6 177	10 295				8 326	16 643	24 960	10 384	22 820	35 255
Food contact materials and packaging	123	491	858				99	100	100	222	591	959
Metal plating and manufacture of metal products ^c	0.5	6	11.4							1	6	11
Consumer mixtures										23	23	23
Cosmetics										0.015	32	64
Ski wax										1	1	1
Applications of fluorinated gases ^{d,e}				<i>38 806</i> <i>1 696</i>	<i>38 806</i> <i>1 696</i>	<i>38 806</i> <i>1 696</i>				<i>38 806</i> <i>1 696</i>	<i>38 806</i> <i>1 696</i>	<i>38 806</i> <i>1 696</i>
Medical devices	128	239	350	3 772	5 586	7 400	32	76	120	3 932	5 901	7 870
Transport ^d							<i>269</i> <i>35</i>	<i>439</i> <i>58</i>	<i>609</i> <i>80</i>	<i>269</i> <i>35</i>	<i>439</i> <i>58</i>	<i>609</i> <i>80</i>
Electronics and semiconductors	348	513	677	7	7	7	11	152	292	366	671	976
Energy sector	42	42	42				12	13	13	53	55	56
Construction products	88	152	216				1 364	2 338	3 311	1 451	2 489	3 527
Lubricants	0.11	0.6	1.1	29	46	62	123	174	225	152	220	288
Petroleum and mining ^c	0.3		2.3							0	1	2
TOTAL^f	2 842	7 707	12 571	42 923	46 418	49 912	10 251	19 958	29 660	56 038	74 137	92 232
Total ^g	2 842	7 707	12 571	5 813	9 308	12 802	10 017	19 577	29 131	18 694	36 646	54 593

a: In some cases a basis for providing a range is lacking. There the available estimate is applied throughout; b: TULAC = Textile, upholstery, leather, apparel and carpets; c: No data available for emission of polymeric PFASs; d: For these sectors the emissions relate to stock (presented in italics). For reference only, the emissions from tonnage brought new to market in 2020 are also given; e: Includes emissions of fluorinated gases in transport sector.

f: Total based on emissions from best available data (stock if available, new to market if stock is not available); g: For reference only, also the total emissions from tonnage brought new to market in 2020 are presented.

PFASs (including the group Other PFASs) used for the impact assessment (see Annex E.2.). These emissions may be an underestimation of environmental emissions and exposure, as not all PFAS uses were researched, emissions from technical stock (PFASs in products already in use) are not taken into account, except for HVACR (as stock information for this sector was available). Waste stage emissions are not taken into account in Emissions from technical stock may have a considerable contribution to the yearly emissions, especially for products that have a long life cycle. Besides PFASs in technical stock, the environmental monitoring data (see B.4.2.6 and B.4.2.7) show that there already is an environmental stock of PFASs. This environmental pollution of PFAS may already exceed planetary boundaries (Cousins et al., 2022), so all additional emissions contribute further to the environmental stock and associated risks of PFAS. There is a delay in time and space when and where the emissions could be demonstrated in the environment. Based on the available information from the different sectors it is clear that polymeric PFASs and fluorinated gases have the highest emissions. For fluorinated gases, this can also be explained by the fact that technical stock emissions are used for HVACR.

B.9.21. Human exposure

In each of the PFAS use sections described above, human exposure is briefly described for each use sector. In the text below the general picture for human exposure is described in more detail.

Human exposure to PFASs has been extensively studied through biomonitoring studies and intake estimations via different exposure routes. The wealth of studies unambiguously demonstrates that humans world-wide are exposed to a wide range of PFASs with the highest levels reported for workers and community residents living close to contaminated sites (hot spots).

Exposure to PFAAs occurs either via direct intake of arrowhead PFAAs, which are not further metabolised in the body, or indirectly via intake of precursor compounds that can be metabolised to arrowhead PFAAs and thus contribute to the internal levels of these compounds. The ubiquitous presence of PFASs in environmental media (see B.4.2.6 and B.4.2.7) and widespread use in many types of consumer products lead to an array of potential exposure sources (Figure B.79). For the general population (i.e. individuals who are not occupationally exposed or living in contaminated hot spots), exposure routes include ingestion of food and water, intake of indoor dust, inhalation of air and contact with consumer products (De Silva et al., 2021; Haug et al., 2011a; Poothong et al., 2020; Vestergren et al., 2012; Vestergren and Cousins, 2009). The dominating exposure route varies greatly for different PFAAs, reflecting their physico-chemical properties and use patterns. For hydrophobic and bioaccumulative long-chain PFAAs, dietary intake (especially of fish and meat) is typically the most important exposure route, whereas for highly water soluble short-chain PFAAs, drinking water and other food categories, such as vegetables, tend to be the dominating exposure routes (EFSA, 2020; Vestergren et al., 2012). For precursor compounds, exposure to consumer products (e.g. impregnation products) via the indoor environment (air and dust) is probably the major exposure route (Vestergren et al., 2008). Regarding other non-polymeric PFASs, such as PFAEs, the relative contribution from different exposure routes in the general population has not been described. For occupationally exposed individuals, who may have a higher exposure, the primary routes to PFAA exposure are inhalation, ingestion of dust and dermal uptake at the workplace (De Silva et al., 2021; Fu et al., 2015).

The bioavailability and thus the potential for human exposure to fluoropolymers has been an issue for discussion and is further described in B.5.1.2. In summary, it has been proposed that absorption of fluoropolymers in humans is obstructed due to their large sizes (Henry et al., 2018). On the contrary, it has been argued that the production, processing, use, and end-of-life treatment of fluoropolymers lead to emissions of bioavailable compounds (e.g. monomers, oligomers, decomposition and combustion products, PFAA/PFEA polymerization aids, additives, unintentional PFAS by-products, impurities, and particles, etc.), which may be relevant for human exposure (Lohmann et al., 2020). Regarding side-chain fluorinated polymers, potential degradation to more bioavailable PFASs may add to the exposure to these compounds in humans.

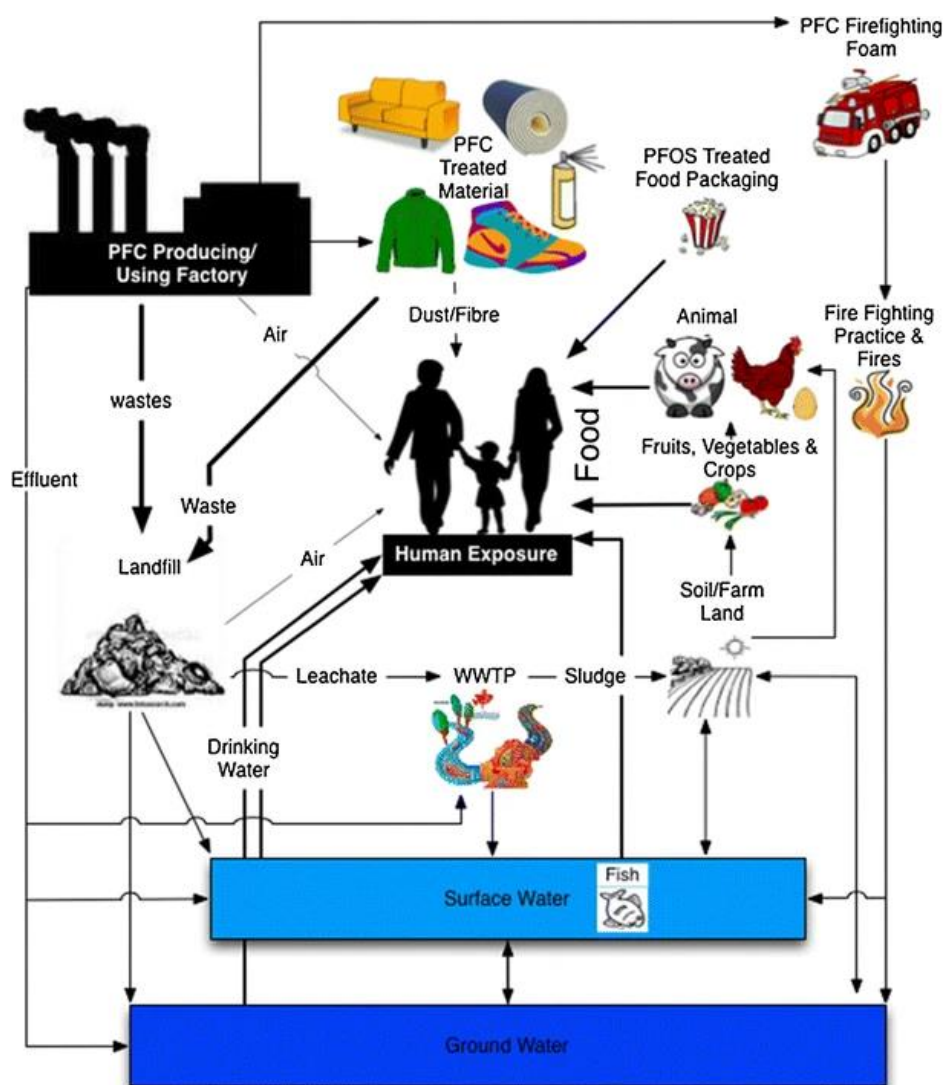


Figure B.79. PFAS exposure pathways to humans from Oliaei et al. (2013).

Children are exposed to PFASs prenatally via placental transfer and postnatally via breast milk, as demonstrated by the presence of PFASs in umbilical cord blood, placenta, breast milk and in the blood of breastfed children. There is a known association between the length of the breastfeeding period and higher levels of PFASs in the child, and conversely, lower levels in the nursing mother, illustrating the importance of breast milk as an exposure route for the infant (Brantsaeter et al., 2013; Haug et al., 2011a; Haug et al., 2010b; Koponen et al., 2018).

Results of several studies have highlighted notable differences among exposure to PFASs across different life stages (e.g. breastfed infants versus adults) and genders. In adults, PFAS blood levels are often higher in men compared to women of the same population, which can partly be explained by physiological factors, such as menstruation, pregnancy, breastfeeding and gender-dependent differences in urinary elimination, leading to a faster excretion in women (Brantsaeter et al., 2013; Gomis et al., 2017; Wong et al., 2014). However, the lower blood levels in women may also reflect different exposure patterns between genders.

B.9.21.1. Dietary exposure

In recent years, the environmental persistence of PFASs and their biomagnification in food webs have generated a notable interest and a large number of publications in this regard. For the already regulated PFASs, of chain lengths ranging between eight to fourteen carbons, food (primarily fish, egg, meat) is generally the major exposure route (EFSA, 2020). For shorter chain PFASs, the available data set is less robust, however the data indicate that these substances are present in food, such as vegetables, but that the dietary intake may be less important for the total exposure (EFSA, 2020; Vestergren et al., 2012).

The most extensive overview of PFASs in food in Europe was presented in the EFSA risk assessment of PFASs in food (EFSA, 2020). The dataset contained >97 000 food samples collected between 2000 – 2016 in 16 European countries. Quantitative data were available for 17 PFASs, of which eight are not restricted and in the scope of this restriction proposal – PFBA, PFPeA, PFHpA, PFPeDA, PFHxDA, PFDoDA, PFBS, and PFHpS. A cut-off value of 1 µg/kg was applied based on Commission recommendation 2010/161/EC (EC, 2010). The result showed that PFBA, PFPeA, PFHpA, PFBS, and PFHpS were detected in food samples, however close to or below the cut-off value. Of the >97 000 samples, the levels in approximately 24 500 samples were below the cut-off value 1 µg/kg. In the total dietary exposure assessment, PFBA was estimated to contribute with 16% to the total PFAS exposure via diet. PFPeDA, PFHxDA and PFDoDA were not detected in any samples.

A number of scientific studies has also analysed PFASs in food in other European countries not covered by the EFSA report. The results confirmed the findings by EFSA, i.e., that the levels of unregulated PFAAs were in the low µg/kg range or lower (data not shown).

Contaminated sites may result in highly contaminated foodstuffs, which is illustrated by several studies. For example, high levels of PFOS, up to 230 µg/kg, was found in veal meat close to a firefighting training site in Denmark where the animals had been consuming contaminated grass (DVFA, 2021). This subsequently led to highly elevated blood levels of PFOS in a population consuming the veal meat. Another example is a recent study of individuals living within a 3 km radius from the 3M facility in Zwijndrecht, Belgium, which showed that consumption of locally produced food (especially eggs) was associated with higher blood levels of e.g. PFOS (VITO and PIH, 2021). Furthermore, HFPO-DA (which was not covered by the overview by EFSA) has been detected in the Netherlands at low µg/kg levels in vegetables in the vicinity of a fluoropolymer production plant and close to a company processing products from the fluoropolymer production plant (reviewed in Gebbink and van Leeuwen (2020)). In addition to populations living in areas with higher levels of PFASs in food, certain dietary habits may lead to high exposure to PFASs. A potentially highly exposed group is fishermen, with a diet high in fish, where elevated serum levels of PFASs (including unregulated PFASs) have been shown (Hu et al., 2018; Shi et al., 2016; Zhou et al., 2014).

In addition to exposure to PFASs via foodstuff, there is also a possibility for additional exposure via the use of PFASs in food contact materials. Transfer of PFCAs/PFSAs, PAPs and fluorotelomers from food contact materials to the food have been shown (Elizalde et al., 2018; Gebbink et al., 2013; Lerch et al., 2022; Zabaleta et al., 2020) with higher transfer at increased temperatures (Elizalde et al., 2018) and where the tolerable daily intake (TDI) for PFAS in food set by (EFSA, 2020) was exceeded in children (Lerch et al., 2022). In the risk assessment of PFAS in food, EFSA concluded that although PTFE cookware may contain residual PFOA in the low µg/kg range and that food packaging may contain PFASs because of their grease-resistant properties, and that the use of this type of material is likely to contribute to human exposure to PFASs, the contribution is small compared with other sources of exposure, see also section B.9.4.3.

In the literature search for this section, no studies on TF, EOF or TOPA in food were found.

B.9.21.2. Exposure via drinking water

PFASs are often found in European drinking water (Domingo and Nadal, 2019; Kaboré et al., 2018; Lindfeldt et al., 2021). For example, a recent Swedish national survey reported that approximately half of drinking water samples from 154 Swedish municipal water works contained detectable levels of one or several analysed PFASs (Lindfeldt et al., 2021). Thus, drinking water can be a relevant exposure route for the general population, especially for short-chained PFASs (EFSA, 2020; Vestergren et al., 2012). Monitoring of PFASs in drinking water is further discussed in B.4.2.1.3, B.4.2.6 and B.4.2.7.

Drinking water is a particularly important exposure route in areas near point sources of PFASs. For example, elevated levels of PFASs, including non-regulated compounds, have been found in drinking water in areas near fluorochemical manufacturing facilities, firefighting training sites, landfills and agricultural land treated with industrial-waste derived soil improvers in Europe, the US and China (Frisbee et al., 2009; Gebbink and van Leeuwen, 2020; Glynn et al., 2015; Gyllenhammar et al., 2015; Ingelido et al., 2018; Kotlarz et al., 2020; Scher et al., 2018; Wilhelm et al., 2008; Xu et al., 2020c). As a consequence of the high levels in drinking water, populations residing these contaminated sites often display elevated PFAS levels in blood. For example, Glynn et al. (2020) showed that blood levels in children can be significantly elevated already at relatively low levels of PFAAs in the drinking water (<10 ng/L of single PFAAs).

B.9.21.3. Exposure via outdoor air

Outdoor air is not considered to be an important exposure route to PFASs in the general population (Egeghy and Lorber, 2011). However, for populations living in areas close to atmospheric point sources, exposure via outdoor air may be of relevance (De Silva et al., 2021). For example, elevated internal levels of PFOA were detected in a population living near the Dupont/Chemours facility in Dordrecht, the Netherlands. The drinking water did not contain elevated levels of PFOA and thus, the air was deemed the most likely exposure route.

B.9.21.4. Exposure via consumer products and the indoor environment

PFASs are present in a wide range of consumer products in the indoor environment. From these products, non-volatile PFASs can be released by abrasion, whereas volatile and semi-volatile PFASs can be released by volatilisation (Winkens et al., 2018). Released PFAS partition to dust and air, which constitute potential exposure routes to individuals residing the indoor environment. Consumers may also be exposed to PFASs directly from products via e.g. inhalation, dermal uptake or hand-to-mouth exposure. Impregnation products for floors, carpets and furniture have been hypothesised to be especially important for elevated indoor levels of PFASs (Beesoon et al., 2012; Knobeloch et al., 2012; Kubwabo et al., 2005; Zhou et al., 2022). The hypothesis that consumer products are the origin to PFASs in indoor environments is supported by the composition of PFASs in dust and air, which shows that precursors used in consumer products dominate the concentration profiles (see Appendix B.9.21. Table B.111 and Table B.112).

In indoor dust, n:2 monoPAPs/diPAPs (precursors to PFCAs) are found at the highest levels (De Silva et al., 2012; Eriksson and Kärrman, 2015; Winkens et al., 2018). Other precursors (e.g. FOSAs, FOSEs and FTOHs) and arrowhead PFAAs (mainly PFOS and PFOA) are found at varying but largely comparable levels. Among the PFAEs, 6:2 Cl-PFESA have been detected in indoor dust from China (Xu et al., 2021a; Zhang et al., 2020a), but only at a low detection frequency (2%) in Finnish dust samples (Winkens et al., 2018). ADONA and HFPO-DA were not detected in any dust sample in these studies (Winkens et al., 2018; Zhang et al., 2020a). Significant correlations between PFAA levels in household dust and in resident's serum, which could indicate that dust can be a relevant exposure route, have been reported but not consistently found in all studies (Haug et al., 2011a; Kim et al.,

2019a; Poonthong et al., 2020; Wu et al., 2015). Although the relative contribution from dust to the total exposure is generally regarded to be low (but highly variable) in adults, this exposure route can be important for small children, due to their higher absolute intake of dust (EPA-US, 2011). In a recent review, the median contribution from dust was estimated to account for 25%, 13%, 7% and 3% of the total internal levels of PFHxS, PFOA, PFNA and PFOS, respectively (DeLuca et al., 2022).

Indoor air generally contains higher concentrations of PFASs compared to outdoor air (Yao et al., 2018). FTOHs dominate the concentration profile in indoor air, followed by other precursors, such as FOSAs, FOSEs and FTAs. Partitioning of these compounds to air is expected due to their low water solubility and high vapor pressure (Jian et al., 2017; Winkens et al., 2018). Biotransformation of inhaled precursors add to the indirect exposure to arrowhead PFASs. Levels of ionic PFASs, such as PFOS and PFOA, in indoor air are generally low and inhalation of indoor air is not regarded to be a large direct exposure route to these substances. In a recent review, indoor air generally contributed with 2-4% of individual PFAA serum levels (DeLuca et al., 2022).

Regarding exposure to PFASs from the use of consumer products, the very limited information found (Vestergren et al., 2008; Washburn et al., 2005), related to the already regulated substances PFOS and PFOA, estimate the contribution to systemic exposure from consumer products to be low. Washburn et al. (2005) estimated that the use of consumer products containing PFOA would not lead to detectable levels of PFOA in serum (<0.5 ng/mL). However, acute inhalation toxicity has been reported from use of impregnation sprays, indicating that high short-term exposure can occur (summarised in ECHA (2017a)). Little is known about the exposure to PFASs from cosmetics or personal care products, but it has been suggested to be of relevance, in particular for children (Winkens et al., 2017b).

The very limited available data on exposure to fluorinated gases in consumer products suggests that the consumer exposure is very low (EPA-DK, 2015b).

For more information on consumer exposure related to different use sectors, see the following sections: B.9.3.3, B.9.4.3, B.9.6.3, B.9.7.3, B.9.8.3, B.9.10.3, B.9.11.3, B.9.12.3, B.9.13.3, B.9.14.3, B.9.15.3, B.9.16.3.

B.9.21.5. Occupational exposure

For industrial and professional workers, the primary exposure routes to PFASs are inhalation, ingestion of dust and dermal uptake (De Silva et al., 2021; Fu et al., 2015) during PFASs production, product manufacturing as well as professional use and disposal of PFAS-containing products (Lohmann et al., 2020).

Workers at several fluorochemical and fluoropolymer production facilities have been shown to have elevated levels of PFAAs and related precursors in their blood (Gao et al., 2018; Gebbink and van Leeuwen, 2020; Girardi and Merler, 2019; Olsen and Zobel, 2007). For example, at the Rimar-Miteni factory in the Italian Veneto region, where PFOA had been produced since 1968, workers displayed heavily elevated levels of PFOA in serum (geometric mean: 4 048 ng/mL; range 19–91 900 ng/mL) when sampled in the period 2000–2013 (Girardi and Merler, 2019). Workers at facilities manufacturing PFAS-containing products, such as textiles, may also be highly exposed to (precursors to) PFAAs (Heydebreck et al., 2016). In addition, high serum levels of Cl-PFESAs have been reported in Chinese metal plating workers, due to the use of mist suppressant F-53B (containing Cl-PFESAs) in this particular industry (Shi et al., 2016).

Groups of professional workers that may be exposed to PFASs are for example firefighters (Rotander et al., 2015b), ski waxers using old methods (see B.9.8.3)(Freberg et al., 2010; Nilsson et al., 2010a), waste recycling workers (Peng et al., 2022) and workers who

frequently use impregnation sprays (summarised in ECHA (2017a)). For case studies of acute and long-term occupational inhalation exposures and health effects, see B.5.4.

Occupational exposures to fluorinated gases in plant manufacturing equipment or when putting the gases into products should be small, given the need to use closed systems (mentioned by many respondents to the CfE). Outside of the manufacturing plant, however, there may be greater exposure of workers, for example during service and at sites reclaiming refrigeration equipment at the end of its service life in case of accidental releases (EPA-DK, 2015b). According to a review by Tsai (2005b) exposure to HFCs could occur via inhalation during accidental spills or leakages from the refrigeration system, recycling system for electronic appliances, degreasing process for precision cleaning, gas delivery pipeline of the semiconductor manufacturing or medical delivery systems for the treatment of asthma. Short-term moderate exposure to HFCs has been reported during refrigeration repair work (Gjølstad et al., 2003). In addition, several studies have demonstrated that health care workers and veterinarians may be exposed to fluorinated anesthetics (e.g. isoflurane, sevoflurane) via inhalation during surgical operations (Saber and Hougaard, 2009; Scapellato et al., 2014).

For more information on worker exposure related to different use sectors, see B.9.5.3, B.9.8.3, B.9.10.3, B.9.11.3, B.9.12.3, B.9.13.3, B.9.14.3, B.9.15.3, B.9.16.3.

B.9.22. Combined human exposure assessment

Blood serum and plasma are the most common matrices for PFAS analyses in humans. To a lesser extent, PFASs have been measured in other human matrices, such as whole blood, breast milk, placenta, urine, hair and nails, etc. For most of the studied PFASs, the levels in matched plasma and serum are comparable, whereas the levels in whole blood are generally half of the corresponding serum or plasma levels (Ehresman et al., 2007; Jin et al., 2020b; Poothong et al., 2017). In contrast to other studied PFASs, PFHxA and PFOSA are detected in much higher levels in whole blood compared to serum or plasma (Poothong et al., 2017). Consequently, whole blood is deemed to be the most suitable blood matrix for analysis of PFHxA and PFOSA. For most PFASs, the ratios between serum, plasma and whole blood are not known and should therefore not be presumed.

There are several reviews and reports presenting compilations of PFAS levels in human matrices, mostly focusing on PFAAs in blood (e.g. ECHA (2018a); EFSA (2020)). Several of the most frequently analysed PFAAs and their respective related substances are covered by the Stockholm Convention on POPs or by existing or proposed REACH restrictions (PFOS, PFOA, PFHxA, PFHxS, C9-C14 PFCAs), whereas other non-restricted PFASs are often omitted from the compilations. Therefore, the Dossier Submitters have done a non-exhaustive compilation of non-restricted PFASs measured in different human matrices. This compilation also includes studies of total extractable organofluorine and non-target and suspect screening studies. Summaries of these studies are tabulated further down in this chapter and in Appendix B.5.1.1.2. Table B.91 and Table B.95.

B.9.22.1. Unknown organic fluorine in humans

This restriction proposal covers known PFASs, but also PFASs of unknown identity. Thus, unspecific methods, such as extractable organic fluorine (EOF) analysis, are needed to estimate the total exposure to organofluorine compounds. Part of these unknown compounds will be currently non-restricted PFASs, but a fraction of these unknown compounds could be precursors to already restricted PFASs. In addition, EOF may contain organofluorine compounds originating from medicinal products, biocidal products or plant protection products. More information about the analytical techniques is given in E.7. Total organic fluorine measurements in environmental matrices are summarised in B.4.2.6.1.

The Dossier Submitters literature search found eight studies of EOF in human matrices (

Table B.61). For the EOF analysis, all except one study used the combustion ion chromatography (CIC) method, which has not been standardized to date. However, in a Swedish interlaboratory comparison of water and sludge samples, the EOF-CIC method showed good accuracy and reasonable interlaboratory precision (KEMI, 2021a).

Based on fluorine mass balance analysis⁵⁵, the proportion of unidentified organic fluorine (UOF) to the total EOF varied substantially between the studies, ranging from 0 up to 97% (

Table B.61). The differences in the proportion of UOF between the studies can be explained by variations in the exposure of the studied populations but also by the study design, including the choice of reported summary statistics, matrix, extraction method, detection limit and the number of PFASs included in the target analysis (i.e. the known organofluorine fraction). Thus, comparisons between different studies should be made with caution. Furthermore, the reported EOF levels are often close to their respective LOD/LOQ, which entails uncertainties in the quantification of EOF and estimated UOF.

⁵⁵ Comparison of the total EOF concentration to the amount of fluorine from the identified PFASs (analysed with targeted methods) in the sample.

Table B.61. Biomonitoring studies of extractable organofluorine (EOF). DF=detection frequency, CIC=combustion ion chromatography, CNAA=cyclic neutron activation analysis, WB=whole blood, S=serum, P=plasma, N PFAS=the number of individual PFASs constituting the known fraction.

Country, year	Matrix (n)	N PFAS	DF EOF	Mean EOF (ng F/mL or ng F/g)	% UOF	Method	LOD/LOQ	Reference
Sweden, 2018	WB (147)	63	88%	9.0 ^a	54	CIC	3 (mean)	(Aro et al., 2021c)
Sweden, 2014	WB Exposed (20)	63	95%	234 ^a	36	CIC	7.1-107	(Aro et al., 2022)
2015	WB Reference (9)	63	100%	24.8	84	CIC	7.1	
Austria, 2017-19	Maternal S (21 pools)	61	29%	3.8 ^b	24	CIC	2.7	(Kaiser et al., 2021b)
	Cord S (11 pools)	61	64%	1.6 ^b	9	CIC	1.1	
	Placenta (13 pools)	61	46%	1.3 ^b	51	CIC	0.92	
China, 2009	S (60)	11	100%	210	87	CNAA	20	(Liu et al., 2020a)
Sweden, 1996-2017	S (57 pools)	61	33%	41 ^b	60	CIC	25	(Miaz et al., 2020)
USA, 2001	P (4)	22	4 of 4	18-59 (range)	0-15	CIC	6	(Miyake et al., 2007b)
Japan, 2003	WB (3)	22	1 of 3	<6-8.9 (range)	16	CIC	6	
Japan, 2004	WB, S Worker (2)	22	2 of 2	424-505 (WB, range) 1020-1070 (S, range)	0-3 0	CIC	30	
China, 2004	WB (47)	52	>70%	ND-94 (range)	14-69	CIC	4	(Yeung and Mabury, 2016)
Germany (Muster), 1982-2009	P (80)	52	100%	24	0-48	CIC	4	
Germany (Halle), 1995-2009	P (42)	52	100%	16	0-43	CIC	4	
China, 2004	WB (30)	13	N.R.	<6-43 ^c	15-66 ^d	CIC	6	(Yeung et al., 2008)

a) Values <LOQ were set to zero

b) EOF values <LOD were excluded from the statistics

c) Range of means in five cities

d) Range of means in the four cities where EOF was >LOD

Aro et al. (2021c) performed a fluorine mass balance analysis of 147 whole blood samples from residents in five Swedish municipalities. The average EOF concentration was 9.0 ng F/mL (range 0.59–57 ng F/mL) and the UOF accounted for 54% of the total EOF. In a second study, the same research group analysed 20 whole blood samples from residents in Ronneby (Sweden) who had been exposed to drinking water contaminated with firefighting foam (Aro et al., 2022). The exposure had ceased less than one year prior to the sampling. The exposed population had an average EOF concentration of 234 ng F/mL (range <116–592 ng F/mL), which was more than twenty times higher than in the general population. In addition, the average level of UOF was higher in the exposed population (79 ng F/mL) compared to the general population (6.2 ng F/mL). Although the levels of UOF was higher in the exposed population, this population had a lower fraction (36%) of UOF in blood compared to the general population (54%).

In another Swedish study, fluorine mass balance analysis was applied in serum samples from first-time mothers, collected in yearly sampling campaigns between 1996 and 2017 (Miaz et al., 2020). Some of these women had been exposed to PFAS contaminated drinking water until the year 2012. Only 33% of the samples had detectable EOF levels, which could be due to a relatively high detection limit (25 ng F/mL). Over the entire period, detectable levels of EOF ranged from 26 to 74 ng F/mL and UOF accounted for 25–89% (mean 60%) of the total EOF. The concentration of EOF did not significantly decrease over time, whereas the sum of identified PFASs declined significantly, probably reflecting the known declining trend for some legacy PFAAs (see section B.9.22.5). Consequently, the proportion of UOF to the EOF increased by approximately 4% per year. However, the time trend should be interpreted with caution as it was based on only 19 samples.

Yeung and Mabury (2016) measured EOF in 122 plasma samples collected in the German cities Halle and Münster between the years 1982 and 2009. The fraction of UOF accounted for 0–48% of the EOF. The levels of identified PFASs decreased significantly over time, whereas there was no significant trend in EOF concentrations. After the year 2000, the amount and proportion of UOF increased in the Münster samples, whereas no trend was observed in the Halle samples.

Kaiser et al. (2021a) measured EOF in maternal serum, placental tissue, and cord serum from Austrian women. On average, 42% of the samples showed detectable EOF levels. The mean EOF concentration was 3.8 ng F/mL in maternal serum, 1.3 ng F/g in placenta and 1.6 ng F/mL in cord serum, which is relatively low compared to other studies. The fraction of UOF was highest in placenta (51%), followed by maternal serum (24%) and cord serum (9%).

In addition to studies in the European population, fluorine mass balance analysis has been applied to human blood samples from China, Japan and USA and in nails and hair from China (Liu et al., 2020a; Miyake et al., 2007b; Yeung and Mabury, 2016; Yeung et al., 2008). The levels of EOF in these studies are generally comparable to the levels reported for Europeans except for a Chinese study that reported significantly higher levels (Liu et al., 2020a). However, the latter study analysed EOF with the CNAA method, for which the comparability to the CIC method is uncertain.

Another method to analyse unknown PFASs is the total oxidizable precursor assay (TOPA), which estimates the amount of unknown precursors in a sample. This method has been successfully applied to e.g. water, soil and biota (see B.4.2.6.2). However, to the best of the Dossier Submitters knowledge, TOPA has not been applied to human matrices to date.

In conclusion, studies of European populations demonstrate that a considerable fraction of the extractable organofluorine detected in human samples is not explained by the PFASs that are routinely analysed in target analyses. Consequently, humans are exposed to a considerable amount of PFASs with unknown identity and regulatory status. Furthermore, limited data sets suggest that the proportion of unknown PFASs in relation to known PFASs

in humans increases over time.

B.9.22.2. Targeted analyses of PFAAs in humans

The EFSA risk assessment of PFASs in food (EFSA, 2020) included a comprehensive compilation of European biomonitoring studies conducted between the years 2007 and 2016. In these studies, the most frequently analysed and most abundant PFAAs in serum or plasma from adults were PFOS, PFOA, PFHxS and PFNA, contributing with 64%, 16%, 5.6% and 5.1% to the sum of PFASs, respectively. The median serum or plasma levels of these and other PFASs that are already covered by (proposed) restrictions are presented in Table B.62 and can serve as reference for comparison to the levels of non-restricted PFAAs discussed below (Table B.63) and in Appendix B.5.1.1.2. Table B.91 to Table B.92. The levels of precursors (i.e. FOSA, 8:2 monoPAP, 8:2 diPAP, EtFOSA, EtFOSAA and PFOSI) were found in low levels compared to the PFAAs in Table B.62.

Table B.62. Median levels (ng/mL) of restricted (or proposed for restriction) PFAAs in plasma or serum of European adults (EFSA, 2020).

	PFHxA	PFHxA (WB ^b)	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTTrDA	PFHxS	PFOS
Median of medians	0.03	0.62	1.9	0.61	0.30	0.28	0.05	-	0.67	7.7
Range of medians	0.01-0.045	0.62-0.62	0.76-4.9	0.30-2.6	0.07-1.3	0.06-2.5	0.03-0.54	-	0.20-152	1.7-27
Number of studies^a	2	1	32	37	33	22	7	0	37	32

For studies with median concentration lower than LOQ, the LOQ was used for calculations. a) Only studies where median is > LOQ are included in this number. b) WB = whole blood.

Within the recently finalized European Human Biomonitoring Initiative (HBM4EU), PFASs were measured in serum or plasma of 1957 teenagers from 9 European countries. Overall, 14.3% of the teenagers exceeded the guidance value of 6.9 µg/L for the sum of PFOA, PFOS, PFNA and PFHxS based on the EFSA tolerable weekly intake (EFSA, 2020; VITO, 2022).

The reported detection frequencies of the **non-restricted PFASs and PFCAs** vary substantially between studies (Table B.63). In addition to the possibility of varying exposure patterns between European subpopulations, the variability of detection frequencies can depend on the magnitude of the reporting limits, which complicates the comparability of the studies. Blood levels of non-restricted PFAAs in the European population are generally lower than the levels of e.g. PFOS, PFOA, PFHxS and PFNA. PFHpS is generally the most frequently detected and most abundant non-restricted PFAA in European blood samples, with median levels in the range of 0.04-0.5 ng/mL (Table B.63). Detection frequencies of PFBA, PFPrA, PFBA, PFPeA, PFHpA, PFHxDA, PFETs, PFPrS, PFBS, PFPeS, PFNS, and PFDS are varying but generally moderate to low, whereas the levels of PFOcDA, PFUnDS and PFDoDS were below the reporting limits in all studies included in the Dossier Submitters compilation.

A PFAA that has rarely been included in target analysis is TFA. In Swedish studies of whole blood, TFA was found in 62% of the samples from the general population (Aro et al., 2021c) and in 1 out of 20 samples from consumers of contaminated drinking water (Aro et al., 2020b). In these two studies, the levels of TFA in blood were not reported due to low recovery. In a Chinese study, TFA was detected in 97% of the analysed serum samples with a median level of 8.6 ng/mL, which accounted for 17% of the sum of the 21 PFASs analysed in the population (Duan et al., 2020).

PFPAAs and PFPIAs have been analysed in blood matrices in a few European studies. In two Norwegian studies, PFHxPA was detected in 52-100% of plasma, serum and whole

blood samples from adults (Poonthong et al., 2017; Thépaut et al., 2021). On the contrary, PFHxPA was not detected in Austrian or Swedish studies (Aro et al., 2021c; Aro et al., 2020b; Kaiser et al., 2021a). The remaining analysed PFPAs (PFOPA and PFDPA) and PFPiAs (C6/C6 PFPiA) were generally not found in these studies (Aro et al., 2021c; Aro et al., 2020b; Kaiser et al., 2021a; Poonthong et al., 2017; Thépaut et al., 2021).

Fetuses are exposed to PFASs in their mothers' blood via **placental transfer** but measured levels in cord blood are generally lower than in matched maternal blood (EFSA, 2020). In **human breast milk**, PFOA and PFOS are the most abundant PFAAs (Awad et al., 2020; Cariou et al., 2015; Karrman et al., 2007; Lee et al., 2018b). Detectable levels of other long-chain PFCAs, PFHxS and PFHxA are also reported in some studies, whereas the levels of other PFAAs generally are very low or below the reporting limits. Breast milk concentrations are considerably lower than serum concentrations, with milk:serum ratios in the range of 0.01-0.12 for different PFAAs (PFOS, PFOA, PFHxS, PFNA, PFDA, PFUnDA and FOSA) (Cariou et al., 2015; EFSA, 2020; Karrman et al., 2007; Liu et al., 2011). Although the levels in breast milk are low compared to blood, breast milk is the major exposure source to PFASs in nursing children (Haug et al., 2011a) and it is therefore important to keep these levels as low as possible.

In addition to blood matrices, **urine** has been analysed in several studies, which show generally lower levels of PFAAs in urine compared to serum (Kato et al., 2018; Wang et al., 2018c; Xu et al., 2020c). The urine:serum ratios are generally highest for short-chain PFAAs, which illustrates their faster renal clearance due to their relatively higher water-solubility and shorter biological half-lives (EFSA, 2020). There are some studies reporting higher detection rates and/or levels of PFPeA, PFBA and PFHpA in urine compared to matched serum (Kato et al., 2018; Kim et al., 2019b; Kim et al., 2014; Zhou et al., 2014). These studies indicate that urine may be a relevant matrix for detecting exposure to certain short-chained PFASs that may otherwise be overlooked.

PFAA levels in **hair and nails** have been analysed in several studies, however the relevance of these non-invasive methods for assessing the internal exposure remains unclear, for example due to the risk of contamination from the surrounding environment (Kim et al., 2019b; Kim and Oh, 2017; Liu et al., 2020a; Martin et al., 2019; Piva et al., 2021; Wang et al., 2018b).

Concentrations of PFASs in **internal organs and other matrices** (liver, follicular fluid, cerebrospinal fluid, semen, etc) are tabulated in Appendix B.5.1.1.2. Table B.94 and Table B.95 and discussed in section B.5.1.1.2.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.63. Detection frequencies of PFAAs (not covered by existing or proposed restrictions) in human blood samples from the general and highly exposed populations in Europe. S=serum, P=plasma, WB=whole blood. For details and full references, see Appendix B.5.1.1.2.

Table B.91.

Country	Samples	Year	N	TFA	PFPrA	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFEtS	PFPrS	PFBS	PFPeS	PFHpS	PFNS	PFDS	PFUnD S	PFDOD S
GENERAL EUROPEAN POPULATIONS																			
Norway	15-19 years, S	2010-11	940					75%					3%	0%	98%	14%	0%		0%
France	Maternal, S	2010-13	100			0%	0%	0%					1%		50%		0%		
Faroe I	13 years, S	2011	51			0%	0%	96%					0%		100%		12%		
France	Adult, S	2011	277			0%	0%	0.4%					0%		7%		0%		
Sweden	Adult, S	2011-14	579					63%											
Faroe I	5 years, S	2012	51			4%	0%	18%					0%		92%		33%		
Norway	Adult, S	2012-15	158					45%					37%	0%	96%	0%	0%		
Belgium	Adult, S	2014	205										3%						
Norway	Adult, S	2013-14	61				0%	13%					51%		100%		77%		
Sweden	Maternal, S	2013-17	15 Pool			13%	0%	13%	0%	0%			66%				0%		
Sweden	11-12 years, S	2014	200					79%	0%	0%			2%				1%		
France	Adult, S	2014-16	744			1%	0%	3%					0%		53%		0%		
Germany	3-17 years, p	2014-17	1 109			0%	0%	1%					0%						
UK	Adult, S	2015	59			0%	49%	17%					7%				0%		
Belgium	Adult, S	2015	242				0%	21%					0%						
Czech R.	Adult, S	2015	300			0%	0%	45%					20%				2%		
Italy	Adult, S	2015-16	250			17%	40%	66%					18%						
Sweden	Adult, S	2016	51					73%											
Germany	S	2016	158										0%						

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Country	Samples	Year	N	TFA	PFPrA	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFEtS	PFPrS	PFBS	PFPeS	PFHpS	PFNS	PFDS	PFUnD S	PFDoD S
Belgium	14-15 years, S	2017-18	410				0%	1%					0%		2%				
Sweden	Adult, S	2017-19	110			0%	0%	4%	0%	0%			1%	26%	43%		0%	0%	
Germany	Adult, P	2009-19	100			0%	4%	5%	0%	0%			0%		6%		0%		
Italy	6-11 years, S	2016	61			22%	3%	8%					0%		50%		0%		
Norway	Adult, S	2016-17	142				19%	59%					68%		100%		90%		
Sweden	Adolescents, S	2016-17	1 098					11%	0.5%	0.4%				2.8%	9.5%	0%	0%	0%	
Germany	Adult, S	2017	72										0%						
Austria	Maternal, S	2017-19	21 Pool			0%	0%	67%					90%	76%	100%	0%	0%		
Sweden	Child&Adult WB	2018	148	62%	22%	3%	2%	1%	9%	0%	49%	1%	27%	49%	99%	0%	0%		0%
Czech R.	Adult, S	2018-19	395					44%					4%						
Czech R.	Adult, S	2019-20	242					17%					28%						
HIGHLY EXPOSED POPULATIONS IN EUROPE																			
Faroe I	Adult, S	2006	10					60%							100%		60%		
Germany	Child, P	2006	90		0%								33%						
Germany	Maternal, P	2006	164		0%								4%						
Germany	Adult, P	2006	101		0%								13%						
Norway	Adult, S	2008-09	13			0%		100%							100%				
Sweden	Adult, WB	2014	20	5%	0%	0%	0%	5%	5%	0%	15%	0%	5%	100%	100%	0%	0%		0%
Sweden	S	2014-15	901					56%											
Italy	Adult, S	2015-16	257			7%	26%	51%					31%						

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Country	Samples	Year	N	TFA	PFPrA	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFEtS	PFPrS	PFBS	PFPeS	PFHpS	PFNS	PFDS	PFUnD S	PFDoD S
Italy	Child&Adult, S	2017- 19	18 122			0	0.1%	1%					3%						
Germany	Child&Adult, S	2018	906										16%						
Sweden	Adult, S	2018	26					100%					81%	100%	100%				
Belgium	Child&Adult S	2021	796			5%	0%	11%					3%		30%				

B.9.22.3. Targeted analyses of PFAEs and cyclic PFASs in humans

According to the Dossier Submitters literature search, the most studied PFAEs to date are 6:2 Cl-PFESA, ADONA, and HFPO-DA (Table B.64). In addition, the cyclic PFECBS is sometimes included in target analyses of human matrices.

6:2 Cl-PFESA has been analysed in populations from Sweden, Germany and Austria. These studies all indicate a low exposure, with detection frequencies ranging from 0 to 12% (Aro et al., 2021c; Aro et al., 2020b; Awad et al., 2020; Gockener et al., 2020a; Gyllenhammar et al., 2020; Kaiser et al., 2021a; Miaz et al., 2020; Nystrom et al., 2022). In contrast to European populations, several biomonitoring studies show a wide exposure to Cl-PFESAs in the Chinese population. In these studies, 6:2 Cl-PFESA has been found in close to all analysed blood samples from Chinese adults at median levels ranging from 1.5 to 8.6 ng/mL (Chen et al., 2017b; Duan et al., 2020; Jin et al., 2020b; Kang et al., 2020; Li et al., 2020c; Yu et al., 2021c). At these levels, 6:2 Cl-PFESA is generally the third most abundant PFAS in blood, following PFOA and PFOS. In addition to blood matrices, Cl-PFESAs have been detected in placenta, breast milk, follicular fluid, semen, urine, hair and cerebrospinal fluid from the Chinese population (Awad et al., 2020; Chen et al., 2017b; Kang et al., 2020; Lu et al., 2021; Pan et al., 2019a; Wang et al., 2018a; Wang et al., 2018b). Metal plating workers and high consumers of freshwater fish have been identified as highly exposed groups, showing median serum levels of 51 ng/mL and 94 ng/mL, respectively (Shi et al., 2016). Although the levels of Cl-PFESAs are currently low in Europe, the available data from China demonstrate that these compounds can reach high internal levels in several human matrices.

ADONA has been measured in European studies from Sweden, Germany, Austria and the Czech Republic. These studies report non-detectable or low (≤ 0.1 ng/mL) levels of ADONA in serum, whole blood, placenta, and breast milk (Aro et al., 2020a; Awad et al., 2020; Cerna et al., 2020; Fromme et al., 2018; Gockener et al., 2020b; Gyllenhammar et al., 2020; Kaiser et al., 2021a; Livsmedelsverket Naturvårdsverket, 2020; Menzel et al., 2021; Miaz et al., 2020; Wang et al., 2018a). In a German study of adult populations living close to or 80 km away from a production plant where ADONA has been used in the production of fluoropolymers, ADONA was found in 9% and 16% of the plasma samples, respectively, but in none of the samples from a reference population (Fromme et al., 2017). Regarding non-European populations, ADONA has not been detected in blood or urine from the US (Calafat et al., 2019; Kato et al., 2018) and in low or non-detectable levels in blood serum and breast milk from China (Awad et al., 2020; Duan et al., 2020).

HFPO-DA has not been detected in any whole blood or serum sample from Sweden or Germany (Aro et al., 2021c; Aro et al., 2020a; Gockener et al., 2020b; Gyllenhammar et al., 2020; Miaz et al., 2020) or in breast milk from the Czech Republic (Cerna et al., 2020). In accordance with these European studies, HFPO-DA has not been detected in blood or urine from North American populations without known elevated exposure to PFASs (Kato et al., 2018; Kotlarz et al., 2020; Mottaleb et al., 2020), with exception of a detection frequency of 1.2% in urinary samples (N=2 682) analysed within the US NHANES program (Calafat et al., 2019).

PFECBS has been found in Swedish, Austrian and German studies with detection frequencies of 0-84% and at low median levels ranging from 0.002 to 0.02 ng/mL (Aro et al., 2021c; Aro et al., 2020a; Gockener et al., 2020b; Kaiser et al., 2021a).

Table B.64. Findings of 6:2 Cl-PFESA, ADONA, HFPO-DA and PFECHS in serum presented with detection frequencies (%), median concentrations (bold) and ranges (ng/mL). A detailed summary is found in Appendix B.5.1.1.2. Table B.92.

Year, country	N	6:2 Cl-PFESA	ADONA	HFPO-DA	PFECHS	Reference
2009, 2015 Germany	86 FCP		9% (<0.2-14)			(Fromme et al., 2017)
	110 FCP		16% (<0.2-0.7)			
2014, 2016 Germany	200 Ref		0% (<0.2)			
2014 Sweden, WB	20 CDW	0% (<0.01)	0% (<0.007/<0.02)	0% (<0.022)	15% (<0.01-0.06)	(Aro et al., 2020b)
1996-2017 Sweden	30 P	10%	0%	0%		(Miaz et al., 2019)
2016 Germany	158 Ref		0% (<0.25)			(Fromme et al., 2018)
2018 Germany	906 CDW		0.3% (<0.25-1.0)			
2017 Germany	72		0% (<0.25)			(Menzel et al., 2021)
2018 Sweden, WB	148	12% (<0.01-0.02)	16% (<0.007/<0.02-0.04)	0% (<0.022)	80% 0.02 (<0.01-0.11)	(Aro et al., 2021c)
2009-2019 Germany	100	0% (<0.25)	0% (<0.25)	0% (<0.25)	0% (<0.25)	(Gockener et al., 2020b)
2016-2017 Sweden	1098	5.4% (<0.005/<0.06-1.2)	0.1% (<0.02/<3.6-0.07)			(Nystrom et al., 2022)
2017-2019 Sweden	110	1% (<0.08-0.2)	0% (<0.08)	0% (<NR)		(Gyllenhammar et al., 2020)
2017-2019, Austria	21 P	0% (<0.0002/0.004)	52% 0.006 (<0.0006/<0.01-0.074)		84% 0.003 (<LOD-0.011)	(Kaiser et al., 2021a)
2017-2019, Austria,	11 P	0% (<0.0002/0.004)	73% 0.008 (<0.0006/<0.01-		82% 0.002 (<NR-0.007)	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year, country	N	6:2 CI-PFESA	ADONA	HFPO-DA	PFECHS	Reference
CS			0.027)			
China	19 MPW	100% 51 (2.0-5040)				(Shi et al., 2016)
China	45 HFC	100% 94 (2.0-357)				
China	8 Ref	100% 4.8 (1.9-5.9)				
China	1516	98% 2.2 (<0.04-500)				(Jin et al., 2020b)
USA	100			0% (<0.05)		(Mottaleb et al., 2020)
2014- 2017 Australia	NR P				0% (<0.06)	(Toms et al., 2019)
2015- 2016 China	32	100% 1.5 (0.23-4.4)				(Chen et al., 2017b)
2015- 2016 China	117	98% 3.6 (<0.1-NR)				(Li et al., 2020c)
2016 USA	50	0% (<0.1)	0% (<0.1)	0% (<0.1)		(Kato et al., 2018)
2017 China	15 OE	93% 0.42 (<0.026-1.4)				(Gao et al., 2018)
	15	60% 0.22 (<0.026-0.31)				
2017 China	252	100% 8.6	17% (<0.015-NR)		2% (<0.002-NR)	(Duan et al., 2020)
2015- 2016 China	1228	100% 1.75		1.2% (<0.5-NR)		(Yu et al., 2021c)
2016 China	48 FCP	100% 4.2 (<0.01-9.9 ^{P95})		37% (<0.14- 1.7 ^{P95})		(Pan et al., 2017)
2018 USA	213 CDW	0% (<0.1)	0% (<0.1)	0% (<0.1)		(Barton et al., 2020)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year, country	N	6:2 Cl-PFESA	ADONA	HFPO-DA	PFECHS	Reference
2018 USA	30 FCP	0% (<0.1)	0% (<0.1)	0% (<0.1)		(Pritchett et al., 2019)
2018-2019 China	28	100% 1.6 (<0.45-4.3)				(Kang et al., 2020)

CDW=contaminated drinking water, OE=occupationally exposed, MPW=metal plating workers, ref=reference population, HFC=population with high fish consumption, FCP=population living close to a fluorochemical manufacturing facility, WB=whole blood, CS=cord serum, P=pooled samples, NR=not reported

A wider range of **PFAEs** have been analysed in **populations living close to fluorochemical manufacturing facilities** in the US and China. Kotlarz et al. (2020) assessed the exposure to PFAEs in a population from Wilmington, North Carolina, who had been exposed via drinking water from the Cape Fear River, which had received discharged wastewater from a fluorochemical manufacturing facility between the years 1980 and 2017. Serum samples were collected in the years 2017-2018 and analysed for 10 PFAEs. Nafion by-product 2, PFO4DA, and PFO5DoA were detected in more than 88% of the samples (Table B.65). In a reference population of 20 unexposed individuals, none of these PFAEs were found. In the exposed Wilmington population, PFO3OA, NVHOS and PEPA were detected in 28%, 15% and 10% of the samples, respectively. In addition, Hydro-EVE (the carboxylate form of Nafion by-product 2) was detected in a subset of samples but was not quantified. In the Wilmington population, the detected and quantified PFAEs contributed with 24% of the total PFAS level in serum. Although HFPO-DA had historically been detected in the drinking water, this substance was not detected above the reporting limit (2 ng/mL) in serum. This is in line with a study by the NC Department of Health and Human Services that did not detect HFPO-DA in serum or urine from individuals who had historically consumed private well water containing HFPO-DA but had switched to bottled water 4-14 months before the sampling (NCDHHS 2018). It can be speculated that HFPO-DA has a short half-life in humans and is therefore not detectable if the exposure has ceased since several months.

Yao et al. (2020) analysed 13 PFAEs in serum samples from non-occupationally exposed residents living close to one of the largest fluoropolymer production facilities in Asia. PFMOAA, 6:2 Cl-PFESA, HFPO-TA, PFO5DoA, PFO4DA, and Nafion by-product 2 were detected in more than 96% of the samples. In addition, 8:2 Cl-PFESA and PFO2HxA were found in 70% of the samples and PFO3OA, PF4OPeA, HFPO-DA, and 4:2 Cl-PFESA were found in <30% of the samples. The detected PFAEs contributed with 13% of the total PFAS in serum.

Table B.65. Serum levels (ng/mL) of PFAEs presented with detection frequencies, median (USA) or geometric mean (China) in populations living in areas near fluorochemical manufacturing facilities in the US (Kotlarz et al., 2020) and China (Yao et al., 2020).

Substance	China	USA
4:2 CI-PFESA	4.5%	
6:2 CI-PFESA	100% -	
8:2 CI-PFESA	70% 0.03	
Nafion by-pr.1		0.3% -
Nafion by-pr.2	99% 0.09	99% 2.7
HFPO-DA	8% -	0% -
HFPO-TA	99% 1.8	
PEPA		9.6% -
PMPA		0.3% -
PF4OPeA	17% -	
PF5OHxA	0% -	
PFMOAA	100% 12.7	
PFO2HxA	70% 0.03	0.3% -
PFO3OA	30% -	28% -
PFO4DA	96% 0.14	99% 2.5
PFO5DoA	100% 0.98	88% 0.3
NVHOS		15% -
3,6-OPFHpA	0% -	

B.9.22.4. Targeted analyses of other PFASs in humans

Standard analytical methods used for low molecular weight PFASs cannot be used to analyse fluoropolymers, perfluoropolyethers or side-chain fluorinated polymers *per se*. Thus, the Dossier Submitters have not identified any biomonitoring studies of these compounds. Potential bioavailability of fluoropolymers/fluoropolymer fractions is further discussed in B.5.1.2.

No human biomonitoring studies of fluorinated gases in the general population have been identified. However, according to a study by Ernstgård et al. (2014), blood and exhaled air could be used for biomonitoring of hydrofluorocarbon exposure. Biomonitoring of the degradation products e.g. TFA, PFBA is discussed under B.9.22.2. Several studies have assessed occupational exposure to the fluorinated anaesthetics (i.e. sevoflurane and isoflurane) or their metabolites in urine or exhaled air (Saber and Hougaard, 2009; Scapellato

et al., 2014). These studies show that health care workers and veterinarians can be exposed to fluorinated anaesthetics during surgical procedures.

B.9.22.5. Time trends of individual PFASs in humans

European biomonitoring studies of temporal trends have demonstrated that the levels of several PFASs and PFCAs increased from the early 1970s until the turn of the millennium (EFSA, 2020; Land et al., 2018). Since then, the levels of the restricted PFOS and PFOA have declined gradually. In line with these findings, the levels of several precursors (i.e., FOSA, FOSAAs and 8:2 FTS) have also declined over time. However, the direction of temporal trends for the long-chain PFCAs (>C9) vary between studies (Gockener et al., 2020b; Land et al., 2018; Miaz et al., 2020).

Levels of non-restricted PFCAs and PFASs are often close to the reporting limits and the data is therefore less robust for time trend analyses. Furthermore, differences in e.g. study period, location and reporting limits make the studies difficult to reliably compare. Thus, no firm conclusions on time trends can be drawn for these compounds.

To the best of the Dossier Submitters knowledge, there are no European time trend studies of other non-restricted PFASs, except for one study of PFECBS, which showed declining levels in Swedish mothers between the years 2000 and 2017. This is in line with the 3M phase-out of PFECBS in the year 2002, concurrent with other perfluorooctyl-based substances (Miaz et al., 2020). Time trends of PFASs in the environment are discussed under B.4.2.7.9.

B.9.22.6. Non-target and suspect screening of PFASs in humans

Non-target and suspect screening analyses have been used to tentatively identify previously unanalysed PFASs in Australian firefighters (Rotander et al., 2015a), Chinese women (Kang et al., 2020; Li et al., 2020c; Wang et al., 2021a), Swedish pregnant women (Miaz et al., 2020) as well as American populations of fishermen (Baygi et al., 2021), firefighters (Grashow et al., 2020), pregnant women (Gerona et al., 2018), mothers and newborns (Wang et al., 2021a) and consumers of contaminated drinking water (McDonough et al., 2021b). Thus, available screening studies have mostly been applied in non-European populations and several of them have focused on highly exposed individuals. Non-target or suspect screening studies of the general European population are scarce.

The confidence level of the identification of each compound is indicated by the Schymanski scale, where 1 is the highest and 5 is the lowest level of confidence (Schymanski et al., 2014). Non-regulated PFASs identified with confidence levels 2 or 3 include PFESAs, PFECAs, ketone-PFASs, unsaturated perfluorinated alcohols and unsaturated PFASs. These results indicate that humans are exposed to non-regulated PFASs that have not been reliably identified or quantified to date. The reported semi-quantification of the tentatively identified PFASs have inherent uncertainties. Thus, it is not possible to estimate the levels of these compounds in relation to the unknown fraction of EOF in blood. However, these studies do not consistently indicate that there are any new dominating PFASs that could close the gap of between the fraction of known PFASs and the total EOF in human blood samples.

In addition to human samples, non-target and suspect screening methods have been used to identify PFASs in various environmental compartments, which is described in chapter B.4.2.6.3.

B.9.22.7. Summary of combined human exposure assessment

Fluorine mass balance analyses of human blood show substantial variation in the proportion of unknown organofluorine to the total concentration of EOF reported in different studies (0-97%). Thus, humans are exposed to a highly variable but considerable amount of PFASs for which the identity and consequently the regulatory status are unknown. Attempts to

characterise the unknown PFAS fraction have been performed with non-target and suspect screening methods. These studies suggest that for example PFESAs, PFECAs, ketone-PFASs, unsaturated perfluorinated alcohols and unsaturated PFASs may partly constitute the unknown fraction. However, the gap between the known and the total EOF concentration remains unexplained.

Human biomonitoring studies of known PFASs unambiguously demonstrate world-wide exposure to a wide range of PFASs, with especially high exposure levels in populations living in areas close to PFAS point sources as well as in occupationally exposed individuals. In the general European population, PFOS, PFOA, PFHxS and PFNA are the most studied and most abundant PFAAs. In a considerable part of the population, the serum levels of these four PFAAs exceed the tolerably weekly intake. The high detection frequencies for PFASs that have been phased out show that the historic exposure takes a long time to reverse. Non-regulated PFAAs are found at lower levels and generally at moderate to low detection frequencies. However, it is evident that the European population is exposed to non-regulated PFAAs. Furthermore, the few studies of TFA in human matrices indicate that part of the European population have detectable levels of TFA in blood.

Blood levels of PFAEs (ADONA, HFPO-DA) are low in the general European population. However, in the US and China, several PFAEs have been detected in blood from populations living close to fluorochemical manufacturing facilities. These studies indicate that a potential increased use of PFAEs as substitutes for legacy PFASs could lead to increased human exposure also in Europe. In addition, studies from China show a widespread human exposure to 6:2 Cl-PFESA, which is generally the third most abundant PFAS in blood of the Chinese population. European biomonitoring studies indicate low current exposure to Cl-PFESAs in the general population. However, the available Chinese data demonstrate that these compounds can reach high internal levels in several human matrices.

Appendices to Annex B

Appendix B.1.2. Physicochemical Properties

Table B.66. Basic substance information and physical chemical properties of PFCAs (Perfluoroalkylcarboxylic acids).

abbrevi a-tion	C2-PFCA	C4-PFCA	C5-PFCA	C6-PFCA	C7-PFCA	C8-PFCA	C9-PFCA	C10- PFCA	C11- PFCA	C12- PFCA	C13- PFCA	C14- PFCA
acronym	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTTrDA	PFTeDA
IUPAC name	trifluoroacetic acid	butanoic acid, heptafluoro-	pentanoic acid, nonafluoro-	hexanoic acid, undecafluoro-	heptanoic acid, tridecafluoro-	octanoic acid, pentadecafluoro-	nonanoic acid, heptadecafluoro-	decanoic acid, nonadecafluoro-	undecanoic acid, henicosafluoro-	dodecanoic acid, tricosafuoro-	tridecanoic acid, pentacosafuoro-	tetradecanoic acid, heptacosafuoro-
molecular formula	CF ₃ -COOH	CF ₃ (CF ₂) ₂ -COOH	CF ₃ (CF ₂) ₃ -COOH	CF ₃ (CF ₂) ₄ -COOH	CF ₃ (CF ₂) ₅ -COOH	CF ₃ (CF ₂) ₆ -COOH	CF ₃ (CF ₂) ₇ -COOH	CF ₃ (CF ₂) ₈ -COOH	CF ₃ (CF ₂) ₉ -COOH	CF ₃ (CF ₂) ₁₀ -COOH	CF ₃ (CF ₂) ₁₁ -COOH	CF ₃ (CF ₂) ₁₂ -COOH
CAS number	76-05-1	375-22-4	2706-90-3	307-24-4	375-85-9	335-67-1	375-95-1	335-76-2	2058-94-8	307-55-1	72629-94-8	376-06-7
physico-chemical data												
molecular weight g/mol	114.02	214.04	264.05	314.05	364.06	414.07	464.08	514.08	564.09	614.10	664.11	714.11
partitioning coefficient log K _{ow}	0.79 ± 0.48 at 25 °C (calculated with QSAR; REACH registration data (2021-	3.39 ± 0.60 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs)	3.43 (calc. using COSMOTHERM (Arp et al., 2006) 3.40 (Predicted using US EPA	4.06 (calc., COSMOTHERM (temp. not specified) (Wang et al., 2011c) 4.13 (exp.	3.82 (calc. using COSMOTHERM (Arp et al., 2006) 5.33 (Predicted using US EPA	5.30 (calc., COSMOTHERM (temp. not specified) (Wang et al., 2011c) 4.30 (calc.	5.9 (calc., COSMOTHERM, (Wang et al., 2011c)) 7.27 (Predicted using US EPA	6.5 (calc., COSMOTHERM, (Wang et al., 2011c)) 7.667 (exp. value, MSDS	7.2 (calc., COSMOTHERM, (Wang et al., 2011c)) 8.548 (exp. value, MSDS	7.8 (calc., COSMOTHERM, (Wang et al., 2011c)) 9.429 (exp. value, MSDS	8.25 (calc., COSMOTHERM, (Wang et al., 2011c))	8.90 (calc., COSMOTHERM, (Wang et al., 2011c)) 11.191 (exp. value, MSDS

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevi a-tion	C2-PFCA	C4-PFCA	C5-PFCA	C6-PFCA	C7-PFCA	C8-PFCA	C9-PFCA	C10- PFCA	C11- PFCA	C12- PFCA	C13- PFCA	C14- PFCA
acrony m	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
	05-31)) ⁵⁶ 0.50 (Predicted using US EPA EPI-Suite (KOWWI N v1.67))	Software V11.02) 2.43 (Predicted using US EPA EPI-Suite (KOWWIN v1.67))	EPI-Suite (KOWWI N v1.67))	value, MSDS LabNetw ork) [Royal Society of Chemistr y, ChemSpi der database] ⁵⁷ 3.26 (calc. using COSMOth erm (Arp et al., 2006)	(KOWWI N v1.67))	using COSMOth erm (Arp et al., 2006)	(KOWWI N v1.67)) 4.84 (calc. using COSMOth erm (Arp et al., 2006)	rk) [Royal Society of Chemistr y, ChemSpi der database] ⁵⁷ 5.30 (calc. using COSMOth erm (Arp et al., 2006)	rk) [Royal Society of Chemistr y, ChemSpi der database] ⁵⁷	rk) [Royal Society of Chemistr y, ChemSpi der database] ⁵⁷		rk) [Royal Society of Chemistr y, ChemSpi der database] ⁵⁷
log K _{OA}	5.843 at 25 °C (Estimate from Log K _{ow} [0,50 (KowWin estimate)] and log	4.743 at 25 °C (Estimate from Log K _{ow} [2.43 (KowWin estimate)] and log	4.992 at 25 °C (Estimate from Log K _{ow} [3.40 (KowWin estimate)]) and	6.63 (calc., COSMOth erm (Wang et al., 2011c)	5.480 at 25 °C (Estimate from Log K _{ow} [5.33 (KowWin estimate)] and log	7.23 (calc., COSMOth erm, (Wang et al., 2011c))	7.50 (calc., COSMOth erm, (Wang et al., 2011c))	7.77 (calc., COSMOth erm, (Wang et al., 2011c))	8.08 (calc., COSMOth erm, (Wang et al., 2011c))	8.36 (calc., COSMOth erm, (Wang et al., 2011c))	8.63 (calc., COSMOth erm, (Wang et al., 2011c))	8.87 (calc., COSMOth erm, (Wang et al., 2011c))

⁵⁶ <https://echa.europa.eu/information-on-chemicals/registered-substances>, date of access: 2022-09-30.

⁵⁷ <http://www.chemspider.com/>, date of access: 2022-09-30.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevi a-tion	C2-PFCA	C4-PFCA	C5-PFCA	C6-PFCA	C7-PFCA	C8-PFCA	C9-PFCA	C10- PFCA	C11- PFCA	C12- PFCA	C13- PFCA	C14- PFCA
acrony m	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
	Kaw [-5.343 (exp. database)]; Predicted using US EPA EPI- Suite (KOAWIN v1.10 estimate))	Kaw [-2.313 (HenryWi n estimate)]; Predicted using US EPA EPI- Suite (KOAWIN v1.10 estimate))	log Kaw [-1.592 (HenryWi n estimate)]; Predicted using US EPA EPI- Suite (KOAWI N v1.10 estimate))		Kaw [- 0.150 (HenryWi n estimate)]; Predicted using US EPA EPI- Suite (KOAWIN v1.10 estimate))							
log Kaw	-5.343 at 25 °C (exp. database US EPA) [Royal Society of Chemistr y, ChemSpi der database] ⁵⁷	-2.313 at 25 °C (Predicted using US EPA EPI-Suite (HenryWi n v3.10 estimate))	-3.04 (calc. using EPIsuite (Arp et al., 2006)) -1.592 at 25 °C (Predicted using US EPA EPI-Suite (HenryWi n v3.10 estimate))	-2.66 (calc., (ECHA, 2016a)) -2.66 (calc. using EPIsuite (Arp et al., 2006))	-2,37 (calc. using EPIsuite (Arp et al., 2006)) -0.150 at 25 °C (Predicted using US EPA EPI-Suite (HenryWi n v3.10 estimate))	-1.93 (calc., COSMOth erm, (Wang et al., 2011c)) -2.03 (calc. using EPIsuite (Arp et al., 2006))	-1.58 (calc., COSMOth erm, (Wang et al., 2011c)) -1.79 (calc. using EPIsuite (Arp et al., 2006))	-1.27 (calc., COSMOth erm, (Wang et al., 2011c)) -1.52 (calc. using EPIsuite (Arp et al., 2006))	-0.92 (calc., COSMOth erm, (Wang et al., 2011c))	-0.58 (calc., COSMOth erm, (Wang et al., 2011c))	-0.38 (calc., COSMOth erm, (Wang et al., 2011c))	0.03 (calc., COSMOth erm, (Wang et al., 2011c))
dissocia	pKa	0.32–	pKa	-0.16	pKa	0.5	<1.6	<1.6	<1.6	pKa	pKa	pKa

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevi a-tion	C2-PFCA	C4-PFCA	C5-PFCA	C6-PFCA	C7-PFCA	C8-PFCA	C9-PFCA	C10- PFCA	C11- PFCA	C12- PFCA	C13- PFCA	C14- PFCA
acrony m	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
tion constan t	0.05±0.1 0 (calculate d using Advanced Chemistr y Develop ment (ACD/Lab s) Software V11.02)	0.42 (exp. value, potentio metric titration of aq. sol.; (Cabala et al., 2017)	0.40±0.1 0 (calculat ed using Advance d Chemistr y Develop ment (ACD/La bs) Software V11.02)	(Zhao et al., 2014)	0.47±0.1 0 (calculate d using Advanced Chemistr y Develop ment (ACD/Lab s) Software V11.02)	(calculate d from exp. values, (Vierke, 2014)) 1.3 (López- Fontán et al., 2005)	(calculate d from exp. values, (Vierke, 2014)) 0.82 (calc., COSMOth erm, (Wang et al., 2011c)) 2.58 (exp. value, measure ment of the PFCAs solubility change with pH; (Cabala et al., 2017)	(calculate d from exp. values, (Vierke, 2014)) 2.58 (Moroi et al., 2001) 2.61 (exp. value, measure ment of the PFCAs solubility change with pH; (Cabala et al., 2017)	(calculate d from exp. values, (Vierke, 2014)) 3.13 (exp. value, measure ment of the PFCAs solubility change with pH; (Cabala et al., 2017)	0.52±0.1 0 (calculate d using Advanced Chemistr y Develop ment (ACD/Lab s) Software V11.02)	0.52±0.1 0 (calculate d using Advanced Chemistr y Develop ment (ACD/Lab s) Software V11.02)	0.52±0.1 0 (calculate d using Advanced Chemistr y Develop ment (ACD/Lab s) Software V11.02)
partitio n coeffici ents log K _d (sedime	n.a.	n.a.	n.a.	1.4 – 3.1 (Li et al., 2011)	n.a.	0.04 (Ahrens et al., 2010b)*	0.6 (Ahrens et al., 2010b)*	1.8 (Ahrens et al., 2010b)*	3.0 (Ahrens et al., 2010b)*	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevi a-tion	C2-PFCA	C4-PFCA	C5-PFCA	C6-PFCA	C7-PFCA	C8-PFCA	C9-PFCA	C10- PFCA	C11- PFCA	C12- PFCA	C13- PFCA	C14- PFCA
acronym	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
nt and overlap ping dissolve d phase)												
log K _{oc} (sedime nt organic carbon- normali sed distribu tion coeffici ent)	0.437 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66))	1.767 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66))	2.431 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66))	1.63 – 2.35 (Sepulveda et al., 2011)	3.761 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66))	2.06 (Higgins and Luthy, 2006) 1.09 (Ahrens et al., 2010b)*	2.39 (Higgins and Luthy, 2006) 2.4 (Ahrens et al., 2010b)*	2.76 (Higgins and Luthy, 2006) 3.6 (Ahrens et al., 2010b)*	3.3 (Higgins and Luthy, 2006) 4.8 (Ahrens et al., 2010b)*	n.a.	n.a.	n.a.
water solubility	miscible with water (>10 g/cm ³)(exp. result; REACH registrati on data (2021- 05-31)) ⁵⁶ 1 000 g/L at 20 °C, fully	0.7657 g/L at 25 °C (Estimate from Log Kow [2.43 (KowWin est)]; Predicted using US EPA EPI- Suite (WSKOW v1.41))	61.11 mg/L at 25 °C (Estimate from Log Kow [3.40 (KowWin est)]; Predicted using US EPA EPI- Suite (WSKOW v1.41))	15.7 g/L (25 °C) (Zhao et al., 2014)	0.3527 mg/L at 25 °C (Estimate from Log Kow [5.33 (KowWin est)]; Predicted using US EPA EPI- Suite (WSKOW v1.41))	9.5 g/L (25 °C) 4.14 g/L (22 °C) (ECHA, 2013)	practical ly insoluble in water (exp. result; MSDS Alfa Aesar) [Royal Society of Chemistr y, ChemSpi der	5.14 g/L at 25 °C (ECHA, 2016b)	1.2·10 ⁻⁴ g/L; pH 1 at 25 °C 9.0·10 ⁻⁴ g/L; pH 2 at 25 °C 8.5·10 ⁻³ g/L; pH 3 at 25 °C 0.056 g/L; pH 4 at 25 °C	2.9·10 ⁻⁵ g/L pH 1 at 25 °C 2.2·10 ⁻⁴ g/L pH 2 at 25 °C 2.0·10 ⁻³ g/L pH 3 at 25 °C 0.014 g/L pH 4 at 25 °C	7.3·10 ⁻⁶ g/L; pH 1 at 25 °C 5.5·10 ⁻⁵ g/L; pH 2 at 25 °C 5.1·10 ⁻⁴ g/L; pH 3 at 25 °C 3.5·10 ⁻³ g/L; pH 4 at	1.9·10 ⁻⁶ g/L; pH 1 at 25 °C 1.4·10 ⁻⁵ g/L; pH 2 at 25 °C 1.3·10 ⁻⁴ g/L; pH 3 at 25 °C 9.3·10 ⁻⁴ g/L; pH 4 at

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevi a-tion	C2-PFCA	C4-PFCA	C5-PFCA	C6-PFCA	C7-PFCA	C8-PFCA	C9-PFCA	C10- PFCA	C11- PFCA	C12- PFCA	C13- PFCA	C14- PFCA
acrony m	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
	miscible (exp. data, SRC PhysProp database, REACH registrati on data (2021- 05-31)) ⁵⁶						database] ⁵⁷ 1.882·10 ⁻⁶ g/L (Estimate from Log Kow [7.27 (KowWin est)]); Predicted using US EPA EPI- Suite (WSKOW v1.41))		0.14 g/L; pH 5 at 25 °C 0.16 g/L; pH 6-10 at 25 °C (calculate d) (ECHA, 2012b)	0.034 g/L pH 5 at 25 °C 0.039 g/L pH 6 at 25 °C 0.040 g/L pH 7 at 25 °C 0.041 g/L pH 8-10 at 25 °C (calculate d) (ECHA, 2012e)	25 °C 8.6·10 ⁻³ g/L; pH 5 at 25 °C 0.0100 g/L; pH 6-10 at 25 °C (calculate d) (ECHA, 2012d)	25 °C 2.2·10 ⁻³ g/L; pH 5 at 25 °C 2.6·10 ⁻³ g/L; pH 6-10 at 25 °C (calculate d) (ECHA, 2012c)
vapour pressur e	12.4 kPa at 20 °C (interpol ated from exp. results; REACH registrati on data (2021- 05-31)) ⁵⁶ 15.5 kPa at 25 °C	1.3 kPa at 25 °C (calculat ed using Advanced Chemistr y Developm ent (ACD/Lab s) Software V11.02)	1.06 kPa at 25 °C (calculat ed using Advance d Chemistr y Develop ment (ACD/Lab s) Software	1.98 mm Hg at 25 °C; equals to 263.93 Pa US EPA; Estimatio n Program Interface (EPI) Suite.	71.9 Pa at 25 °C (calculat ed using Advanced Chemistr y Develop ment (ACD/Lab s) Software V11.02)	4.2 Pa (25 °C) extrapola ted from measured data 2.3 Pa (20 °C) extrapola ted from measured data 128 Pa	22.8 Pa at 25 °C (calculat ed using Advanced Chemistr y Develop ment (ACD/Lab s) Software V11.02)	3.1 to 99.97 kP a (129.6 to 218.9 °C) (calculat ed) (ECHA, 2016b)	0.6 to 99.97 kP a (112 to 237.7 °C) (calculat ed) (ECHA, 2012b)	1.25 Pa at 25 °C (calculat ed) (ECHA, 2012e)	0.48 Pa at 25 °C (calculat ed) (ECHA, 2012d)	0.18 Pa at 25 °C (calculat ed) (ECHA, 2012c)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevi a-tion	C2-PFCA	C4-PFCA	C5-PFCA	C6-PFCA	C7-PFCA	C8-PFCA	C9-PFCA	C10- PFCA	C11- PFCA	C12- PFCA	C13- PFCA	C14- PFCA
acrony m	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
	(Predicted using US EPA EPI-Suite (Mean VP of Antoine & Grain methods, MPBPWIN v1.42)) 12.8 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)		V11.02)	Ver. 4.11. Nov, 2012. Available from, as of Jan 11, 2015		(59.3 °C) measured (ECHA, 2013)						
boiling point	71.78 °C (extrapolated, exp. result, ebulliometer; REACH	120.0 °C (Cabala et al., 2017)	140 °C (exp. value, Alfa Aesar) [Royal Society of	157 °C (Savu, 2000)	-63.5 °C (exp. result; SRC [Syracuse Research Corporati	189.0 °C (Cabala et al., 2017)	218 °C (ECHA, 2015b)	218 °C measured (ECHA, 2016b)	238.4 °C (calculated) (ECHA, 2012b)	249 °C (ECHA, 2012e)	260.7 °C (calculated) (ECHA, 2012d)	270 °C (ECHA, 2012c)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevi a-tion	C2-PFCA	C4-PFCA	C5-PFCA	C6-PFCA	C7-PFCA	C8-PFCA	C9-PFCA	C10- PFCA	C11- PFCA	C12- PFCA	C13- PFCA	C14- PFCA
acrony m	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
	registrati on data (2021- 05-31)) ⁵⁶ 73 °C (Handboo k data: CRC; REACH registrati on data (2021- 05-31)) ⁵⁶ 72.4 °C (Handboo k data: Merck index; REACH registrati on data (2021- 05-31)) ⁵⁶		Chemistr y, ChemSpi der database] ⁵⁷		on of Syracuse , New York (US))]							
Henrys Law constan t	4.31E- 006 atm- m3/mole at 25 °C (Predicted using US EPA EPI-Suite (Bond	1.19E- 004 atm- m3/mole at 25 °C (Predicted using US EPA EPI-Suite (Bond	6.26E- 004 atm- m3/mole at 25 °C (Predicted using US EPA EPI-Suite (Bond	3.29E- 003 atm- m3/mole at 25 °C (Predicted using US EPA EPI-Suite (Bond	1.73E- 002 atm- m3/mole at 25 °C (Predicted using US EPA EPI-Suite (Bond	9.08E- 002 atm- m3/mole at 25 °C (Predicted using US EPA EPI-Suite (Bond	4.77E- 001 atm- m3/mole at 25 °C (Predicted using US EPA EPI-Suite	n.a.	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevi a-tion	C2-PFCA	C4-PFCA	C5-PFCA	C6-PFCA	C7-PFCA	C8-PFCA	C9-PFCA	C10- PFCA	C11- PFCA	C12- PFCA	C13- PFCA	C14- PFCA
acrony m	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
	Method, HENRYWI N v3.10))	Method, HENRYWI N v3.10))	Method, HENRYWI N v3.10))	Method, HENRYWI N v3.10))	Method, HENRYWI N v3.10))	Method, HENRYWI N v3.10))	(Bond Method, HENRYWI N v3.10))					
	$H^{\text{CP}}=8.9 \times 10^1$ [mol/(m ³ Pa)] (Sander, 2015)	$H^{\text{CP}}=8.2 \times 10^{-2}$ [mol/(m ³ Pa)] (Sander, 2015)	n.a.	$H^{\text{CP}}=4.4 \times 10^{-1}$ [mol/(m ³ Pa)] (Sander, 2015)	$H^{\text{CP}}=5.0 \times 10^{-2}$ [mol/(m ³ Pa)] (Sander, 2015)	$H^{\text{CP}}=4.9 \times 10^{-2}$ [mol/(m ³ Pa)] (Sander, 2015)	$H^{\text{CP}}=4.3 \times 10^{-2}$ [mol/(m ³ Pa)] (Sander, 2015)	$H^{\text{CP}}=2.5 \times 10^{-2}$ [mol/(m ³ Pa)] (Sander, 2015)	$H^{\text{CP}}=1.3 \times 10^{-2}$ [mol/(m ³ Pa)] (Sander, 2015)	$H^{\text{CP}}=6.4 \times 10^{-3}$ [mol/(m ³ Pa)] (Sander, 2015)	n.a.	$H^{\text{CP}}=1.6 \times 10^{-3}$ [mol/(m ³ Pa)] (Sander, 2015)

Table B.67. Basic substance information and physical chemical properties of PFSA (Perfluoroalkane sulfonic acids).

abb rev ia- tio n	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acr ony m	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFDoDS	PFTrDS	PFTeDS
IUP AC na me	Trifluor ometha nesulfo nic acid	Pentaflu oroetha nesulfo nic acid	1,1,2,2 ,3,3,3- Heptaflu oro-1- propan esulfoni c acid	1,1,2,2 ,3,3,4, 4,4- Nonaflu oro-1- butane	1,1,2,2, 3,3,4,4, 5,5,6,6, 6- Tridecaflu oro-1- hexane-	1,1,2,2,3, 3,4,4,5,5, 6,6,7,7,8, 8,8- Hepta- decafluoro -1-	1,1,2,2,3,3,4, 4,5,5,6,6,7,7, 8,8,9,9,10,10, 10- henicosafuoro decane-1- sulfonic acid	1,1,2,2,3,3,4,4,5, 5,6,6,7,7,8,8,9,9, 10,10,11,11,12,1 2,12- Pentacosafuorodo decane-1- sulphonic acid	1,1,2,2,3,3,4,4,5,5, 6,6,7,7,8,8,9,9,10,1 0,11,11,12,12,13,13 ,13- Heptacosafuorotride cane-1-sulfonic acid	1,1,2,2,3,3,4,4,5,5,6, 6,7,7,8,8,9,9,10,10,1 1,11,12,12,13,13,14,1 4,14- Nonacosafuorotetradecane-1-sulfonic acid

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abb rev ia- tio n	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acr ony m	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFTeDS
				- sulfo nic acid	sulfonic acid	octanesulf onic acid				
oth er na me s	Triflic acid	Perfluor oethane sulfonic acid	Perfluor opropane sulfonic acid	Perfluor obutane sulfonic acid	Perfluor ohexane sulfonic acid	Perfluoroo ctanesulf onic acid	Perfluorodeca nesulfonic acid	Perfluorododecane sulfonic acid	Perfluorotridecanesu lfonic acid	Perfluorotetradecanes ulfonic acid
mol ecu lar for mul a	CF ₃ - SO ₃ H	CF ₃ (CF ₂) ₂ -SO ₃ H	CF ₃ (CF ₂) ₂ - SO ₃ H	CF ₃ (CF ₂) ₃ - SO ₃ H	CF ₃ (CF ₂) ₅ -SO ₃ H	CF ₃ (CF ₂) ₇ - SO ₃ H	CF ₃ (CF ₂) ₉ - SO ₃ H	CF ₃ (CF ₂) ₁₁ -SO ₃ H	CF ₃ (CF ₂) ₁₂ -SO ₃ H	CF ₃ (CF ₂) ₁₃ -SO ₃ H
CA S nu mb er	1493- 13-6	354-88- 1	423- 41-6	375- 73-5	355-46- 4	1763-23-1	335-77-3	79780-39-5	791563-89-8	1379460-39-5
EC nu mb er	216- 087-5	-	-	206- 793-1	206- 587-1	217-179-8	206-401-9	279-259-9	-	-
physico-chemical data										
mol ecu	150.1	200.1	250.1	300.1	400.1	500.1	600.2	700.2	750.2	800.2

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevia- tion	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acronym	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFTeDS
lar weight g/ mol										
parti- oni- ng coe- ffici- ent log K _{ow}	<0.3 at 25 °C and pH 1, (exp. result, HPLC method , OECD 117; REACH registra- tion data (2021- 05- 21)) ⁵⁶ -0.49 (QSAR estimat- ion (KOWW	0.48 (Predict- ed using US EPA EPI- Suite (KOWW IN v1.67 estimat- e))	1.45 (Predict- ed using US EPA EPI- Suite (KOWW IN v1.67 estimat- e))	-0.34 at 23 °C and pH 1.7 (exp. result, shake flask metho- d EU Method A.8; REACH registr- ation data (2021- 05- 26)) 2.41 (Predic	5.17 (calc., COSMO therm, (Wang et al., 2011c)) 4.57 (exp. value, MSDS LabNet work) [Royal Society of Chemist- ry, ChemS- pider databas- e] ⁵⁷	4.512±0.8 62 at 25 °C (calculate d using Advanced Chemistry Developm- ent (ACD/Labs) Software V11.02) 4.49 (Predicted using US EPA EPI- Suite; HSDB, National Library of Medicine	5.972±0.891 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	7.432±0.916 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	8.161±0.927 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	8.891±0.939 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abb rev ia- tio n	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acr ony m	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFT _e DS
	IN); REACH registra tion data (2021- 05- 21)) ⁵⁶			ted using US EPA EPI- Suite (KOW WIN v1.67 estimat e)) 2.808 (exp. value, MSDS LabNet work) [Royal Society of Chemis try, ChemS pider databa se] ⁵⁷	4.34 (Predict ed using US EPA EPI- Suite (KOW WIN v1.67 estimat e))	(US)) ⁵⁸				

⁵⁸ <https://pubchem.ncbi.nlm.nih.gov/>, date of access: 2022-09-30.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abb rev ia- tio n	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acr ony m	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFTeDS
log K _{OA}	4.902 at 25 °C (Estimate from Log K _{ow} [- 0.49 (K _{ow} W _i n estimat e)] and log K _{aw} [-5.392 (Henry Win estimat e)]; Predict ed using US EPA EPI- Suite (KOAW IN v1.10	5.152 at 25 °C (Estimate from Log K _{ow} [0.48 (K _{ow} W _i n estimat e)] and log K _{aw} [-4.672 (Henry Win estimat e)]; Predict ed using US EPA EPI- Suite (KOAW N v1.10 estimat e))	5.401 at 25 °C (Estimate from Log K _{ow} [1.45 (K _{ow} W _i n estimat e)] and log K _{aw} [-3.951 (Henry Win estimat e)]; Predict ed using US EPA EPI- Suite (KOAW IN v1.10	5.640 at 25 °C (Estimate from Log K _{ow} [2.41 (K _{ow} W _i n estimat e)] and log K _{aw} [-3.23 0 (Henry Win estimat e)]; Predict ed using US EPA EPI- Suite	7.55 (calc., COSMO therm, (Wang et al., 2011c)) 6.130 at 25 °C (Estimate from Log K _{ow} [4.34 (K _{ow} W _i n estimat e)] and log K _{aw} [-1.790 (Henry Win estimat e)]; Predict ed using	n.a.	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevia- tion	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acronym	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFT _e DS
	estimate))		estimate))	(KOAW IN v1.10 estimate))	US EPA EPI- Suite (KOAWI N v1.10 estimate))					
log K _{AW}	-5.392 at 25 °C (Predicted using US EPA EPI- Suite (Henry Win v3.10 estimate))	-4.672 at 25 °C (Predicted using US EPA EPI- Suite (Henry Win v3.10 estimate))	-3.951 at 25 °C (Predicted using US EPA EPI- Suite (Henry Win v3.10 estimate))	-3.230 at 25 °C (Predicted using US EPA EPI- Suite (Henry Win v3.10 estimate))	-2.38 (calc., COSMO therm, (Wang et al., 2011c)) -1.790 at 25 °C (Predicted using US EPA EPI- Suite (Henry Win v3.10 estimate))	n.a.	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevia- tion	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acronym	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFTeDS
					e))					
dis- socia- tion con- stant	pKa<0 (REACH registra- tion data (2021- 05- 25)) ⁵⁶	pKa -3. 86±0.5 0 (calcula- ted using Advanc- ed Chemist- ry Develop- ment (ACD/L abs) Softwar- e V11.02)	pKa -3. 63±0.5 0 (calcula- ted using Advanc- ed Chemis- try Develo- pment (ACD/L abs) Softwar- e V11.02)	pKa -3. 57±0.5 0 (calcula- ted using Advanc- ed Chemis- try Develo- pment (ACD/L abs) Softwa- re V11.02)	-3.45 (calc., COSMO therm, (Wang et al., 2011c)) pKa -3. 34±0.5 0 (calcula- ted using Advanc- ed Chemist- ry Develop- ment (ACD/L abs) Softwar- e V11.02)	pKa -3.27 ±0.50 (calculate d using Advanced Chemistry Developm- ent (ACD/Labs) Software V11.02)	pKa -3.26±0. 50 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	pKa -3.26±0.50 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	pKa -3.26±0.50 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	
parti- titi	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abb rev ia- tio n	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acr ony m	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFT _e DS
on coe ffici ent s log K _d (se dim ent and ove rla ppi ng dis sol ved pha se)										
log K _{oc} (se dim ent org ani	0.352 (Predict ed using US EPA EPI- Suite	1.016 (Predict ed using US EPA EPI- Suite	1.681 (Predict ed using US EPA EPI- Suite	2.345 (Predict ed using US EPA EPI- Suite	3.675 (Predict ed using US EPA EPI- Suite	n.a.	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevia- tion	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acronym	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFT _e DS
carbon- normalise d distribu- tion coefficient)	(PCKOC WIN v1.66 estimate))	(PCKOC WIN v1.66 estimate))	(PCKOC WIN v1.66 estimate))	(PCKO CWIN v1.66 estimate))	(PCKOC WIN v1.66 estimate))					
water solubility	≥1 604 g/L at 20 °C (exp. result, flask method , OECD 105; REACH registra	17.04 g/L at 25 °C (Estima te from Log Kow [0.48 (KowWi n est)]; Predict	1.378 g/L at 25 °C (Estima te from Log Kow [1.45 (KowWi n est)]; Predict	≥1 000 g/L at 20 °C (exp. result, flask metho d, EU Method A.6; REACH	2.3 g/L (calc., COSMO therm, (Wang et al., 2011c))	7.5 g/L in unbuffere d water (pH 1.82) at 25 °C (calculate d using Advanced Chemistry Developm ent	0.42 g/L in unbuffered water (pH 1.82) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software	0.026 g/L in unbuffered water (pH 4.43) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	6.7 x 10 ⁻³ g/L in unbuffered water (pH 5.05) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	1.8 x 10 ⁻³ g/L in unbuffered water (pH 5.65) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abb rev ia- tio n	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acr ony m	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFT _e DS
	tion data (2021- 05- 25)) ⁵⁶ 1.975·1 0 ⁵ g/L at 25 °C (Estima te from Log Kow [- 0.49 (KowWi n est)]; Predict ed using US EPA EPI- Suite (WSKO W v1.41))	d using US EPA EPI- Suite (WSKO W v1.41))	ed using US EPA EPI- Suite (WSKO W v1.41))	registr ation data (2021- 05- 26)) ⁵⁶ 999 g/L in unbuff ered water (pH - 0.52) at 25 °C (calcul ated using Advanc ed Chemis try Develo pment (ACD/L abs) Softwa		(ACD/Labs) Software V11.02)	V11.02)			

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbreviation	C-PFSA	C2-PFSA	C3-PFSA	C4-PFSA	C6-PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acronym	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFT _e DS
				re V11.02)						
vapour pressure	2.4 hPa (at 20 °C), 3.2 hPa (at 25 °C), 12.9 hPa (at 50 °C) (exp. result, OECD 104 (Vapour Pressure Curve); REACH registration data (2021-05-	36.3 Pa at 25 °C (Predicted using US EPA EPI-Suite (Mean VP of Antoine & Grain method s, MPBPWIN v1.42))	10.01 Pa at 25 °C (Predicted using US EPA EPI-Suite (Modified Grain method , MPBPWIN v1.42))	7 Pa at 20 °C (exp. result; OECD 104 (Vapour Pressure Curve) ; REACH registration data (2021-05-26)) ⁵⁶ 6.9 Pa at 25 °C (Predicted	58.9 Pa (calc., (Wang et al., 2011c))	0.267 Pa at 25 °C (Predicted using US EPA EPI-Suite (Antoine method); HSDB, National Library of Medicine (US)) ⁵⁸	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abb rev ia- tio n	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acr ony m	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFTeDS
	25)) ⁵⁶			using US EPA EPI- Suite (Modifi ed Grain metho d, MPBPW IN v1.42))						
boil ing poi nt	161- 162 °C (exp. result; MSDS Alfa Aesar) [Royal Society of Chemis try, ChemS pider databas e] ⁵⁷	178 °C (exp. databas e US EPA) [Royal Society of Chemist ry, ChemS pider databas e] ⁵⁷	196 °C (exp. databas e US EPA) [Royal Society of Chemis try, ChemS pider databas e] ⁵⁷	198 °C at 1013 hPa (exp. result; EU Method A.2; REACH registr ation data (2021- 05-	238- 239 °C (exp. result; HSDB, National Library of Medicin e (US)) ⁵⁸	249 °C (exp. result; HSDB, National Library of Medicine (US)) ⁵⁸	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abb rev ia- tio n	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acr ony m	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFT _e DS
	e] ⁵⁷ 162 °C (handb ook data; REACH registra tion data (2021- 05- 25)) ⁵⁶			26)) ⁵⁶						
He nry s La w con sta nt	9.92·10 ⁻⁸ atm- m ³ /mol e at 25 °C (Predict ed using US EPA EPI- Suite (Bond Method , HENRY	5.21·10 ⁻⁷ atm- m ³ /mol e at 25 °C (Predict ed using US EPA EPI- Suite (Bond Method, HENRY WIN	2.74·10 ⁻⁶ atm- m ³ /mol e at 25 °C (Predict ed using US EPA EPI- Suite (Bond Method , HENRY	1.44·10 ⁻⁵ atm- m ³ /mol e at 25 °C (Predic ted using US EPA EPI- Suite (Bond Method , HENRY	3.97·10 ⁻⁴ atm- m ³ /mol e at 25 °C (Predict ed using US EPA EPI- Suite (Bond Method, HENRY WIN	n.a.	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbrevia- tion	C- PFSA	C2- PFSA	C3- PFSA	C4- PFSA	C6- PFSA	C8-PFSA	C10-PFSA	C12-PFSA	C13-PFSA	C14-PFSA
acronym	TFMS, TFSA, HOTf or TfOH			PFBS	PFHxS	PFOS	PFDS	PFD _o DS	PFT _r DS	PFTeDS
	WIN v3.10))	v3.10))	WIN v3.10))	HENRY WIN v3.10))	v3.10))					
	-	-	-	$H^{CP}=2.0$ [mol/(m ³ Pa)] (Sander, 2015)	$H^{CP}=5.1 \times 10^{-1}$ [mol/(m ³ Pa)] (Sander, 2015)	$H^{CP}=9.0 \times 10^{-4}$ [mol/(m ³ Pa)] (Sander, 2015)	-	-	-	-

Table B.68. Basic substance information and physical chemical properties of PFCs (Perfluoroalkanes).

abbrevia- tion	C-PFC	C2-PFC	C3-PFC	C4-PFC	C6-PFC	C8-PFC	C10-PFC	C12-PFC
IUPAC name	Tetrafluoromethane	Hexafluoroethane	Octafluoropropane	Decafluorobutane	Tetradecafluorohexane	Octadecafluorooctane	Docosafluorodecane	Hexacosfluorododecane
other names	Carbon tetrafluoride	Perfluoroethane	Perfluoropropane	Perfluorobutane	Perfluorohexane	Perfluorooctane	Perfluorodecane	Perfluorododecane
molecular formula	CF ₄	C ₂ F ₆	C ₃ F ₈	C ₄ F ₁₀	C ₆ F ₁₄	C ₈ F ₁₈	C ₁₀ F ₂₂	C ₁₂ F ₂₆
CAS number	75-73-0	76-16-4	76-19-7	355-25-9	355-42-0	307-34-6	307-45-9	307-59-5
EC number	200-896-5	200-939-8	200-941-9	206-580-3	206-585-0	206-199-2	-	206-204-8
physico-chemical data								

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbreviati on	C-PFC	C2-PFC	C3-PFC	C4-PFC	C6-PFC	C8-PFC	C10-PFC	C12-PFC
molecular weight g/mol	88.01	138.01	188.02	238.03	338.04	438.06	538.07	638.09
partitionin g coefficient log Kow	1.18 (HSDB, National Library of Medicine (US); REACH registration data (2021-05-31)) ⁵⁶ 1.19 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	2.00 (exp. database US EPA, Hansch, C et al. (1995)) [Royal Society of Chemistry, ChemSpider database] ⁵⁷ 2.15 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate)) 2.15 (estimated with QSAR; REACH registration data (2021- 05-31)) ⁵⁶	2.8 at 25 °C (calculated; REACH registration data (2021- 05-31)) ⁵⁶ 3.12 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	4.09 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate)) 4.822 (exp. value, MSDS LabNetwork) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	6.02 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate)) ≥ 4.5 (OECD 107 (Shake Flask Method), estimation method (solubility ratio); REACH registration data (2021- 06-09)) ⁵⁶ 8.346 (exp. value, MSDS LabNetwork) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	7.95 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate)) ca. 6.2 at 25 °C, pH 7 (estimated using US EPA EPI-Suite; REACH registration data (2021- 06-09)) ⁵⁶ 8.346 (exp. value, MSDS LabNetwork) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	8.011±0.865 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	9.470±0.893 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02) 11.87 (exp. value, MSDS LabNetwork) [Royal Society of Chemistry, ChemSpider database] ⁵⁷
log Koa	-1.143 at 25 °C (Estimate from Log Kow [1.18 (exp. database)] and log Kaw [2.323 (exp.	-0.919 at 25 °C (Estimate from Log Kow [2.00 (exp. database)] and log Kaw	-0.010 at 25 °C (Estimate from Log Kow [3.12 (KowWin estimate)])	-0.346 at 25 °C (Estimate from Log Kow [4.09 (KowWin estimate)])	0.144 at 25 °C (Estimate from Log Kow [6.02 (KowWin estimate)])	0.633 at 25 °C (estimate from Log Kow [7.95 (KowWin estimate)])	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbreviati on	C-PFC	C2-PFC	C3-PFC	C4-PFC	C6-PFC	C8-PFC	C10-PFC	C12-PFC
	database)); Predicted using US EPA EPI- Suite (KOAWIN v1.10 estimate)) -0.950 (exp. database US EPA) [Royal Society of Chemistry, ChemSpider database] ⁵⁷ -0.95 (HSDB, National Library of Medicine (US)) ⁵⁸	[2.919 (exp. database)); Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	and log Kaw [3.130 (exp. database)); Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	and log Kaw [4.436 (HenryWin estim.)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	and log Kaw [5.876 (HenryWin estim.)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	and log Kaw [7.317 (HenryWin estim.)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))		
log K _{AW}	2.323 (exp. database US EPA) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	2.919 (exp. database US EPA) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	3.130 (exp. database US EPA) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	4.436 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	5.876 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	7.317 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	n.a.	n.a.
dissociatio n constant	no dissociable groups	no dissociable groups	no dissociable groups	no dissociable groups	no dissociable groups	no dissociable groups	no dissociable groups	no dissociable groups
partition coefficient s log K _d (sediment and overlappin	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbreviati on	C-PFC	C2-PFC	C3-PFC	C4-PFC	C6-PFC	C8-PFC	C10-PFC	C12-PFC
g dissolved phase)								
log Koc (sediment organic carbon- normalise d distributio n coefficient)	1.687 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	2.352 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	3.016 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	3.681 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	5.010 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	6.339 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	n.a.	n.a.
water solubility	18.8-20 mg/L (exp. result; REACH registration data (2021-05-31)) ⁵⁶ 4.1 g/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.52 g/L at 25 °C (exp. result, OECD 105, column elution method; REACH registration data (2021- 05-31)) ⁵⁶ 0.36 g/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software	5.7 mg/L at 20 °C (calculated value; REACH registration data (2021- 05-31)) ⁵⁶ 5.7 mg/L at 15 °C (HSDB, National Library of Medicine (US)) ⁵⁸	1.612 mg/L at 25 °C (Estimate from Log Kow [4.09 (KowWin est)]; Predicted using US EPA EPI-Suite (WSKOW v1.41)) 1.4 mg/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development	≤0.1 mg/L at 20 °C, pH 7.1-7.2 (exp. result, extrapolated, slow-stirring flask method; REACH registration data (2021- 06-09)) ⁵⁶ 0.0096 mg/L at 25 °C (Estimate from Log Kow [6.02 (KowWin est)]; Predicted using US EPA EPI-Suite	ca. 10 µg/L at 20 °C, pH 7 (exp. result; WoE, REACH registration data (2021- 06-09)) ⁵⁶ 0.052 µg/L at 25 °C (Estimate from Log Kow [7.95 (KowWin est)]; Predicted using US EPA EPI-Suite (WSKOW v1.41)) 0.048 µg/L	0.00031 µg/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.00031 µg/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

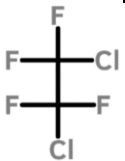
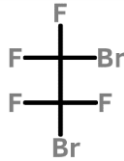
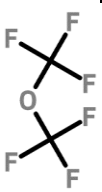
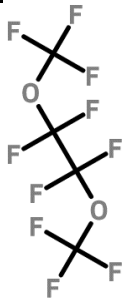
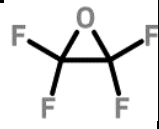
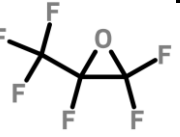
abbreviati on	C-PFC	C2-PFC	C3-PFC	C4-PFC	C6-PFC	C8-PFC	C10-PFC	C12-PFC
		V11.02)		(ACD/Labs) Software V11.02)	(WSKOW v1.41)) 0.0081 mg/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)		
vapour pressure	2.3 ·10 ⁷ Pa at 25 °C (exp. result; REACH registration data (2021-05-31)) ⁵⁶ 1.13 ·10 ⁷ Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	2902.1 kPa at 18 °C (exp. result, static cell method; REACH registration data (2021- 05-31)) ⁵⁶ 3.2 ·10 ⁶ Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	883.9 kPa at 25 °C (exp. result; HSDB, National Library of Medicine (US)) ⁵⁸ 767 kPa at 20 °C (exp. value, handbook data; REACH registration data (2021- 05-31)) ⁵⁶	268.0 kPa at 25 °C (exp. result; HSDB, National Library of Medicine (US)) ⁵⁸ 258.6 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	ca. 26.5 kPa at 25 °C (calculated with QSAR; REACH registration data (2021- 06-09)) ⁵⁶ 30.4 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	ca. 3 kPa at 25 °C (exp. result; WoE, REACH registration data (2021- 06-09)) ⁵⁶ 5.17 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	599.95 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	92.39 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
boiling point	-127.9 °C (handbook	-78.1 °C (exp. result; HSDB,	-37 °C (exp. value,	-2.1 °C (handbook	58.45 °C (exp. result,	105.9 °C (exp. result;	150 °C (exp. result; source:	178 °C (exp. result; source: Haszeldine,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbreviati on	C-PFC	C2-PFC	C3-PFC	C4-PFC	C6-PFC	C8-PFC	C10-PFC	C12-PFC
	data; CRC Handbook of Chemistry and Physics. 95th Edition)	National Library of Medicine (US)) ⁵⁸	handbook data; REACH registration data (2021-05-31)) ⁵⁶	data; CRC Handbook of Chemistry and Physics. 95th Edition)	EU Method A.2; REACH registration data (2021-06-09)) ⁵⁶	HSDB, National Library of Medicine (US)) ⁵⁸	Benning, Anthony F.; US2490764, 1949; Scifinder [CAS])	R. N.; Journal of the Chemical Society, (1950); Scifinder [CAS])
Henry's Law constant	5.15 atm-m ³ /mole (exp. database US EPA) [Royal Society of Chemistry, ChemSpider database] ⁵⁷ 4.59 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	20.3 atm-m ³ /mole (exp. database US EPA) [Royal Society of Chemistry, ChemSpider database] ⁵⁷ 24.1 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	33.0 atm-m ³ /mole (exp. database US EPA) [Royal Society of Chemistry, ChemSpider database] ⁵⁷ 24.5 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Group Method, HENRYWIN v3.10))	245 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Group Method, HENRYWIN v3.10))	2.45·10 ⁴ atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Group Method, HENRYWIN v3.10))	2.45·10 ⁶ atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Group Method, HENRYWIN v3.10))	n.a.	n.a.
	H ^{CP} =2.1×10 ⁻⁶ [mol/(m ³ Pa)] (Sander, 2015)	H ^{CP} =6.5×10 ⁻⁷ [mol/(m ³ Pa)] (Sander, 2015)	H ^{CP} =1.2×10 ⁻⁷ [mol/(m ³ Pa)] (Sander, 2015)	H ^{CP} =1.5×10 ⁻⁸ [mol/(m ³ Pa)] (Sander, 2015)	H ^{CP} =5.4×10 ⁻¹⁰ [mol/(m ³ Pa)] (Sander, 2015)	-	-	-

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.69. Basic substance information and physical chemical properties of PFAEs (Haloperfluoroalkanes and Perfluoroalkylethers; acyclic and cyclic).

abbreviatio n/acronym	Cryofluoran e	Fluobrene	PFME	PFEE	Perfluorogly me	Perfluorodigl yme	Tetrafluor ooxirane	HFPO
IUPAC name	1,2- Dichlorotetrafl uoroethane	1,2- Dibromotetrafl uoroethane	Trifluoro(trifluorom ethoxy)methane	1,1,1,2,2- Pentafluoro-2- (pentafluoroet hoxy)ethane	1,1,2,2- Tetrafluoro- 1,2- bis(trifluoromet hoxy)ethane	1,1,2,2- Tetrafluoro-1- [1,1,2,2- tetrafluoro-2- (trifluorometh oxy)ethoxy]- 2- (trifluorometh oxy)ethane	2,2,3,3- Tetrafluoro oxirane	2,2,3-Trifluoro-3- (trifluoromethyl)o xirane
other names	Cryofluorane	Fluobrene	Perfluorodimethyl ether; Perfluoromethyl ether	Perfluorodieth yl ether; Perfluoroethyl ether	Perfluoroglyme	Perfluorodigly me	Tetrafluoro oxirane	Trifluoro(trifluoro methyl)oxirane; Hexafluoro-1,2- epoxypropane
molecular formula	C ₂ Cl ₂ F ₄	C ₂ Br ₂ F ₄	C ₂ F ₆ O	C ₄ F ₁₀ O	C ₄ F ₁₀ O ₂	C ₆ F ₁₄ O ₃	C ₂ F ₄ O	C ₃ F ₆ O
structural formula								
CAS number	76-14-2	124-73-2	1479-49-8	358-21-4	378-11-0	40891-99-4	694-17-7	428-59-1
EC number	200-937-7	204-711-9	-	-	-	-	211-767-8	207-050-4
physico-chemical data								

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbreviation/acronym	Cryofluorane	Fluobrene	PFME	PFEE	Perfluoroglyme	Perfluorodiglyme	Tetrafluorooxirane	HFPO
molecular weight g/mol	170.92	259.82	154.01	254.03	270.03	386.04	116.01	166.02
partitioning coefficient log K _{ow}	2.82 (exp. database US EPA; source: Hansch,C et al. (1995))	2.96 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	2.00 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	3.93 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	6.120±0.807 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	5.55 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	1.10 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	1.72 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))
log K _{oa}	0.761 at 25 °C (Estimate from Log K _{ow} [2.82 (exp. database)] and log K _{aw} [2.059 (exp. database)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	2.139 at 25 °C (Estimate from Log K _{ow} [2.96 (KowWin estimate)] and log K _{aw} [0.821 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	1.660 at 25 °C (Estimate from Log K _{ow} [2.00 (KowWin estimate)] and log K _{aw} [0.340 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	2.148 at 25 °C (Estimate from Log K _{ow} [3.93 (KowWin estimate)] and log K _{aw} [1.782 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	n.a.	6.437 at 25 °C (Estimate from Log K _{ow} [5.55 (KowWin estimate)] and log K _{aw} [-0.887 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	2.214 at 25 °C (Estimate from Log K _{ow} [1.10 (KowWin estimate)] and log K _{aw} [-1.114 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	2.113 at 25 °C (Estimate from Log K _{ow} [1.72 (KowWin estimate)] and log K _{aw} [-0.393 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))
log K _{aw}	2.059 (exp. database US	0.821 at 25 °C	0.340 at 25 °C (Predicted using US	1.782 at 25 °C (Predicted	n.a.	-0.887 at 25 °C	-1.114 at 25 °C	-0.393 at 25 °C (Predicted using

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbreviation/acronym	Cryofluorane	Fluobrene	PFME	PFEE	Perfluoroglyme	Perfluorodiglyme	Tetrafluorooxirane	HFPO
	EPA)	(Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	EPA EPI-Suite (HenryWin v3.10 estimate))	using US EPA EPI-Suite (HenryWin v3.10 estimate))		(Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	(Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	US EPA EPI-Suite (HenryWin v3.10 estimate))
dissociation constant	no dissociable groups	no dissociable groups	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
partition coefficients log K _d (sediment and overlapping dissolved phase)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
log K _{oc} (sediment organic carbon-normalised distribution coefficient)	2.352 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	2.352 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	1.330 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	2.660 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	4.706 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	1.946 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	0.932 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	1.596 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))
water solubility	130 mg/L at 25 °C (exp. result; HSDB; source: Riddick et al. (1985))	3 mg/L at 25 °C (exp. result; HSDB; source: Horvath et al. (1999))	7.4 g/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs)	0.23 g/L unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry	0.17 g/L unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry	5 mg/L unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry	110 g/L unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry	1.2 g/L unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbreviation/acronym	Cryofluorane	Fluobrene	PFME	PFEE	Perfluoroglyme	Perfluorodiglyme	Tetrafluorooxirane	HFPO
			Software V11.02) 1.431 g/L at 25 °C (Estimate from Log Kow [2.00 (KowWin est)]); Predicted using US EPA EPI-Suite (WSKOW v1.41))	Development (ACD/Labs) Software V11.02) 9.882 mg/L at 25 °C (Estimate from Log Kow [3.93 (KowWin est)]); Predicted using US EPA EPI-Suite (WSKOW v1.41))	Development (ACD/Labs) Software V11.02)	Development (ACD/Labs) Software V11.02)	Development (ACD/Labs) Software V11.02)	Software V11.02)
vapour pressure	268.51 kPa at 25 °C (exp. result; HSDB; source: Riddick et al. (1985))	43.33 kPa at 25 °C (exp. result; HSDB; source: Daubert et al. (1989))	3.60·10 ⁶ Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	127.86 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	110.92 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	4.27 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	3.57·10 ⁶ Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	946.59 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
boiling point	3.5 °C (handbook data; CRC Handbook of Chemistry and Physics. 91th Edition)	47.35 °C (handbook data; CRC Handbook of Chemistry and Physics. 86th Edition)	-59 °C (exp. result; source: Simons, J. H.; US2500388, 1950; Scifinder (CAS))	2.5 °C (exp. result; source: Dresdner, R. D.; Journal of Organic Chemistry, (1959), 24,	13 °C (exp. result; source: Simons, J. H.; US2500388, 1950; Scifinder (CAS))	66 °C (exp. result; Modena, S.; Journal of Fluorine Chemistry, (1988), 40(2-	-63.5 °C (exp. result; SRC [Syracuse Research Corporation of Syracuse, New York (US)])	-27.4 °C (exp. result; SRC [Syracuse Research Corporation of Syracuse, New York (US)])

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

abbreviatio n/acronym	Cryofluoran e	Fluobrene	PFME	PFEE	Perfluorogly me	Perfluorodigl yme	Tetrafluor ooxirane	HFPO
				698-700; Scifinder (CAS))		3), 349-57; Scifinder (CAS))	Syracuse, New York (US))	
Henrys Law constant	1.51 atm- m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	0.162 atm- m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	0.0535 atm- m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	1.48 atm- m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	n.a.	0.00317 atm- m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	0.00188 atm- m ³ /mole at 25 °C (Predicted using US EPA EPI- Suite (Bond Method, HENRYWIN v3.10))	0.0099 atm- m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))
	H ^{CP} =9.0×10 ⁻⁶ [mol/(m ³ Pa)] (Sander, 2015)	H ^{CP} =2.7×10 ⁻⁷ [mol/(m ³ Pa)] (Sander, 2015)	-	-	-	-		H ^{CP} =8.8×10 ⁻⁶ [mol/(m ³ Pa)] (Sander, 2015)

Table B.70. Basic substance information and physical chemical properties of PFPAs (Perfluoroalkylphosphonic acids).

acron ym	PFMPA	PFEPa	PFBPA	PFPPA	PFHxPA	PFOPA	PFDPa	PFDopa
IUPAC name	(Trifluoro methyl)- phosphon ic acid	(Pentaflu roethyl)- phosphoni c acid	(Nonafluorobut yl)phosphonic acid;	(Undecafluoropen tyl)phosphonic acid	(Tridecafluorohex yl)phosphonic acid	Heptadecafluoroo ctylphosphonic acid	(Henicosaflluorode cyl)phosphonic acid	(Pentacosaflluorodod ecyl)phosphonic acid
other name s	Trifluoro methyl- phosphic acid; Perfluoro	Pentafluor oethyl- phosphoni c acid; Perfluoroe	Perfluorobutyl- phosphonic acid	Perfluoropentyl- phosphonic acid	Perfluorohexanep hosphonic acid	Perfluorooctyl- phosphonic acid	Perfluorodecylpho sphonic acid	Perfluorododecylpho sphonic acid

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	PFMPA	PFEPA	PFBPA	PFPPA	PFHxPA	PFOPA	PFDPA	PFDoPA
	methyl phosponic acid	thyl phosponic acid						
molecular formula	CH ₂ F ₃ O ₃ P	C ₂ H ₂ F ₅ O ₃ P	C ₄ H ₂ F ₉ O ₃ P	C ₅ H ₂ F ₁₁ O ₃ P	C ₆ H ₂ F ₁₃ O ₃ P	C ₈ H ₂ F ₁₇ O ₃ P	C ₁₀ H ₂ F ₂₁ O ₃ P	C ₁₂ H ₂ F ₂₅ O ₃ P
CAS number	374-09-4	103305-01-7	52299-24-8	2109769-70-0	40143-76-8	40143-78-0	52299-26-0	63225-55-8
EC number	-	-	-	-	-	-	-	-
physico-chemical data								
molecular weight g/mol	149.99	200.00	300.02	350.02	400.03	500.05	600.06	700.08
partitioning coefficient log K _{ow}	-0.28 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	0.68 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	4.093±0.674 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	4.659±0.696 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	5.389±0.741 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02) 4.55 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	6.849±0.834 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	8.308±0.917 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	9.768±0.993 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
log	8.126 at	8.366 at	n.a.	n.a.	9.353 at 25 °C	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	PFMPA	PFEPA	PFBPA	PFPPA	PFHxPA	PFOPA	PFDPA	PFDoPA
K _{OA}	25 °C (Estimate from Log K _{ow} [-0.28 (KowWin estimate)] and log K _{aw} [-8.406 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	25 °C (Estimate from Log K _{ow} [0.68 (KowWin estimate)] and log K _{aw} [-7.686 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))			(Estimate from Log K _{ow} [4.55 (KowWin estimate)] and log K _{aw} [-4.803 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))			
log K _{AW}	-8.406 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	-7.686 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	n.a.	n.a.	-4.803 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	n.a.	n.a.	n.a.
dissociation	pK _a 0.37±0.1	pK _a 0.64±0.1	pK _a 0.64±0.10 (calculated)	pK _a 0.72±0.10 (calculated using	pK _a 0.74±0.10 (calculated using	pK _a 0.78±0.10 (calculated using	pK _a 0.78±0.10 (calculated using	pK _a 0.78±0.10 (calculated using

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	PFMPA	PFEPA	PFBPA	PFPPA	PFHxPA	PFOPA	PFDPA	PFDoPA
constant	0 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	using Advanced Chemistry Development (ACD/Labs) Software V11.02)	Advanced Chemistry Development (ACD/Labs) Software V11.02)	Advanced Chemistry Development (ACD/Labs) Software V11.02)	Advanced Chemistry Development (ACD/Labs) Software V11.02)	Advanced Chemistry Development (ACD/Labs) Software V11.02)	Advanced Chemistry Development (ACD/Labs) Software V11.02)
partition coefficients log K _d (sediment and overlapping dissolved phase)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
log K _{oc} (sediment organic carbon-)	0.654 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	1.318 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	n.a.	n.a.	3.977 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	PFMPA	PFEPA	PFBPA	PFPPA	PFHxPA	PFOPA	PFDPA	PFDoPA
normalised distribution coefficient)	)							
water solubility	85 g/L in unbuffered water (pH 0.49) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	22 g/L in unbuffered water (pH 1.10) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	3.6 g/L in unbuffered water (pH 1.96) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	1.7 g/L in unbuffered water (pH 2.33) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.8 g/L in unbuffered water (pH 2.71) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.19 g/L in unbuffered water (pH 3.44) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.038 g/L in unbuffered water (pH 4.18) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	5.7 mg/L in unbuffered water (pH 4.98) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
vapour pressure	10.15 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	105.59 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	40.80 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	18.67 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	8.12 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	1.40 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.227 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	35.60 mPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	PFMPA	PFEPA	PFBPA	PFPPA	PFHxPA	PFOPA	PFDPA	PFDoPA
	s) Software V11.02)	Software V11.02)						
boiling point	210.5±45.0 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	426.42 °C at 101325 Pa (exp. result, extrapolated; MSDS Oakwood)	186.0±50.0 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	199.9±50.0 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	214.3±50.0 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	243.6±50.0 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	272.4±50.0 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	300.2±52.0 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
Henry's Law constant	9.60·10 ⁻¹¹ atm·m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	5.04·10 ⁻¹⁰ atm·m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	n.a.	n.a.	3.85·10 ⁻⁷ atm·m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	n.a.	n.a.	n.a.
	-	-	-	-	-	-	-	-

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.71. Perfluoroalkylamines. Basic substance information and physical chemical properties.

acronym	PFMAm	PFEAm	PFPrAm	PFBAm	PFHxAm	
IUPAC name	1,1,1-Trifluoro-N,N-bis(trifluoromethyl)met hanamine	1,1,2,2,2-Pentafluoro-N,N-bis(pentafluoroethyl) ethanamine	1,1,2,2,3,3,3-Heptafluoro-N,N-bis(1,1,2,2,3,3,3-heptafluoropropyl)- 1-propanamine	1,1,2,2,3,3,4,4,4-Nonafluoro-N,N-bis(nonafluorobuty l)-1-butanamine	1,1,2,2,3,3,4,4,5,5, 6,6,6-Tridecafluoro-N,N-bis(tridecafluorohex yl)-1-hexanamine	1,1,2,2,2-Pentafluoro-N-(pentafluoroethyl)-N-(trifluoromethyl)e thanamine
other names	Tris(trifluoromethyl)ami ne; Perfluorotrimethylamine	Pentadecafluorotriet hylamine; Perfluorotriethylamin e	Heneicosafluorotripr opylamine; Perfluorotripropylam ine; Perfluamine	Tris(perfluoro-bu tyl)amine; Perfluorotributyla mine	Perfluorotrihexylam ine	Perfluoromethyldi ethyl-amine; Perfluorodiethylm ethylamine
molecular formula	C ₃ F ₉ N; [(C F ₃) ₃ N]	C ₆ F ₁₅ N; [(C ₂ F ₅) ₃ N]	C ₉ F ₂₁ N; [(C ₃ F ₇) ₃ N]	C ₁₂ F ₂₇ N; [(C ₄ F ₉) ₃ N]	C ₁₈ F ₃₉ N; [(C ₆ F ₁₃) ₃ N]	C ₅ F ₁₃ N
CAS number	432-03-1	359-70-6	338-83-0	311-89-7	432-08-6	758-48-5
EC number	-	206-632-5	206-420-2	206-223-1	-	-
physico-chemical data						
molecular weight g/mol	221.02	371.05	521.07	671.09	971.14	321.04
partitioning coefficient log Kow	1.29 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	4.18 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate)) 6.462 (exp. value, MSDS LabNetwork) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	≥5.3-≤6.1 (read-across: log Kow of 5.3 is for PFHp (perfluoroheptanes); log Kow of 6.1 is for PTBA (perfluorotributylami nes); REACH registration data (2021-06-14)) 9.105 (exp. value, MSDS LabNetwork) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	15.109±0.941 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02) 11.748 (exp. value, MSDS LabNetwork) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	19.103±0.998 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	3.22 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	PFMAm	PFEAm	PFPrAm	PFBA	PFHxAm	
log K _{OA}	1.428 at 25 °C (Estimate from Log K _{ow} [1.29 (KowWin estimate)] and log K _{aw} [-0.138 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	2.155 at 25 °C (Estimate from Log K _{ow} [4.18 (KowWin estimate)] and log K _{aw} [2.025 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	n.a.	n.a.	n.a.	1.916 at 25 °C (Estimate from Log K _{ow} [3.22 (KowWin estimate)] and log K _{aw} [1.304 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))
log K _{AW}	-0.138 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	2.025 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	n.a.	n.a.	n.a.	1.304 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))
dissociation constant	pK _a -28.74±0.50 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	pK _a -27.46±0.50 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	pK _a -27.02±0.50 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	pK _a -26.84±0.50 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	pK _a -26.31±0.50 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	pK _a -28.57±0.50 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
partition coefficients log K _d (sediment and overlapping dissolved phase)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	PFMAm	PFEAm	PFPrAm	PFBA	PFHxAm	
log K _{oc} (sediment organic carbon-normalised distribution coefficient)	3.104 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	5.098 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	n.a.	n.a.	n.a.	4.433 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))
water solubility	0.21 g/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	1.2 mg/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.381 µg/L (exp. result, mean value, EPA OPPTS 830.7840 (Water Solubility), flask method; REACH registration data (2021-06-14))	insoluble (exp. result; HSDB, National Library of Medicine (US)) 0.081 µg/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	5.2·10 ⁻¹¹ g/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	5.5 mg/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
vapour pressure	394.6 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	17.3 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.516 kPa at 20 °C (exp. result, ASTM E1719-97; REACH registration data (2021-06-14))	73.33 Pa (exp. result; HSDB, National Library of Medicine (US))	0.45 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	46.93 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
boiling point	-10.5 °C (exp. result; source: Young, John A.; Journal of the American Chemical Society, (1958), 80, 1889-92; Scifinder (CAS))	72 °C (exp. result; source: Felling, Kyle W.; Journal of Fluorine Chemistry, (2003), 123(2), 233-236; Scifinder (CAS))	132 °C (exp. result, ASTM E-1719-97 and ASTM D1120-94; REACH registration data (2021-06-14))	178 °C (handbook data; CRC Handbook of Chemistry and Physics. 83rd Edition)	258 °C (exp. result; source: Kauck, Edward A.; GB666733, 1952 https://scifinder-cas.org/navigate/	45 °C at 978.59 hPa (exp. result; source: Kauck, Edward A.; GB666733, 1952 https://scifinder-cas.org/navigate/

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	PFMAm	PFEAm	PFPrAm	PFBAm	PFHxAm	
					?appId=c45de92f-c9dd-48de-ac3f-512e39d817e2&clearSearch=true&resultType=reference&resultView=DETAIL&state=searchDetail.reference&suppressNavigation=true&uiContext=369&uiSubContext=607&uriForDetails=document/pt/document/18419826; Scifinder (CAS))	n.cas.org/navigate/?appId=c45de92f-c9dd-48de-ac3f-512e39d817e2&clearSearch=true&resultType=reference&resultView=DETAIL&state=searchDetail.reference&suppressNavigation=true&uiContext=369&uiSubContext=607&uriForDetails=document/pt/document/18419826; Scifinder (CAS))
Henrys Law constant	0.0178 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	2.59 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	n.a.	n.a.	n.a.	0.493 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))
	-	-	-	H ^{CP} = 1.8×10 ⁻¹⁰ [mol/(m ³ Pa)] (Sander, 2015)	-	-

Table B.72. Basic substance information and physical chemical properties of FTOHs (Fluorotelomer alcohols, C4 to C10).

acronym	4:2 FTOH	6:2 FTOH	8:2 FTOH	10:2 FTOH
IUPAC name	3,3,4,4,5,5,6,6,6-Nonafluoro-1-hexanol	3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-octanol	3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-decanol	3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10,11,11,12,12,12-Henicosafuoro-1-dodecanol

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	4:2 FTOH	6:2 FTOH	8:2 FTOH	10:2 FTOH
other names	2-(Perfluorobutyl)ethanol	2-(Perfluorohexyl)ethanol	2-(Perfluorooctyl)ethanol	2-(Perfluorodecyl)ethanol
molecular formula	C ₆ H ₅ F ₉ O	C ₈ H ₅ F ₁₃ O	C ₁₀ H ₅ F ₁₇ O	C ₁₂ H ₅ F ₂₁ O
CAS number	2043-47-2	647-42-7	678-39-7	865-86-1
EC number	218-050-9	211-477-1	211-648-0	212-748-7
physico-chemical data				
molecular weight g/mol	264.1	364.1	464.1	564.1
partitioning coefficient log K _{ow}	3.66 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	5.60 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	7.53 (Predicted using US EPA EPI-Suite (KOWWIN v1.67 estimate))	6.995±0.855 at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02) 9.213 (exp. value, MSDS LabNetwork) [Royal Society of Chemistry, ChemSpider database] ⁵⁷
log K _{OA}	4.314 at 25 °C (Estimate from Log K _{ow} [3.66 (KowWin estimate)] and log K _{aw} [-0.654 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	4.812 at 25 °C (Estimate from Log K _{ow} [5.60 (KowWin estimate)] and log K _{aw} [0.788 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	5.301 at 25 °C (Estimate from Log K _{ow} [7.53 (KowWin estimate)] and log K _{aw} [2.229 (HenryWin estimate)]; Predicted using US EPA EPI-Suite (KOAWIN v1.10 estimate))	n.a.
log K _{AW}	-0.138 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	-0.138 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	-0.138 at 25 °C (Predicted using US EPA EPI-Suite (HenryWin v3.10 estimate))	n.a.
dissociation constant	pK _a 14.16±0.10 (calculated using	pK _a 14.26±0.10 (calculated using	pK _a 14.28±0.10 (calculated using Advanced Chemistry Development	pK _a 14.28±0.10 (calculated using Advanced Chemistry Development (ACD/Labs) Software

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	4:2 FTOH	6:2 FTOH	8:2 FTOH	10:2 FTOH
	Advanced Chemistry Development (ACD/Labs) Software V11.02)	Advanced Chemistry Development (ACD/Labs) Software V11.02)	(ACD/Labs) Software V11.02)	V11.02)
partition coefficients log K _d (sediment and overlapping dissolved phase)	n.a.	n.a.	n.a.	n.a.
log K _{oc} (sediment organic carbon-normalised distribution coefficient)	2.726 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	4.055 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	5.384 (Predicted using US EPA EPI-Suite (PCKOCWIN v1.66 estimate))	5.2 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
water solubility	1.1 g/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.058 g/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.003 g/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	0.17 mg/L in unbuffered water (pH 7) at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
vapour pressure	1.72 kPa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	50.9 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	22.7 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	2.77 Pa at 25 °C (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)
boiling point	140-143 °C (exp. value, Sigma Aldrich,	88-95 °C at 28 mmHg (exp. value, Sigma	112-114 °C at 10 mmHg (exp. value, Alfa Aesar, MSDS) [Royal	145 °C at 10 mmHg (exp. value, Alfa Aesar, MSDS) [Royal Society of Chemistry, ChemSpider

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

acronym	4:2 FTOH	6:2 FTOH	8:2 FTOH	10:2 FTOH
	MSDS) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	Aldrich, MSDS) [Royal Society of Chemistry, ChemSpider database] ⁵⁷	Society of Chemistry, ChemSpider database] ⁵⁷	database] ⁵⁷
Henrys Law constant	5.42E-003 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	1.50E-001 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	4.14 atm-m ³ /mole at 25 °C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	n.a.
	H ^{cp} = 6.6×10 ⁻³ [mol/(m ³ Pa)] (Sander, 2015)	H ^{cp} = 1.7×10 ⁻⁴ [mol/(m ³ Pa)] (Sander, 2015)	H ^{cp} = 2.0×10 ⁻⁴ [mol/(m ³ Pa)] (Sander, 2015)	H ^{cp} = 1.3×10 ⁻⁴ [mol/(m ³ Pa)] (Sander, 2015)

Appendix B.4.1.2. Key arrowhead subgroups

On the reliability and training sets of QSAR models

The below assessment of the training sets of the QSAR models relates to the modelling of PFAS persistence described in section B.4.1.2.

Biodegradability estimates are likely to be less accurate for compounds outside the molecular weight (MW) range of the training set compounds. Therefore, the substance's MW should be in the range of the training set substance's MW. The training set encompasses substances with MW ranging from 31–698 (BIOWIN 1 and 2), MW 53–698 (BIOWIN 3 and 4), MW 30–1215 (BIOWIN 5 and 6), and MW 46 – 885 (BIOWIN 7). In the present study, the analysed PFAS' MW ranged from 214 to 971. In this sense, all predictions may be considered reliable except for the perfluorotrihexylamine (MW = 971.143), which was outside the training set MW for most BIOWIN models.

Furthermore, it is important that fragment coefficients have been developed for all functional group(s) or other structural features of the substances, as they might be relevant for biodegradation. Table B.73 shows all fragments present in each of the 18 substances analysed herein, followed by the presence or absence of this fragment in the training set, for different BIOWIN models. One major issue in predicting biodegradability of PFAS is that PFAS contain fluorine [-F] fragments, whose coefficients were not developed either for the linear/non-linear models (BIOWIN 1 and 2), nor for the primary/ultimate biodegradation models (BIOWIN 3 and 4), compromising the robustness and reliability of the results. On the other hand, MITI models (BIOWIN 5 and 6) lack a fragment coefficient for trifluoromethyl groups [-CF₃]. Therefore, the influence of the fluorine atoms and bonds on PFAS aerobic biodegradation will be underestimated, as no BIOWIN model is complete to predict all fluorine fragments in the molecule.

For anaerobic biodegradation, fragment coefficients values for the fragments [-F] and [-CF₃] returned as zero for all 18 studied PFAS. If a chemical for estimation contains unique or unusual substructures not included in a model's fragment library, these structural features should not be considered in the prediction process. It should be noted, however, that a model can still have value even if there is a "missing fragment" deemed important. Considering that these fragments are not listed in the training set of BIOWIN 7 (anaerobic), it is likely that coefficients were not developed despite displayed in the output tables.

As for fragments that categorize the PFAS substances into different groups, aliphatic acid [-C(=O)-OH], sulfonic acid, tertiary amine and aliphatic ether [C-O-C] have fragment coefficients developed for BIOWIN models, while the fragment phosphonic acid is not included in the training sets.

Table B.73. Presence (YES) or absence (NO) of fragments for different BIOWIN models present in each modelled PFAS in the training set.

Group and substance	Fragment	BW 1, 2	BW 3, 4	BW 5, 6	BW 7
Carboxylic acids PFOA PFHxA PFBA	Carbon with 4 single bonds & no hydrogens	YES	YES	YES	YES
	Aliphatic acid [-C(=O)-OH]	YES	YES	YES	YES
	Trifluoromethyl group [-CF ₃]	YES	YES	NO	UNL
	Fluorine [-F]	NO	NO	YES	UNL
Sulfonic acids PFOS PFHxS PFBS	Carbon with 4 single bonds & no hydrogens	YES	YES	YES	YES
	Sulfonic acid/salt -> aliphatic attach	YES	YES	NO	YES
	Trifluoromethyl group [-CF ₃]	YES	YES	NO	UNL

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Group and substance	Fragment	BW 1, 2	BW 3, 4	BW 5, 6	BW 7
	Fluorine [-F]	NO	NO	YES	UNL
Phosphonic acids PFOPA PFHxPA PFBPA	Carbon with 4 single bonds & no hydrogens	YES	YES	YES	YES
	Phosphonic acid -> aliphatic attach	NO	NO	NO	NO
	Trifluoromethyl group [-CF3]	YES	YES	NO	UNL
	Fluorine [-F]	NO	NO	YES	UNL
Perfluoroalkanes Perfluorohexane Perfluorooctane Perfluorodecaline*	Carbon with 4 single bonds & no hydrogens	YES	YES	YES	YES
	Trifluoromethyl group [-CF3]	YES	YES	NO	UNL
	Fluorine [-F]	NO	NO	YES	UNL
Perfluoroalkyl amines Perfluoramine Perfluoromethyldiethylamine Perfluorotrihexylamine	Carbon with 4 single bonds & no hydrogens	YES	YES	YES	YES
	Tertiary amine	YES	YES	YES	YES
	Trifluoromethyl group [-CF3]	YES	YES	NO	UNL
	Fluorine [-F]	NO	NO	YES	UNL
Ethers Perfluorodiethyl ether CF3-O-CF2-CF2-O-CF3 2,2,3,3,4,4,5-heptafluorotetrahydro-5-(nonafluorobutyl)furan	Carbon with 4 single bonds & no hydrogens	YES	YES	YES	YES
	Aliphatic ether [C-O-C]	YES	YES	YES	YES
	Trifluoromethyl group [-CF3]	YES	YES	NO	UNL
	Fluorine [-F]	NO	NO	YES	UNL

BW – BIOWIN model; *Perfluorodecaline does not have [-CF3] groups; UNL - unlikely

There are maximum instances of fragments in the substances used in the training set. Therefore, it is recommended that the substance to be predicted has no more than the maximum fragment instances used in the training set. Table B.74 shows the maximum instances of each fragment in the training set library (grey cells), as well as the number of each fragment in the modelled substances.

As it can be seen from Table B.73 and Table B.74, no PFAS could be accurately predicted by all BIOWIN models. Similarly, different applicability domains were found to different PFAS groups, mainly due to the presence and instances of characteristic fragments.

Table B.74. Maximum number of instances of each fragment in the training set (grey) versus the number of instances of each fragment in the modelled PFAS (colours). The colours indicate which set of BIOWIN models cover the instances of the fragments in the training set.

Fragment	Maximum instances of the fragment in the training set				Instances of the fragment in the modelled PFAS																	
					Carboxylic acid			Sulfonic acid			Phosphonic acid			Perfluoroalkane			Perfluoroalkylamine			Ether		
	BW 1,2	BW 3,4	BW 5,6	BW 7	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
Carbon with 4 single bonds & no hydrogens	2	3	12	3	6	4	2	7	5	3	7	5	3	4	6	10	6	2	15	2	2	7
Trifluoromethyl group [-CF ₃]	1	1	0	0	1	1	1	1	1	1	1	1	1	2	2	0	3	3	3	2	2	1
Fluorine [-F]	0	0	27	0	15	11	7	17	13	9	17	13	9	14	18	18	21	13	39	10	10	16
Aliphatic acid [-C(=O)-OH]	4	1	3	3	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sulfonic acid / salt -> aliphatic attach	1	2	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Phosphonic acid - aliphatic attach	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0
Tertiary amine	4	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0
Aliphatic ether [C-O-C]	2	5	5	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	1

A. PFOA; B. PFHxA; C. PFBA; D. PFOS; E. PFHxS; F. PFBS; G. PFPOA; H. PFHxPA, I. PFBPA; J. Perfluorohexane; K. Perfluorooctane; L. Perfluorodecaline; M. Perfluoramine; N. Perfluoromethyldiethylamine; O. Perfluorotrihexylamine; P. Perfluorodiethylether; Q. 1,1,2,2-Tetrafluoro-1,2-bis(trifluoromethoxy)ethane; R. 2,2,3,3,4,4,5-heptafluorotetrahydro-5-(nonafluorobutyl)furan

	Within training set of all models
	Within training set of models 3-7
	Within training sets of models 1-4
	Within training set of MITI models (5 and 6)
	Outside training sets

Appendix B.4.1.3.1. Degradation of PFCA precursors

Table B.75. Summary of formed PFCAs during degradation of n:2 FTOHs and the intermediate products (5:3 acid, fluorotelomer carboxylic acid (FTCA) and fluorotelomer unsaturated carboxylic acid (FTUCA)).

Substance	Compartment	Study duration	C4-PFCA [%]	C5-PFCA [%]	C6-PFCA [%]	C7-PFCA [%]	C8-PFCA [%]	C9-PFCA [%]	C10-PFCA [%]	Reference
6:2 FTOH	Atmosphere		+	+	+	+				(Ellis et al., 2004)
	Atmosphere			+	+	+				(Styler et al., 2013)
	Soil (flow through)	84 d	0.8	4.2	4.5	-				(Liu et al., 2010b)
	Soil (closed system)	180 d	1.8	30	8.1	-				(Liu et al., 2010c)
	Mixed bacterial culture	90 d	<0.5	<0.5	5	-				(Liu et al., 2010c)
	WWTP-activated sludge	60 d	-	4.4 mol%	11 mol%	-				(Zhao et al., 2013b)
	Aerobic river sediment system	100 d	1.5 mol%	10.4 mol%	8.4 mol%	-				(Zhao et al., 2013a)
	Anaerobic digester sludge	90 d		-	0.2 mol%	-				(Zhang et al., 2013b)
		176 d		-	0.4 mol%	-				
	Anaerobic sediment	100 d	-	-	0.6 mol%					(Zhang et al., 2016c)
5:3 acid (5:3 FTCA)	WWTP-activated sludge	90 d		0.8 mol%	5.9 mol%					(Wang et al., 2012)
8:2 FTOH	Atmosphere		0.1	0.1	0.24	0.32	1.5	1.6		(Ellis et al., 2004)
	Aqueous photolysis – H ₂ O ₂ solution	10 h					40	+		(Gauthier and Mabury, 2005)
	Aqueous photolysis – synthetic field water	140-146 h					1-8	+		

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Compartment	Study duration	C4-PFCA [%]	C5-PFCA [%]	C6-PFCA [%]	C7-PFCA [%]	C8-PFCA [%]	C9-PFCA [%]	C10-PFCA [%]	Reference
	Aqueous photolysis –Lake Ontario						3	+ (but below LOQ)		
	mixed microbial system (sediment and groundwater)	81 d				-	3	-		(Dinglasan et al., 2004)
	mixed bacterial culture	90 d			1	Not evaluated	6	-		(Wang et al., 2005a)
	activated sludge	28 d				Not evaluated	2.1	-		(Wang et al., 2005b)
	Soil	197 d			1-4	-	10-40 (average 25)			(Wang et al., 2009)
	Anaerobic digester sludge	181 d			-	-	0.3 mol%			(Zhang et al., 2013b)
	Anaerobic activated sludge	150 d	1.9	1.2	5.4	8.9	17			(Li et al., 2018b)
8:2 FTCA	Sediment-water system	50 d					21 mol% (water) 9.3 mol% (sed.)			(Myers and Mabury, 2010)
8:2 FTUCA	Sediment-water system	35 d				12 mol% (water, at day 22)	27 mol% (water) 9 mol% (sed.)	<1 mol%	<1 mol%	(Myers and Mabury, 2010)
10:2 FTOH	soil	30 d					5.1 mol%	4.3 mol%	59.7 mol%	(Zhao and Zhu, 2017)
	Soil-earthworm						8.7 mol%	7.3 mol%	74.9 mol%	
	Soil-wheat						8.9 mol%	5.9 mol%	77.8 mol%	
	Soil-earthworm-wheat						9.9 mol%	6.0 mol%	74.8 mol%	
10:2 FTCA	Sediment-water system	50 d							11 mol% (sed.)	(Myers and Mabury, 2010)
10:2 FTUCA	Sediment-water system	35 d				0.37 mol%	1.9 mol% (sed.)	1.1 mol% (water)	6 mol% (water)	(Myers and Mabury, 2010)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Compartment	Study duration	C4-PFCA [%]	C5-PFCA [%]	C6-PFCA [%]	C7-PFCA [%]	C8-PFCA [%]	C9-PFCA [%]	C10-PFCA [%]	Reference
						(sed.)		1.7 mol% (sed.)	22 mol% (sed.)	

[+] detected, but not quantified; [-] not detected; [] not evaluated

Table B.76. Summary of formed PFCAs during degradation of n:2 fluorotelomer derivatives.

Substance	Compartment	Study duration	C4-PFCA [%]	C5-PFCA [%]	C6-PFCA [%]	C7-PFCA [%]	C8-PFCA [%]	C9-PFCA [%]	C10-PFCA [%]	Reference
<i>n:2 Fluorotelomer iodides (FTIs)</i>										
6:2 FTI	Soil	91 d	-	20 mol%	3.8 mol%	16 mol%				(Ruan et al., 2010)
4:2 FTI	Atmosphere		+	+						(Young et al., 2008; Young and Mabury, 2010)
FTI	Hydrolysis (modelling)				Corresponding FTOHs and PFCAs					(Nielsen, 2014; Rayne and Forest, 2010)
<i>Esters of n:2 fluorotelomer alcohols</i>										
8:2 fluorotelomer stearate monoester	Agricultural soil	80 d			0.16 mol%	0.38 mol%	1.7 mol%	0.009 mol%		(Dasu et al., 2013)
8:2 fluorotelomer stearate monoester	Forest soil	94 d			0.2 mol%	0.9 mol%	4 mol%			(Dasu et al., 2013)
8:2 Fluorotelomer citrate triester	Forest soil	218 d			0.2 mol%	0.8 mol%	4 mol%			(Dasu et al., 2013)
n:2FT(M)A (n=2-12)	Hydrolysis (modelling)				Corresponding FTOHs and PFCAs					(Nielsen, 2014; Rayne and Forest, 2010)
8:2 FTA	Soil	105 d			<0.4 mol%	1.3 mol%	8 mol%			(Royer et al., 2015)
8:2 FTMA	Soil	105 d			<0.4 mol%	3.4 mol%	10.3 mol%			(Royer et al., 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Compartment	Study duration	C4-PFCA [%]	C5-PFCA [%]	C6-PFCA [%]	C7-PFCA [%]	C8-PFCA [%]	C9-PFCA [%]	C10-PFCA [%]	Reference
4:2 FTA	Atmosphere	10 d	Corresponding PFCAs (1-10 mol%)							(Butt et al., 2009)
<i>n:2 Polyfluoroalkyl phosphoric acid mono-/diesters (monoPAPs/diPAPs)</i>										
n:2 diPAPs (n = 4, 6, 8, 10)	Rats		Corresponding FTOHs and PFCAs							(D'Eon J and Mabury, 2011)
6:2 monoPAP	Wastewater and sewage sludge	92 d		0.7 mol%	2.1 mol%	8.4 mol%				(Lee et al., 2010)
6:2 diPAP	Wastewater and sewage sludge	92 d		1.5 mol%	6.2 mol%	7.3 mol%				
n:2 monoPAPs (n = 4, 6, 8, 10)	Wastewater and sewage sludge	92 d	Corresponding FTOHs (1-2% after 92 days) and PFCAs							
6:2 diPAP	Soil and plant	5.5 months	+	+	+	+				
6:2 diPAP	Activated sludge	30 d		0.47 mol%	2 mol%	0.04 mol%				(Lewis et al., 2016)
6:2 diPAP	Soil	112 d	0.73	6.4	6					(Liu and Liu, 2016)
8:2 diPAP	Soil	112 d			0.34	0.25	2.1			
8:2 diPAP	compost amended soil 2.4	108 d			+	+	10%			(Bizkarguena ga et al., 2016)
	compost amended substrate				+	+	62%			
	in presence of crops (carrot)	3 months	+	+	+	+	+	+		
	in presence of crops (lettuce)	1 month					+			
8:2 monoPAP and diPAP	Hydrolysis	14 d					8:2 FTOH			(D'Eon and Mabury, 2007;

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Compartment	Study duration	C4-PFCA [%]	C5-PFCA [%]	C6-PFCA [%]	C7-PFCA [%]	C8-PFCA [%]	C9-PFCA [%]	C10-PFCA [%]	Reference
										Nielsen, 2014; Rayne and Forest, 2010)
8:2 monoPAP and diPAP	Rats	15 d			-	+	+	-		(D'Eon and Mabury, 2007)
<i>n:2 Fluorotelomer urethane (monomers)</i>										
toluene-2,4-di-(8:2 fluorotelomer urethane) (FTU)	Agricultural soil	180 d					+ (from residual 8:2 FTOH)			(Dasu and Lee, 2016)
	Forest soil	117 d			0.07 mol%	0.11 mol%	0.84 mol%			
hexamethylene-1,6-di(8:2 fluorotelomer urethane) (HMU)	Forest soil	180 d			0.06 mol%	0.14 mol%	0.94 mol%			
<i>n:2 Fluorotelomer sulfonic acids (FTSAs)</i>										
6:2 FTSA	WWTP-activated sludge	90 d	0.14	1.5	1.1	-				(Wang et al., 2011b)
6:2 FTSA	Aerobic sediment	90 d	-	21 mol%	20 mol%	0.55 mol%				(Zhang et al., 2016c)
	Anaerobic sediment	100 d	-	-	-	-				
<i>n:2 Fluorotelomer thioether amido sulfonates (FTTAoSs) [belonging to the PFAS subgroup n:2 fluorotelomer -thiol derivatives]</i>										
n:2 FTTAoS (n=4,6,8)	Soil amended with an AFFF solution	60 d	+	+	+	+				(Harding-Marjanovic et al., 2015)
<i>n:2 Fluorotelomer olefins (FTOs)</i>										
n:2 Fluorotelomer olefins	Atmosphere		Corresponding FTOHs and PFCAs							(Nielsen, 2014; Sulbaek Andersen et

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Compartment	Study duration	C4-PFCA [%]	C5-PFCA [%]	C6-PFCA [%]	C7-PFCA [%]	C8-PFCA [%]	C9-PFCA [%]	C10-PFCA [%]	Reference
										al., 2005; Young and Mabury, 2010)
<i>n:2 Fluorotelomer silanes</i>										
n:2 Fluorotelomer silanes	Atmosphere		Corresponding PFCAs							(Nielsen, 2014; Zhu et al., 2019)

[+] detected, but not quantified; [-] not detected; [] not evaluated

Appendix B.4.2.1.3. Mobility in water

Table B.77. Concentrations of PFASs in ground water described by detection frequency (% or x/xx), median value (ng/L) in bold and range in brackets. Grey cells indicate sampling sites near known PFAS point sources. NR=not reported.

Location	Pollution	N	TFA	PFEtS	PFPrA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	Reference
Denmark		247	89% (<50-2 400)								(Miljøstyrelsen, 2020)
11 European countries	Partly polluted areas	2 000-7 000				46%	29%	25%		24%	(WFD CIS, 2020)
Germany		42	~800 (NR-7 500)								(Janda et al., 2019)
Germany, Baden-Württemberg	Polluted sampling sites	5	(~800-2 200)		(NR-56)						
Sweden (Ground-/surface water)	Suspected contamination	23		100% (0.07-5 700)		100% (4.8-24 000)	100% (4.8-65 000)	100% (3.4-90 000)	100% (2.6-29 000)	100% (1.4-26 000)	(Ericson Jogsten and Yeung, 2017)
Sweden	Near landfills	52-196				61% 129 (<LOQ-6 700)	60% 80 (<LOQ-2 900)	66% 77 (<LOQ-2 500)	56% 23 (<LOQ-530)	71% 54 (<LOQ-1 000)	(Miljösamverkan Sverige, 2022)
Table continued											
		PFPrS	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^φ	PFNS	PFDS	PFD _o DS	
Denmark											(Miljøstyrelsen, 2020)
11 European countries	Partly polluted areas		26%		37%		21%				(WFD CIS, 2020)
Germany											(Janda et al., 2019)
Germany, Baden-Württemberg	Polluted sampling sites										

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Pollution	N	TFA	PFEtS	PFPrA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	Reference
Sweden (Ground-/surface water)	Suspected contamination	96% (<0.4-39 000)	100% (2.6-46 000)	96% (<0.86-59 000)	100% (4.4-92 000)	96% (<1.9-77 000)	100% (10-140 000)	83% (<0.02-6.8)	61% (<0.02-1.2)	9% (<0.07-0.3)	(Ericson Jogsten and Yeung, 2017)
Sweden	Near landfills		54% 95 (<LOQ-4 100)	17% 4.6 (<LOQ-160)	57% 58 (<LOQ-7 100)	14% 0.87 (<LOQ-44)	58% 67 (<LOQ-7 700)	0%	1% (<LOQ-0.4)	2% (<LOQ-2.3)	(Miljösamverkan Sverige, 2022)

‡ PFOS can be reported as linear (L), branched (Br) or Total (L+Br), which is generally not indicated in the table.

Table B.78. Concentrations of PFASs in surface water described by detection frequency (% or x/xx), mean value (ng/L) in bold and range in brackets. Grey cells indicate sampling sites near known PFAS point sources. NR=not reported, nd=not detected, FCPP=fluorochemical production plant (mainly fluoropolymer production).

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS‡	PFECHS	6:2 Cl-PFESA	HFPO-DA	Other	Reference
Switzerland (rivers)	1996-97		80	TFA: 87 (12-328)															(Berg et al., 2000)
Switzerland (midland lakes)	1996-97		20	TFA: 119 (37-204)															
Switzerland (mountain lakes)	1996-97		8	TFA: 141 (46-360)															
Switzerland, (moor water)	1996-97		3	TFA: 107 (59-175)															
Sweden (snow, rain)				PFEtS: (nd-															(Ericson Jogsten and

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFES A	HFPO-DA	Other	Reference
and rivers)				2.9) PFPoS: (nd-1.4)															Yeung, 2017)
Faroe Islands (lakes)	2012		4		3/4 (<0.4-1.2)	0/4	0/4	3/4 (<0.05-0.14)	4/4 (0.23-0.42)	0/4		0/4		2/4 (<0.09-0.57)				PFDS: 1/4 (0.001-0.06)	(Eriksson et al., 2013)
Netherlands	2009		10											10/10 (3.3-25)				PFHxPA, PFDPA: nd PFOPA: 1/10 (nd~1)	(Esparza et al., 2011)
Germany			43	TFA: ~500* (NR-17 000)															(Janda et al., 2019)
German Bight	2017		28		100% 1.5 (1.1-2.2)	100% 0.40 (0.27-0.64)	100% 0.84 (0.47-1.3)	100% 0.28 (0.17-0.45)	100% 0.50 (0.27-0.71)	100% 0.55 (0.44-0.72)		100% 0.16 (0.12-0.23)		100% L: 0.044 (0.02-0.08) Br: 0.039 (0.02-0.08)	0%		100% 1.6 (0.92-2.5)		(Joerss et al., 2019)
Elbe river	2017		17		100% 1.5 (1.2-1.9)	100% 1.1 (0.65-1.7)	100% 3.1 (1.5-4.6)	100% 0.88 (0.48-1.2)	100% 1.4 (0.87-2.1)	100% 0.75 (0.43-0.99)		100% 0.32 (0.22-0.49)		100% L: 0.20 (0.10-0.33) Br: 0.17	6% (nd-0.06)		100% 0.40 (0.07-1.5)		

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFES A	HFPO-DA	Other	Reference
														(0.06-0.28)					
Baltic sea	2017		42		100% 0.46 (0.33-0.99)	100% 0.16 (0.10-0.75)	100% 0.32 (0.22-0.84)	100% 0.20 (0.13-0.38)	100% 0.32 (0.20-0.70)	100% 0.25 (0.15-0.43)		95% 0.25 (nd-0.48)		100% L: 0.043 (0.02-0.08) Br: 0.05 (0.03-0.1)	86% 0.06 (nd-0.14)		100% 0.05 (0.03-0.08)		
Germany/ Netherlands (Rhine River)	2013		23		100% 1.7 (0.2-2.7)	100% 4.7 (3.2-11)	100% 2.7 (1.8-5.4)	100% 1.9 (1.2-2.9)	100% 4.8 (3.5-7.1)	100% 16 (1.4-40)		100% 1.7 (0.8-3.6)		74% 1.2 (nd-2.7)			17% (nd-108)		(Heydebreck et al., 2015)
Germany (Elbe river)	2014		22		91% 1.0 (nd-1.9)	100% 2.4 (0.4-4.8)	100% 2.8 (1.5-4.1)	68% 0.6 (nd-1.8)	100% 2.0 (0.8-3.6)	100% 2.3 (0.8-3.6)		100% 0.8 (0.3-1.4)		36% (nd-11)			0%		
Germany (Elbe estuary/ North sea)	2014		19		100% 1.0 (0.3-1.8)	100% 0.8 (0.2-1.4)	100% 1.9 (0.4-4.0)	74% 0.6 (nd-1.3)	100% 1.6 (0.4-5.1)	100% 1.1 (0.7-1.6)		100% 0.5 (0.1-1.0)		95% (nd-2.6)			42% (nd-3.7)		
Germany, (Ems estuary/ North sea)	2014		18		50% (nd-3.7)	28% (nd-3.8)	100% 1.3 (0.3-4.4)	78% 2.8 (nd-8.4)	100% 4.6 (1.4-12)	100% 1.2 (0.6-2.7)		61% 0.4 (nd-1.6)		11% (nd-0.8)			89% (nd-2.0)		
Greenland Sea, Norwegian Sea, North Sea, Fram	2018		40				100% 0.056 (0.017-0.11)	100% 0.040 (0.02-0.10)	100% 0.066 (0.038-0.17)	100% 0.039 (0.015-0.093)		39% (nd-0.054)	0% (<0.03)	L: 0.042 (nd-0.11)	0% (<0.02)	0% (<0.02)	90% 0.03 (nd-0.12)	HPFO-TrA: 0% HFPO-TeA: 0% PFDS: 0%	(Joeress et al., 2020b)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFES A	HFPO-DA	Other	Reference
Strait																		ADONA: 0%	
North Atlantic Ocean	1995			TFA: 70-250															(Jordan and Frank, 1999)
Longyearbyen (river)	2006		6		1.2	1.0	0.26	0.15	0.31										(Kwok et al., 2013)
(Isdammen lake)			1		0.43	1.4	0.07	0.06	0.17										
(Adventfjorden)	2006		3		0.057	0.35	0.056	0.015	0.074										
Nordic countries	2017		13	PFES: 11/12 (<0.06-0.88) PFPrA: 2/13 (<LOD-0.39) PFPrS: 2/12 (<LOD-0.18)	9/13 (<LOD-3.5)	6/13 (<LOD-5.9)	9/13 (<LOD-11)	13/13 (0.09-3.2)	13/13 (0.1-4.1)	6/13 (<LOD-1.6)	3/13 (<LOD-0.47)	8/13 (<LOD-4.3)	1/13 (<LOD-0.25)	13/13 L- (0.22-10)	2/13 (<LOD-0.94)	0/13 (<LOD)	0/13 (<LOD)	PFNS, PFDS, PFDoDS, PFHxPA, PFOPA, PFDPA, ADONA: 0/13	(Kärman et al., 2019)
Germany	2010-12		24		33% (nd-23)	17% (nd-9.4)	29% (nd-13)	38% (nd-24)	29% (nd-6.5)			21% (nd-5.6)		13% (nd-4.6)					(Llorca et al., 2012a)
Spain	2010-12		24		71% 30 (nd-125)	21% (nd-13)	25% (nd-31)	38% (nd-27)	63% 13 (nd-68)			21% (nd-37)		46% (nd-2 709)					
Norway (Inner Oslo)	2017		2			9.1	5.4	3.3	5.9	1.4				4.7					(NEA, 2019)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFESA	HFPO-DA	Other	Reference
fjord)																			
England (Thames River)			6		100% 7.0 (4.6-9.8)	100% 16 (10-20)	100% 12 (7.3-15)	100% 4.1 (2.6-5.2)	100% 8.5 (5.6-12)	100% 5.1 (3.3-6.7)		100% 7.1 (5.0-11)		100% 14 (8.1-19)		100% 0.05 (0.001-0.08)	100% 1.1 (0.70-1.6)	HFPO-TrA: 4/6 0.16 (0.05-0.21) 6:2 H-PFESA; ADONA: 0%	(Pan et al., 2018)
Germany/Netherlands (Rhine River)			20		100% 4.3 (0.84-6.2)	100% 2.6 (0.42-4.0)	100% 2.9 (0.83-4.6)	100% 1.2 (0.2-2.0)	100% 2.6 (0.86-3.7)	100% 22 (0.46-146)		100% 2.0 (0.12-3.9)		100% 4.4 (0.23-8.6)		100% 0.08 (0.02-0.38)	100% 0.99 (0.59-2.0)	HFPO-TrA: 14/20 0.16 (<LOQ-0.31) 6:2 H-PFESA: 0% ADONA: 15/20 0.09 (<LOQ-1.5)	
Sweden (Mälaren Lake)			10		100% 2.3 (1.7-3.0)	100% 2.1 (1.0-3.2)	100% 1.7 (0.89-2.9)	100% 0.86 (0.55-1.3)	100% 2.3 (1.1-3.3)	100% 1.4 (0.75-1.9)		100% 1.3 (0.56-2.8)		100% 3.1 (1.0-8.2)		80% 0.02 (<0.01-0.05)	100% 1.5 (0.88-2.7)	HFPO-TrA: 8/10 0.20 (<LOQ-0.39) 6:2 H-PFESA: 0% ADONA: 0%	
Germany (Elbe and Weser river)	2011				1.1 (<0.14-2.5)	0.83 (<0.05-4.4)	2.0 (0.50-5.3)		2.3 (0.8-5.1)	6.3 (0.24-238)		0.54 (<0.03-1.2)		1.0 (0.13-3.0)					(Zhao et al., 2015)
Germany (North	2011				0.92 (<0.1	0.22 (<0.0	0.45 (<0.09		0.84 (0.1-	1.2 (<0.03		0.24 (<0.03		0.51 (<0.07					

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFESA	HFPO-DA	Other	Reference
Sea)					4-2.2)	5-0.41)	-1.8)		2.4)	-2.9)		-0.51)		-2.7)					
Europe Arctic (seawater 0.5m)	2019		5		0.13 ± 0.28	0.03 9 ± 0.054	0.083 ± 0.068	0.34 ± 0.26	0.69 ± 0.55	<MDL				0.031 ± 0.055					(Garnett et al., 2021)
(seawater 5m)	2019		5		<MDL	0.01 6 ± 0.036	0.009 ± 0.019	0.11 ± 0.049	0.16 ± 0.057	0.084 ± 0.19				0.010 ± 0.023					
(melt pond)	2019		6		0.83 ± 0.17	0.06 0 ± 0.015	0.058 ± 0.013	0.12 ± 0.025	0.042 ± 0.010	<MDL				0.004 ± 0.009					
Canada, Great Lakes															(0.16–5.7)				(De Silva et al., 2011)
Canada (creeks and rivers)	2005-07		30						83% (nd-87)					97% (nd-40)				PFHxPA: 40% (nd-1.2) PFOPA: 80% (nd-3.4) PFDPA: 73% (nd-0.9)	(D'eon et al., 2009)
Canadian Arctic	2010-11						0.43-30§	0.30-25§	0.60-17§	0.06-4.9§		0.01-30§		0.02-41§	0.06-4.3§			PFD _o DS: 0.0001-0.003§	(Lescord et al., 2015)
Canadian arctic (Barrow Strait)	2011		7		0.75 (0.05-2.0)	0.47 (0.21-0.85)	0.38 (0.98-1.2)	0.12 (0.056-0.18)	0.32 (0.042-0.77)	(<0.001)		0.002 (0.001-0.003)	(<0.001)	0.008 (0.001-0.012)	(<0.001)			PFDS: <0.001	(Muir et al., 2015)
Canadian arctic, Barrow	2012		12		1.6 (0.05-5.4)	0.05 0 (0.00	0.094 (0.041-0.25)	0.056 (0.025-0.13)	0.13 (0.064-0.27)	(<0.001)		0.001 (<0.001-1)	(<0.001)	0.014 (0.001-0.095)	0.025 (0.004-			PFDS: <0.001	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFES A	HFPO-DA	Other	Reference
Strait)						5-0.41)						0.0015)			0.064)				
West Arctic (Canada Basin)	1998			TFA: (34-181)															(Scott et al., 2005)
East Arctic (Nares Strait)	1998			TFA: (8.0-170)															
Amundsen Basin (1-10m)	2012		2				(0.014-0.030)	(0.016-0.017)	(0.009-0.037)	(0.015-0.018)		(<0.001-0.009)		(<0.001-0.014)				PFDS: <0.001	(Yeung et al., 2017)
North Barents Sea (1-10m)	2012		1				0.012	0.022	0.032	0.011		0.015		0.041				PFDS: <0.001	
Nansen Basin (1-10m)	2012		1				<0.001	<0.001	0.015	0.015		<0.001		0.019				PFDS: <0.026	
S. Beaufort sea shelf (1-10m)	2012		7				0/7 (<0.001)	6/7 (<0.001-0.030)	7/7 (0.02-0.056)	3/7 (<0.001-0.009)		4/7 (<0.001-0.008)		7/7 (0.006-0.033)				PFDS: <0.001	
China, Beijing (landscape water)	2012			TFA: 643 ±169															(Zhai et al., 2015)
Netherlands, Dordrecht (river)	2016	Upstream FCPP + control site	5		5/5 8.1 (4.1-14)	4/5 5.7 (<4-9.2)	5/5 6.0 (5.1-6.4)	5/5 2.0 (1.8-2.2)	5/5 3.0 (2.8-3.2)	5/5 19 (12-22)		5/5 2.0 (1.7-2.2)	5/5 0.15 (0.13-0.2)	5/5 4.3 (3.1-7.1)		0%	1/5 (<0.2-22)	ADONA: 0%	(Gebbinck et al., 2017)
		Down-stream	13		13/13 7.8	10/13 5.1	13/13 5.3	13/13 1.9	13/13 4.6	13/13 21		13/13 2.0	13/13 0.1	13/13 3.4		0%	13/13 178	ADONA: 0%	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFES A	HFPO-DA	Other	Reference
		FCPP			(4.6-13)	(<4-8.2)	(4.0-6.4)	(1.5-2.2)	(3.4-12)	(16-27)		(1.5-2.2)	(0.09-0.2)	(2.7-6.5)			(1.7-812)		
Germany (Alz river)	2018	Upstream industry	2		0.87 (0.65-1.1)	0.65 (0.3-1)	0.52 (0.38-0.67)	0.40 (0.25-0.55)	1.6 (0.77-2.5)	0.44 (0.44-0.44)		(nd)	(nd)	0.43 (0.42-0.45)	(nd)	(nd)	13 (0.55-25)	ADONA: 19 (1.2-37)	(Joerss et al., 2020a)
		Downstream industry (eg FCPP)	3		153 (130-190)	233 (200-280)	88 (75-110)	31 (26-37)	73 (20-180)	3.4 (3.1-3.7)		0.03 (0.02-0.32)	(nd)	0.44 (0.40-0.47)	(nd)	(nd)	2600 (1900-3600)	ADONA: 2100 (1800-2500)	
Germany (Ruhr river)	2018	Upstream industry	2		3.8 (3.8-3.8)	2.9 (2.8-3.0)	3.2 (3.2-3.3)	1.5 (1.4-1.5)	2.4 (2.3-2.4)	3.4 (3.1-3.8)		1.8 (1.8-1.8)	(nd)	2.2 (2.1-2.2)	(nd)	(nd)	0.05 (0.05-0.05)	ADONA: nd	
		Downstream industry (eg metal plating)	6		6.5 (5.8-6.9)	5.1 (4.7-5.4)	7.5 (7.3-7.7)	3.7 (3.2-5.3)	5.1 (4.8-5.4)	5.1 (4.8-5.7)		0.6 (0.56-0.63)	(nd)	3.0 (2.6-4.7)	0.14 (0.11-0.16)	(nd)	0.07 (0.06-0.08)	ADONA: (nd-0.08)	
Germany (Rhine river)	2018	Downstream industry (eg pesticides)	3		4.2 (4.0-4.4)	2.8 (2.8-2.8)	3.2 (3.1-3.3)	1.5 (1.4-1.6)	2.4 (2.3-2.5)	45 (34-66)		1.9 (1.8-2.0)	(nd)	2.6 (2.3-2.9)	(nd)	(nd)	0.05 (0.04-0.06)	ADONA: nd	
Germany, (Tributary to Rhine)	2018	Up- & down-stream industry	6		3.9 (3.1-5.2)	2.3 (1.9-2.6)	3.2 (2.8-3.6)	1.5 (1.3-1.8)	2.3 (1.9-2.7)	3.2 (2.4-3.7)		1.2 (0.87-1.4)	(nd)	1.3 (1.0-2.0)	(nd-0.12)	(nd)	0.13 (0.03-0.21)	ADONA: nd	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFESA	HFPO-DA	Other	Reference
China (Xiaoqing River)	2019	FCPP			383 ± 154	237 ± 89	284 ± 104	284 ± 104	27 600 ± 11 367	9.4 ± 9.6		5.9 ± 1.5		22 ± 6.6		3.3 ± 1.9	828 ± 224	HFPO-TrA: 1218 ± 412 HFPO-TeA: 0.93 ± 0.82 6:2H-PFESA: 0.65 ± 0.34 PFMOAA: 1 675 ± 924 PFO2HxA: 1 899 ± 887 PFO3OA: 1 638 ± 879 PFO4DA: 253 ± 156 PFO5DoA: 41 ± 28 PF4OPeA: 44 ± 25 PF5OHxA: 9.0 ± 4.4 PFMO2OESA: 3.6 ± 1.2 Nafion by-p 2: 20 ± 8.9	(Li et al., 2021e)
China (Xiaoqing River)	2015	Upstream	6		100% 6.9 (2.8-9.7)	100% 2.2 (0.93-3.3)	100% 3.1 (1.1-4.4)	100% 1.7 (0.66-3.3)	100% 45 (15-79)	6/6 0.85 (0.71-1.0)		100% 0.64 (0.31-1.3)		100% 3.0 (2.0-4.3)		100% 8.2 (3.7-16)	100% 2.3 (1.6-3.6)	HFPO-TrA: 100% 27 (4.0-48)	(Pan et al., 2017)
		Down-	11		100%	100%	100%	100%	100%	100%		100%		100%		100%	100%	HFPO-	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFES A	HFPO-DA	Other	Reference
		stream FCPP			1 346 (273-3 970)	1 176 (235-3 370)	1 342 (343-3 690)	1 161 (280-3 470)	64 773 (20 500-197 000)	1.3 (0.94-2.5)		0.34 (0.14-0.57)		4.8 (2.7-10)		5.1 (1.5-9.6)	783 (118-2 060)	TrA: 100% 20 160 (5 200–68 500)	
USA (Cape fear river)	2014	Down-stream FCPP			32	22	12	12	11	<10		<10		17			3 100	PMPA: 1 300 PEPA: 420 Nafion b-p2: 670 NVHOS: 44 HydroEVE: 1 200	(Zhang et al., 2019a)
	2018	Down-stream FCPP			<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ		<LOQ		<LOQ			<LOQ	PMPA, PEPA, NVHOS, HydroEVE Nafion b-p2: <LOQ	
USA (Ohio River)	2016	Upstream FCPP ø	5		1/5 (<LOQ-11)	0/5	0/5	0/5	0/5	0/5		0/5		0/5			0/5		(Galloway et al., 2020)
	2016	Downstream FCPP	12		0/12	0/12	0/12	0/12	4/12 (<LOQ-15)	0/12		0/12		0/12			2/12 (<LOQ-11)		
Tributaries to Ohio River	2016	Downstream landfill used by FCPP	5		1/5 (<LOQ-27)	1/5 (<LOQ-17)	1/5 (<LOQ-20)	1/5 (<LOQ-34)	5/5 (51-1250)	0/5		0/5		0/5			1/5 (<LOD-71)		
Watersheds, Ohio	2016	Close to FCPP	4		1/4 (<LOQ)	1/4 (<LOQ)	1/4 (<LOQ)	1/4 (<LOQ)	3/4 (<LOQ)	0/4		0/4		0/4			1/4 (<LOQ)		

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl-PFES A	HFPO-DA	Other	Reference
					-10)	Q-15)	-15)	-24)	-463)								D-59)		
Little Hocking watershed, Ohio	2016	<16 km to FCPP	25		100% (32-203)	56% (<LOD-66)	100% (14-95)	96% (<LOQ-94)	100% (319-2570)	0%		12% (<LOD-79)		24% (<LOD-72)			85% (<LOD-227)		
Little Hocking and beyond, Ohio	2016	<48 km to FCPP	40		30% (<LOQ-20)	5% (<LOD-17)	22% (<LOQ-20)	20% (<LOD-36)	90% (<LOQ-1306)	2% (<LOD-28)		7% (<LOD-14)		7% (<LOD-19)			42% (<LOD-137)		
China, Beijing	2014	Downstream airport	16		100% 20 (11-41)	100% 11 (8.9-14)	100% 6.4 (1.8-13)	100% 3.3 (0.97-8.4)	100% 12 (4.0-24)	100% 18 (2.9-51)		100% 10 (0.66-45)		100% 4.8 (0.33-13)	100% 0.13 (1.0-195)	87% (<MLQ-5.3)		PFPCPeS: 38% (<MLQ-129)	(Wang et al., 2016a)
		Upstream airport + ref. site	4		100% 12 (7.3-15)	100% 7.6 (2.9-11)	100% 2.3 (1.7-2.9)	100% 1.1 (0.8-1.6)	100% 7.2 (5.0-10)	100% 7.8 (0.6-16)		2/4 (<MLQ-1.2)		3/4 (<MLQ-2.0)	0%	0%		PFPCPeS: 0%	
Jinan, China (rivers)	2016	Close to FCPP (including production of TFA)	13	TFA: 884 ± 180															(Xie et al., 2020a)
Jinan, China (landscape waters)			2	TFA: 1 842 ± 436 & 2 688 ± 117															
Sweden	2019	Leachate (waste-to-energy-plant)			(21-29)	45 (37-56)	(41-64)	(16-24)	(29-45)	15 (12-20)	(0.8-1.1)	(4.1-6.3)	(nd-0.4)	8.3 (4.9-11)				PFNS: nd	(Bjorklund et al., 2021)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^o	PFECHS	6:2 Cl- PFES A	HFPO- DA	Other	Reference
Sweden		Water/ leachate near suspected point- sources	34	<i>TFA</i>: 61% 110* (<34- 14 000) <i>TFMS</i>: 94% 30* (<1.8- 940) <i>PFEtS</i>: 71% (<1.8- 1 700) <i>PFPrA</i>: 79% 13* (<3.1- 53 000) <i>PFPrS</i>: 88% 8.4* (<0.00 9-15 000)	94% 16* (<1.9- 11 000)	97% 30* (<0.3- 12 000)	91% 73* (<0.7- 79 000)	91% 15* (<1.2- 7 800)	91% 33* (<0.3- 39 000)	97% 40* (<0.3- 58 000)	94% 8.5* (<0.00 5-64 000)	94% 73* (0.3- 350 000)	91% 7.9* (<0.00 2-100 000)	97% 87* (<6.9- 220 0000)				<i>PFNS</i>: 41% (<0.01-3 900) <i>PFDS</i>: 32% (<0.04-1 000) <i>PFDoDS</i>: 21% (<0.01-540)	(Björnsdotte r et al., 2019)
Sweden	2020	Leachate from	17		89% 1 232	96% 745	99% 897	96% 271	98% 147	94% 1 242	76% 156	94% 229	53% 19	97% 427				<i>PFNS</i>: 0% <i>PFDS</i>: 0%	(Miljösamver kan Sverige,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C2-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS [¶]	PFECH ₃ S	6:2 Cl-PFES A	HFPO-DA	Other	Reference
		landfills	123		(<LOQ-74 600)	(<LOQ-34 400)	(<LOQ-28 100)	(<LOQ-9 990)	(<LOQ-8 180)	(<LOQ-40 500)	(<LOQ-984)	(<LOQ-5 530)	(<LOQ-222)	(<LOQ-22 800)				PFDoS: 0%	(2022)
Sweden	2020	Surface water near landfills	74-150		59% 15 (<LOQ-354)	55% 19 (<LOQ-390)	61% 19 (<LOQ-300)	57% 8.2 (<LOQ-160)	65% 18 (<LOQ-420)	53% 30 (<LOQ-2 110)	31% 2.1 (<LOQ-41)	58% 8.1 (<LOQ-210)	17% 0.99 (<LOQ-40)	67% 25 (<LOQ-1 400)				PFNS: 1.4% (<LOQ-1.8) PFDS: 0% PFDoS: 0%	(Miljösamverkan Sverige, 2022)

[¶] PFOS can be reported as linear (L), branched (Br) or total (L+Br), which is generally not indicated in the table.

*Median.

§ Range of means in 6 lakes.

ø PFOA had been used for 62 years at the fluoropolymer production facility, but phased-out 3 years prior to sampling, concurrently with HFPO-DA being introduced as replacement.

Table B.79. Concentrations of PFASs in drinking water described by detection frequency (% or x/xx), mean value (ng/L) in bold and range in brackets. Grey cells indicate sampling sites near known PFAS point sources. NR=not reported, nd=not detected, FCPP=fluorochemical production plant, dw=drinking water.

Location	Year	Pollution	N	C1-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS [¶]	HFPO-DA	Other	Reference
Switzerland	1996-97		6	TFA: 71 (16-123)													(Berg et al., 2000)
Sweden			2	PFPrA: 2/2 (2.3-28) TFMS: 1/2 (<5.1-7.8) PFES: 0/2 (<2.1)	1/2 (<0.9-3.1)	1/2 (<0.2-1.7)	1/2 (<0.7-1.9)	0/2	1/2 (<0.3-1.3)	2/2 (1.2-1.9)	2/2 (0.3-0.8)	2/2 (1.6-2.3)	1/2 (<0.002-0.1)	1/2 (<0.4-1.5)		PFNS, PFDS, PFDoS: 0/2	(Björnsdotter et al., 2019)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C1-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^φ	HFPO-DA	Other	Reference
				PFPrS: 2/2 (0.1-0.2)													
Germany (tap dw)			21	TFA: ~500* (NR-11 000) PFPrA: (NR-11)													(Janda et al., 2019)
Germany (Sources of dw)	2020		46	TFA: 96% 900* (<LOQ-12 400) TFMS: 100% 8.0* (<LOQ-2112) PFEtS: 0% PFPrA: 80% 13* (12-179) PFPrS: 85% (<LOD-1.3)	85% (<LOD-23)	91% (<LOD-10)	100% 2.0 (0.1-11)	100% 1.3 (<LOQ-11)	100% 2.3 (0.2-8.0)	96% (<LOD-17)	80% (<LOD-1.2)	89% (<LOD-3.6)	54% (<LOD-0.2)	93% 2.1 (<LOD-19)	2.2% (<LOD-0.9)	PFNS: 13% (<LOD-1.3) PFDS: 30% (<LOD-2.1) FAP: 11% (0.1-0.7) NTf2: 20% (<LOD-1.9)	(Neuwald et al., 2022)
France			19				0%	47%	16%	32%		0%		26%		PFDS: 5%	(Schwanz et

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C1-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^φ	HFPO-DA	Other	Reference
(bottled dw)								(nd-25)	(nd-7.4)	(nd-6.7)				(nd - 11)		(<LOD-23)	al., 2016)
France (tap dw)			8				2/8 (nd - 6.8)	3/8 (nd - 33)	2/8 (nd - 18)	5/8 (nd - 15)		0%		3/8 (nd -3)		PFDS: 3/8 (<LOD-12)	
Spain (bottle dw)			10				20% (nd - 12)	40% (nd - 17)	20% (nd - 11)	0%		0%		0%		PFDS: 0%	
Spain (tap dw)			29				7% (nd - 58)	34% (nd - 42)	21% (nd - 29)	31% (nd - 24)		0%		38% (nd - 140)		PFDS: 0%	
Germany (tap dw)	2010-12		5		1/5 (<LOD -0.4)	1/5 (<LOD -1.2)	4/5 0.9 (<LOD -1.8)	5/5 9.2 (0.23-24)	2/5 (<LOD -1.9)	0/5		0/5		1/5 (<LOD-0.4)		PFOPA: 0/5 PFDPa: 1/5 (<LOD-10)	(Llorca et al., 2012a)
Spain (tap dw)	2010-12		84		52% 10 (<LOD -27)	38% (<LOD -17)	18% (<LOD -11)	13% (<LOD-16)	37% (<LOD -35)	35% (<LOD -36)		36% (<LOD -28)		51% 46 (<LOD-258)		PFOPA: 6% (<LOD-25) PFDPa: 6% (<LOD-23)	
Several countries (bottle dw)			38		58% 0.20	32%	50%	42%	34%	47%		32%		18%		PFDS: 0%	(Kaboré et al., 2018)
(tap dw)			59		92% 1.5	68% 0.44	64% 0.59	90% 0.33	86% 0.67	88% 0.24		78% 0.30		85% 1.0		PFDS: 5% PFECHS: 3% (nd-1.2)	
(bottle & tap)			97	PFETs:							(nd-		(nd-1.2)				

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C1-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^φ	HFPO-DA	Other	Reference
dw)				(nd-0.51) PFPrS: (nd-0.94)							3.9)						
USA (bottle dw)			101	PFPrA: 22% (nd-6.5) PFPrS: 2% (nd-0.18)	3% (nd-1.4)	2% (nd-3.3)	6% (nd-2.0)	8% (nd-0.94)	25% (nd-1.9)	17% (nd-1.4)	2% (nd-0.23)	5% (nd-0.64)		7% (nd-0.86)			(Chow et al., 2021)
China, Beijing (tap dw)	2012			TFA: 155±7													(Zhai et al., 2015)
Netherlands, Dordrecht		Within 50 km of FCPP	6		2/6 (<5-10)	2/6 (<4-5.1)	6/6 (1.6-5.9)	4/6 (<1-3.2)	6/6 (2.4-7.1)	6/6 (2.5-11)		3/6 (<0.5-1.3)	0/6 (<0.5)	5/6 (<1-2.6)	6/6 4.3 (1.4-8.0)		(Brandsma et al., 2019)
Netherlands, Dordrecht	2016	Near FCPP	4		1/6 (<2-13)	2/6 (<4-5.7)	5/6 2.7 (<0.1-5.3)	3/6 (<0.05-2.4)	4/6 (<0.3-11)	6/6 3.9 (0.54-19)		6/6 0.2 (0.02-0.43)	3/6 (<0.02-0.03)	5/6 0.3 (<0.03-0.41)	3/6 (<0.2-11)	ADONA: 0% 6:2 Cl- PFESA: 0%	(Gebbink et al., 2017)
USA (Cape Fear River dw intake A)	2013				33 (<10-99)	62 (14-191)	78 (<10-318)	67 (<10-324)	46 (<10-137)	(<10-80)		14 (<10-193)		44 (<25-346)	(<10)		(Sun et al., 2016)
intake B					12 (<10-38)	19 (<10-38)	11 (<10-42)	11 (<10-85)	(<10-32)	(<10-11)		(<10-14)		(<25-43)	(<10-10)		
intake C		Downstr- eam FCPP			22 (<10-104)	36 (<10-116)	(<10-24)	(<10-24)	(<10-17)	(<10)		(<10-14)		(<25-40)	631 (55-4560)		

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	N	C1-C3 PFAAs	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^φ	HFPO-DA	Other	Reference
USA (Cape fear river dw intake)	2015	140 km downstream FCPP			26	26	27	22	19	<10		18		27	780	<i>PFMOAA</i> : 110 000 <i>PFO2HxA</i> : 7 800 <i>PFO3OA</i> : 6 300 <i>PFO4DA</i> : 350 <i>PFO5DoA</i> : 200 <i>PMPA</i> : 690 <i>Nafion b-p</i> <i>2</i> : 83 <i>NVHOS</i> : 19 <i>HydroEVE</i> <i>:</i> 20	(Zhang et al., 2019a)
Jinan, China (well/tap dw)	2016	Near FCPP (incl. TFA)		<i>TFA</i> : 384 ± 7 (tap dw) 319 ± 8 (well dw)													(Xie et al., 2020a)

^φ PFOS can be reported as linear (L), branched (Br) or total (L+Br), which is generally not indicated in the table.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.80. Concentrations of PFASs in precipitation described by detection frequency (% or x/xx), mean value (ng/L) in bold and range in brackets. Grey cells indicate sampling sites near known PFAS point sources. NR=not reported, nd=not detected, FCPP=fluorochemical production plant.

Location	Year	Matrix (N)	TFA	PFPrA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFHxS	PFHpS	PFOS [†]	PFDS	PFECHS	HFPO-DA	ADONA	Reference
Germany (8 locations over 12 months)	2018-19	Precipitation (187)	93% 335 (<LOQ-38000)															(Freeling et al., 2022)
Canada, Nova Scotia	2002	Precipitation	(4-100)	(<0.1-59)	(<0.1-2.9)													(Scott et al., 2006)
Ontario			(8-220)	(1.2-36)	(0.5-11)													
Japan	2007	Precipitation	(39-76)	(8.9-10)	(0.77-2.2)													(Taniyasu et al., 2008)
China (nationwide)	2016	Precipitation (39)	100% 93* (8.8-1800)	90% 0.79* (<LOQ-24)	95% 3.6* (<LOQ-41)	41% (<LOQ-22)	97% 1.6* (<LOQ-18)	95% 1.4* (<LOQ-54)	100% 3.4* (<LOQ-100)	56% 0.37* (<LOQ-4.3)	64% 0.5* (<LOQ-4.3)		100% 6* (0.9-20)				0%	(Chen et al., 2019a)
Poland, Gdansk	1996	Rain	(26-1100)															(von Sydow et al., 2000)
Ireland, Mace Head	1996	Rain	(2-92)															
Germany	2018	Rain (12)			2.6 (1.4-6.9)	2.5 (0.97-7.6)	2.0 (0.85-5.4)	4.9 (0.16-179)	2.2 (1.3-4.6)									(UBA, 2021a)
Switzerland	1996-1997	Rain/snow (73)	151 (<3-1550)															(Berg et al., 2000)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Matrix (N)	TFA	PFPrA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFHxS	PFHpS	PFOS ^ø	PFDS	PFECHS	HFPO-DA	ADONA	Reference
Northern Sweden	2009	Surface snow			(0.017-0.82)	(<LOD-0.59)	(0.018-0.15)	(<LOD-0.042)	(<LOD-0.12)	(<LOD-2.2)	(<LOD-0.65)		(0.003-0.25)					(Codling et al., 2014a)
European High Arctic	2019	Snow (6)			2.6 ± 0.70	0.088 ± 0.030	0.070 ± 0.049	0.12 ± 0.086	0.041 ± 0.017	<MDL			<MDL					(Garnett et al., 2021)
		Sea Ice (34)			1.4 ± 3.1	0.030 ± 0.055	0.080 ± 0.19	0.085 ± 0.087	0.15 ± 0.29	1.3 ± 3.4			0.013 ± 0.018					
Longyearbyen town	2006	Snow (5)			0.25	0.081	0.089	0.12	0.4									(Kwok et al., 2013)
Longyearbyen glacier	2006	Snow (4)			0.11	0.03	0.075	0.017	0.11		<LOQ							
	2006	Ice core (13)			0.023	0.006	0.013	<LOQ	0.019		<LOQ		0.009 (L)					
	2007	Ice core (13)			0.08	0.021	0.011	<LOQ	0.024		<LOQ		0.009 (L)					
	2008	meltwater (4)			0.29	0.84	0.1	0.11	0.11		<LOQ							
Canada, Devon Ice Cap	2008	Surface snow (1)			0.26	0.06	<0.001	<0.002	0.079	0.095	<0.001	<0.002	0.002 (Br)	<0.002	0.02			(MacInnis et al., 2017)
Arctic Canada, Lake Hazen catchment	2013	Snow pack (8)			8.9 (1.2–52)	0.35 (0.097–1.6)	0.40 (0.12–1.3)	1.1 (0.38–4.3)	2.2 (0.35–10)	(<0.002-0.40)	(<0.001-0.44)		0.19 (0.009–1.0)	(<LOQ)	0.031 (<0.001-0.059)			(MacInnis et al., 2019)
	2014	Light snow (9)			2.7 (1.8–3.8)	0.14 (0.083–0.21)	0.25 (0.16–0.38)	0.45 (0.29–0.70)	0.71 (0.46–1.1)	0.006 (<0.002-0.011)	(<0.0007)		0.029 (0.009–0.051)		0.008 (<0.001-0.022)			
	2014	Dark snow (9)			4.8 (2.3–11)	0.67 (0.18–)	0.89 (0.36–)	1.5 (0.54–)	2.2 (0.92–)	0.013 (<0.003-	(<0.001-		0.18 (0.035–)		0.007 (<0.001-			

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Matrix (N)	TFA	PFPr A	PFBA	PFPe A	PFHx A	PFHp A	PFOA	PFBS	PFHxS	PFHpS	PFOS [¶]	PFDS	PFECH S	HFPO-DA	ADON A	Reference
						1.5)	1.6)	2.9)	4.9)	0.024)	0.004)		0.44)		0.009)			
Arctic Canada Devon ice cap	2014	Ice	40	41	0.21													(Pickard et al., 2020)
	1977-2014	Ice	32 (4.2-129)	19 (3.1-192)	0.39 (<0.04 -1.3)													
Arctic Canada Mt. Oxford icefield	2016	Ice	137	6.3	1.5													
	1967-2016	Ice	28 (<0.3 -148)	4.1 (0.3-73)	0.35 (<0.087 -1.9)													
Arctics	2016	Surface snow (11)				0.17 (0.073-0.45)	0.22 (0.092-0.37)	0.18 (0.094-0.27)	0.36 (0.27-0.54)	0.024 (0.017-0.035)	0.006 (0.001-0.012)	0.0015 (0.0006-0.004)	0.046 (0.036-0.062)	0.0003 (0.0001-0.0008)		0.0092 (0.0063-0.013)		(Xie et al., 2020b)
China, Beijing	2012	Snow	282 ± 68															(Zhai et al., 2015)
China, Tianjin. Upwind, downwind or above landfills	2016	dry deposition/g (10)	100% (1-100-3700)	100% (78-740)	100% (11-55)	60%	80%	100%	100% (15-46)	80% (<0.03 -1.2)	60%		100% (0.73-2.3)					(Tian et al., 2018)

*Median.

† precipitation-weighted average.

¶ PFOS can be reported as linear (L), branched (Br) or total (L+Br), which is generally not indicated in the table.

Appendix B.4.2.3. Soil

Table B.81. Concentrations of PFASs in sediment and soil described by detection frequency (% or x/xx), mean value (ng/g dry weight) in bold and range in brackets. Grey cells indicate sampling sites near known PFAS point sources. nd=not detected, FCPP=fluorochemical production plant.

Location	Year	Pollution	Matrix (N)	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFHxS	PFHpS	PFO S ^φ	PFDS	PFPCPeS	PFECHS	6:2 Cl-PFESA	Other	Reference
Netherlands	2009		Sediment (4)										4/4 (0.07-1.9)					PFHxPA, PFOPA, PFDPA: 0/4	(Esparza et al., 2011)
North Sea & Baltic Sea	2017		Sediment (24)		67% 0.11 (nd-0.54)		8% (nd-0.06)	25% (nd-0.12)	42% (nd-0.65)	0%			L: 83% 0.13 (nd-0.39) Br: 17% (nd-0.03)						(Joeress et al., 2019)
China Bohai Bay,		Erosion inhibitor factories	Sediment													50% (nd-0.18)			(Liu et al., 2019c)
China, Beijing	2014	Downstream airport	sediment (14)		100% 0.7 (0.4-1.6)	0%	0%	0%	100% 1.1 (0.6-2.0)	100% 0.7 (0.06-2.2)	29% (<MLQ-0.95)		93% 2.3 (0.17-15)		14% (<MLQ-0.39)	43% (<MLQ-1.9)	43% (<MLQ-1.9)		(Wang et al., 2016a)
Canadian Arctic	2010-2011		Sediment				<LOQ -0.67 †	<LOQ -0.81 †	0.04-1.78 †	<LOQ 0.08 †	LOQ-1.0 †	<LOQ 0.26 †	0.02-49 †	<LOQ 0.63 †		<LOQ 0.07 †			(Lescord et al., 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	Matrix (N)	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFHxS	PFHpS	PFO _S	PFDS	PFPCPeS	PFECHeS	6:2 Cl-PFESA	Other	Reference
China, Xiaoqing River	2019	FCPP	Sediment		0.26 ± 0.13	0.16 ± 0.09	0.37 ± 0.25	0.16 ± 0.10	10 ± 5.8	0.39 ± 0.00			0.07 ± 0.02				0.02 ± 0.01	HFPO-DA: 0.23 ± 0.09 HFPO-TrA: 1.2 ± 0.65 HFPO-TeA: 0.01 ± 0.00 Nafion by-p 2: 0.01 ± 0.00 PFMO2OESA: 0.03 ± 0.03 PFMOAA: 1.4 ± 0.91 PFO2HxA: 1.4 ± 0.81 PFO3OA: 0.79 ± 0.49 PFO4DA: 0.31 ± 0.25 PFO5DoA: 0.05 ± 0.03 PF4OPeA: 0.02 ± 0.02 PF5OHxA, 6:2 H-PFESA: nd	(Li et al., 2021e)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	Matrix (N)	TFA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFHxS	PFHpS	PFO _S [†]	PFDS	PFPCPeS	PFECHS	6:2 Cl-PFESA	Other	Reference
Ohio	2004	FCPP ø	Soil (3)		3/3 (3.3-3.8)	2/3 (1.2-2.1)	3/3 (8.4-18)	3/3 (41-104)	3/3 (57-66)									HFPO-DA: 0/3	(Galloway et al., 2020)
	2016	4-48 km to FCPP ø	Soil (8)		2/8 (<LOQ-1.2)	3/8 (<LOD-49)	2/8 (<LOD-3.6)	2/8 (<LOD-7.6)	6/8 (<LOQ-27)									HFPO-DA: 2/8 (<LOD-8.1)	
	2018	1-45 km to FCPP ø	Soil (7)		1/7 (<LOQ-3.5)	7/7 (1.4-15)	2/7 (<LOQ-3.1)	2/7 (<LOQ-3.1)	7/7 (2.9-11)									HFPO-DA: 3/7 (<LOD-3.1)	
China, Jinan	2016	Near FCPP (incl. TFA production)	Soil	1.7 ±0.28 (site1) 0.59 ±0.014 (site2) 0.11 ±0.017 (site3)															(Xie et al., 2020a)
		Reference area	Soil	0.077 ±0.002															

† Range of means in different lakes, ‡ PFOS can be reported as linear (L), branched (Br) or Total (L+Br), which is generally not indicated in the table. ø PFOA had been used for 62 years at the fluoropolymer production facility, but phased-out 3 years prior to sampling, concurrently with HFPO-DA being introduced as replacement.

Appendix B.4.2.6.1. EOF/AOF

Table B.82. Studies of EOF, AOF and/or TF in abiotic environmental samples presented as mean (bold text) and range (in brackets). Note that the levels of fluorine measured by EOF and AOF, respectively, are not directly comparable. Grey cells indicate sampling sites near known PFAS point sources. N PFAS=number of individual PFAS included in targeted analysis (i.e. known fraction), DF=detection frequency, CIC=combustion ion chromatography, HR-CF-GFMS=high resolution-continuum source-graphite furnace molecular absorption spectrometry, PIGE=particle-induced gamma ray emission, WW=wastewater, AFFF=aqueous film-forming foam, MDL=method detection limit, NR=not reported, dw=dry weight.

Country, year	Matrix (N)	N PFAS	DF EOF	Mean EOF (range)	Mean AOF (range)	Mean TF (range)	% unknown organic fluorine	Analytical method	LOD/ LOQ	Reference
Denmark, Faroe Islands, Iceland, Sweden, Green-land, Finland, Norway, 2017	Effluent water (14)	73	100%	839 ng/L (183-1 460)			90 (63-98)	CIC	LOQ: 123–200 ng/L	(Aro et al., 2021b)
	Sludge (12)		83%	108 ng/L (<LOQ-210)			48			
Norway, 2018	Lake surface water (9) (polluted)	37	58%	1 750 ng/L (<LOD-4 030)			99.8	CIC	LOD: water neutral fr.: 36 ng/L, anionic fr.: 40 ng/L; passive samples: 119 000 ng/L; sediment: 22 ng/g	(Aro et al., 2021a)
	Lake sediment (3)	37	33%	(<LOD-388 ng/g)			99.9			
	River sediment (2)		100%	(23-44 ng/g)			99.6			
	Sewage water (5)		100%	(919-1 460 ng/L)			99			
Scotland	Sea water (3)	6	100%			<100 ng/L		HR-GFMS	LOD: 300 ng/L LOQ: 1 000 ng/L	(Akhthar et al., 2020)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Country, year	Matrix (N)	N PFAS	DF EOF	Mean EOF (range)	Mean AOF (range)	Mean TF (range)	% unknown organic fluorine	Analytical method	LOD/ LOQ	Reference
	River water (3)		100%			14 500 ± 100 ng/L				
	Effluent (3)		100%			<1 000 ng/L				
	Wastewater (3)		100%			<1 000 ng/L				
Sweden, 2019	Water leachate (5)	34	100%	(690-1 450 ng/L)			88	CIC	MDL: 399 ng/L	(Bjorklund et al., 2021)
USA, 2010	Surface sediment (27)	25	100%	1.6 mg/g dw (0.6–4.8)		571 mg/g dw (96-1 181)	99.9	CIC		(Codling et al., 2014b)
	Sediment cores (48)		100%	2.2 mg/g dw (0.8-4.8)		782 mg/g dw (375-1 322)	99.8			
Canada, 2012-16	Surface water rural area (5)	23	100%	(~100-500 ng/L)			30-99.7 (Lower-end UOF from contaminated waters)	CIC		(D'Agostino and Mabury, 2017)
	Surface water urban area (5)		100%	(~150-600 ng/L)						
	Surface water (14) (polluted by AFFF)		100%	(~200-1 000 ng/L)						
Germany, 2020	River water (10)			(50-550 ng/L)		~190 000 ng/L		HR-CS- GFMAS		(Gehrenkemper et al., 2021)
USA, 2019-20	Killian Creek surface water (polluted by AFFF)	29	100%	87 000 ng/L	66 000 ng/L			CIC	300 ng/L 400 ng/L	(Han et al., 2021b)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Country, year	Matrix (N)	N PFAS	DF EOF	Mean EOF (range)	Mean AOF (range)	Mean TF (range)	% unknown organic fluorine	Analytical method	LOD/ LOQ	Reference
	Caper Fear river surface water (polluted by industry WW)		100%	440 000 ng/L	110 000 ng/L					
	Fayetteville groundwater (polluted by industry WW)		100%	2 600 ng/L	1 200 ng/L					
	Mallard Creek groundwater (polluted by domestic WW)		100%	110 ng/L	880 ng/L					
Sweden, 2016	Water site A (4) (AFFF)	25	100%	(320-2 480 ng/L)			95-98	CIC	MDL: 71–217 ng/L	(Koch et al., 2019)
	Water site R (4) (AFFF)		100%	(408-3 930 ng/L)			45-61			
	Water site K (1) (industry WW)		100%	1 110 ng/L			92			
Sweden, 2016-17	Pond surface water (3) (AFFF)	24					42-58	CIC		(Koch et al., 2021)
China, 2008-10	Surface water (12)	22		41 ng/L				CIC	LOQ: <0.10 ng/L	(Loi et al., 2011)
	Sediment (6)	22		360 ng/L					LOQ: <26 pg/g	
Germany, 2017	Surface water (14)		100%	(50-300 ng/L)		(35 000-70 000 ng/L)		HR-CS-GFMS	LOD: 5 ng/L LOQ: 18 ng/L	(Metzger et al., 2019)
Japan,	Seawater reference	12	100%	93 ng/L			~92	CIC	2 ng/L	(Miyake et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Country, year	Matrix (N)	N PFAS	DF EOF	Mean EOF (range)	Mean AOF (range)	Mean TF (range)	% unknown organic fluorine	Analytical method	LOD/ LOQ	Reference
2003-2004	site(2)									2007a)
	Seawater (polluted) (2)	12	100%	562 ng/L			~65			
USA, 2017-2019	Surface water (7) (AFFF)	27	5 of 7	(<LOD-29 nM F)			37-77	CIC	MDL: 1.95-3.26 nM	(Ruyle et al., 2021)
Nepal, 2010	Surface soil (14)	16	100%	(35-200 ng/g)		(335-739 ng/g)	98-100	CIC	LOD: 0.03-0.30 ng/g	(Tan et al., 2014)
Japan, 2003-2004	Sea water (13) (partly AFFF)	9	100%				~65-98	CIC	LOQ: 0.03-2 ng/L	(Taniyasu et al., 2015)
	Runoff (5) (partly AFFF)	9	100%				~60-85			
	Snow (3) (partly AFFF)	9	100%				~40-75			
	Lake/pond water (3)	9	100%				~80-98			
Germany, 2015-2017	Surface water (74)	24	100% (AOF)		4 500-10 200 ng/L			CIC	LOD: 1 300 ng/L LOQ: 2 000 ng/L	(von Abercron et al., 2019)
	Municipal wastewater (116)	24	85% (AOF)		3 200-3 800 ng/L					
	Industrial wastewater (33)	24	N.R. (AOF)		(74 000-555 000 ng/L)		95-99.6			
	Gound water (93)	24	40% (AOF)		(2 000-6 100 ng/L)					
Canada, 2006-2008	Sediment (26)	14	100%	(<10-203 ng/g dw)			56-98	CIC	LOQ: 10 ng/g	(Yeung et al., 2013a)
USA, 2018	Dust and wipes (88)	24	100%			157 000* ng/g (6170-	98.8	PIGE	MDL: 25 000 ng/g	(Young et al., 2021)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Country, year	Matrix (N)	N PFAS	DF EOF	Mean EOF (range)	Mean AOF (range)	Mean TF (range)	% unknown organic fluorine	Analytical method	LOD/ LOQ	Reference
						952 000)				
China, 2008	Soil (14)	22	100%	(31-208 ng/g dw)		(219-608 ng/g dw)	99.2	CIC		(Wang et al., 2013a)
Germany, 2013	Surface water (2)	10	100%		1 000 ng/L		95	CIC	LOD: 100 ng/L LOQ: 300 ng/L	(Wagner et al., 2013)
	Ground water (3) (AFFF)	10	100%		(1 300–2 500 ng/L)		50-58			
Germany, 2012	Surface water (23) (including WWTP)	17	19 of 23		(880-1 980 ng/L)		95-98	CIC	LOQ: 770 ng/L	(Willach et al., 2016)
	Ground water (4) (contaminated site)	17	100%		(162 000-782 000 ng/L)		49-68	CIC		
Denmark, Faroe Islands, Iceland, Greenland, Sweden, Finland, Norway, 2017	Surface water (12)	22	5 of 12	239 ng/L (<30-849)			92 (83-98)	CIC	LOD: <30–34 ng/L	(Kärrman et al., 2019)
	WWTP effluent (14)	73	100%	437 ng/L (<123-893)			89 (56-98)	CIC	LOD: 57–126 ng/L	
	WWTP sludge (10)	27 + PFAA precursors	10 of 12	663 ng/L (<556–767)			91 (79–97)	CIC	LOD: 475 ng/g	

‡ Range of means.

*Median.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.83. Studies of EOF and/or TF in biota described as mean EOF and/or TF in bold text and range in brackets. CIC=combustion ion chromatography. N PFAS=number of individual PFAS included in targeted analysis (i.e. known fraction), DF=detection frequency.

Country, year	Matrix (N)	N PFAS	DF	Mean EOF (range)	Mean TF (range)	% unknown organic fluorine	Analytical method	LOD/LOQ	Reference
East Greenland, 2012-17	Bear, whale, seal, dolphin (8)	36		1 104 ng/g ww (<158-3 537)	(408-5 563 ng/g)	0-75	CIC		(Spaan et al., 2020)
Sweden, 2011-16	Seal, porpoise (5)	36		384 ng/g ww (<158-973)	(569-1 086 ng/g)				
USA, 2000-12	Porpoise, seal, whale (4)	36		1 174 ng/g ww (293-3 288)	(560-1 560 ng/g)				
Iceland, 2009-10	Seal (3)	36		(<71-52 ng/g ww)	(298-9 196 ng/g)				
West Greenland, 2000-16	Whale, porpoise, seal (5)	36		<158 ng/g ww	(540-1 488 ng/g)				
China, 2003-2007	Humpback dolphin liver (10)	10	100%	740 ng/g ww (267-1 590)	1 270 ng/g ww (618-3220)	~70	CIC	LOQ: 6 ng/mL	(Yeung et al., 2009b)
	Finless porpoise liver (10)	10	100%	439 ng/g ww (234-707)	1 610 ng/g ww (447-9540)				
Japan, 2004-2006	Wild rat blood (10)	12	100%	(61 000-134 000 ng/L)	(60 000-192 000 ng/L)	44 (11-91)	CIC		(Yeung et al., 2009a)
Baltic Sea, 5 years 1981-2013	Cod liver (10 per year)	28	100%	Fraction 1: 124-338 † Fraction 2: 21-43 ng/g †	102-369 ng/g †	93-98	CIC		(Schultes et al., 2020a)
China, 2008-2010	Fish liver and body (21)	26		liver: 46-124 ng/g ww ¥ body: <9-32 ng/g ww ¥	liver: 156-362 ng/g ww¥ body: 775-7 980 ¥		CIC	LOQ: 9.1 ng/g ww	(Loi et al., 2011)
	Shrimp (4)	26		23-33 ng/g ww ¥	6 340-7 820 ng/g ww ¥	88-90			
	Worm (7)	26		123-145 ng/g ww¥	14 200-15 300 ng/g	99.5-96.3			

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Country, year	Matrix (N)	N PFAS	DF	Mean EOF (range)	Mean TF (range)	% unknown organic fluorine	Analytical method	LOD/LOQ	Reference
					ww¥				
	Gastropod (2)	26		140 ng/g ww	32 400 ng/g ww	99.6			
Norway, 2018	Fish liver (4)	16	50%	(<LOD-309 ng/g)		83.8	CIC	88-145 ng/g ww	(Aro et al., 2021a)
Sweden, 2017	Aquatic invertebrates (7)	24		(912-3 970 ng/g)		0 in 4 of 6	CIC	89 ng/g	(Koch et al., 2021)
	Aquatic insects (4)	24		(97-666 ng/g)		0-37			
	Terrestrial invertebrates (5)	24		(78-342 ng/g)		87-99			
Faroe islands, Denmark, Finland, Greenland, Sweden, Iceland, Norway, 2017	Bird eggs (11)	78	9 of 11	221 ng/g (<40-649)		32	CIC	30 ng/L	(Kärrman et al., 2019)
	Marine fish (6)	78	10 of 19	243 ng/g (<132-355)		58			
	Freshwater fish (13)	78		241 ng/g (<140-488)		74			
	Marine mammals (12)	78	7 of 12	707 ng/g (<40-2 056)		63			
	Terrestrial mammals (9)	78		249 ng/g (76-427)		82			

† Range of geometric means for each year.

¥ Range of arithmetic means for each species.

Appendix B.4.2.7. Monitoring of specific PFASs in environmental samples

Table B.84. Concentrations of PFASs in air described by detection frequency (% or x/xx), mean value (pg/m³) in bold and range in brackets. Grey cells indicate sampling sites near known PFAS point sources. WWTP=wastewater treatment plant, FCPP=fluorochemical production plant, nd=not detected.

Location	Year	Pollution	N	TFA	PFPrA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFHxS	PFOS [¶]	PFNS	PFDS	Reference
Arctic Canada Alert station	2006-2014					99% 3.6 (<LOD-29)	26% (<LOD-0.19)	30% (<LOD-0.39)	57% 0.055 (<LOD-0.47)	89% 0.19 (<0.006-1.3)	66% 0.066 (<LOD-1.5)	39% (<LOD-0.62)	96% 0.19 (<0.006-2.8)	8% (<LOD-0.022)		(Wong et al., 2018)
China, Beijing,	2012-2013		144	1 580 ± 558												(Wu et al., 2014)
Canada	2009	Reference site	1			44	<0.26	2.2	3.7	7.4			3.0			(Ahrens et al., 2011)
	2009	Above WWTPs	8			89 (55-116)	11 (3.4-24)	33 (10-63)	11 (3.3-20)	15 (4.4-28)	(nd)	(nd)	112 (43-171)		(nd)	
	2009	Above landfills	2			101 (101-102)	11 (2.7-20)	35 (7.2-62)	10 (2.5-18)	25 (3.0-46)			3.9 (3.2-4.6)			
China, Jinan	2016	Near FCPP (incl. production TFA)		4 106 ± 1 780												(Xie et al., 2020a)
China, Tianjin	2016	Upwind, down-wind or above landfills	12	100% (1 400-3 000)	58% (64-360)	100% (180-590)	58%	100% (3.6-24)	100% (7.0-54)	100% (22-100)	100% (4.8-70)	100% (<0.02-4.2)	100% (4.4-23)			(Tian et al., 2018)

[¶] PFOS can be reported as linear (L), branched (Br) or Total (L+Br), which is generally not indicated in the table.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.85. Concentrations of PFASs in WWTP influent and effluent described by detection frequency (% or x/xx), mean value (ng/L) in bold and range in brackets.

Lo-cation	Year	Matrix (N)	PFEtS	PFPrA	PFB A	PFPeA	PFHxA	PFHpA	PFOA	PFPrS	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^φ	PFNS	PFDS	PFECHS	Other	Reference
Spain	2010	Influent (15 pool)			20.5	7.8	1870	14.3	19		12		15.5	14.6	118	3.3	ND			(Campo et al., 2014)
		Effluent (15 pool)			13	8.1	4.9	9.6	16		8.6		14.1	2.2	77	0.04	ND			
	2011	Influent (16 pool)			54	9.3	1.1	13	22		19		42	8.8	78	5.6	ND			
		Effluent (16 pool)			58	14	17	7.5	15		58		38	2.9	91	0.04	ND			
Canada	2004 / 2007	Effluent (7)							7/7 (5.8-180)						6/7 (nd-72)				PFHxPA: (D'eon et al., 2009) 4/7 (nd-6.5) PFOPA: 6/7 (nd-2.5) PFDPA: 3/7 (nd-0.46)	
Nordic countries	2017	Effluent (14)	5/14 (<0.54-1.3)	13/14 (<1.4-47)	14/14 (0.58-14)	14/14 (0.58-14)	14/14 (2.4-27)	14/14 (0.27-16)	14/14 (0.50-33)	9/14 (<0.14-6.0)	14/14 (0.81-13)	11/14 (<0.03-1.2)	14/14 (0.23-4.3)	10/14 (<0.02-0.58)	L:14/14 (1.3-20)	3/14 (<0.02-0.73)	4/13 (<0.01-0.29)	5/14 (<0.02-0.37)	PFDoDS: 4/13 (<0.01-0.78) PFHxPA, PFOPA, HFPO-DA, ADONA 6:2 Cl-	(Kärman et al., 2019)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Lo- cation	Year	Matrix (N)	PFEtS	PFPrA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFPrS	PFBS	PFPeS	PFHxS	PFHpS	PFOS [¶]	PFNS	PFDS	PFECHS	Other	Referenc e
																			PFESA: 0/14	
Nor- way	2017	Effluent (2)				6.5 (5.5- 7.6)	5.8 (4.7- 6.9)	3.1 (3.0- 3.2)	6.4 (5.6- 7.2)		3.7 (3.3- 4.1)	(<LOD)	0.85 (0.77- 0.93)		2.0 (1.7- 2.3)		(<LOD)			(NEA, 2019)

[¶] PFOS can be reported as linear (L), branched (Br) or total (L+Br), which is generally not indicated in the table.

Table B.86. Concentrations of PFASs in WWTP sludge described by detection frequency (% or x/xx), mean value (ng/g dry weight) in bold and range in brackets. nd=not detected.

Year	N	PFEtS	PFPrA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFPrS	PFBS	PFPeS	PFHxS	PFHpS	PFOS [¶]	PFNS	PFDS	PFECHS	Other	Referenc e
2010				203 (41- 442)	2.5 (0.13- 11)	11 (11- 11)	3.3 (0.33- 12)	1.8 (0.13- 3.5)		38 (0.41- 175)		(<LOD)	(<LOD)	229 (3.1-1 790)	0.13 (0.13- 0.13)	(<LOD)			(Campo et al., 2014)
2011				399 (0.13- 1 800)	193 (0.13- 1 080)	1.3 (1.3- 1.3)	6.4 (0.33- 55)	22 (0.13- 103)		0.78 (0.41- 4.1)		0.01 (0.01- 0.01)	2.0 (0.13- 9.4)	41 (0.01- 497)	2.1 (0.13- 12)	0.01 (0.01- 0.01)			
2009	4													4/4 (35- 48)				PFHxPA , PFOPA, PFDPA: 0/4	(Esparza et al., 2011)
2011	14				50% 1.7 (nd- 5.6)	50% 0.8 (nd- 2.2)	0% 7.3 (1.3- 16)	100%		0%		0%	0%	100% 7.3 (4.6- 11)		0%			(Stasinaki s et al., 2013)
2017		0/3 (<0.2)	0/10 (<3.7)	0/12 (<0.04)	7/9 (<0.04 -0.84)	11/12 (<0.04 -1.6)	2/12 (<0.2 - 0.51)	8/12 (<0.5 - 1.5)	0/3 (<0.04)	0/8 (<0.04)	1/12 (<0.04 -0.2)	0/12 (<0.04)	0/12 (<0.04)	L:10/1 1 (<0.04 -12)	0/12 (<0.04)	0/12 (<0.04)	0/12 (<0.04)	PFD _o DS , PFHxPA , PFOPA, PFDPA,	(Kärrman et al., 2019)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year	N	PFEtS	PFPrA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFPrS	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^φ	PFNS	PFDS	PFEC HS	Other	Reference
																		HFPO-DA, ADONA, 6:2 Cl-PFESA: 0/12	
2017	2				(<LOD)	(<LOD)	(<LOD)	1.0 (0.72-1.4)		(<LOD)	0.10 (<LOD-0.2)	(<LOD)	(<LOD)	5.3 (4.9-5.6)	(<LOD)	0.32 (<LOD-0.64)			(NEA, 2019)
2008 - 2013	4981					0.5% 0-0.45§ (<LOQ-680)	0.5% 0-0.36§ (<LOQ-123)	7% 0.32-7.8§ (<LOQ-1043)		0.4% 0.04-0.13§ (<LOQ-49)		0.7% 0-0.32§† (<LOQ-84)		43% 12-46§ (<LOQ-7600)		0.6% 0-0.29§ (<LOQ-67)			(Ulrich et al., 2016)

§ range of means per year.

^φ PFOS can be reported as linear (L), branched (Br) or total (L+Br), which is generally not indicated in the table.

Table B.87. Concentrations of PFASs in biota described by detection frequency (% or x/xx), mean value (ng/g) in bold and range in brackets. Grey cells indicate sampling sites near known PFAS point sources. N.A.=not analysed, nd=not detected, FCPP=fluorochemical production plant (mainly fluoropolymer production).

Location	Year	Pollution	Matrix (N)	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFPrS	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^φ	PFDS	PFEC HS	6:2 Cl-PFESA	HFP O-DA	Other	Reference
Canada, Great Lakes			Fish - top predator													(<MD L-3.7)				(De Silva et al., 2011)
Greenland	2012-13		Ringed seal liver (10)	0/10		0/10	3/10 (<0.02-0.071)	0.56 ± 0.15		0/10 (<0.002)		10/10 0.71 ± 0.06		10/10 93 ± 6	10/10 0.27 ± 0.19		10/10 0.045 ± 0.004			(Gebbinck et al., 2016)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Lo- cation	Yea r	Pollu- tion	Matrix (N)	PFBA	PFPe A	PFHx A	PFHp A	PFOA	PFPr S	PFBS	PFPe S	PFHx S	PFHp S	PFOS φ	PFDS	PFEC HS	6:2 Cl- PFES A	HFP O- DA	Other	Referen ce
			Polar bear liver (8)	0/8		0/8	8/8 0.74 ± 0.16	8/8 13 ± 2		8/8 0.032 ± 0.008		8/8 13 ± 2		8/8 1811 ± 218	8/8 1.5 ± 0.2		8/8 0.27 ± 0.04			
			Killer whale liver (6)	0/6		0/6	6/6 0.16 ± 0.07	6/6 0.27 ± 0.09		4/6 (0.005 - 0.002)		6/6 1.5 ± 0.3		6/6 122 ± 42	6/6 1.2 ± 0.4		5/6 0.02 3 ± 0.009			
Nordic countrie s	201 7		Fresh fish (13)	0/12 (<0.2)	0/12 (<0.2)	0/11 (<1.7)	2/13 (<0.0 4- 0.85)	4/13 (<0.2 1- 0.23)	0/10 (<0.0 4)	0/13 (<0.04)	0/13 (<0.0 4)	3/13 (<0.2 - 0.28)	1/13 (<0.0 4- 0.28)	L:12/ 12 (0.15 -108)	0/12 (<0.0 4)	1/13 (<0.0 4- 0.44)	0/13 (<0.0 4)	0/13 (<0. 4)	PFEtS, PFPrA, PFNS, PFDoDS	(Kärrma n et al., 2019)
			Marine fish (6)	1/6 (<0.2 - 0.24)	0/6 (<0.0 4)	0/6 (<1.7)	0/5 (<0.0 4)	4/5 (<0.2 1- 1.2)	0/4 (<0.0 4)	0/5 (<0.04)	0/5 (<0.0 4)	3/5 (<0.2 - 0.39)	0/5 (<0.0 4)	L:5/5 (2.0- 11)	0/5 (<0.0 4)	4/5 (<0.0 4- 0.39)	0/5 (<0.0 4)	0/6 (<0. 4)	, PFHxPA , PFOPA,	
			Marine mammal s (10)	0/10 (<0.2)	0/10 (<0.2)	1/10 (<0.2 -4.1)	3/10 (<0.0 4- 2.3)	6/10 (<0.0 4- 1.6)	0/7 (<0.0 4)	0/10 (<0.12)	0/10 (<0.0 4)	6/10 (<0.0 4- 2.3)	2/10 (<0.0 4- 0.8)	L:10/ 10 (13- 97)	6/8 (<0.0 4- 0.25)	2/10 (<0.0 4- 0.87)	0/8 (<0.0 4)	0/10 (<0. 2)	PFDPa, and ADONA :	
			Polar bears (2)	0/2 (<0.2)	0/2 (<0.2)	0/2 (<0.2)	2/2 (2.8- 4.0)	2/2 (54- 59)	N.A.	0/2 (<0.12)	0/2 (<0.0 2)	2/2 (17- 20)	2/2 (87- 114)	L:2/2 (567- 819)	N.A.	2/2 (0.10- 0.22)	N.A.	0/2 (<0. 2)	Not detecte d in any sample	
			Bird eggs (11)	2/11 (<0.2 0- 0.26)	0/11 (<0.0 4)	3/11 (<0.3 2- 0.54)	1/11 (<0.0 4- 0.19)	5/11 (<0.2 4- 0.56)	0/5 (<0.0 4)	0/10 (<0.04)	2/11 (<0.0 4- 0.09)	8/11 (<0.2 0- 1.6)	2/11 (<0.0 4- 6.8)	L:11/ 11 (9.9- 528)	0/11 (<0.0 4)	0/11 (<0.0 4)	0/11 (<0.0 4)	0/11 (<0. 4)		
			Terrestri al mammal s (9)	0/9 (<0.2)	0/9 (<0.2)	3/9 (<0.2 -1.4)	3/9 (<0.0 4- 1.5)	7/9 (<0.2 1- 2.0)	0/5 (<0.0 4)	0/9 (<0.12)	0/9 (<0.0 4)	6/9 (<0.1 9- 0.14)	0/7 (<0.0 4)	8/9 L- (<0.0 4-13)	0/7 (<0.0 4)	0/9 (<0.0 4)	0/9 (<0.0 4)	0/9 (<0. 4)		

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Lo- cation	Yea r	Pollu- tion	Matrix (N)	PFBA	PFPe A	PFHx A	PFHp A	PFOA	PFPr S	PFBS	PFPe S	PFHx S	PFHp S	PFOS φ	PFDS	PFEC HS	6:2 Cl- PFES A	HFP O- DA	Other	Referen ce
Canada n Arctic	201 0-11		Arctic char muscle			0.00 1- 0.01 1§	0.00 1- 0.01 6§	0.00 6- 0.09 5§		0.006 - 0.021 §		<LO Q- 0.33§	0.00 1- 0.14§	<LO Q- 32§	<LO Q- 0.02§	nd				(Lescord et al., 2015)
			Chirono- mids & zoo- plankton			0.00 6- 0.56§	0.00 1- 0.47§	0.00 2- 0.47§		<LOQ - 0.022 §		0.00 4- 0.11§	<LO Q- 0.20§	0.02 2- 77§	<LO Q- 0.08§	0.003 - 0.15§				
Canada n Arctic	201 3-14		Polar bears													88- 96% (nd- 1.4)				(Letcher et al., 2018)
China, Xiaoqing River	201 9	FCPP	Plankton , bivalve, crustace an, gastropo d, and fish (50) [see levels below]					100%						100%				26%	HFPO- TrA: 100% HPFO- TeA: 71% PFMOA A: 100% PFO2Hx A: 93% PFO3O A: 93% PFO4D A: 26% PFO5Do A: 59% PF4OPe A: 24% PF5OHx	(Li et al., 2021e)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location	Year	Pollution	Matrix (N)	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFPrS	PFBS	PFPeS	PFHxS	PFHpS	PFOS ^φ	PFDS	PFEC HS	6:2 Cl-PFESA	HFO-DA	Other	Reference
																			A: 37%	
			Plankton (6) ng/g dw					97 (64-165)						3.9 (0.81-9.3)				(nd-0.83)	HFPO-TeA: 35 (14-64) HFPO-TrA: 0.10 (0.05-0.18) PFMOA A: 5.1 (2.2-16) PFO2Hx A: 1.5 (0.73-1.8) PFO3O A: 0.88 (0.59-1.1) PFO4D A, PFO5Do A, PF4OPe A, PF5OHx A: nd	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Lo- cation	Yea r	Pollu- tion	Matrix (N)	PFBA	PFPe A	PFHx A	PFHp A	PFOA	PFPr S	PFBS	PFPe S	PFHx S	PFHp S	PFOS φ	PFDS	PFEC HS	6:2 Cl- PFES A	HFP O- DA	Other	Referen- ce
			Bivalve (11) ng/g dw					339 (53- 682)						4.2 (3.2- 4.9)				(nd- 2.0)	HFPO- TrA: 9.1 (0.84- 14) HPFO- TeA: 0.04 (nd- 0.13) PFMOA A: 509 (237- 721) PFO2Hx A: 20 (13-33) PFO3O A: 6.6 (1.4- 11) PFO4D A: (nd- 2.6) PFO5Do A: 0.35 (nd- 0.66) PF4OPe A: (nd- 0.31) PF5OHx A: nd	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Lo- cation	Yea r	Pollu- tion	Matrix (N)	PFBA	PFPe A	PFHx A	PFHp A	PFOA	PFPr S	PFBS	PFPe S	PFHx S	PFHp S	PFOS φ	PFDS	PFEC HS	6:2 Cl- PFES A	HFP O- DA	Other	Referen ce
			Crustacean (10) ng/g dw					148 (136-171)						9.4 (8.7-11)				(nd)	<i>HFPO-TrA: 72</i> (21-138) <i>HPFO-TeA: 0.3</i> (0.16-0.5) <i>PFMOA A: 93</i> (67-122) <i>PFO2Hx A: 0.97</i> (0.84-1.2) <i>PFO3O A: 0.84</i> (0.61-1.1) <i>PFO4D A: nd</i> <i>PFO5Do A: 0.89</i> (0.71-1.1) <i>PF4OPe A: nd</i> <i>PF5OHx A: 1.0</i> (0.71-1.3)	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Lo- cation	Yea r	Pollu- tion	Matrix (N)	PFBA	PFPe A	PFHx A	PFHp A	PFOA	PFPr S	PFBS	PFPe S	PFHx S	PFHp S	PFOS φ	PFDS	PFEC HS	6:2 Cl- PFES A	HFP O- DA	Other	Referen ce
			Gastropod (5) ng/g dw					46 (45-48)						2.7 (2.5-2.8)				(nd)	HFPO- TrA: 3.2 (2.6-3.6) HPFO- TeA: nd PFMOA A: 16400 (15900-16700) PFO2Hx A: 51 (51-52) PFO3O A: 3.3 (2.9-3.7) PFO4D A, PFO5Do A: nd PF4OPe A: 4.2 (4.1-4.2) PF5OHx A: nd	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Lo- cation	Yea r	Pollu- tion	Matrix (N)	PFBA	PFPe A	PFHx A	PFHp A	PFOA	PFPr S	PFBS	PFPe S	PFHx S	PFHp S	PFOS φ	PFDS	PFEC HS	6:2 Cl- PFES A	HFP O- DA	Other	Referen ce
			Fish (18) ng/g dw					138 (23- 319)						10 (4.2- 24)				(nd- 3.5)	HFPO- TrA: 67 (12- 188) HPFO- TeA: 1.2 (0.11- 3.7) PFMOA A: 54 (3.0- 330) PFO2Hx A: 2.1 (nd- 5.6) PFO3O A: 2.5 (nd- 8.9) PFO4D A: (nd- 12) PFO5Do A: 2.8 (nd-12) PF4OPe A: (nd- 0.26) PF5OHx A: (nd- 1.1)	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Lo- cation	Yea r	Pollu- tion	Matrix (N)	PFBA	PFPe A	PFHx A	PFHp A	PFOA	PFPr S	PFBS	PFPe S	PFHx S	PFHp S	PFOS φ	PFDS	PFEC HS	6:2 Cl- PFES A	HFP O- DA	Other	Referen ce
China, Xiaoqing River	2015	Downstre am FCPP	Common carp liver (15)	100% 1.1* (0.24 -2.7)	100% 0.45* (0.07 -0.94)	100% 0.45* (0.10 -0.88)	100% 1.3* (0.51 -1.9)	100% 449* (93- 935)		35% (nd- 0.04)		94% 0.09* (nd- 0.3)		100% 22* (12- 32)			100% 26* (17- 43)	94% 1.4* (nd- 2.1)	HFPO- TrA: 100% 587 (137- 1220)	(Pan et al., 2017)
China, Beijing	2014	Downstre am airport	Fish liver	1.5 (<ML Q- 2.4)	0% (<ML Q)	(<ML Q- 0.59)	0% (<ML Q)	100% 21 (20- 22)		0.47 (<MLQ -1.4)		100% 2.3 (0.84 -4.1)		L: 100% 352 (271- 496)		100% 79 (41- 125)	100% 11 (7.2- 21)		PFPCPe S: 100% 7.3 (3.8- 12)	(Wang et al., 2016a)
Greenla nd	2012-13		Polar bears (3)	(<0.8 1)	(<0.2 9)	(<0.2 9)	(1.2- 1.5)	(27- 55)		(<2.4)	(<LO Q)	(21- 22)	(15- 20)	(1 784-1 864)	(2.6- 9.9)		(<0.8 4)		PFNS: 0% (<LOQ) ADONA : 0% (<0.8)	(Spaan et al., 2020)
Greenla nd, Sweden, US, Iceland	2000-17		marine mammal s (22)	0/22 (<0.8 1)	0/22 (<0.2 9)	0/22 (<0.2 9)	1/22 (<0.2 9- 0.5)	14/22 (<0.2 9-11)		0/22 (<2.4)	0/22 (<LO Q)	20/22 1.1 (<0.0 1- 7.6)	14/22 (<0.0 1- 2.4)	21/22 148 (<5.6 -858)	19/22 1.3 (<0.0 4- 8.7)		0/22 (<0.8 4)		PFNS: 0% (<LOQ) ADONA : 0% (<0.8)	
Canada, St. Lawrenc e river		Down- stream WWTP	Fish liver													0.54 ± 0.25				(Houde et al., 2013)
			Fish plasma													5.1 ±4.7				

§ Range of means in several lakes.

*Median.

φ PFOS can be reported as linear (L), branched (Br) or total (L+Br), which is generally not indicated in the table.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.88. Concentrations of PFASs in plants described by detection frequency (% or x/xx), mean value (ng/g w.w., unless stated otherwise) in bold and range in brackets. Grey cells indicate sampling sites near known PFAS point sources. FCPP=fluorochemical production plant.

Location	year	Pollution	Matrix (N)	TFA	PFPrA	PFBA	PFPeA	PFHxA	PFHpA	PFOA	PFBS	PFHxS	PFHpS	PFOS [¶]	HFPO-DA	Reference
Netherlands, Dordrecht		<3km from FCPP	Leaves & grass (10)			4/10 (<2.9-42)	2/10 (<0.2-0.7)	0/10 (<0.2)	2/10 (<0.2-0.5)	10/10 (0.4-28)	2/10 (<0.1-0.5)	0/10 (<0.2)	0/10 (<0.2)	0/10 (<0.2)	10/10 (1.0-86)	(Brandsma et al., 2019)
Netherlands,		Control area	Leaves & grass (2)			0/2 (<2.7/<6.4)	0/2 (<0.2/<0.5)	0/2 (<0.2/<0.4)	0/2 (<0.2/<0.4)	0/2 (<0.3/<0.7)	1/2 (<0.1-1.1)	0/2 (<0.2/<0.4)	0/2 (<0.2/<0.4)	0/2 (<0.2/<0.4)	0/2 (<0.3)	
Netherlands, Dordrecht		<4 km from FCPP	Vegetables (74)							40% (<0.1-2.8)					40% (<0.5-5.9)	(Mengelers et al., 2018)
Netherlands, Bilthoven		Control area	Vegetables (7)							0% (<0.1)					0% (<0.5)	
China, Tianjin	2016	Upwind, downwind or above landfills	Plant leaves (70) (ng/g lipid)	100% (6300-42000)	42%	100% 130 & 290 §	38%	55% (0.46-27)	48%	100% (3.3-210)	68%	67%		100% (1.2-32)		(Tian et al., 2018)

§ Means at two different sites.

¶ PFOS can be reported as linear (L), branched (Br) or total (L+Br), which is generally not indicated in the table.

Appendix B.4.2.9. Bioaccumulation

Table B.89. Summary of bioaccumulation studies in fish according to OECD 305 for HFPO-DA, EEA-NTH and ADONA (SVHC dossier for HFPO-DA, ECHA CHEM 2021).

Test substance	Method	Results	Reliability	Reference
EEA-NH4 EC: 700-323-3	<i>Cyprinus carpio</i> Aqueous (freshwater) flow-through; Concentrations tested: 2 and 20 µg/L Total uptake duration: 28 d Details of method: None OECD Guideline 305	BCF: ≤0.59 dimensionless (whole body ww) (kinetic) (concentration 20 µg/L) (The concentration in fish was below the detection limit.) BCF: ≤5.8 dimensionless (whole body ww) (kinetic) (concentration 2 µg/L) (The concentration in fish was below the detection limit) Lipid content: 2.43% (start of exposure) 2.48% (end of exposure)	1 (key study)	Registration dossier
ADONA EC: 480-310-4	<i>Cyprinus carpio</i> Aqueous (freshwater) flow-through; Total uptake duration: 34 d OECD Guideline 305	BCF: 0.094 whole body ww (Time of plateau: 34 d) (steady state) (34d BCF of ADONA at a concentration of 0.1 mg/L active ingredient was 0.094 ± 0.0071.)	1 (reliable without restriction) key study experimental result	Registration dossier
HFPO-DA EC: 700-242-3	<i>Cyprinus carpio</i> Aqueous (freshwater) flow-through; Total uptake duration: 28 days; A depuration phase was not conducted. Japanese new chemical substance testing guidelines which are similar to USEPA OPPTS, 850.1730 and OECD TG 305 test guidelines.	HFPO-DA could not be detected in fish at none of the two concentrations tested (<0.55 mg/kg), which resulted in BCF values <30 and <3 L/kg. Concentrations tested 20 and 198 mg/L Average lipid content of the fish was 3.3% at test initiation and 3.8% at test end	1 (reliable without restriction)	(Hoke et al., 2016)
Ammonium 2,2-difluoro-2-{[2,2,4,5-tetrafluoro-5-	<i>Oncorhynchus mykiss</i> (Rainbow trout); Aqueous (freshwater) flow-through; Total uptake duration: 17 days;	No uptake of the substance was observed. Therefore, no uptake / depuration rates and no bioconcentration factors (steady state and kinetic, respectively) have been calculated.	1 (reliable without restriction)	Registration dossier

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Test substance	Method	Results	Reliability	Reference
EEA-NH4 EC: 700-323-3	<i>Cyprinus carpio</i> Aqueous (freshwater) flow-through; Concentrations tested: 2 and 20 µg/L Total uptake duration: 28 d Details of method: None OECD Guideline 305	BCF: ≤0.59 dimensionless (whole body ww) (kinetic) (concentration 20 µg/L) (The concentration in fish was below the detection limit.) BCF: ≤5.8 dimensionless (whole body ww) (kinetic) (concentration 2 µg/L) (The concentration in fish was below the detection limit) Lipid content: 2.43% (start of exposure) 2.48% (end of exposure)	1 (key study)	Registration dossier
(trifluoromethoxy)-1,3-dioxolan-4-yl]oxy}acetate EC: 682-238-0	Total depuration duration: 7 days OECD 305 test guidelines	Bioconcentration factors at any sampling date during the uptake phase have been calculated based on fish body weight. No depuration rates were calculated since no uptake was observed.		
GX903 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid	<i>Cyprinus carpio</i> (Carp); Aqueous exposure Total uptake phase: 36 days; Total depuration phase: 28 days According to OECD TG 305, under GLP	The reported steady-state BCF values were 8, 7, 2, 1 and 1 L/kg for the increasing nominal exposure concentrations of 0.01, 0.1, 1, 10 and 100 µg/L. Short-comings: Low exposure concentrations; exposure concentrations were not maintained within ±20% of the mean measured concentrations; cross-contamination	2 / 3	(Goodband, 2019)

Appendix B.4.4. Accumulation in plants

Table B.90. Uptake of PFASs in plants.

Method	Plant species (plant parts)	substances	Results	Reference
Hydroponic studies				
climate chamber (100 µg/L of each individual PFAA per litre of nutrient solution at pH 5, pH 6 and pH 7); analysis of plant material after 5 days of exposure	maize (<i>Zea mays</i>) (root, shoot)	PFCAs (C4-C10) PFSAAs (C4, C6, C8)	- All PFAAs reached the shoot of maize plants - Uptake rate by roots: of all PFCAs C4 PFCA had the highest mean uptake rate; of all PFSAs C8 PFSA had the highest mean uptake rate - Shoot:root ratio decreased with increasing carbon chain: Short-chain PFAAs are transferred predominantly and at higher concentrations to the shoot (shoot:root ratio >2). Long-chain PFAAs increasingly accumulated in the roots with increasing carbon chain (shoot:root ratio <1)	(Krippner et al., 2014)
greenhouse – hydroponic system (PFAA-spiked nutrient solution with nominal concentration of 10 ng/L to 10 µg/L of each spiked PFAA)	lettuce (<i>Lactuca sativa</i>) (root, foliage)	PFCAs (C4-C14) PFSAAs (C4, C6, C8)	- Root concentration factors (RCF) for PFSAs increased with increasing carbon chain length - RCF for PFCAs decrease with increasing carbon chain length from C4 to C6, then increase between C6 and C11 and are quite similar for C11 to C14 (U-shaped relationship with chain length) - Foliage to root concentration factor (FRCF) for PFAAs decreased exponentially with increasing carbon chain length (FRCF >1 for C4 and C5 PFCAs) - Translocation of PFAAs from root to foliage can be described by transpiration stream concentration factor (TSCF) (assumption: substance is not degraded in the plant, elimination from the plant is negligible, substance is only taken up through roots). Except for C4 PFCA (TSCF ~ 0.8) the TSCF values were less than 1, which means that transfer from nutrient solution to leaves was inhibited. No simple relationship between the TSCF and carbon chain length of PFAAs could be observed.	(Felizeter et al., 2012)
greenhouse – hydroponic	tomato (<i>Solanum</i>)	PFCAs (C4-C14) PFSAAs (C4, C6, C8)	RCFs increased with increasing chain length and were highest for long-chain PFCAs (≥ C11) in all three plant species. RCFs	(Felizeter et al., 2014)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
system (PFAA-spiked nutrient solution with nominal concentration of 10 ng/L to 10 µg/L of each spiked PFAA)	<i>lycopersicum</i> var. MoneyMaker), cabbage (<i>Brassica oleracea</i> convar. <i>capitata</i> var. <i>alba</i>) and zucchini (<i>Cucurbita pepo</i> var. Black Beauty) (root, stem, leaf, twig, and edible parts)		were a factor of about 2-3 higher for PFSAAs than for PFCAs (with same carbon chain) - Higher stem concentration factors were observed for C8-C11 PFAAs (sharp decrease of stem concentration factors $\geq$ C11 PFCAs) - Leaf concentration factor were in all plant species >1 (except long-chain PFCAs). Compared with the concentration factors of the other aboveground parts of the plants, the leaves show the highest concentration factors for most of the PFAAs. - Edible part concentration factor (cabbage head, tomato and zucchini fruit) were highest for the short-chain PFCAs and decrease with increasing chain length. No concentrations were detected above LOQ for C12-C14 PFCAs. ECF was >1 for C4-C6 PFCAs in cabbage and tomato and for C5 PFCA in zucchini - All other PFAAs than C12-C14 PFCAs were present in the above ground plant parts. They are taken up with the transpiration stream and accumulate primarily in the leaves. Distribution within the plants were similar between plant species and among PFAAs. - Transpiration stream concentration factor was <1 for all compounds in all plant species, which means transfer from the nutrient solution to the vegetative parts of the plants was inhibited. - All edible part /leaf transfer factor factors were <1, which indicates that leafy crops with open leaves (spinach or some lettuce) accumulate higher amounts in the edible part than fruit-bearing crops. Leafy crops pose a higher risk for human exposure.	
semi-static mesocosm study (exposure phase 14 days, depuration period 14 days, individual PFAA	aquatic macrophytes: <i>Echinodorus horemanii</i> (submerged species) and <i>Eichhornia</i>	PFCAs (C5-C14) PFSAs (C4, C6, C8)	- BCFs increased with increasing carbon chain length - Higher BCFs for PFSAs compared to PFCAs with identical chain length - Leaf: BCF = 16.6 – 835 (<i>E. horemanii</i>), BCF = 21.2-349 (<i>E. Crassipes</i>) (higher leaf BCF in submerged species) - Root: BCF = 3.5 – 1620 (<i>E. horemanii</i>), BCF = 3.1-2 590 (<i>E. Crassipes</i>)	(Pi et al., 2017)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
concentration = 20 µg/L)	<i>crassipes</i> (free-floating species)		- Whole-plant: BCF = 13.7 – 910 (<i>E. horemanii</i>), BCF = 18.8 – 1280 (<i>E. Crassipes</i>) - Translocation factors (TF): After exposure phase only C4 PFSA, C5 PFCA and C6-PFCA allocate more in leaf compared to roots (TF >1) in both species. At the end of depuration phase additionally C6 PFSA, C7 PFCA and C8 PFCA were observed to be more allocated in leaf than in roots. During exposure phase TFs were generally higher for the submerged species compared to the free-floating specie (except for C5 and C6 PFCA). During depuration phase TFs were higher in the free-floating species (except for C13 and C14 PFCA). - A sigmoidal relationship between BCFs and chain length as well as membrane-water distribution coefficient, protein-water distribution coefficient and organic carbon-water partition coefficient was observed.	
greenhouse, water augmented with varying concentrations of PFAAs (nominal 0.2-40 µg/L).	lettuce (<i>Lactuca sativa</i>) and strawberry (<i>Fragaria ananassa</i>) (lettuce leaf and strawberry root, shoot, fruit)	PFCAs (C4-C9) PFSAs (C4, C6, C8)	- PFAA plant concentrations increased linearly with the aqueous concentration of PFAAs - PFCAs bioaccumulated to a greater degree than PFSAs - Chain length dependency trends in lettuce shoot and strawberry fruit: decreasing concentrations with increasing chain length - In strawberry fruit concentrations for C7-C9 PFCAs and C6, C8 PFSAs were below LOQ (suggestion that other specific transport mechanisms exist for long-chain PFAAs) - Strawberry: fruit-soil concentration factor (at 10 µg/L water concentration): C4 PFCA = 203, C5 PFCA 243, C6 PFCA 34.5 (overall average decrease of fruit-soil concentration factor per CF2 group was ~0.3 log units) - Lettuce: The BAFs for PFCAs decreased ~0.4 -0.7 log units per additional CF2 group. Dependent on organic carbon content of the soil the BAFs for PFCAs ranged from 0.938 to 3390 and for PFSA from 0.759 to 316 (at 10 µg/L water concentration) - Bioaccumulation potential depends on analyte functional group and chain length, concentration in the reclaimed water,	(Blaine et al., 2014b)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
			and organic carbon content of the soil	
greenhouse study, designed to assess PFAA phytoremediation (PFAA were added weekly to irrigation water (nominal 1 mg/L of each compound), 14 to 18-week establishment period, sand was used as growth media)	herbaceous plant species: amaranth (<i>Amaranthus tricolor</i>), mustard (<i>Brassica juncea</i>), bemudagrass (<i>Cynodon dactylon</i>), horsetail (<i>Esquisetum hyemale</i>), sunflower (<i>Helianthus annuus</i>), tall fescue (<i>Schedonorus arundinaceus</i>), red fescue (<i>Festuca rubra</i>) and Crimson clover (<i>Trifolium incarnatum</i>) woody plant species: river birch (<i>Betula nigra</i>), green ash (<i>Fraxinus pennsylvanica</i>), sweetgun	PFCAs (C5, C6, C8) PFSAAs (C4, C6, C8, C10)	- Highest BCF was observed for C5 PFCA (18.0 – 174.6 in herbaceous plant species, 0.3 – 156.2 in woody plant species) and lowest for C8 PFSA (0.7 – 5.5 in herbaceous plant species, 0.0 – 16.4 in woody plant species) - BCFs for PFCAs were higher than for PFSAAs - BCFs decreased with increasing chain length (except for C4 PFSA) - BCF of the best performing tree species (based on foliage concentrations, <i>Salix nigra</i>) were lower than BCF of the best performing herbaceous species (<i>Festuca rubra</i>) but were generally in the same overall range of the herbaceous plants.	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
	(<i>Liquidambar styraciflua</i>), tulip poplar (<i>Liriodendron tulipifera</i>), sycamore (<i>Platanus occidentalis</i>), loblolly pine (<i>Pinus taeda</i>), black willow (<i>Salix nigra</i>)			
hydroponic model plant system (PFAA concentrations nominal 2 µg/L)	wall cress (<i>Arabidopsis thaliana</i>) (root, shoot)	PFCAs (C4-C10) PFSA (C4, C6, C8)	- Rapid saturation of root concentration occurred for all PFAAs (except C4 PFCA). Shoot concentrations increased continuously. - RCFs and SCFs of PFCAs followed U-shaped trend with increasing chain length (highest for C4, C9 and C10 PFCAs). For PFSA the RCFs and SCFs increased with increasing chain-length.	(Muller et al., 2016)
climate chamber - hydroponic system (nutrient solution spiked with PFAAs at 0.5 mg/L and 1 mg/L; sampling after 1, 2, 6, 13 and 20 days)	grass (<i>Bromus diandrus</i>)	PFCAs (C4, C8, C10) PFSA (C4, C6, C8)	- The transfer factor from nutrient solution to the aerial part of plant increased with exposure time for both concentration levels, except from day 13 to day 20 at the higher concentration level where no increasing transfer factor was observed. - For PFCAs the transfer factor decreased with increasing chain length. No statistical differences in transfer factor values were observed for PFSA. - After 20 days transfer factors were highest for C4-PFCA, but all PFAAs were greater than 1 (2.036 – 5.65)	(Garcia-Valcarcel et al., 2014)
climate chamber - hydroponic system	wheat (<i>Triticum aestivum</i> L.) (root, shoot)	PFCAs (C2-C4, C6, C8) PFSA (C8)	Time-dependent uptake: All PFAAs were efficiently absorbed by wheat roots. C2 and C3 PFCAs were rapidly taken up within the 80-hour exposure period and no steady state was observed. The uptake rates of the C4-C8 PFAAs slowed during	(Zhang et al., 2019c)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
(1. time-dependent: nutrient solution spiked with each PFAA at 0.1 mg/L; sampling after 2, 4, 8, 6, 32 and 80 hours; 2. concentration-dependent: nutrient solution spiked with PFAA at 0, 0.1, 0.5, 0.7, 1.0, 1.5, 2.0, 2.5 mg/L; sampling after 4 hours; 3. effect of metabolic, aquaporin and anion-channel inhibitors)			the late exposure period. The C8 PFAAs reached a steady state at the end of exposure period. Root concentrations of PFCAs decreased with increasing chain length, achieving a minimum at C6 PFCA, and then increased again with the chain length. • The concentrations in shoots were lower than in roots, except C4 PFCA. The final shoot concentration decreased with increasing chain length. • The translocation factors (concentration ratio shoot:root) were all less than 1 and declined with increasing chain length except for C4 PFCA (translocation factor = 1.1). The relatively low translocation factor for C2 and C3 PFCA could be a result due to their high concentrations in roots and the short exposure time (80 hours). Therefore, an increase is expected as the bioaccumulation proceeds for a longer time. • Concentration-dependent uptake: The uptake of PFAAs was nonlinear and followed Michaelis-Menden model well, indicating that the uptake is a carrier-mediated process. • The absorption of different types of PFAAs (PFCAs and PFSAs) and different chain lengths may follow different pathways in wheats. The uptake of PFAAs by wheat is mainly an energy-dependent active process, whereas for C2 and C3 PFCAs, anion channels and aquaporins also participate in the uptake process.	
greenhouse study, hydroponic system exposed with three different solutions: effluents from two WWTPs (C4-C8 PFCAs and C4, C8 PFSAs)	lettuce (<i>Lactuca sativa</i> L.) and spinach (<i>Spinacia oleracea</i> L.) (root, shoot)	PFCAs (C4-C14) PFSAs (C4, C6, C8)	• The root concentration factor showed similar pattern under different treatments. The root concentration factor values ranged from 5.4 (C4 PFSA) to 2400 (C11 PFCA) for lettuce and from 1.7 (C4 PFSA) to 1500 (C12 PFCA) for spinach, respectively. The root concentration factor was generally higher in lettuce than spinach. The values for PFCAs decreased from C4 to C6 and from C11 to C14, while it increased in the range between C6 and C11. For PFSAs the root concentration factor increased with increasing chain length. • The leaf concentration factor showed similar pattern under	(Dal Ferro et al., 2021)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
detected in effluent) and a PFAAs-spiked drinking water solution (nominal concentration of 500 ng/L for each PFAA); exposure time: 45 (lettuce) and 55 (spinach) days			different treatments. The highest leaf concentration factor was observed for C4 PFCA (median values between 47 and 440) followed by C5 PFCA (49-64) and C6 PFCA (9.8-22). The translocation factor from root to shoot decreased with increasing carbon chain length (except for C5 PFCA in spinach which has a higher TF than C4 PFCA). For lettuce, the translocation factor was >1 only for C4 PFCA and C5 PFCA for the treatment with WWTP effluents. For all other PFAAs and treatments the translocation factor was less than 1. For spinach, translocation factors >1 were observed for C4 – C6 PFCAs and C4 PFSA in all treatments and additionally C7 PFCA in treatment with PFAA-spiked solution. Comparing PFCAs and PFSAs with the same carbon chain length, show that PFCAs had a greater affinity to shoots accumulation than PFSAs.	
climate chamber - hydroponic system (nutrient solution spiked with 6:2 FTSA at 1.100 nmol/mL; exposure time: 12 days)	pumpkin (<i>Cucurbita maxima</i> L.) (root, shoot)	6:2 fluorotelomer sulfonic acid (6:2 FTSA) PFCAs (C2-C8) PFSAs (C4, C6, C8)	6:2 FTSA and all tested PFAAs had a root concentration factor >1. The root concentration factor of 6:2 FTSA was 2.6-24.2-fold as high as those of PFAAs of the same or much shorter carbon chain length, demonstrating much higher bioaccumulative ability of 6:2 FTSA in pumpkin roots. - C2-C7 PFCAs were found as metabolites in roots and shoots. C7 PFCA and C4 PFCA were the major metabolite in roots, while C4 PFCA was the major metabolite in shoots. - Neither the PFAAs nor 6:2 FTSA had higher concentrations in shoots than in roots, leading to translocation factors lower than 1. The translocation factor decreased with increasing perfluorinated carbon chain length (and increasing log K_{ow}).	(Zhao et al., 2019)
hydroponic greenhouse study (nutrient solution spiked with FOSA at 1.856 nmol/mL; exposure time: 12 days)	soybean (<i>Glycine max</i> L. <i>Merrill</i>) and pumpkin (<i>Cucurbita maxima</i> L.) (root, shoot)	Perfluorooctane sulfonamide (FOSA) + degradation products (C8 PFSA is also present as impurity (~8 mol%) in the FOSA standard)	- The translocation factor of FOSA from roots to shoots was 1.5-fold higher for pumpkin (0.09) than for soybean (0.06). The higher root lipid content of pumpkin might be an explanation. - C4, C6 and C8 PFSA were found as metabolites in roots and shoots of pumpkin and soybean. The concentration in roots were higher than in shoots for all metabolites. The concentration increased with increasing chain length.	(Zhao et al., 2018a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
growth chamber (nutrient solution spiked with C8 PFSA or F53-B concentrations at 0.05 and 0.1 µg/mL; exposure time: 7 days)	wheat (<i>Triticum aestivum</i> L.) (root, shoot)	C8 PFSA, commercial F53-B (6:2 CI-PFESA as major component and 8:2 CI-PFESA as impurity)	- Root concentrations of C8 PFSA and CI-PFESAs were an order of magnitude higher than those in shoots. - There was no significant difference in BCF_{shoot} values between C8 PFSA and 6:2 CI-PFESAs at both tested levels (BCF_{shoot} = 2.614 – 4.182). The BCF_{shoot} values for 8:2 CI-PFESA were about 70-76% lower than for C8 PFSA. On the contrary, the BCF_{root} values for 8:2 CI-PFESA were 1.4-1.9-fold higher than for C8 PFSA (BCF_{root} 8:2 CI-PFESAs = 194.7 and 266.7). - The translocation factor values from root to shoot were similar for C8 PFSA and 6:2 CI-PFESA (0.023-0.029) and quite lower for 8:2 CI-PFESA (0.004 and 0.005). 6:2 CI-PFESAs had a similar accumulation pattern as C8 PFSA, whereas 8:2 CI-PFESA was predominantly restricted to the roots, which might be attributed to their hydrophobicity and carbon chain length.	(Lin et al., 2020b)
Soil studies				
field study (biosolid amended soils; biosolids applied = 4.5, 9, 18, 36 t/(ha·y))	wheat (<i>Triticum aestivum</i> L.) (root, straw, husk, grain)	PFCAs (C4-C11, C14) PFSA (C4, C6, C8)	- No correlation between the root concentration factor and carbon chain length of PFAAs - Transfer potential from roots to straws and further to the grains was higher for short-chain PFAAs than for long-chain PFAAs - Transfer factor from roots to straws: higher for PFCAs than for PFSA (with same carbon chain) - Transfer factor from straws to grains: higher for PFSA than for PFCAs (with same carbon chain) - PFCAs concentrations in grain increased logarithmically with increasing PFCA concentrations in soils while PFSA concentrations in grain were correlated linearly with PFSA concentrations in soils, indicating that PFCAs and PFSA may have different transport pathways from soil to grain.	(Wen et al., 2014)
pot experiment (soil was spiked with an aqueous solution of 0.25	maize (<i>Zea mays</i>) (straw, kernel)	PFCAs (C4-C10) PFSA (C4, C6, C8)	- Straw: PFAA concentrations decreased significantly with increasing chain length 4-fold increase in spiking (1.00 mg of the individual substances/kg soil versus 0.25 mg/kg soil) leads to a 4-fold	(Krippner et al., 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
mg individual PFAA/kg soil and 1.00 mg individual PFAA/kg soil). After 128 days straw and kernels were harvested.			higher concentration of PFAAs with chain lengths $\geq C6$ in the straw of maize plants. 4-fold increase in spiking concentration leads only to a 2-fold increase of C4 PFCA, C5 PFCA and C4 PFSA in the straw. - Kernel: only C4-C7 PFCAs and C4 PFSA were detected (highest concentration for C5 PFCA) - Concentrations of PFAAs detected in kernels were lower than those measured in the straw - PFCAs are always found in higher concentrations than PFSAs - Highest soil-to-plant transfer for both straw and kernels was determined for short-chain PFAAs. The PFAA transfer from soil to straw decreased with increasing chain length. Transfer factors in straw was >1 for C4-C7 PFCAs and C4 PFSA. Transfer factors in kernels were all below 1. - PFAAs accumulate to a greater degree in vegetative plant parts and only to a small degree in generative organs.	
field study (grass from biosolid-applied fields)	grass (tall fescue, barley, Bermuda grass, Kentucky bluegrass)	PFCAs (C6-C14) PFSAs (C4, C6, C8) n:2 FTOH (n= 6, 8, 10, 12, 14), n:2 sFTOH (n= 7, 9, 11, 13), 8:2 FTA	- The shortest PFCA had the highest grass/soil accumulation factor (GSAF) and the accumulation potentials decreased with increasing carbon chain length (C6 to C9 mean decrease of 32-fold, C9 to C14 mean decrease 2-fold) - The accumulation potential is higher for C8 PFCA than for C8 PFSA (GSAF for other PFSAs were not provided) FTOHs, sFTOH were quantifiable in only a few plant samples and only at very low concentrations compared to PFCAs (e.g. 8:2 FTOH 10-fold lower concentrations than C8 PFCA)	(Yoo et al., 2011)
greenhouse study with biosolids-amended soil (industrially impacted soil (PFAA contaminated biosolids),	lettuce (<i>Lactuca sativa</i>) and tomato (<i>Lycopersicon lycopersicum</i>) (lettuce leaf and tomato fruit)	PFCAs (C5-C10) PFSAs (C4, C6, C7, C8, C10)	Greenhouse study: - The BAFs for PFAAs in greenhouse lettuce decreased approximately 0.3 log units per additional CF₂ group (C4 PFSA excluded from regression calculation) - BAFs in lettuce in industrially impacted soil higher than in municipal soil. BAFs (lettuce, municipal soil) = 0.19 – 28.4, BAFs (lettuce, industrially impacted soil) = 0.52 – 56.8 (C10 PFDS < LOQ); greatest accumulation was seen for C4 PFCA - No apparent linear trend for PFAA log BAFs in tomato. BAF	(Blaine et al., 2013)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
municipal soil) limited-scale field study (fertilization via biosolids with different agronomic rate for nitrogen (0.5x, 1x, 2x, 4x))			decreases approximately 0.5 – 0.9 log units (C4 PFCA excluded from regression calculation) - BAFs (tomato, industrially impacted soil) = 0.1 – 17.1 (C9, C10 PFCAs and C7, C8, C10 PFSA < LOQ); greatest accumulation was seen for C5 PFCA - Bioaccumulation of PFAAs from biosolid-amended soils depend strongly on PFAA concentrations, soil properties, the type of crop, and analyte - transpiration stream concentration factor (TSCF) lettuce: except for C4 PFCA in municipal soil (TSCF ~ 1.25) the TSCF values were less than 1 for all analytes and both biosolids-amended soils Limited-scale field study: - BAFs decreased with increasing chain length (only calculated for 4x plot) - Lettuce: BAFs could only be calculated for C4 PFCA (40.0), C5 PFCA (16.3), C4 PFSA (2.02), C6 PFSA (1.51), C8 PFSA (0.1); concentrations for all other PFAAs were below LOQ - Tomato: BAFs could only be calculated for C4 PFCA (18.2), C5 PFCA (14.9) and C6 PFCA (6.84); concentrations for all other PFAAs were below LOQ	
greenhouse study with biosolids-amended soil (industrially impacted biosolids and municipal biosolids)	radish (<i>Raphanus sativus</i>), celery (<i>Apium graveolens var. dulce</i>), tomato (<i>Lycopersicon lycopersicum</i>), and sugar snap pea (<i>Pisum sativum var. macrocarpon</i>)	PFCAs (C4-C10) PFSA (C4, C6, C8)	- Root-soil concentration factors (RCF) for tomato and pea were independent of PFCA chain length, while radish and celery RCFs showed a slight decrease with increasing chain length (chain length trends were not calculated for PFSA as only three analytes were studied). - PFCAs: Shoot-soil concentration factors (SCF) for all crops showed a decrease with increasing chain length (0.11 to 0.36 log decrease per CF2 group). - PFCAs: Fruit-soil concentration factors (FCF) decreased with increasing chain length (0.54–0.58 log decrease per CF2 group). - Fruit crops were found to accumulate fewer long-chain PFAAs than shoot or root crops presumably due to an increasing	(Blaine et al., 2014a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
	(radish and celery: root and shoot; tomato and pea: root shoot and fruit)		number of biological barriers as the contaminant is transported throughout the plant (root to shoot to fruit). Edible parts: radish root (RCF >1 for C4, C6, C9 PFCA and C4, C6 PFSA), celery shoot (SCF >1 for C4-C7 PFCA and all three PFSA), tomato fruit and pea fruit (FCF >1 for C4-C6 PFCA)	
Outdoor lysimeter (soil spiked with a mixture of PFAAs – nominal concentration of each PFAA: 0.1 mg/kg dw, 1 mg/kg dw, 5 mg/kg dw, 10 mg/kg dw)	Radish (<i>Rapahnus sativus</i>), lettuce (<i>Lactuca sativa</i>), pea (<i>Pisum sativum</i>) and maize (<i>Zea mays</i>) (radish: roots, bulb, foliage; lettuce: roots, foliage; pea: roots, stem, twigs, leaves, pods, peas; maize: roots, stem, leaves, hull leaves, cobs, kernels)	PFCAs (C4-C14) PFSA (C4, C8)	- Phytotoxic effects of PFAAs: radish and lettuce plants grown in the highest exposure level soil were smaller at the time of harvest compared to those growing in lower exposure levels. Pea and maize plants showed no visible effects of phytotoxicity. - Edible part/soil concentration factors ranged over seven orders of magnitude and decreased strongly with increasing PFAA chain length, by a factor of 10 for each additional CF2 group for pea. - Root retention factors increased by a factor 1.7 for each CF2 group. - Fruit/leaf concentration factors decreased by a factor 2.5 for each CF2 group. - Independent of the plant species the highest concentrations were found in leaves and roots of the plants and the lowest in the fruits. Therefore, leafy and root vegetables pose the highest risk for dietary exposure followed by fruit-bearing crops.	(Felizeter et al., 2021)
climate chamber, two biosolid amended soils (anaerobically digested thermal drying sludge)	spinach (<i>Spinacia oleracea</i>), tomato (<i>Solanum lycopersicum</i>)	PFCAs (C4-C16) PFSA (C4, C6, C8, C10) FOA, N-MeFOA, N-EtFOA	Tomato: C8 PFSA (75%) and C7–C10 PFCA (54–96%) preferentially remained in roots and C4–C6 PFCA tended to be translocated to above-ground tissues (leaf: 31–56%, fruit: 32–48%). Transfer factor values for PFASs in fruit were >1 for C4 (30.87 and 69.82), C5 (31.22) and C6 PFCA (3.64). Transfer factors between tomato plant parts were determined	(Navarro et al., 2017)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
and anaerobically digested municipal solid waste compost); exposure time: 28 days (spinach) and 6 months (tomato)	<i>L.</i> , (tomato: root, stem, leaf, fruit)		to evaluate the translocation and distribution within the plant: leaf concentration factor for C5–C8 PFCA >1 (2.69 – 6.92), edible part concentration factor only for C5-PFCA >1 (1.12) - Spinach: only C5, C8 PFCA and C8 PFSA were detected (transfer factor 1.08 – 4.47) - C6 PFSA, C10 PFSA, C13–C16 PFCA, FOSA, N-MeFOSA and N-EtFOSA were not detected in any sample.	
climate chamber, soils fortified by addition of technical mixture of C8 PFSA (~50 mg/kg soil); exposure time: 28 days	maize (<i>Zea mays</i>) (root, leaf)	technical mixture of C8 PFSA	- High levels of C4 and C6 PFSA were also detected in roots and leaves as the commercial mixture of C8 PFSA also contains ~ 1.5% of C4 and C6 PFSA. - C8 PFSA is highly presented in roots (89%), whereas C4 PFSA (88%) and C6 PFSA (82%) were preferentially found in leaves. The transfer factor values in roots were highest for C8 PFSA (8.82) followed by C4 PFSA (5.00) and C6 PFSA (2.62). Transfer factor values in leaves were: 9.39 (C6 PFSA), 4.00 (C4 PFSA) and 0.80 (C8 PFSA).	(Navarro et al., 2017)
greenhouse, water-soil-plant system, derived from a surface flow constructed wetland; surface water enriched with PFAA at two different concentrations (low PFAA concentration 0.18–4.22 µg/L; high PFAA concentration 64–4 300 µg/L)	bulrush (<i>Typha angustifolia</i>) (root, shoot)	PFCAs (C4–C8) PFSA (C4, C6, C8)	- Longer-chain PFAAs showed higher root uptake potential compared to shorter-chain PFAAs. PFSA exhibited higher concentrations in the roots compared to PFCAs. - BAF_{root/water} = 8.1 – 45.7 at low concentrations and 0.7 – 15.6 at higher concentrations; BAF_{shoots/water} = 7.3 – 26.6 at low concentrations and 1.4 – 3.5 at higher concentrations. BAF_{plant/water} decreased with increasing PFAA initial concentrations. - A positive correlation between BAF_{plant/soil} and chain length was observed. - Translocation factor from roots to shoots decreased with increasing chain length (TF >1 for C4–C7 PFCAs and C4 PFSA). Higher translocation factors were observed for PFCAs compared to PFSA with similar chain length.	(Zhang et al., 2020b)
pot experiments	wheat	PFCAs (C4, C6, C8)	Both the root and shoot accumulated PFAAs from soil. The	(Lan et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
in greenhouse with wheat-soil system (PFAA concentrations: 200 and 2 000 µg/kg soil)	(<i>Triticum aestivum</i> L.) (root, shoot)	PFSAAs (C4, C6, C8)	accumulation of PFAAs was enhanced at the higher spiking levels of PFAAs and increased with decreasing chain length. PFCAs showed higher accumulation in wheat than PFSAs of the same chain lengths, which corresponds to their differences of log Kow values. • Root: BAF values were all greater than 1. BAF values for PFCAs decreased with increasing chain length, while the BAF were at similar level for PFSAs • Shoot: BAF values were greater than 1 for C4 and C6 PFAAs. • Transfer factor from root to shoot: no significant difference was observed between the two spiking levels. For C4 and C6 PFAAs the transfer factors were greater than 1 (C4 PFCA: 11.1 and 11.9; C4 PFSA: 4.51 and 1.86; C6 PFCA: 2.6 and 1.9; C6 PFSA: 1.04 and 1.28) indicating their higher accumulation potential in shoot. The limited transfer potential of long-chain PFAAs from root to shoot may be due to their low solubility and greater interaction with biological macromolecules (e.g. protein and lipid) in root.	2018)
greenhouse microcosm experiment (duration 5.5 months; four different treatments: 1. Soil without biosolids; 2. WWTP biosolids-amended soil (16 g biosolids/kg soil); 3. WWTP- and paper fibre biosolids-amended soil)	alfalfa plants (<i>Medicago truncatula</i>) pumpkin (<i>Cucurbita maxima</i>) (root, stalk, flower, leaf, fruit)	DiPAPs PFCAs (C4-C14)	Greenhouse study: • DiPAPs (6:2 diPAP, 6:2/8:2 diPAP, 8:2 diPAP, 8:2/10:2 diPAP, 10:2 diPAP, 10:2/12:2 diPAP) as well as PFCAs (C4-C13) were detected in control soil and biosolid-amended soils prior application. • The majority of the 6:2 diPAP resided in the soil (99%), with minor uptake observed in the plants (1%) • FTOHs were not analysed and the microcosms were open to the atmosphere of the greenhouse. • The following transformation products were observed in the soil-plant microcosm: 6:2 FTCA, 6:2 FTUCA, 5:3 FTCA, C4-C6 PFCAs • The plant-soil accumulation factor for PFCAs decreased with increasing carbon chain length Field study: • several PFCAs were present in the field soil collected prior to	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
(mixture 1:4); 4. 6:2 diPAP-spiked WWTP biosolids-amended soil) and field experiment (compost and paper fibre biosolids (1:4) were applied to two farmfields)			the application. No diPAPs were detected. - DiPAPs can migrate to lower soil depths. 2 months after application 6:2/8:2 diPAP, 8:2 diPAP, 8:2/10:2 diPAP were observed at a soil depth of 5-10 and 6:2 diPAP even at a depth of 10-15 inches - Uptake of diPAPs and PFCAs in the root, stalk, flower, leaf and fruit of pumpkins were observed after 3.5 months	
pot experiment with two different compost amended soils (soil 2.4 and substrate, 8:2 diPAP concentration nominal 500 ng/g) (growth periods: carrot ~ 3 months, lettuce ~1 month)	lettuce (<i>Lactuca sativa</i>) and carrot (<i>Daucus carota ssp sativus</i>) (carrot: peel, core, leaf; lettuce: leaf, heart)	8:2 diPAP + degradation products	- In the presence of crops different degradation products were detected in the soil compared to the experiment in absence of crop. - Degradation products in the absence of crop: 8:2 monoPAP, 8:2 saturated and unsaturated fluorotelomer carboxylate (8:2 FTCA and 8:2 FTUCA), 7:3 FTCA, C6-C8 PFCAs - Carrot experiments: degradation products: C4-C9 PFCAs, 7:3 FTCA; Lower 8:2 diPAP concentrations were observed in the carrot parts compared to the soil. This could mean that the substance retained to the soil or that metabolization occurs. The highest concentrations of PFCAs were found in leaves. BCF and translocation of PFCAs increased with increasing solubility. Independent of type of soil BCF values decreased with increasing chain length. - Lettuce experiments: only C8 PFCA was detected as degradation product in the heart of the lettuce. No translocation through the plant was observed as in the leaves concentrations of 8:2 diPAP and C8 PFCA were below method detection limits (MDL for 8:2 diPAP = 3 ng/g; MDL for C8 PFCA not mentioned).	(Bizkarguenaga et al., 2016)
climate chamber with plant-soil	longhair sedge (<i>Carex</i>	PFAS-ether: 2,2,3,3-Tetrafluoro-3-	All PFAS-ether were taken up by plant roots, translocated to shoots, and accumulated in plant tissues. Exposure	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
system (solutions of PFAS-ether at 500 or 2 000 ng/L of each PFAS-ether; sampling at day 52 and 80)	<i>comosa</i>) (root, shoot)	(trifluoromethoxy)propionic acid (PFMOPrA), perfluoro(4-methoxybutanoic) acid (PFMOBA), 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid (HFPO-DA), ammonium 2,2,3 trifluoro-3-(1,1,2,2,3,3-hexafluoro-3-trifluoromethoxypropoxy), propionate (ADONA), Potassium 2-(6-chloro-1,1,2,2,3,3,4,4,5,5,6,6-dodecafluorohexyloxy)-1,1,2,2-tetrafluoroethane sulfonate (F-53B)	concentration and time positively affected the plant uptake of the PFAS-ether. The uptake in shoots was significantly higher for the other PFAS-ether than for F-53B. F-53B, which has the longest carbon chain among the PFAS-ether in this study and a sulfonic functional group, was largely accumulated in roots with very limited upwards translocation. - Plants exposed to HFPO-DA (500 ng/L, 52 days) had the highest translocation factor. Only F-53B had a translocation factor less than 1. The relatively higher hydrophobicity and lipophilicity of F-53B (log Kow =7.03) could cause greater interactions between the substance and the biological macromolecules in plant roots (e.g. proteins, lipids). This could lead to decreasing penetration of F-53B through the Casparian strip. - The concentration of PFAS-ether in water-soluble fraction increased with decreasing carbon chain length and logKow values and had a positive linear relationship with PFAS-ether mass in whole plants and plant shoots. PFAS-ether that had higher concentration in water-soluble fraction (e.g. PFMOPrA and PFMOBA) may have higher leachability to surrounding environments. Aging process could facilitate PFAS-ether to become non-extractable, hence reducing their mobility in soil and bioavailability to plants.	
pot experiment (soil was spiked with a stock solution of target PFASs to achieve nominal concentrations of 200 ng/g and 500 ng/g; exposure time: 60 days)	wheat (<i>Triticum aestivum</i> L.), maize (<i>Zea mays</i> L.), soybean (<i>Glycine max</i> L. Merrill), and pumpkin (<i>Cucurbita maxima</i> L.) (Wheat: root,	6:2 fluorotelomer sulfonate (6:2 FTS), 6:2 chlorinated polyfluoroalkyl ether sulfonates (6:2 Cl-PFESA, trade name F-53B) and perfluorophosphinates (C6/C6 and C8/C8 PFPIAs)	- All four PFASs were detected in all compartments of all four plant species in both spiked treatments. The concentration of the four PFASs in the plant roots were significantly higher than those in shoots and leaves. - The mean concentrations in the plant roots and aboveground tissues decreased in order of 6:2 FTS > F53-B > C6/C6 PFPIA > C8/C8 PFPIA with increasing hydrophobicity (increasing log Kow). - The root soil concentration factor as well as the translocation factor from root to shoot were inversely proportional to their log Kow for all four plant species. All translocation factor values were below 1.	(Zhou et al., 2020)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Method	Plant species (plant parts)	substances	Results	Reference
	shoot; maize, soybean, pumpkin: root, shoot, leaf)			
Pot experiment in outdoor transparent shelter (irrigation with PFAS contaminated river water from Lee's Creek (AFFF contamination, <1 µg/L PFAS) and PFAS-free water)	Tomato (<i>Solanum lycopersicum</i>), lettuce (<i>Lactuca sativa</i>) and beet (<i>Beta vulgaris ssp. vulgaris</i>) (tomato: root, stem, foliage, flower, foliage; lettuce and beet: root, foliage)	PFCAs (C4-C12) PFASs (C4, C6, C8, C10), PFOSA (perfluorooctanesulfonamide)	- Short-chain PFASs: tomato plants (exception of roots) showed significant increases of short-chain PFAS concentrations with river treatment (highest concentration in flowers). This effect could not be observed in lettuce or beet. - Long-chain PFASs: Concentration of long-chain PFASs only increased in tomato foliage and lettuce roots and foliage. - Tomato: In small fruits higher concentrations of short-chain PFAS but lower absolute PFAS mass were observed. Whereas in larger fruits lower concentration of short-chain PFAS but higher absolute PFAS mass was detected. - Biomagnification of short-chain PFASs in flowers could have implications for pollinators depending on where the contaminants reside (e.g. in pollen or nectar, exposure to insects could be meaningful).	(McDonough et al., 2021a)

Appendix B.5.1.1.2. Distribution

Table B.91 to Table B.95 summarise human biomonitoring studies of PFASs. The tables include precursors and arrowhead PFASs that are not covered by existing or proposed restrictions. Thus, data for PFOA, PFOS, PFHxA, PFHxS and C9-C14 PFCAs and related precursors are not included in these tables.

Table B.91. Serum (S), plasma (P) or whole blood (WB) concentrations (ng/mL) of PFAAs (PFSAs, PFCAs and PFPAs) that are not covered by existing or proposed restrictions described by detection frequency (% or x/xx), median (bold) and range (within brackets). Note that the levels of whole blood are not comparable to plasma/serum. Grey cells indicate sampling sites near known PFAS point sources. NR=not reported, w pp=weeks postpartum; P=pool; cont drw=contaminated drinking water, FPP=fluoropolymer production plant, FCM=fluorochemical manufacturing facility, ref=reference area.

Year Sam ple	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
1977 - 2006 S	40-50 (M)	Norway	24 P	0% (<0.1)	54% 0.076 (<0.05- 0.63)	63% 0.081 (<0.05- 0.14)			67% 0.074 (<0.05- 0.18)		83% 0.20 (<0.05- 0.47)		0% (<0.05)		(Haug et al., 2009)
1982 - 2009 S	20-29 (F,M)	Germany, Muster, Halle	420PFDS 122PFHp S 420PFHp A			100% (0.019-2.2)					100% (0.054- 2.0)		46% Munster (<0.00 5- 0.084) 69% Halle (<0.00 5- 0.097)		(Yeung and Mabury , 2016; Yeung et al., 2013b; Yeung et al., 2013c)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
1982 - 2010 P	20-29 (F,M)	Germany, Munster	258 ^{PFCAs} 158 ^{PFSAs}	11% (<0.5-1.4)	2% (<0.5- 14)	53% (<0.5-2.3)			0% (<0. 5)		45% (<0.5- 2.3)		0% (<0.5)		(Schrot er- Kerman i et al., 2013)
1996 - 2010 S	Primipara, 4 w pp	Sweden, Uppsala	36 P (5-25 /P)			100% (0.056- 0.14)			72% (<0. 013- 0.10)				100% (0.011 -0.26)		(Glynn et al., 2012)
1997 - 2004 P	20-21 (F,M)	Germany, Arns-berg (cont. drw)	30		0% (<1.0)				0% (<0. 1)						(Wilhel m et al., 2009)
1997 - 2012 S	20-42 Primi- para, 4 w pp	Sweden, Uppsala	27 P (10/P)	0% (<0.3)	0% (<0.1)	100% (0.014- 0.10)			70% (<0. 009- 0.05 8)				81% (<0.00 5- 0.091)		(Gebbin k et al., 2015)
2000 - 2008 P		Norway, National survey	3174/ 4295			11% (<0.05- 0.077 ^{P95})					90% 0.15 (<0.05 - 0.34 ^{P95})				(HBM4E U, 2022)
2001 - 2004	70 (F,M)	Sweden, Uppsala	1006		0% (<0.02)	74% 0.05 (F) 78% 0.06			14% (F) 11%				0% (<0.03)		(Saliho vic et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
P						(M)			(M)						(2015)
2002 - 2005 Cord P	Newborn (F,M)	Belgium, 8 locations	8P (48- 162/P)	0% (<0.1)					0% (<0. 02)						(Roose ns et al., 2010)
2002 - 2005 S	14-15 (F,M)		8P(149 -186/P)	0% (<0.1)					0% (<0. 02)						
2002 - 2005 S	50-65 (F,M)		8P (182- 197/P)	0% (<0.1)					0% (<0. 02)						
2003 S	Adults (F,M)	Norway, High fish consumption	175			37% (<0.035- 0.49)					99.5% 0.42 (<0.03 5-2.5)				(Haug et al., 2010b)
2003 - 2008 S	pregnant	Spain	1216						0%						(Manza no- Salgado et al., 2016)
2005 P	Pregnant	Denmark, Aarhus	88			65% 0.08 (<0.05- 1.95)					100% 0.25 (0.03- 0.7)				(Bach et al., 2015)
2005	1-100	USA (OH & WV)	69 030		4.9%	38%									(Frisbe

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFP As	Reference
- 2006 S	(F,M)	Cont. drw			(<0.5- NR)	(<0.5-NR)									e et al., 2009)
2006 S	47-80 (M)	Faroe Island Whalers	10			60% 0.39 (<0.03- 0.49)					100% 0.65 (0.16- 1.1)		60% 0.07 (<0.03 -0.09)		(Hu et al., 2018)
2006 WB	Adults (F,M)	Spain, Catalonia	48			0% (<0.78)			0% (<0. 73)				0% (<0.58)		(Ericso n et al., 2007)
2006 P	Children (F,M)	Germany, Siegen (ref)	80	0% (<1)					5% (<0. 1- 0.1 ^{P9} 5)						(Holzer et al., 2008)
	Mothers		153	0% (<1)					0.7 % (<0. 1- NR)						
	Adults (M)	Germany, Brilon (ref)	103	0% (<1)					3% (<0. 1- NR)						
	Children (F,M)	Germany, Arnsberg	90	0% (<1)					33% (<0. 1- 0.2 ^{P9}						

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
									5)						
	Mothers	Cont. drw	164	0% (<1)					4% (<0.1 - NR)						
	Adults (M)		101	0% (<1)					13% (<0.1 - 0.2 ^{P9} 5)						
NR year Cord WB		Spain, Barcelona	30	20% ($<NR-11.8$)	0%	3% ($<NR-0.51$)	10% ($<NR-19$)	0%	0%				0%		(Llorca et al., 2012b)
2007 - 2008 Cord WB		Greece, Heraklion	30	33% ($<NR-1.5$)	0%	0%	0%	0%	0%				0%		
2007 - 2008 S	25-45 (F)	Norway, Oslo	41			12% (<0.035 - 0.10)					76% 0.079 (<0.03 5-0.19)				(Haug et al., 2011b)
2007 - 2008 S	19-44 (mothers 2 w. pp)	Faroe Island	51	0% (<0.1)	0% (<0.05)	6% (<0.03 - 0.12)			0% (<0.1)		86% 0.09 (<0.03 -0.22)		27% (<0.03 -0.13)		(Hu et al., 2018)
2007	31 ± 4,8	Norway	391			16%					80%				(Berg

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFP As	Reference
- 2009 S	Pregnant					(<0.03- 0.45)					0.1 (<0.06 -1.1)				et al., 2014)
2008 S	4 (F,M)	Sweden, Uppsala	57			79% 0.12 (<0.08-1.0)			65% 0.019 (<0.01- 0.11)						(Gyllen hammar et al., 2016)
	8-9 (F,M)		55			60% 0.08 (<0.08- 0.75)			44% (<0.01- 0.086)						
	12 (F,M)		119			51% 0.06 (<0.08- 0.52)			60% 0.015 (<0.01- 0.23)						
2008	18-75 Fishermen	France	478								>80% 0.6 (<LOD- 13.3)				(Denys et al., 2014)
2008 -	28-53 Ski wax	Norway, After season1 (March)	13	NR% (<0.1-3.7)		100% 2.2 (0.4-					100% 0.49				(Freber g et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFP As	Reference
2009 S	technician					11.0)					(0.16-1.7)				2010)
		Before season2 (Nov)		0% (<0.1)		100% 0.74 (0.14-9.1)					100% 0.40 (0.21-1.4)				
		After season2 (March)		NR% (<0.1 -5.4)		100% 1.5 (0.21-12.0)					100% 0.40 (0.13-1.5)				
2008 - 2009 S	20 (mean) (M)	Denmark	247								100% 0.26 (NR-0.52 ^{P95})				(Joensen et al., 2013)
2008 - 2013 S	Pregnant (w. 9-20)	Denmark, Aarhus	1507		6% (<0.19 -NR)	26% (<0.05 -NR)			1% (<0.07 -NR)		76% 0.2 (<0.11 -1.16)		0% (<0.37)		(Bach et al., 2016b)
2009 S	0-87 (F,M)	China, Fuxin Area near FCM (PFBS, PTFE)	120						93% 0.12 (<0.02 -1.3)						(Bao et al., 2011)
2009 S	18-70 (F,M)	USA	40	57% 0.035 † (<0.005 -0.23)	65% 0.073 † (<0.002 -0.50)	87% 0.097 † (<0.001 -0.42)			15% (<0.01 -				65% 0.04 † (<0.01 -0.15)	Individual & pool;	(Lee and Mabury, 2011)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
									0.06 0)					PFH xPA	
			10 P (>10/P)	100% 0.037 † (0.038- 0.057)	0% (<0.00 2)	100% 0.083 † (0.025- 0.16)			30% (<0. 01- 0.05 9)				100% 0.051 † (0.041 - 0.082)	: 0% (<0. 009) PFO PA: 0% (<0. 005) PFD PA: 0% (<0. 07)	
2009 S	25-42 (F)	Belgium, Antwerp	20	0% (<1.3)		0% (<1.4)			0% (<0. 78)				0% (<0.57)		(Petro et al., 2014)
2009 - 2019 P	20-29 (F,M)	Germany, Munster	100	0% (<0.25)	4% (<0.25- 1.1)	5% (<0.25- 0.31)	0% (<0.5)	0% (<0.5)	0% (<0. 5)		6% (<0.25 -0.42)		0% (<0.25)		(Gocke ner et al., 2020b)
2009 - 2010 S	32.3 Pregnant	Japan	399	0% (<0.25)	0% (<0.19)	6% (<0.15)	0% (<0.13)	0% (<0.14)	1% (<0. 08- 0.11)		3% (<0.14 -0.46)		0% (<0.13)		(Nakay ama et al., 2020)
2009	12-79	Canada	1524						0%						(Health

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
- 2011 P	(F,M)								(<0. 4)						Canada , 2013)
2010 - 2011 S	15-19	Norway, Troms arctic	940			75% 0.11 (<0.07-1.5)			3%	0% (<0.01)	98% 0.15 (<0.01 -7.6)	14% (<0.02 -1.2)	0%	PFD oDS : 0%	(Averin a et al., 2018)
2010 - 2011 S	18-80 (F)	Sweden	270			4.4% (<0.1-NR)									(Bjerm o et al., 2013)
2010 - 2012 Cord S	Newborns (F,M)	Slovakia, National	322	6% (<0.01- 0.019 ^{P95})	13% (<0.01- 0.04 ^{P95})	20% (<0.01- 0.09 ^{P95})			0.3 % (<0. 01- NR)				0% (<0.01)		(Richter ová et al., 2018)
2010 - 2013 S	20-46 Pregnant	France	100	0% (<0.38)	0% (<0.24)	0% (<0.24)			1% (<0. 2- NR)		50% 0.18 ‡ (<0.24 -0.8)		0% (<0.12)		(Cariou et al., 2015)
Cord S				0% (<0.38)	0% (<0.24)	0% (<0.24)			1% (<0. 2- NR)		25% (<0.24 - <0.4 ^{LOQ})		0% (<0.12)		
2010 - 2013	18-44 Pregnant	Greenland	209		0%	16% (<NR-0.26)			0%		87% 0.19 (0.06-		0%		(Long et al., 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFP As	Reference
S											1.44)				
2011 S	18-47 (pregnant)	France	277	0% (<0.6)	0% (<0.3)	0.4% (<0.24-NR)			0% (<0.3)		7% (<0.21-0.24 ^{P95})		0% (<0.3)		(Dereu meaux et al., 2016)
2006 - 2009 S	75 (F,M)	Sweden, Uppsala. (Repeated sampling at 75 & 80)	579			NR% 0.07 (<0.06-NR)									(Stuble ski et al., 2016)
2011 - 2014 S	80 (F,M)		579			63% 0.03 (<0.03-NR)									
2011 - 2014 S	Adults (F)	Greenland	158		0% (<0.06)	85% 0.14 (<0.02-NR)			0% (<0.02)		95% (<0.04-NR)		2% (<0.12-NR)		(Wielso e et al., 2017)
2011 S	13	Faroe Island	51	0% (<0.1)	0% (<0.05)	96% 0.06 (<0.03-NR)			0 (<0.1)		100% 0.19 (NR-NR)		12% (0.03-NR)		(Dassu ncao et al., 2018)
2012 S	5		51	4% (<0.1-NR)	0% (<0.05)	18% (<0.03-NR)			0 (<0.1)		92% 0.07 (<0.03-NR)		33% (0.03-NR)		
2012 S	Ref. group	China, Hubei province	9	0/9 (<0.05)	0/9 (<0.11)	0/9 (<0.03)			1/9 (<0.1-)						(Zhou et al., 2014)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refer ence
									NR)						
	Fishery employees		39	39/39 4.2	0/39 (<0.11)	5/39 (<0.03 -NR)			28/39 11.3 (<0.1 -NR)						
	Fishery family		7	7/7 0.87	0/7 (<0.11)	2/7 (<0.03 -NR)			2/7 (<0.1 -NR)						
2012 - 2015 S	18-39 (F)	Norway, Bergen	158			45%			37%	0%	96% 0.09 (<0.001 -0.41)	0%	0%		(Bjorke - Monsen et al., 2020)
2013 S	18±0.6 (F)	Sweden	104			0.03 (<0.01 - 0.16 ^{P95})	(<0.004 - 0.02 ^{P95})	(<0.009 - 0.04 ^{P95})	($<NR$ - 0.04 ^{P95})				0.02 (NR- 0.15 ^{P95})		(Jönsso n et al., 2014)
	18±0.6 (M)	Sweden	97			0.02 (<0.01 - 0.09 ^{P95})	(<0.004 - 0.01 ^{P95})	(<0.009 - 0.03 ^{P95})	0.01 ($<NR$ - 0.08 ^{P95})				0.02 ($<NR$ - 0.07 ^{P95})		
2013 - 2014	18-45 (F,M)	USA, Alaska	85	0% (<0.5 / <1)	0% (<0.5 / <1)	0% (<0.5 / <1)			0% (<0.5 / <1)						(Byrne et al., 2018)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
S									)						
2013 - 2014 S	20-66 (F,M)	Norway, Oslo	61		0% (<0.09)	13% (<0.045 - 0.34)			51% 0.04 (<0.009 - 0.2)		100% 0.2 (0.06- 0.63)		77% 0.06 (<0.002 - 0.17)	PFH xPA: 62% (<0.045 - 0.21) PFO PA: 15% (<0.009 - 0.03) PFD PA: 0% (<0.009)	(Pootho ng et al., 2017)
2013 - 2017 S	Primipara, 4 w. pp	Sweden, Uppsala	15 P (10/P)	2/15 (<0.004 - 0.22)	0% (<0.004)	2/15 (<0.025 - 0.031)	0% (<0.19)	0% (<0.026)	67% (<0.018 - 0.03 0)				0% (<0.033)		(Miaz et al., 2020)
2014	11-12	Sweden,	200			79%	0%	0%	2%				1%		(Glynn

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
S	(F,M)	6 cities				0.04 (<0.02- 0.25)	(<0.1)	(<0.1)	(<0. 1- 0.18)				(<0.1- 0.1)		et al., 2020)
2014 WB	20-42 (F,M)	Sweden, Ronneby Cont. drw	20	0% (<0.05/0.2 2)	0% (<0.02/ 0.4)	5% (<0.04/0.06 -0.13)	5% (<0.02- 0.03)	0% (<9.8)	5% (<0. 01- NR)	100% 4.3 † (<0.01 -13)	100% 16 † (NR- 56)	0% (<0.02)	0% (<0.01)	TFA: 5% PFet S: 15% PFP rA, PFP rS, PFD oDS , PFH xPA, PFO PA, PFD PA: 0%	(Aro et al., 2022)
2014 S	50-65 (F,M)	Belgium, Flanders	205						3% (<0. 2- 0.29						(Colles et al., 2020)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFP As	Reference
									)						
2013 - 2014 Cord S	Newborns	Belgium, Flanders	269						0% (<0.2)						
2005 /2006 S	1 (F,M)	Finland Repeated sampling at 1, 6 and 10 years	54			67% 0.46 (M) 0.51 (F) (<0.2 / <0.4 - 1.2)					0% (<0.35 / <0.54)		0% (<0.5 / <0.77)		(Koponen et al., 2018)
2010 /2011 S	6 (F,M)		54			4% (<0.2 / <1.0 - 0.37)					0% (<0.4 / <2.0)		0% (<0.4 / <2.0)		
2014 /2015 S	10 (F,M)		54			0% (<0.2)					0% (<0.2)		0% (<0.5)		
2014 - 2015 S	2-82	South Korea, Seoul, Busan	94		16% (<0.28 - 0.75)	26% (<0.09 - 0.28)			0% (<0.06)		77% 0.15 (<0.07 - 0.34)		0% (<0.09)		(Kim et al., 2019b)
2016 S	(F,M)	Sweden, Karlshamn Ref. group	51			73% 0.04 (<0.02 - 0.2 ^{P95})				NR% ($<LOD$ - 0.02)	NR% ($<LOD$ - 0.16)				(Xu et al., 2021b)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
2014 - 2015 S	(F,M)	Sweden, Ronneby 0.5-1.5 years after cont. drw	901			56% 0.06 (<0.05 - 0.8^{P95})									
2014 - 2016 S	18-74 (F,M)	France	744	1% (<0.5 -NR)	0% (<0.05)	3% (<0.2 -NR)			0% (<0.19)		53% 0.18 † (<0.19 - 0.48^{P95})		0% (<0.19)		(Fillol et al., 2021)
	6-17 (F,M)	France	249						0% (<0.19)		3% (<0.19 -NR)		0.4% (<0.19)		
2014 - 2017 P	3-17 (F,M)	Germany, National	1109	0% (<1)	0% (<0.25)	1% (<0.25 - 0.67)			0% (<0.25)						(Duffek et al., 2020)
2015 S	20-45 (F,M)	UK, Hull	59	0% (<0.5)	49% (<0.5 - 2.0)	17% (<0.1 - 0.7)			7% (<0.2 - 0.46)				0% (<0.5)		(Heffer nan et al., 2018)
2015 S	18-76 (F,M)	Belgium, Liege	242		0% (<0.1)	21% (<0.1 - 0.65)			0% (<0.1)						(Pirard et al., 2020)
2015 S	18-65 (F,M)	Czech Republic, 4 cities	300	0% (<0.013)	0% (<0.013)	45% (<0.013 - 0.52)			20% (<0.006 -				2% (<0.006 -		(Sochor ova et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFP As	Reference
									0.05 7)				0.24)		(2017)
2015 S	1-87 (F,M)	China, Fuxin Area near PFBS, PTFE factory	100						100 % 0.14 (<0.05- 1.5)						(Bao et al., 2017)
2015 - 2016 S	20-51 (F,M)	Italy, Veneto Ref. group	250	17% (<NR- 0.35)	40% (<NR- 0.22)	66% (<NR-0.26)			18% (<LO Q- 0.36)						(Ingelido et al., 2018)
	20-51 (F,M)	Italy, Veneto Cont. drw	257	7% (<NR-3.6)	26% (<NR- 0.46)	51% (<NR-0.42)			31% (<LO Q- 4.3)						
2015 - 2017 S	Farmers 20-51	Italy, Veneto Cont. drw.	122			54% 0.06 (<NR- 1.4)									(Ingelido et al., 2020)
2015 - 2016 S	62±14 (F,M)	China, Shenyang	1228	88% 1.49 (<0.008- NR)	25% (<0.01 8-NR)	80% 0.02 (<0.0016- NR)			23% (<0.009- NR)	23% (<0.003- NR)	99.8% (<0.002- NR)	4% (<0.006- NR)	27% (<0.004- NR)		(Yu et al., 2021c)
2015 -	24-41 pregnant	China, Beijing	117								55% 0.16	4% (<0.1-			(Li et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
2016 S											(<0.1- NR)	NR)			2020c)
2015 - 2016 Cord S		China, Beijing	117								67% 0.18 (<0.1- NR)	4% (<0.1- NR)			
2016 S	NR (NR)	US	50	0% (<0.1)	0% (<0.1)	2% (<0.1-0.1)			0% (<0.1)		96% 0.3 (<0.1- 1.0)			PFP rS: 0% (<0.1)	(Kato et al., 2018)
2016 S	6-11 (F,M)	Italy, Sicily	61	22% (<0.1- 0.22)	3% (<0.1- 0.29)	8% (<0.1-0.29)			0% (<0.2)		50% (<0.1- 0.39)		0% (<0.2)		(Ledda et al., 2018)
2016 S		Germany, Munich	158						0% (<0.25)						(Fromm e et al., 2018)
2016 - 2017 P	3-79 (F,M)	Canada, National	2590	4% (<0.07- NR)											(Health Canada , 2019)
2016 - 2017	16-40 Pregnant	Canada, Nunavik	97	0%					0%						(Caron- Beaudoin et al., 2020)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
2016 - 2017 S	25-72 (F,M)	Norway, Oslo & Akershus	142		19% (<0.09 - 0.20^{P95})	59% 0.13 ¥ (F) 0.15 ¥ (M) (<0.045 - NR)			68% 0.08 ¥ (F) 0.11 ¥ (M) (<0.009 - NR)		100% 0.14 ¥ (F) 0.27 ¥ (M)		90% 0.03 ¥ (F) 0.05 ¥ (M) (<0.002 -NR)	PFHxPA : 52% 0.05 ¥ (<0.04 - NR) PFOPA : 0% (<0.009) PFDPA : 0% (<0.009)	(Thépa ut et al., 2021)
2014 - 2015 S	0-60+ (F,M)	Australia	2400 in 24 P	57% (<0.08 - NR)	0% (<0.05)	36% (<0.06 -NR)			11% (<0.08 - NR)	0% (<0.08)	61% (<0.13 -NR)	0% (<0.13)	0% (<0.1)	PFD oDS : 0% (<0.21)	(Toms et al., 2019)
2016 - 2017 S	0-60+ (F,M)	Australia	2400 in 24 P	14% (<0.08 - NR)	0% (<0.05)	32% (<0.06 -NR)			11% (<0.08 - NR)	0% (<0.08)	61% (<0.13 -NR)	0% (<0.13)	0% (<0.1)	PFD oDS : 0% ($<0.$)	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
														21)	
2016 - 2017 S	10-21 (F,M)	Sweden, 7 citites	1098			11% (<0.02/<0. 1-0.60)	0.5% (<0.02/ <1.5- 0.095)	0.4% (<0.31/ <0.86- 8.5)		2.8% (<0.04 /<0.2- 1.9)	9.5% (<0.02 /<0.1- 5.8)	0% (<0.02 /<3.3)	0% (<0.08 /<0.6)	PFPeDA : 0.4 % (<0. 02- 0.36) PFUnDS : 0% (<0. 02- 3.4)	(Nystro m et al., 2022)
2017 S	19-87 (F,M)	China, Tianjin	252	86% 0.6 (<0.015- NR)	30% (<0.44- NR)	67% 0.11 (<0.013- NR)			17% (<0. 012- NR)				0% (<0.00 5)	TFA: 97% 8.5 (<0. 12- NR) PFP rA: 77% 0.48 (<0. 07-	(Duan et al., 2020)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFBs	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFP As	Reference
														NR)	
2017 S	Adults	China, Wuhan Ref. group	15	60% 0.18 † (<0.013- 0.64)	20% (<0.02- 0.17)		0% (<0.03)	0% (<0.03)	100% 1.3 † (NR- 7.2)	0% (<0.02 1)	33% (<0.02 3-0.11)	0% (<0.02 3)	0% (<0.02 2)	PFDoDS : 0% (<0. 025) PFHxPA : 0% (<0. 05) PFOPA : 0% (<0. 02)	(Gao et al., 2018)
		China, Wuhan Workers at FCM	15	100% 8.2 † (2.1-63)	40% (<0.02- 3.1)		13% (<0.03- 0.36)		100% 101 † (1.4- 340)	33% (<0.02 1-0.23)	53% 2.3 † (<0.02 3-10.9)	0% (<0.02 3)	33% (<0.02 2-0.17)	PFDoDS : 0% (<0. 025) PFHxPA : 0% (<0. 05) PFOPA : 0%	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam- ple	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth- er PFC As/ PFS As/ PFP As	Refere- nce
														0% (<0.02)	
2017 P	30-57 (F,M)	Germany, Berlin	72						0% (<0.25)						(Menzel et al., 2021)
2017 - 2018 S	14-15 (F,M)	Belgium, Flanders	410		0% (<0.2)	1.2% (<0.2 -NR)			0% (<0.2)		2.4% (<0.2 -NR)				(Luys, 2021)
2008 - 2009 S	30-44 (F)	USA, NC Ref. group	20			0% (<0.3)									(Kotlarz et al., 2020)
2017 - 2018 S	6-86 (F,M)	USA, Wilmington (NC) Cont. drw	344	5.5% (<0.8 -3.2)	12% (<3.9 -~39)	63% 0.3 (<0.3 -1.3)			7% (<1.5 -4.1)						
2017 - 2019 S	21-45 Primipara	Sweden, Uppsala	110	0% (<0.04)	0% (<0.04)	4% (<0.08 -0.2)	0% (<1.15)	0% (<3.9)	1% (<0.072 -0.08)	26% (<0.08 -0.43)	43% (<0.078 -0.29)		0% (<0.08)	PFU nDS : 0% (<0.08)	(Gyllen- hamma r et al., 2020)
2017 - 2019 S	Mothers	Austria, 3 areas	136	0%	0%	3% ($<LOD$ -0.17)			0%		0%		0%		(Kaiser, 2021)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFP As	Reference
2017 - 2019 Cord S		Austria, 3 areas	136	0%	0%	6% (<LOD- 0.19)			0%)		0%		0%		
2017 - 2019 S	Pregnant (sampling at delivery)	Austria, 3 areas (samples with highest PFAS- levels out of 136 samples)	54 in 21P	0% (<0.07)	0% (<0.03)	14/21 0.017 (<0.06- 0.09)			19/2 1 0.00 8 (<0. 005- 0.02 2)	16/21 0.005 (<0.00 5- 0.032)	21/21 0.043 (0.02- 0.16)	0% (<0.00 8)	0% (<0.00 5)	PFH xPA : 0% (<0. 01)	(Kaiser et al., 2021a)
Cord S			27 in 11P	0% (<0.07)	0% (<0.03)	10/11 0.022 (<0.06- 0.07)			9/11 0.00 6 (<0. 005- 0.01)	9/11 0.003 4 (<0.00 5- 0.008)	9/11 0.017 (<0.00 5- 0.037)	0% (<0.00 8)	0% (<0.00 5)	PFH xPA : 0% (<0. 01)	
2017 - 2019 S	14-39 (F,M)	Italy,Veneto Cont. drw	18122	2% (<0.5-24)	0.1% (<0.5- 1.3)	1.4% (<0.5-15)			3% (<0. 5- 8.9)						(Pitter et al., 2020a)
2018 S	7-85 (F,M)	Germany, Altötting Cont. drw	906						16% (<0. 25- 0.98						(Fromm e et al., 2018)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
									)						
2018 S	19-93 (F,M)	USA, El Paso County. Cont. drw 2012-15	213	0% (<0.1)	0% (<0.1)	9% (<0.1-NR)			0.5 % (<0.1- NR)		83% 0.2 (<0.1- NR)				(Barton et al., 2020)
2018 S	14-79 (F,M)	USA, Bladen county. Area near FCM. bottled water last 4-14 months.	30	0% (<0.1)	0% (<0.1)	NR% (<0.1-0.6)			0% (<0.1)						(NCDH HS, 2018)
2018 S	22-62 (F,M) airport workers	Sweden, Arvidsjaur Cont. drw	26			100% 0.46 (0.07-2.2)			81% 0.33 (<0.05- 1.3)	100% 6.9 (1.4-17)	100% 1.3 (0.28-6.2)				(Xu et al., 2020c))
2018 WB	11-79 (F,M)	Sweden, 5 areas	148	3% (<0.22- 0.22)	2% (<0.04- 0.29)	1% (<0.06- 0.07)	9% (<0.02- 0.28)	0% (<9.8)	27% (<0.019- 0.11)	49% (<0.01- 0.26)	99% 0.20- 0.37 (<0.01- 2.5)	0% (<0.02)	0% (<0.01)	TFA : 62% PFP rA : 22% PFEt S : 49% (<NR- 0.04	(Aro et al., 2021c)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxD A	PFOcD A	PFB S	PFPeS	PFHpS	PFNS	PFDS	Oth er PFC As/ PFS As/ PFP As	Refere nce
														) PFP rS: 1% (<N R- 0.09) PFD oDS : 0% (<0. 02) PFH xPA : 1% (<0. 05- 0.09) PFO PA: 0% (<0. 21) PFD PA: 0% (<0.	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFP As	Reference
														011)	
2018 - 2019 S	(F)	China, Beijing	28			75% 0.011 (<0.003- 2.0)			29% (<0. 007- 0.01 2)						(Kang et al., 2020)
2018 - 2019 S	18-65 (F,M)	Czech Republic	395			44% (<0.027- 0.15)			4% (<0. 027- 0.03 5)						(SZU, 2021)
2019 - 2020 S	Adults (F,M)	Czech Republic, 4 cities	242			17% (<0.50- 0.49)			28% (<0. 11- 3.1)						(SZU, 2021)
2019 - 2020 S	0-96 (F,M)	China, Huantai Area near FPP	977	99.4% 0.53 ¥ (<0.05-15)	0% (<0.07)	99.9% 0.38 ¥ (<0.01-11)			55% 0.01 0 ¥ (<0. 01- 0.16)		99,8% 0.14 ¥ (<0.01 -4.6)				(Yao et al., 2020)
NR year S	17-80 (F,M)	USA, Kentucky	100			59% 1.0 (<0.05- 2.3)			7% (<0. 05- 2.7)						(Mottal eb et al., 2020)
NR	1-91	China,	1516	31%	5%	41%			19%						(Jin et

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age (gender)	Country, area	N	PFBA	PFPeA	PFHpA	PFHxDA	PFOcDA	PFB S	PFPeS	PFHpS	PFNS	PFDS	Other PFC As/ PFS As/ PFPA s	Reference
year S	(F,M)	7 cities		(<0.06- 6.3)	(<0.09- 0.60)	(<0.03-2.0)			(<0. 05- 1.6)						al., 2020b)
2021 S	>12 (F,M)	Belgium, Zwijndrecht <3km from 3M facility	796	4.5% (<0.2-NR)	0% (<0.2)	11% (<0.2- 0.53 ^{P95})			2.6 % (<0. 2- NR)		30% (<0.2- 1.0 ^{P95})				(VITO and PIH, 2021)

‡ Arithmetic mean, ¥ Geometric mean, § Mean per area.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.92. Serum (S), plasma (P) or whole blood (WB) concentrations (ng/mL) of PFAEs , cyclic PFAS and precursors that are not covered by existing or proposed restrictions, described by detection frequency (% or x/xx), median (bold) and range (within brackets) . Note that the levels of whole blood are not comparable to plasma/serum. Grey cells indicate sampling sites near known PFAS point sources. NR=not reported, P95=95th percentile, w pp=weeks postpartum; P=pool; cont. drw =contaminated drinking water, FPP= fluoropolymer production plant, FCM=fluorochemical manufacturing facility, ref=reference area.

Year Sam ple	Age (gen der)	Country , area	N	6:2 Cl- PFESA	8:2 Cl- PFESA	ADON A	HFP O- DA	PFECH S	C6/C 6 PFPIA	3:3 FTC A	4:2 FTSA /FTS	Other PFASs	Reference
1982 - 2009 S	20- 29 (F,M)	Germany , Munster, Halle	32 0									4:2/4:2 diPAP: 40% (<0.0007-0.095)	(Yeung et al., 2013c)
1996 - 2017 S	Primi para, 4 w. pp	Sweden, Uppsala	57 P (5- 25 /P)	5% (<0.01- 0.017)	0% (<0.09)	0% (<0.00 4)	0% (<0. 72)	NR% (0.06- 0.28)			0% (<0.0 01)	3:3 FTA (FPrPA): 0% (<0.34)	(Miaz et al., 2020)
1997 - 2012 S	20- 42 Primi para, 4 w pp	Sweden, Uppsala	27 P (1 0/ P)									4:2 monoPAP: 0% (<0.3) 4:2/4:2 diPAP: 0% (<0.001)	(Gebblink et al., 2015)
2009 - 2019 P	20- 29 (F,M)	Germany , Munster	10 0	0% (<0.25)	0% (<0.25)	0% (<0.25)	0% (<0. 25)	0% (<0.25)			0% (<0.5)	7H-PFHpA: 0% (<0.5%)	(Gockener et al., 2020b)
2009, 2015 P	Adults (F,M)	Germany Near FPP	86			9% (<0.2- 14.4)							(Fromme et al., 2017)
		Germany 80 km from FPP	110			16% (<0.2- 0.7)							
2014 , 2016	Adult s (F,M)	Germany ,Munich Ref.	20 0			0% (<0.2)							

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam- ple	Age (gen- der)	Country , area	N	6:2 Cl- PFESA	8:2 Cl- PFESA	ADON A	HFP O- DA	PFECH S	C6/C 6 PFPIA	3:3 FTC A	4:2 FTSA /FTS	Other PFASs	Reference
P		group											
2014 WB	20-42 (F,M)	Sweden, Ro- nneby Cont. drw	20	0/20 (<0.01)	0/20 (<0.01)	0/20 (<0.02)	0/20 (<0.02 - 2)	3/20 (<0.01 - 0.06)	0%	0/20 (<0.0 5)	0/20 (<0.005)	FBSA: 0% (<0.015 / <0.03) MeFSBA: 0% (<0.21)	(Aro et al., 2022)
2016 - 2017 S	10- 21 (F,M)	Sweden, 7 cities	10 98	5.4% (<0.005 / <0.06 - 1.2)	0.6% (<0.06 / <0.03 - 0.03)	0.1% (<0.02 / <3.6 - 0.07)				0% ($<0.$ 1/ $<$ 12)	0.1% (<0.0 6- 0.56)		(Nystrom et al., 2022)
2017 P	30- 57 (F,M)	Germany , Berlin	72			0% (<0.25)							(Menzel et al., 2021)
2017 - 2019 S	21- 45 Primi para	Sweden, Uppsala	11 0	1% (<0.08 - 0.2)	0% (<0.14)	0% (<0.08)	0%				0% (<0.0 8)	3:3 FTA (FPrPA): 0% (<0.29)	(Gyllenhammar et al., 2020)
2017 - 2019 S	Preg nant (at deliv ery)	Austria, 3 areas (samples with highest	54 in 21 P	0% (<0.000 2/ <0.004)	0% (<0.000 4/ <0.006)	11/21 0.006 (<0.00 06/ <0.01 - 0.074)		16/19 0.003 ($<NR$ - 0.011)	0% (<0.0 02- 0.04)	0% ($<0.$ 002/ $<0.$ 02)	0% (<0.0 002/ <0.00 4)	FBSA: 0% (<0.001 / <0.02) MeFBSA: 0% (<0.008 / <0.12)	(Kaiser et al., 2021a)
Cord S		PFAS- levels out of 136 samples)	27 in 11 P	0% (<0.000 2/0.004)	0% (<0.000 4/0.006)	8/11 0.008 (<0.00 06/ <0.01 - 0.027)		9/11 0.002 ($<NR$ - 0.007)	0% (<0.0 02- <0.04)	0% ($<0.$ 002/ $<0.$ 02)	0% (<0.0 002/ <0.00 4)	FBSA: 0% (<0.001 / <0.02) MeFBSA: 0% (<0.008 / <0.12)	
2018 WB	11- 79 (F,M)	Sweden, 5 areas	14 8	12% (<0.01 - 0.02)	0% (<0.01)	16% (<0.02 -0.04)	0% ($<0.$ 022)	80% 0.02 † (<0.01 -0.11)	0%	0% ($<0.$ 05)	0% (<0.0 05)	FBSA: 2% (<0.015 / <0.03 - 0.05) MeFBSA: 0% (<0.21)	(Aro et al., 2021c)
2018	7-85	Germany,	906			0.3%							(Fromme et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam- ple	Age (gen- der)	Country , area	N	6:2 Cl- PFESA	8:2 Cl- PFESA	ADON A	HFP O- DA	PFECH S	C6/C 6 PFPIA	3:3 FTC A	4:2 FTSA /FTS	Other PFASs	Reference
S	(F,M)	Altötting Cont. drw				(<0.25- 1.0)							(2018)
2016 S	NR	Germany , Munich (ref)	15 8			0% (<0.25)							
2014 - 2015 S	0- 60+ (F,M)	Australia	24 00 in 24 P					0% (<0.06)			0% (<0.1 0)		(Toms et al., 2019)
2016 - 2017 S			24 00 in 24 P					0% (<0.06)			0% (<0.1 0)		
2009 S	18- 70 (F,M)	USA	40						50% (<0.0 01- 0.05)		10% (<0.0 05- 0.018)	4:2 diPAP: 12% (<0.008-0.022)	(Lee and Mabury, 2011)
			10 P (> 10 /P)						90% (<0.0 01- 0.05)		0% (<0.0 05)	4:2 diPAP: 0% (<0.008)	
2008 - 2009 S	30- 44 (F)	USA, North Carolina Ref. group	20									Nafion by-prod.2: 0% (<0.1) PFO4DA: 0% (<0.1) PFO5DoA: 0% (<0.1)	(Kotlarz et al., 2020)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gen der)	Country , area	N	6:2 Cl- PFESA	8:2 Cl- PFESA	ADON A	HFP O- DA	PFECH S	C6/C 6 PFPIA	3:3 FTC A	4:2 FTSA /FTS	Other PFASs	Reference
2017- 2018 S	6-86 (F,M)	USA, Wilmington (NC) Cont. drw	344				0% (<2)					Nafion by-prod.1: 0.3% (<0.1-0.4) Nafion by-prod.2: 99% 2.7 (<0.1-8.4 ^{P95}) PEPA: 9.6% (<0.1/0.5-2) PMPA: 0.3% (<0.4/1.5-1.5) PFO2HxA: 0.3% (<0.5/5.8-1.9) PFO3OA: 28% (<0.1/1.3-3.7) PFO4DA: 99% 2.5 (<0.1-12.8 ^{P95}) PFO5DoA: 88% 0.3 (<0.1-1 ^{P95}) NVHOS: 15% (<0.1/0.2-4.6)	
NR year S	17- 80 (F,M)	USA, Kentuck y	10 0				0% (<0. 05)				0% (<0.0 5)		(Mottaleb et al., 2020)
2016 S	NR	USA	50	0% (<0.1)		0% (<0.1)	0% (<0. 1)						(Kato et al., 2018)
2018 S	14-79 (F,M)	USA, Bladen county, Area near FCM. Bottled water last	30	0% (<0.1)		0% (<0.1)	0% (<0.1)						(NCDHHS, 2018)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gen der)	Country , area	N	6:2 CI- PFESA	8:2 CI- PFESA	ADON A	HFP O- DA	PFECH S	C6/C 6 PFPIA	3:3 FTC A	4:2 FTSA /FTS	Other PFASs	Reference
		4-14 months.											
2018 S	19-93 (F,M)	USA, El Paso County. Cont. drw 2012-15	213	0% (<0.1)		0% (<0.1)	0% (<0.1)						(Barton et al., 2020)
NR year S		China, Shandong Metal plating workers	19	100% 51.5 (2.0- 5040)	100% 1.6 (0.37- 90.7)							10:2 CI-PFESA: 0% (<0.045)	(Shi et al., 2016)
		China, Hubei fresh water fish consumer s	45	100% 93.7 (2.0-357)	NR 1.6 (<0.04- 3.4)							10:2 CI-PFESA: 0% (<0.045)	
		China, Wuhan, Hubei (ref)	8	100% 4.8 (1.9- 5.9)	100% 0.08 (0.04- 0.10)							10:2 CI-PFESA: 0% (<0.045)	
NR S	1-91 (F,M)	China, 7 cities	15 16	98% 2.2 (<0.04- 500)	13% (<0.05- 67.5)							10:2 CI-PFESA: 0.3% (<0.07-3.3)	(Jin et al., 2020b)
2015 - 2016 S	27.1 ±2.8 Preg nant	China, Wuhan	32	100% 1.5 (0.23- 4.4)	84% 0.01 (<0.004 -0.21)								(Chen et al., 2017b)
Cord S			32	100% 0.6	81% 0.01								

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam- ple	Age (gen- der)	Country , area	N	6:2 Cl- PFESA	8:2 Cl- PFESA	ADON A	HFP O- DA	PFECH S	C6/C 6 PFPIA	3:3 FTC A	4:2 FTSA /FTS	Other PFASs	Reference
				(0.1- 2.6)	(<0.004 -0.08)								
2015 - 2016 S	24- 41 Preg nant	China, Beijing	11 7	98% 3.6 (<0.1- NR)	31% (<0.1- NR)								(Li et al., 2020c)
Cord S			11 7	96% 1.6 (<0.1- NR)	29% (<0.1- NR)								
2015 - 2016 S	61.8 ±14. 4 (F,M)	China, Shenyan g	12 28	100% 1.75	69% 0.01		1.2%				0.5%		(Yu et al., 2021c)
2016 S	53 (mean) (F,M)	China, Huntai Near FPP	48	100% 4.2 (0.01- 9.9 ^{P95})	100% 0.06 (0.01- 0.2 ^{P95})		37% (<0.14 -1.7 ^{P95})					4:2 Cl-PFESA: 98% 0.04 (<0.01-0.1 ^{P95}) HFPO-TA: 98% 2.9 (<0.1-53 ^{P95})	(Pan et al., 2017)
2017 S	19- 87 (F,M)	China, Tianjin	25 2	100% 8.6	70% 0.06	17%		2%					(Duan et al., 2020)
2017 S	Workers at FCM	China, Wuhan	15	93% 0.42 † (<0.026- 1.4)	13% (<0.038- 0.31)				13% (<0.017 -0.09)		20% (<0.031 -0.08)		(Gao et al., 2018)
	Adult s ref. grou p	China, Wuhan	15	60% 0.22 † (<0.026 -0.31)	0% (<0.038)				0% (<0.0 17)		0% (<0.0 31)		
2018 - 2019	Adult s (F)	China, Beijing	28	100% 1.6 (0.45-	100% 0.017 (0.005-							HFPO-TA: 25% (<0.05-0.48)	(Kang et al., 2020)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sam ple	Age (gen der)	Country , area	N	6:2 Cl- PFESA	8:2 Cl- PFESA	ADON A	HFP O- DA	PFECH S	C6/C 6 PFPIA	3:3 FTC A	4:2 FTSA /FTS	Other PFASs	Reference
S				4.3)	0.10)								
2019 - 2020 S	0-96 (F,M)	China, Huantai Near FPP	97 7	100% 2.2 ¥ (0.06- 29.9)	70% 0.03 ¥ (<0.02- 1.8)		8% (<0. 05- 0.65)					4:2 Cl-PFESA: 4.5% (<0.01-1.4) Nafion by-prod. 2: 99% 0.095 ¥ (<0.01-24) HFPO-TA: 99% 1.8 ¥ (<0.05-429) PF4OPeA/PFMPA: 17% (<0.01-0.38) PF5OHxA / PFMBA: 0% (<0.02) PFMOAA: 100% 12.7 ¥ (0.42-158) PFO2HxA: 70% 0.033 ¥(<0.01-12) PFO3OA: 30% (0.05-5.9) PFO4DA: 96% 0.14 ¥ (<0.02-3.4) PFO5DoA: 100% 0.98 ¥ (0.03-43) 3,6-OPFHpA: 0% (<0.02)	(Yao et al., 2020)

† Arithmetic mean, ¥ Geometric mean

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.93. Breast milk concentrations (ng/mL) of PFASs (PFAAs, precursors, PFAEs and PFECs) that are not covered by existing or proposed restrictions, described by detection frequency (% or x/xx), median (bold) and range (within brackets). Grey cells indicate sampling sites near known PFAS point sources. P95=95th percentile, w pp=weeks postpartum, P=pool.

Year	Sampling	Country, area	N	PFBA	PFPeA	PFHpA	PFBS	PFHpS	PFDS	ADONA	6:2 Cl-PFESA	8:2 Cl-PFESA	Other PFASs	Reference
2004,2007,2009,2011	Primipara	Sweden, Uppsala	50		0% (<0.03)	12% (<0.015-0.02)	20% (<0.4-0.39)		0% (<0.009)					(Kärman et al., 2013)
2007		France	48	17% (<0.07-0.13)	0% (<0.07)	2% (<0.07-0.074)	0% (<0.07)	0% (<0.07)						(Antignac et al., 2013)
2007	Primipara 5-9 w pp	Spain, Catalonia	10			0% (<0.02)	0% (<0.02)							(Karrman et al., 2010)
2008	40 w pp	Spain, Barcelona	20						6/20 (<0.004-0.07)					(Llorca et al., 2010)
2010		Czech Republic	50	0% (<0.02)	0% (<0.02)	0% (<0.006)	0% (<0.006)		0% (<0.006)					(Lankova et al., 2013)
2010		France	30	1/30 (<0.01-NR)	0% (<0.002)	0% (<0.01)	0% (<0.001)	0% (<0.001)						(Kadar et al., 2011)
2010-2013	<1 w pp	France	61	0% (<0.04)	0% (<0.04)	0% (<0.04)	0% (<0.04)	0% (<0.03)	0% (<0.04)					(Cariou et al., 2015)
2010-2013	6 w pp	Slovakia	238	2.5% (<0.01-NR)	28% (<0.01-0.16 ^{P95})	1.7% (<0.01-NR)			0% (<0.005)					(HBM4EU, 2022)
2012	Primipara. 18 month pp (mean)	Spain, Valencia	10	100% 0.035 (0.006-0.15)	0% (<0.0006)	7/10 0.067 (<0.0003-0.7)	2/10 (<0.0006-0.009)	3/10 (<0.0006-0.45)	1/10 (<0.0001-0.025)				PFHxDA: 0% (<0.0001) PFOcDA: 0% (<0.0001)	(Lorenzo et al., 2016)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year	Sampling	Country, area	N	PFBA	PFPeA	PFHpA	PFBS	PFHpS	PFDS	ADONA	6:2 Cl-PFESA	8:2 Cl-PFESA	Other PFASs	Reference
2016	2-14 w pp	Sweden, Stockholm	10			1/10 ($<0.01-0.011$)	7/10 ($<0.001-0.021$)		1/10 ($<0.001-0.003$)	0% (<0.003)	0% (<0.002)	0% (<0.002)		(Awad et al., 2020)
2016	Primipara 3-8 w pp	Ireland	92 in 16P				0% (<0.1)							(Abdallah et al., 2020)
2017	Primipara 2-8 w pp	Czech Republic	232	0% (<0.006)	0% (<0.006)	0% (<0.003)	1.3% ($<0.003-NR$)		0% (<0.03)	0% (<0.015)	0% (<0.015)	0% (<0.015)	HFPO-DA: 0% (<0.015)	(Cerna et al., 2020)
2019	Primipara	USA, Seattle	50		0% (<0.0007)	98% 0.006 ($<0.0002-0.046$)	0% (<0.003)	74% 0.001 ($<0.0003-0.007$)	4% ($<0.001-0.001$)				PFPeS: 8% ($<0.0001-0.002$) PFNS: 58% 0.0004 ($<0.0003-0.001$) 4:2 FTS: 14% ($<0.0006-0.035$) PFHxDA, PFPrS, PFECHS, 4:2 FTOH, 8Cl-PFOS: 0%	(Zheng et al., 2021)
2013		South Korea	264		82% 0.05	67% 0.03	42%		40%					(Kang et al., 2016)
2010-2016		China	30			10% ($<0.01-0.017$)	43% ($<0.003-0.011$)		0% (<0.002)	27% ($<0.003-0.008$)	100% 0.09 ($0.017-0.98$)	60% 0.003 ($<0.002-0.09$)		(Awad et al., 2020)
2018-2019	1 w pp	China, Hangzhou	174	63% 0.003 ($<0.003-0.11$)	68% 0.002 ($<0.002-0.02$)	0% (<0.003)	0.6% ($<0.01-0.03$)				100% 0.016 ($0.008-0.20$)	20% ($<0.001-0.014$)		(Jin et al., 2020a)

‡ Arithmetic mean, ¥ Geometric mean

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Table B.94. Concentrations of PFAAs in urine, follicular fluid, semen and cerebrospinal fluid (ng/mL) and hair, nail, placenta and internal organs (ng/g) that are not covered by existing or proposed restrictions, described by detection frequency (% or x/xx), median (bold) and range (within brackets). Grey cells indicate sampling sites near known PFAS point sources. P=pool, FCM=fluorochemical manufacturing facility

Year Sample	Age Gender	Country, Area	N	PFBA	PFPeA	PFHpA	PFBS	PFPeS	PFHpS	PFDS	Other PFCA/PFSA/PFPA	Reference
2010 Urine	20-88 (F,M)	China, Handan & Shijiazhuang	86			67% 0.0008 (<0.0002-0.019)						(Zhang et al., 2013d)
2012 Urine	5-13	South Korea, Dae-gu	120	0% (<0.17)	70% 0.35† (<0.22-12)	36% (<0.12-4.4)	1% (<0.11-0.49)		0% (<0.11)	0% (<0.14)		(Kim et al., 2014)
	22-77		57	1% (<0.17-1.7)	25% (<0.22-17.6)	7% (<0.12-1.1)	0% (<0.11)		0% (<0.11)	0% (<0.14)		
2012 Urine	Reference group	China, Hubei	9	7/9 0.054	9/9 0.35	1/9	1/9					(Zhou et al., 2014)
	Fishery employees		39	39/39 0.94	39/39 1.1	29/39 0.016	36/39 1.6					
	Fishery family		7	7/7 0.29	7/7 0.22	4/7 0.012	4/7 0.25					
2013-2014 Urine	>6 (F,M)	USA, National	2682	13% (<0.1-3.4)	0% (<0.1)	1.1% (<0.1-0.3)	0% (<0.1)		<0.1% (<0.1-0.1)			(Calafat et al., 2019)
2014-2015 Urine	2-82	South Korea, Seoul & Busan	94		84% 1.7 (<0.13-9.3)	4% (<0.041-0.06)	2% (<0.058-0.064)		9% (<0.056-0.077)	0% (<0.12)		(Kim et al., 2019b)
Hair (matche					59% 0.42	30% (<0.41-	0% (<0.80)		0% (<0.28)	2% (<0.42-		

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age Gender	Country, Area	N	PFBA	PFPeA	PFHpA	PFBS	PFPeS	PFHpS	PFDS	Other PFCA/PFSA/PFPA	Reference
d)					(<0.36-2.3)	1.0)				7.4)		
2015 Urine	3-68 (F,M)	China, Shijiazhuang	41	98% 0.016 (<0.00003-0.05)	93% 0.014 (<0.00002-0.06)	95% 0.0042 (<0.00001-0.02)	95% 0.014 (<0.000007-0.04)					(Wang et al., 2018b)
Hair (matched)				34% (<0.09-3.8)	10% (<0.11-6.9)	17% (<0.03-2.9)	63% 0.24 (<0.012-2.7)					
Nails (matched)				0% (<0.22)	0% (<0.34)	0% (<0.019)	85% 0.80 (<0.05-3.2)					
2016 Urine	25-46 (F,M)	Austria	11		8/11 0.003 † (<0.0005-0.008)	10/11 0.0004 † (<0.0002-0.001)			0% (<0.0003)	0% (<0.0003)		(Hartmann et al., 2017)
2016 Urine	NR	USA	50	56% 0.2 (<0.1-0.8)	0% (<0.1)	0% (<0.1)	0% (<0.1)		0% (<0.1)		PFPrS: 0% (<0.1)	(Kato et al., 2018)
2017-2018 Urine	4-6 (F,M)	Hong Kong	53			75% 0.0006 (<0.00001-0.013)						(Li et al., 2021c)
Hair (matched)			27			70% 0.023 (<0.002-0.080)						
2018 Urine	14-79 (F,M)	USA, Bladen county	30	0% (<0.1)	0% (<0.1)	0% (<0.1)	0% (<0.1)					(NCDHHS, 2018)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age Gender	Country, Area	N	PFBA	PFPeA	PFHpA	PFBS	PFPeS	PFHpS	PFDS	Other PFCA/PFSA/PFPA	Reference
		(NC) Near FCM. Bottled water last 4-14 months.										
2018 Urine	24-61 (F,M) Airport workers	Sweden, Arvidsjaur Cont. drw	17			0.025 (<0.01-0.08)		100% 0.072 (0.021-0.12)				(Xu et al., 2020c)
2019 Urine	8-12 (F,M)	China, Shainghai	189			99.5% 0.046 (<0.005-1.0)	87% 0.021 (<0.012-0.062)			0% (<0.01)		(Li et al., 2021a)
2019-2021 Urine	6-10 (F, M)	Austria	85		96% 0.0035 (<0.0005-0.037)	99% 0.0015 (<0.0002-0.007)		1.2% (<0.0004-0.0014)	0%	0%	PFNS: 0%	(Kaiser, 2021)
2020 Urine	50.3±9.65 (F,M)	China, Shanxi & Shandon g	80			12% (<0.02-NR)	44% (<0.01-NR)					(Ji et al., 2021)
2009 Hair	19-26 (F,M)	China, Guangdo ng	49		40% (<0.41-18)	44% (<0.022-12)						(Liu et al., 2020a)
2013 Hair	NR	Belgium	30	77% 0.21 † (<0.019-1.5)	30% (<0.017-0.086)	0% (<0.017)	100% 0.055 † (0.03-0.12)	0% (<0.008)	0% (<0.004)	3% (<0.006-0.03)	PFDoDS: 63% 0.046† (<0.003-0.091)	(Alves et al., 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age Gender	Country, Area	N	PFBA	PFPeA	PFHpA	PFBS	PFPeS	PFHpS	PFDS	Other PFCA/PFSA/PFPA	Reference
											PFNS: 0% (<0.015)	
2017-2018 Hair	16-85 (F,M)	India, 14 cities	39	15% (<0.1/0.4-0.59)	0% (<0.4/1-7)	0% (<0.1/0.4)	21% (<0.02/0.08-0.23)			31% (<0.19/0.83-1.2)	PFocDA, PFHxDA, PFEtS & PFPrS: 0% (<0.02/<0.09)	(Ruan et al., 2019)
NR Hair	NR	Spain, Seville	6	0/6 (<3.2)	3/6 (<0.9-13)	5/6 1.9 (<0.2-10)						(Martin et al., 2016)
NR Hair	4-90 (F,M)	Spain, Seville	42	14% (<1.0-15.5)	26% (<0.9-13.3)	86% 2.4 (<0.2-10.1)						(Martin et al., 2019)
NR Hair	NR	Italy	11	3/11 (<0.1-15)	0% (<0.1)	0% (<0.1)	1/11 (<0.02-0.50)	0/11 (<0.02)	0/11 (<0.02)			(Piva et al., 2021)
NR Hair	Adults	South Korea, Busan	47		36% (<0.36-1.5)	19% (<0.41-0.74)	0% (<0.80)		0% (<0.28)	2% (<0.42-0.42)		(Kim and Oh, 2017)
2009 Nails	19-26 (F,M)	China, Guangdong	39		58% 5.5 (<0.41-44)	63% 9.8 (<0.22-65)						(Liu et al., 2020a)
2012 Nails	Fishery employees	China, Wuhan	8	0%	0%	0%	8/8 4.1 (0.15-7.7)					(Wang et al., 2018b)
NR Nails	children & adults (F,M)	Spain	12	7/12 (<1-15)	11/12 4 (<1-7)	9/12 5 (<0.7-6)						(Martin-Pozo et al., 2020)
2012-	NR age	China,	103	100%	100%	100%	94%				PFPrA: 100%	(Song et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age Gender	Country, Area	N	PFBA	PFPeA	PFHpA	PFBS	PFPeS	PFHpS	PFDS	Other PFCA/PFSA/PFPA	Reference
2013 Semen		Guangzhou		3.1	1.7	0.36	0.076				0.95	2018b)
2015-2016 Semen	29.4±5.4	China, Nanjing	664	0% (<0.075)	0% (<0.05)	3% (<0.01-0.06)	6% (<0.01-0.094)					(Pan et al., 2019a)
2015 Follicular fluid	20-45	UK, Hull	59	0% (0.2)	0% (<0.3)	15% (<0.1-0.53)	21% (<0.2-0.44)			0% (<0.1)		(Heffernan et al., 2018)
2006-2011 Follicular fluid	23-42	Australia, Queensland	97	38% (<0.08-NR)		90% 0.01 † (<0.06-0.6)			96% 0.1 † (<0.13-1.1)			(Kim et al., 2020c)
2008-2009 Follicular fluid	25-42	Belgium, Antwerp	38	0% (<1.3)		0% (<1.4)	0% (<0.78)			0% (<0.57)		(Petro et al., 2014)
2018-2019 Follicular fluid		China, Beijing	28			79% 0.012 ¥	29% (<NR-0.009)					(Kang et al., 2020)
2016 Placenta		China, Henan	54			41% (<0.002-0.052)	0% (0.05)	0% (<0.02)	0% (<0.04)	0% (<0.01)	PFDoDS: 0% (<0.006) PFNS: 0% (<0.02)	(Lu et al., 2021)
2017-2019 Placenta		Austria, 3 areas (samples with highest PFAS-levels out of 136 samples)	32 in 13P	5/13 (<0.002-0.053)	0% (<0.001)	10/13 0.009 (<0.003-0.019)	0% (<0.00005)	0% (<0.00007)	13/13 0.012 (0.006-0.026)	1/13 (<0.00005-0.004)	PFDoDS: 1/13 (<0.0002-0.0006) PFHxPA: 0/13 (<0.00003)	(Kaiser et al., 2021a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year Sample	Age Gender	Country, Area	N	PFBA	PFPeA	PFHpA	PFBS	PFPeS	PFHpS	PFDS	Other PFCA/PFSA/PFPA	Reference
2017-2018 Cerebrospinal fluid	2-81 (F,M)	China	223			0%	0%		6.7% (<LOQ-0.04)			(Wang et al., 2018a)
2008 Liver	27-79 (F,M)	Spain, Catalonia	12			0% (<0.06)	0% (<0.03)					(Karrman et al., 2010)
2011-2014 Kidney	45-86 (F,M)	France	9	0/9								(Abraham et al., 2021)
2011-2014 Lung	64-80 (F,M)	France	7	1/7 (<NR-0.17)								

¥ Geometric mean

Table B.95. Concentrations of precursors, PFAEs and PFECHS in urine, follicular fluid, semen, and cerebrospinal fluid (ng/mL) and hair, nail and placenta (ng/g), which are not covered by existing or proposed restrictions, described by detection frequency (% or x/xx), median (bold) and range (within brackets). Grey cells indicate sampling sites near known PFAS point sources. FCM=fluorochemical manufacturing facility, P=pool.

Year, Sample	Age (gender)	Country, area	N	6:2 Cl-PFESA	8:2 Cl-PFESA	10:2 PFESA	ADONA	HFPO-DA	Other PFASs	Reference
2012 Urine	Highly exposed	China, Wuhan	8	5/8 0.01 (<NR-0.03)	0/8 (<NR)	0/8 (<NR)				(Wang et al., 2018b)
Nail	fishery employees			8/8 2.8 (0.4-7.6)	0/8 (<NR)	0/8 (<NR)				
2013-2014 Urine	>6 (F, M)	USA, National	26 82	0% (<0.1)			0% (<0.1)	1.2% (<0.1-0.4)		(Calafat et al., 2019)
2015 Urine	3-68 (F, M)	China, Shijiazhu	41	95% 0.0020	2%	0%				(Wang et al., 2018b)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year, Sample	Age (gender)	Country, area	N	6:2 Cl-PFESA	8:2 Cl-PFESA	10:2 PFESA	ADONA	HFPO-DA	Other PFASs	Reference
		ng		(<0.000008-0.01)	(<0.00002-0.0007)	(<0.00002)				
Hair				88% 0.53 (<0.015-9.3)	61% 0.35 (<0.03-2.9)	0% (<0.06)				
Nail				95% 1.0 (<0.04-3.6)	56% 0.46 (<0.06-1.5)	0 (<0.09)				
2016 Urine	NR	USA	50	0% (<0.1)			0% (<0.1)	0% (<0.1)		(Kato et al., 2018)
2018 Urine	14-79 (F, M)	USA, Bladen county (NC) Near FCM. Bottle water last 4-14 months.	30	0% (<0.1)			0% (<0.1)	0% (<0.1)		(NCDHHS, 2018)
NR Hair	NR	Italy	11	0% (<0.02)	0% (<0.05)		0% (<0.07)		PF4OPeA (PFMPA): 0% (<0.12) PF5OHxA (PFMBA): 0% (<0.1) PFEESA: 0% (<0.02)	(Piva et al., 2021)
2015-2016 Semen	29.4±5.4	China, Nanjing	664	100% 0.064 (<0.005-1.4)	31% (<0.005-0.08)					(Pan et al., 2019a)
2018-2019 Follicula	NR	China, Beijing	28	100% 1.1 (0.24-5.2)	100% 0.02 (0.008-0.13)				HFPO-TA: 36% (<NR-0.36)	(Barton et al., 2020)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Year, Sample	Age (gender)	Country, area	N	6:2 Cl-PFESA	8:2 Cl-PFESA	10:2 PFESA	ADONA	HFPO-DA	Other PFASs	Reference
r fluid										
2017-2019 Placenta	NR	Austria, 3 areas (samples with highest PFAS levels out of 136 samples)	32 in 13 P		0% (<0.00005/<0.0002)		0% (<0.0002/<0.0008)		3:3 FTCA: 4/13 (<0.00002-0.0014) 4:2 FTSA: 13/13 0.0058 (0.0023-0.011) FBSA, MeFBSA & 6:6 PFPiA: 0%	(Kaiser, 2021)
2016 Placenta	NR	China, Henan	54	100% 0.08 (0.02-0.34)	24% (<0.002-0.025)				4:2 FTS: 0% (<0.05)	(Lu et al., 2021)
2015-2016 Placenta	NR	China, Wuhan	32	100% 0.34 (0.04-1.8)	28% (<0.009-0.07)					(Chen et al., 2017b)
2017-2018 Cerebrospinal fluid	2-81 (F,M)	China	223	95% 0.051 ¥ (<LOQ-2.0)	13% 0.003 ¥ (<LOQ-0.068)				4:2 Cl-PFESA: 0%	(Wang et al., 2018a)

Appendix B.7.5. Endocrine activity and endocrine disruption

Table B.96. Studies investigating the EA / ED of PFAS.

Substance	Activity/Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
4:2 FTOH, 6:2 FTOH, 8:2 FTOH, 8:2 diPAPs, 10:2 diPAPs, 8:2 triPAPs, PFBA, PFPeA, PFHxA, PFHpA	4:2 FTOH increased ER-activity (3-4 fold) 6:2 FTOH significantly increased 17β-estradiol levels and increased ER-activity (1,5-5 fold) 8:2 FTOH increased ER-activity (1.5 fold) 8:2 monoPAPs increased ER-activity (2 fold) 8:2 diPAPs inhibited testosterone synthesis 10:2 diPAPs did not show activity in any of the assays 8:2 triPAPs decreased ER-activity (0.8 – 0.5 fold) PFBA increased PPARα-activity PFPeA, PFHxA and PFHpA increased PPARα- and PPARγ-activity	<i>In vitro</i>: ER-reporter gen assay: stably transfected human ovarian adenocarcinoma cell-line (BG1Luc4E2) AR-reporter gene assay: Chinese hamster ovary cell-line (ATCC) transiently transfected with receptors, pSVAR0 (antagonist mode) or pSVAR13 (toxicity) and the reporter gene, MMTV-LUC PPARα, PPARγ reporter gene assay: NIH-3T3 cells transiently transfected with plasmids, expressing the ligand-binding domain of murine PPARα or PPARγ as well as a plasmid containing the upstream-activating sequence (UAS) Steroidogenesis assay: H295R cells from an ex vivo rat fetal testis culture system (FEGA)	6:2 FTOH and PFHxA were recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	(Rosenmai et al., 2016)
6:2 FTOH	females: - the increase of E2 was accompanied by up-regulated hepatic estrogenic receptor a	<i>In vivo</i>: Zebrafish (<i>Danio rerio</i>): 18 weeks old at start of exposure Exposure to 0, 0.03, 0.3 and	6:2 FTOH was recently assessed for its endocrine	(Liu et al., 2009)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity/Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	(ERα) and vitellogenin (VTG1 and VTG3) expression - significantly increased plasma estradiol (E2) and testosterone (T) levels - reduced ratio of T/E2 males: - elevation of the T level is consistent with the up-regulation of cytochrome P450 c17-hydroxylase, 17, 20-lase (CYP17) and the down-regulation of cytochrome P450 aromatase A (CYP19A) - significantly increased plasma estradiol (E2) and testosterone (T) levels - increased ratio of T/E2 results suggest that FTOHs may disturb fish reproduction through endocrine disrupted activity	3.0 mg/L 6:2 FTOH for 7 days.	disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	
8:2 FTOH	Females: - plasma testosterone and estradiol levels were significantly increased - promotion of oocyte maturation, upregulated follicle-stimulating hormone β (FSHβ) and luteinizing hormone β (LHβ) in the pituitary - down-regulation of gene transcription of vtg1 and zp2α,	<i>In vivo:</i> Zebrafish (<i>Danio rerio</i>): 16 weeks old at start of exposure Exposure to 0, 10, 30, 90, 270 µg/L for 4 weeks	Effects with relevance on population level	(Liu et al., 2010a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	associated with decreased fecundity Males: - T levels were decreased and E2 levels increased, - retarded spermiation, - downregulated FSHβ and LHβ, - Up-regulation of vitellogenin (VTG1) and zona pellucida protein 2 (ZP2a) gene transcription, indicating estrogenic activity F1: - number of eggs spawned and sperm production were reduced - thinning of eggshell, and reduced protein content and egg diameter - reduced hatching rates in the offspring General: - exposure to 8:2 FTOH caused disruption of sex hormone biosynthesis and impaired reproduction in adult zebrafish, ultimately resulting in decreased hatching rates in the offspring			
PFNA, PFHxS, + others	short-chain PFASs, such as PFNA and PFHxS, activated the PPAR transcription factor receptor, which led to increased metabolism of fatty acids, increased	Many different: <i>in vitro</i> and <i>in vivo</i> test systems (but only <i>in vitro</i> studies mentioned here)	Also of relevance for HH	(Mokra, 2021) (Review)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	apolipoprotein I (apo A1) level (Rosen et al., 2017)] PFHxS caused an almost 10-fold stronger expression of the oxidoreductase, one of regulators of lipid metabolism, and stearoyl coenzyme A desaturase (Scd), compared to PFOA, PFOS and PFNA (Watkins et al., 2015) the binding affinity of PFASs with the same number of carbon atoms in chain is dependent on terminal groups and decreases as follows: sulfo group > carboxylic acid group > alcohol group (Qiu et al., 2020)			
GenX, PFBA, PFBS, 6:6 PFPiA, 6:8 PFPiA, 8:8 PFPiA, PFHxS + others	<i>In vitro:</i> - short-chain PFAS had no cytotoxic effects on rat thyroid cells and did not interfere with thyroid-stimulating hormone (TSH)-dependent cyclic adenosine monophosphate (cAMP) production (Croce et al., 2019) - FRTL-5 cells exposed to increasing concentrations of GenX displayed both genotoxic and cytotoxic effects (Coperchini et al., 2020) <i>In vivo:</i>	Many different: <i>in vitro</i> , <i>in vivo</i> test systems	Also of relevance for HH	(Coperchini et al., 2021) (Review)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	- GenX caused a dose-responsive up-regulation of 28 different genes involved in the PPAR signaling pathway (Conley et al., 2019) - After exposure to 0.5–50 nM of 8:8 PFPiA in zebrafish larvae, an increase of T4 and T3 was observed. In addition, corticotropin-releasing hormone (CRH) and TSHb were down-regulated and uridinediphosphate-glucuronosyltransferase (UGT1AB) resulted up-regulated. The authors suggested that this should be regarded as a compensatory response to the hyperthyroid status (Liu et al., 2019b) - Contrary to above study by Kim et al., showed an up- regulation of corticotropin releasing hormone b (CRHB), thyrotropin receptor (TSHR), and thyroid transcription factor-1 (NKX2.1) genes which was suggestive of a negative feedback in response to decreased circulating thyroid hormones (Kim et al., 2020b) - study performed on dams exposed to PFHxS reported no statistically significant effects on thyroid gland weights and			

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	histopathology (Ramhoj et al., 2020)			
6:2 FTOH, 8:2 FTOH, 8:2 FTOAcr, PFOA, PFNA, PFDA, PFUnDA, PFPeA, PFHxA, PFHpA, PFOS, PFDS, E2 + others	<i>In silico:</i> - computational model based upon crystal structure from human Era: PFOA, PFNA, PFDA, and PFOS all efficiently docked with Era from different species in a similar manner to BPA and nonylphenol <i>In vitro:</i> - PFOA, PFNA, PFDA, PFUnDA, and PFOS significantly enhanced human Era-dependent transcriptional activation at concentrations ranging from 10–1000 nM - All PFAAs tested weakly bound to trout liver ER with IC₅₀ values of 15.2–289 mM <i>In vivo:</i> - PFOA, PFNA, PFDA, PFUnDA all potent inducers of vtg <i>in vivo</i> (at high concentrations of 50 ppm) - Structure-activity relationship for PFAAs was observed, where eight to ten fluorinated carbons and a carboxylic acid end group were optimal for maximal vtg induction	<i>In silico:</i> - ICM-virtual ligand screening (VLS) procedure (Molsoft ICM v3.5-1p) - proteins were built based upon 1ERE as the 3Dtemplate with Molsoft ICM v3.5-1p <i>In vitro:</i> - ER saturation binding assays and competitive binding assays with trout liver cells (cytosol fraction of liver homogenate) - Era reporter gene assay with HEK-293T cells co-transfected with XTEL luciferase reporter plasmid containing a consensus estrogen-responsive element (ERE) sequence from the Xenopus Vtg promoter human Era expression vector <i>In vivo:</i> - Rainbow trout (<i>Oncorhynchus mykiss</i>): Dietary exposure of juvenile individuals (5 months old for VTG analysis, 11 months old for other) 14 day PFAS mixture exposure (in the ratio of 1:1:1:1, mix A	6:2 FTOH and PFHxA were recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	(Benninghoff et al., 2011)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
		composed of 5 mg/L individual PFAS (PFOA, PFNA, PFDA, PFUnDA), mix B composed of 50 mg/L individual PFAS, mix C composed of 250 mg/L individual PFC) - For VTG: PFOA and PFDA exposure, 0.026, 0.128, 0.64, 3.2, 16, 80, 400, 2 000 mg/L PFOA or PFDA; DMSO vehicle (0.05 mg/L);		
PFOSA	Hepatocellular fatty acids content, gene expression (lipid metabolism, oxidative stress),	<i>In vivo</i> : Atlantic salmon (<i>Salmo salar</i>) hepatocytes, Static exposure (12 h and 24 h); 0.01% DMSO (solvent control), 2, 20, 50 µM PFOSA	Only abstract available	(Wåggbø et al., 2012)
PFAA mixture (PFOA, PFOS, PFBS, PFNA)	Cellular level changes in the endocrine organs, including follicle cell degeneration in male fish and follicle cell atrophy significant increase in vtg expression relative to the control in the F2 generation (but not significant for F0, or F1 generation) at 5 µg/L reduced fecundity: suppression of hatching rate in F1 generation survival rate of F1 and F2 generation >80% for all treatment groups	<i>In vivo</i> : Japanese medaka (<i>Oryzias latipes</i>), 238 d exposure at 0.5 and 5 µg/L (nominal) mixture ratio 1:1:1:1	Effects with relevance on population level	(Lee et al., 2017)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity/Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	sex ratio: PFAA high concentration caused the shifting into male portion			
6:2 FTOH, 8:2 FTOH, NFDH, PFOS, PFOA	Treatments with 6:2 FTOH, 8:2 FTOH and NFDH dose-dependently induced hER-mediated transcriptional activity with interaction between the hERα or hERβ ligand binding domain and TIF2 estrogenic effects of FTOHs on hERα were higher than those on hERβ, indicating a differential responsiveness of hERs to FTOHs estrogenic effects for hERα and hERβ descended in the order of estradiol-17β > 6:2 FTOH > NFDH > 8:2 FTOH	<i>In vitro</i>: yeast two-hybrid assay: modified by incorporation of hER isoforms (hERα or hERβ)	6:2 FTOH was recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	(Ishibashi et al., 2007)
4:2FTOH, 6:2 FTOH, 8:2 FTOH, PFOS, PFOA	Dose-dependent vtg induction after exposure to 6:2 FTOH but not 4:2 FTOH or 8:2 FTOH Significant vtg induction after 12 h (6:2 FTOH) exposure, and 72h exposure (4:2 and 8:2 FTOH (but not dose dependent)) Co-exposure with E2 inhibited E2-induced hepatocellular VTG production in a dose-dependent manner except for 4:2 FTOH suggesting an anti-estrogenic activity Co-exposure with known estrogen receptor inhibitor tamixofen inhibited	<i>In vitro</i>: non-competitive enzyme-linked immunosorbent assay (ELISA) investigating vtg induction in in primary cultured hepatocytes of freshwater male tilapia (<i>Oreochromis niloticus</i>)	6:2 FTOH was recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	(Liu et al., 2007)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	the ability of test compounds to stimulate vitellogenesis: estrogenic effect of PFAS may be mediated by the estrogen receptor pathway			
PFBS	No treatment-related mortalities or effects on body weight, weight gain, feed consumption, histopathology measures, or reproductive parameters evaluated in the study when compared to the control group	<i>In vivo</i> : Northern bobwhite quail (<i>Colinus virginianus</i>) reproduction study: adult quail were exposed to nominal dietary concentrations of 100, 300, or 900 mg PFBS/kg, ww feed for up to 21 weeks		(Newsted et al., 2008)
PFBA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDODA, PFTeDA, 7H-PFHpA, 6:2 FTUA, PFBS, PFHxS, PFOS, L-PFDS, L-PFOSi, 6:2 FTOH, 8:2 FTOH, N-MeFOSE, N-EtFOSE, FOSA, N,N-ME2FOSA, N-MeFOSA, N-EtFOSA	binding potency decreased in the order: perfluorohexane sulfonate > perfluorooctane sulfonate/perfluorooctanoic acid > perfluoroheptanoic acid > sodium perfluoro-1-octanesulfinate > perfluorononanoic acid maximum potency at a chain length of eight carbons (PFOA). The binding potency is clearly associated with the degree of fluorination of the alkyl chain For PFASs with a carbon chain length of four to eight, TTR binding potencies were significantly higher for compounds containing a sulfonate functional group than for those containing a carboxylic acid functional group QSAR models indicated the dependence on molecular size and functional groups	<i>In vitro</i> : radioligand-binding assay testing for binding capacity to human TTR	Modelled binding to human TTR. Of relevance for ENV due to high conservation of HPT axis 6:2 FTOH and PFHxA were recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	(Weiss et al., 2009)

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Substance	Activity/Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	(but only preliminary result, more detailed description of chemical properties and data for validation needed) Of the six PFASs with the same fluorinated carbon chain length (C8) but with different sulfate-based functional groups, highest binding potency was observed for the sulfonate (PFOS), followed by the ulfonate (perfluorinated octane ulfonate) and the sulfonamide (perfluoro-1-octane sulfonamide) Test compounds with the sulfonamide functional group protected by an alkyl group had no TTR binding potency themselves but seemed to cause a slight increase in T4-TTR binding at high test concentrations			
PFBA, PFBS, PFHxA, PFHxS, PFHpA, and PFHpS	Chicken: - PFAS < C8 altered the expression of TH-responsive genes (D2, D3, TTR, and RC3) in chicken embryonic neuronal cells to a greater extent than PFAS > C8 - chicken: D2 upregulated after exposure to PFHxA, PFHpA, and PFNA - D3 mRNA expression increased twofold to fivefold following exposure to several PFCs (PFBS, PFHxA, and PFHxS)	<i>In vitro</i>: primary cultures of avian neuronal cells of two avian species: the domestic chicken (<i>Gallus domesticus</i>) and herring gull (<i>Larus argentatus</i>). Measurement of mRNA levels of thyroid hormone (TH)-responsive genes D2, D3, TTR, Oct-1, myelin basic protein and RC3 after exposure to PFBA, PFBS, PFHxA, PFHxS, PFHpA, and PFHpS at five concentrations: 0.01, 0.1, 1, 3, and 10IM	PFHxA was recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	(Vongphachan et al., 2011)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	- PFHxS treatment significantly decreased TTR mRNA expression - PFHpA exposure increased TTR mRNA levels - PFBS and PFHxS treatment increased RC3mRNAexpression - MBP mRNA expression was upregulated at 3 and 10 µM following PFHxA treatment - no changes to Oct-1 mRNA levels Herring gull: - upregulation in RC3 mRNA expression (Fig. 4A) following PFHpA exposure - RC3 mRNA expression did not change - increase in Oct-1 mRNA following treatment with PFBS, PFHxA, and PFHxS General: - study provided evidence that the brain may be a target organ for PFAS effects and that these contaminants have the potential to alter TH homeostasis in birds			
6:2 FTOH, 8:2 FTOH	6:2 FTOH & 8:2 FTOH induce cell proliferation at 10 µM small but relevant up-regulation of the estrogen receptor as a consequence of exposures to 6:2 FTOH or 8:2 FTOH.	<i>In vitro</i>: proliferation-promoting capacity of 6:2 FTOH and 8:2 FTOH with an Escreen assay of MCF-7 cell lines	6:2 FTOH was recently assessed for its endocrine disrupting properties in the	(Maras et al., 2006)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity/Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	Up regulated genes: TFF1, PGR, ESR1, PDZK1 Down regulated genes: ERBB2		course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	
PFECHS (acyclic perfluoroalkane sulfonic acid used as an erosion inhibitor in aircraft hydraulic fluid)	significant decrease of the transcription of VTG1 in exposed organisms transcriptomic and cellular results indicated that exposure to PFECHS reduced VTG in <i>D. magna</i> no effects were observed on the survival, the frequency of molting, the number of neonates produced or the growth of exposed organisms	<i>In vivo</i> : sublethal exposure (12 d) of <i>Daphnia magna</i> to PFECHS (0.06, 0.6, and 6 mg/L), microarray and quantitative real-time PCR		(Houde et al., 2016)
PFOS, PFBS	neither PFOS nor PFBS had a significant effect on the survival and growth caused hepatohistological impairment at higher concentrations (100; 1 000 ug/L) PFBS had no effect on the sex ratio and gonadal histology. PFOS and PFBS promoted expression of estrogen receptor (ER) and androgen receptor (AR), but not affected aromatase expression in the brain	<i>In vivo</i> : growth and sexual development of <i>Xenopus laevis</i> tadpoles exposure to series of concentrations of PFOS and PFBS (0.1; 1; 100; 1 000 ug/L) as well as 17-beta-estradiol (E2, 100 ng/L) and 5 alpha-androstan-17-beta-ol-3-one (DHT, 100 ng/L) from stage 46/47 to 2 months postmetamorphosis		(Lou et al., 2013)
PFBA, PFHxA,	PFOA, PFOS and PMOH enhanced	<i>In vitro</i> :	PFHxA was	(Behr et al.,

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
PFOA, PFBS, PFHxS, PFOS	17beta-estradiol-stimulated estrogen receptor beta activity PFOS, PMOH, PFHxA and PFBA enhanced dihydrotestosterone-stimulated androgen receptor activity H295R steroidogenesis assay, PFOA and PFOS slightly enhanced estrone secretion, and progesterone secretion was marginally increased by PFOA. All effects were only observed at concentrations above 10 µM, and none of the PFAS displayed any effect on any of the molecular endocrine endpoints at concentrations of 10 µM or below	Cell Lines: H295R, HEK293T, LNCaP, MCF-7, MDA-kb2 Exposure Duration : 24 h – 6 d Exposure Range : 0.001 – 500 µM Types of Endpoints: Androgen related, Cytotoxicity, Estrogen related, Steroidogenesis, Cell proliferation	recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	2018)
PFHxA, PFHxS	Pipping success (pip = first break in eggshell) was reduced to 63% at the highest dose of PFHxS; PFHxS exposure (38,000 ng/g) decreased tarsus length and embryo mass. PFHxS and PFHxA accumulated in the three tissue compartments analyzed as follows: yolk sac > liver > cerebral cortex. Type II and type III 5'-deiodinases (D2 and D3) and cytochrome P450 3A37 mRNA levels were induced in liver tissue of chicken embryos exposed to PFHxS	<i>In vivo</i>: Chicken (<i>Gallus gallus domesticus</i>): determined in ovo effects of PFHxS and PFHxA exposure (maximum dose = 38,000 and 9700 ng/g egg, respectively) on embryonic death, developmental endpoints, tissue accumulation, mRNA expression in liver and cerebral cortex, and plasma TH levels	PFHxA was recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table* In vivo effects of PFHxS but not PFHxA	(Cassone et al., 2012)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	D2, neurogranin (RC3), and octamer motif binding factor 1 mRNA levels were upregulated in cerebral cortex. Plasma TH levels were reduced in a concentration-dependent manner following PFHxS exposure no effects were observed for PFHxA.		Effects with relevance on population level	
PFBS	PFBS exposure decreased the levels of 3,5,3'-triiodothyronine (T3) in F0 female blood; increased T3 or thyroxine (T4) levels in F0 brains, in which hyperthyroidism suppressed the local transcription of 5'-deiodinase 2 (Dio2). Decreased T3 was transferred to F1 eggs, although the parental influences were reversed in F1 larvae. Delayed hatching was coupled with elevated T3 levels in F1 larvae. F1 adults showed comparable symptoms of thyroidal disruption with F0 adults. Slight recovery was noted in the F2 generation, although F2 larvae still exhibited thyroid disruption and synthesized excessive T4. Results suggested that the offspring	<i>In vivo:</i> Exposure of F0 marine medaka (<i>Oryzias melastigma</i>) eggs to PFBS at different concentrations (0, 1.0, 2.9, and 9.5 µg/L) until sexual maturity. The F1 and F2 generations were reared without continued exposure.	Effects with relevance on population level!	(Chen et al., 2018b)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity/Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	suffered more severe dysfunction of the thyroidal axis albeit without direct exposure			
6:2 chlorinated polyfluorinated ether sulfonate (F-53B)	<i>In silico</i> - F-53B binds to transthyretin (TTR) by forming hydrogen bonds with Lys123 and Lys115, thereby interfering with thyroid hormone homeostasis <i>In vitro</i> - F-53B enhanced cell proliferation in a dose-dependent manner, indicative of thyroid receptor agonistic activity. <i>In vivo</i> - In zebrafish larvae, F-53B exposure induced significant developmental inhibition and increased thyroxine (T4) but not 3,5,3'-triiodothyronine (T3) levels accompanied by a decrease in thyroglobulin (TG) protein and transcript levels of most genes involved in the hypothalamic-pituitary-thyroid (HPT) axis	<i>In silico</i> - Based on the homology-modeled structure of zebrafish TTR, F-53B was docked automatically into the binding site of zfTTR using AutoDock Vina 1.1.2 <i>In vitro</i> - Molecular docking study to TTR Cell proliferation assay with GH3 cell line <i>In vivo</i> - Zebrafish (<i>Danio rerio</i>) embryos (2 hpf) exposed for 5 days to 0, 0.5, 20 and 200 µg/L F-53B followed by depuration in clean water for 5 days		(Deng et al., 2018)
PFOA, TBBPA, TDCPP, DOPO, PFBA	Reduced surface area of swim bladder (3 dpf) and significant changes in gene expression patterns (3 dpf)	<i>In vivo</i> : Zebrafish (<i>Danio rerio</i>) embryos exposed to PFOA, TBBPA, TDCPP, DOPO, PFBA. Sub-chronic (0-6days post fertilization (dpf)) and chronic		(Godfrey et al., 2017)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
		(0-28dpf) exposures at 1% of LC ₅₀		
TDCCP, PFOA, PFBA	Females displayed significantly larger swim bladders (which are under thyroid hormone control) after exposure to all chemicals with the exception of triiodothyronine, which caused the opposite effect	<i>In vivo</i> : Japanese Medaka (<i>Oryzias latipes</i>) embryos were exposed to sublethal concentrations of TDCPP, 0.019 mg/L, PFOA, (4.7 mg/L) and PFBA (137 mg/L). Exposure from 0 – 10 dpf		(Godfrey et al., 2019)
PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFBS, PFHxS, PFOS	IEFs for the PFAS was as follows: PFOA (IEF: 1)>PFHpA (0.89)>PFNA (0.61)>PFPeA (0.50)>PFHxS (0.41)>PFHxA (0.38) approximately PFDA (0.37)>PFBA (0.26)=PFOS (0.26)>PFUnDA (0.15)>>PFDoDA and PFBS (not activated). SAR analysis showed that PFCAs having more than seven perfluorinated carbons had a negative correlation (r=-1.0, p=0.017) between the number of perfluorinated carbons and the IEF of PFCAs, indicating that the number of perfluorinated carbon of PFCAs is one of the factors determining the transactivation potencies of the BS PPARα. PFCAs were more potent than PFASs with the same number of perfluorinated carbons	<i>In vitro</i> reporter gene assay Transactivation of the Baikal seal (<i>Pusa sibirica</i>) peroxisome proliferator-activated receptor alpha (BS PPARα) by PFAS (C4-C12) estimated the PFOA induction equivalency factors (IEFs), a ratio EC ₅₀ of PFOA to the concentration of each compound that can induce the response corresponding to 50% of the maximal response of PFOA	PFHxA was recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	(Ishibashi et al., 2011)
6:2 CI-PFESA and 8:2 CI-PFESA (PFOS	6:2 CI-PFESA and 8:2 CI-PFESA bound to PPARs with affinity higher than PFOS	<i>In vitro</i> : fluorescence competitive binding assay		(Li et al., 2018a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
alternatives in China)	showed agonistic activity toward PPARs signaling pathways with potency similar to (6:2 CI-PFESA) or higher than (8:2 CI-PFESA) PFOS CI-PFESAs fitted into the ligand binding pockets of PPARs with very similar binding mode as PFOS	luciferase reporter gene transcription assay (Cell Lines Used: 3T3-L1, HEK293T)		
HFPO-TA, HFPO-DA	receptor binding experiment showed HFPO-TA exhibited 4.8-7.5 folds higher binding affinity with PPAR γ than PFOA, whereas HFPO-DA exhibited weaker binding affinity than PFOA. Agonistic activity toward PPAR γ signaling pathway in HEK 293 cells in the order of HFPO-TA > PFOA > HFPO-DA. Molecular docking simulation indicated HFPO-TA formed more hydrogen bonds than PFOA, whereas HFPO-DA formed fewer hydrogen bonds than PFOA. HFPO-TA promoted adipogenic differentiation and lipid accumulation in both mouse and human preadipocytes with potency higher than PFOA. Adipogenesis in human preadipocytes is a more sensitive end point than mouse preadipocytes	<i>In vitro</i> : investigation of receptor binding, receptor activity, and cell adipogenesis effects (Cell Lines Used: 3T3-L1, HEK293T, Preadipocytes) to compare potential disruption effects of HFPO-TA, HFPO-DA, and PFOA on peroxisome proliferator-activated receptor gamma (PPAR γ) via the		(Li et al., 2019)
PFHpS, PFOS, PFNA + others	PFAS dominated the summed HOCs concentrations in both species (77% in	<i>In vivo</i> : Assessed plasma concentrations of		(Nøst et al., 2012)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
	kittiwakes and 69% in fulmars). Positive associations between total thyroxin (TT4) and PFAS (PFHpS, PFOS, PFNA) were reported by the authors for both species. The authors qualify that "Although correlations do not implicate causal relationships per se, the correlations are of concern as disruption of TH homeostasis may cause developmental effects in young birds"	halogenated organic contaminants (HOCs) in chicks of two seabird species: black-legged kittiwake (<i>Rissa tridactyla</i>) and northern fulmar (<i>Fulmarus glacialis</i>) to investigate possible correlations of HOCs with circulating thyroid hormone (TH) concentrations. Plasma chicks were sampled in Kongsfjorden, Svalbard in 2006. Samples were analyzed for thyroid hormones and a wide range of HOCs (polychlorinated biphenyls (PCBs), hydroxylated (OH-) and methylsulphoned (MeSO-) PCB metabolites, organochlorine pesticides (OCPs), brominated flame retardants (BFRs), and perfluorinated compounds (PFAS)		
6:2 FTOH, 8:2 FTOH, 10:2 FTOH, PFBS, PFHxS, PFOS, PFBA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTTrDA, PFTeDA,	Most of the tested PFASs bound TTR with relative potency (RP) values of 3×10^{-4} to 0.24 when compared with that of the natural ligand thyroxine, whereas fluorotelomer alcohols did not bind Structure-binding analysis revealed that PFASs with a medium chain length and a sulfonate acid group are optimal for TTR binding, and PFASs with lengths longer than 12 carbons are optimal for TBG binding Molecular docking showed that the	<i>In vitro</i>: fluorescence displacement assay was used to determine the binding affinities of 16 PFASs with two major TH transport proteins, transthyretin (TTR) and thyroxine-binding globulin (TBG)	Not included in overview table as no new information regarding substance activity but interesting to describe trends 6:2 FTOH and PFHxA were recently assessed for its endocrine	(Ren et al., 2016)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

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	PFASs bind to TTR with their acid group forming a hydrogen bond with K15 and the hydrophobic chain towards the interior. PFASs were modeled to bind TBG with their acid group forming a hydrogen bond with R381 and the hydrophobic chain extending towards R378		disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	
PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTeDA, PFBS, PFHxS, PFOS, FOSA	Cellular concentration of PFCAs increased with perfluorocarbon chain length up to PFDoDA. PPARα activity of PFCAs increased with chain length up to PFOA. Maximum induction of PPARα activity was similar for short-chain (PFBA and PFPeA) and long-chain PFCAs (PFDoDA and PFTeDA) (approximately twofold). PPARα activities were induced at lower cellular concentrations for the short-chain homologs compared to the long-chain homologs	<i>In vitro:</i> investigated the relationship between PPARα activity and cellular concentration in HepG2 cells: Cellular concentrations were determined by high-performance liquid chromatography–tandem mass spectrometry and PPARα activity was determined in transiently transfected cells by reporter gene assay	Partly included in overview table as no new information regarding substance activity but relevant to describe trends In line with results from Zhang et al 2014 PFHxA was recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More	(Rosenmai et al., 2018)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

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			details are provided below the table*	
PFBS	PFBS-exposed embryos had significantly increased caudal fin deformities, delayed swim bladder inflation, and impaired yolk utilization Incidence of fish with significantly stunted growth and truncated exocrine pancreas length was significantly increased, although these two effects occurred independently. Islet morphology revealed an increased incidence of severely hypomorphic islets (areas lower than the 1st percentile of controls) and an elevated occurrence of fragmented islets. RNA-Seq data (4 dpf) also identify disruptions in regulation of lipid homeostasis	<i>In vivo</i>: Dechorionated zebrafish (<i>Danio rerio</i>) embryos from two different transgenic fish lines (Tg[insulin:GFP], Tg[ptf1a:GFP]): exposed to 0 (0.01% DMSO), 16, or 32 µM PFBS daily from 1 – 7 dpf. Were examined using fluorescent microscopy for islet area and morphology, and exocrine pancreas length		(Sant et al., 2019)
6:2 CI-PFESA (F-53B)	F-53B accumulated in the F0 gonads and transferred to the F1 generation via maternal eggs, and even remained in F1 adult fish and their eggs (F2) after 180d depuration In the F0 generation, F-53B exposure significantly inhibited growth and induced reproductive toxicity, including decreased gonadosomatic index and egg	<i>In vivo</i>: Adult zebrafish (<i>Danio rerio</i>) (F0 generation) were chronically exposed to different concentrations of F-53B (0, 5, 50, and 500 µg/L) for 180d using a flow-through exposure system, with F1 and F2 generations reared without exposure. The reproductive toxicity endpoints were assessed in F0 and F1 adult fish	Effects with relevance on population level (Two follow up studies investigated the ED effects further to identify possible MoA ((Shi et al.,	(Shi et al., 2018a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

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	production/female, changes in the histological structure of the gonads, and increased serum testosterone levels serum estradiol and vitellogenin levels were significantly increased in 5 ug/L F-53B-exposed adult males. Transcriptional levels of several genes along the hypothalamic-pituitary-gonadal axis were altered in F0 generation fish. Testis transcriptome analysis revealed that F-53B exposure disrupted spermatogenesis in F0 male zebrafish. Maternal transfer of F-53B also induced adverse effects on growth and reproduction in the F1 generation. Higher occurrence of malformation and lower survival in F1 and F2 embryos indicated that parental exposure to F-53B could impair the embryonic development of offspring		2019a; Shi et al., 2019b) not mentioned here)	
PFHxS, PFPeA, PFHxA, PFHpA + others	no estrogenic responses to PFASs	<i>In vitro</i> : MMV-LUC cell line reporter gene assay was used to assess estrogenic activity of PFAs (C6-C12) and other chemicals	PFHxA was recently assessed for its endocrine disrupting properties in the course of the substance	(Wielogórska et al., 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Substance	Activity / Effect (in some cases direct quotes from the referenced source are used)	Test System / Methods (in some cases direct quotes from the referenced source are used)	Remark	Reference
			evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	
6:2 FTOH, 8:2 FTOH, PFBA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTeDA, PFBS, PFHxS, PFOS	binding affinity was strongly dependent on their carbon number and functional group. For PFCAs the binding affinity increased with their carbon number from 4 to 11, and then decreased slightly. For PFSA binding affinity was stronger than their PFCA counterparts. No binding was detected for the two fluorotelomer alcohols (FTOHs)	<i>in vitro</i>: binding of 16 PFASs to human PPARγ ligand binding domain (hPPARγ-LBD) and their activity on the receptor in cells were investigated using HepG2/C3A cells	Partly included in overview table as no new information regarding substance activity but relevant to describe trends 6:2 FTOH and PFHxA were recently assessed for its endocrine disrupting properties in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA. More details are provided below the table*	(Zhang et al., 2014)
6:2 CI-PFESA	relative epididymis and testis weights decreased in the 1.0 mg/kg/d group	<i>In vivo</i> : subchronic exposure study to	Study with higher relevance	(Zhou et al., 2018)

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	compared with the control. No changes were observed in the serum levels of testosterone, estradiol, follicle-stimulating hormone (FSH), or luteinizing hormone (LH), nor in the histopathological structure of the epididymis and testis and sperm count. 56 d of consecutive gavage of 1.0 mg/kg/d of 6:2 Cl-PFESA did not affect male mouse fertility. RNA sequencing showed that no genes were significantly altered in the testes after 6:2 Cl-PFESA exposure	investigate the reproductive toxicity of 6:2 Cl-PFESA exposure (0, 0.04, 0.2, and 1.0 mg/kg/d body weight, 56 d) in adult male BALB/c mice	to HH but interesting to compare to other studies with 6:2 Cl-PFESA	

* Results of a FSDT (OECD TG 234) performed with 6:2 FTOH as one main degradation product of FTA/FTMA in the course of the substance evaluation (SEv) for 6:2 FTA and 6:2 FTMA indicate an estrogenic MoA for the substances: increased VTG levels in male fish as well as changes in the secondary sex characteristics (significant decrease in the number of anal fin papillae in males) were observed. Additionally, there are hints (not statistically significant in the presented study most likely due to discrepancy between nominal and measured concentrations) for an influence of FTOH on the sex ratio. The ED expert group supported the conclusion that considering all data available, there is sufficient evidence on the estrogenic modality to identify FTOH as ED for the environment. During the substance evaluation of FTA/FTMA also an AMA (OECD TG 231) assay was performed for PFHxA the other main degradation product of FTA/FTMA. The result of this test clearly shows a thyroid agonistic activity with a dose-dependent acceleration in metamorphosis of the test animals. During the ED EG discussion the view was expressed that the thyroid mediated adversity could already be concluded based on the effects observed in the submitted AMA study. A summary report of the discussion at ED EG 21 can be found here: https://echa.europa.eu/documents/10162/1459379/flashreport_edeg-21_en.pdf/e530deb9-5baf-7fd4-dc35-8a4cd7c73f33?t=1639059043393, date of access: 2022-09-29.

The SEv for FTA/FTMA was recently concluded, stating “The assays requested for 6:2FT-OH and PFHxA during the substance evaluation of FTA and FTMA, together with available in vitro data, leads the EMSCA to the conclusion that the WHO/IPCS criteria for an endocrine disruptor in the environment are fulfilled for both substances under evaluation.”

“For 6:2-FTOH it is concluded that both in vitro and in vivo data in different fish species provide sufficient evidence to prove an estrogenic activity of the substance that can be linked to adverse and population relevant effects like feminization of male fish and the loss of male specific secondary sex characteristics, possibly leading to an impairment of mating success.”

“For PFHxA it is concluded that in vitro and amphibian in vivo data provide sufficient evidence to prove a thyroid agonistic activity of PFHxA that can be linked

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

to adverse and population relevant effects (accelerated development in amphibians).”

Once published, the conclusion document can be found here: <https://echa.europa.eu/de/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table/-/dislist/>, date of access: 2022-09-29.

Appendix B.9.3. Textiles, upholstery, leather, apparel and carpets

Table B.97. TULAC – emission estimates (ERC assumptions).

Life cycle phase	ERC	Applicable PFAS	Total release into the environment	Comments
Manufacturing phase				
Manufacture of non-woven membranes for use in textile applications.	ERC 12A Processing of articles at industrial with low release.	Fluoropolymers and Side Chain Fluorinated polymers.	Emissions to air: 2.5% w.w Emissions to soil: 2.5% w.w Releases into wastewater system: 2.5% w.w TOTAL: 7.5% w.w	Applied ERC12A to the production of membranes. Fluoropolymers are highly stable, but assume emissions relate to dusts and any cutting activities.
Manufacture of mixtures for use in textile applications.	ERC 2 – Formulation into mixture.	Non-polymeric PFAS (PFAA precursors C2-C3 and PFAA precursors $\geq$ C4) and PFPE.	Emissions to air: 2.5% w.w Emissions to soil: 0.01% w.w Releases into wastewater system: 2% w.w TOTAL: 4.51% w.w	Applied the standard ERC for mixtures.
The manufacture of solid articles where the PFAS is used as processing aid. PFAS is not intentionally retained in the article.	ERC 6B Use of reactive processing aid at industrial site (no inclusion into or onto article).	Non-polymeric PFAS.	Emissions to air: 0.1% w.w Emissions to soil: 0.03% w.w Releases to wastewater system: 5% TOTAL: 5.13% w.w	Data from the CfE suggests that use or processing aids for production of textile materials is carried out within closed systems. Therefore applied ERC 6B
The treatment of textiles with commercial textile mixtures.	ERC 6A: Use of intermediate meaning use of chemical building blocks (feedstock).	Non-polymeric PFAS (PFAA precursors C2-C3 and PFAA precursors $\geq$ C4) and PFPE.	Emissions to air: 5% w.w Emissions to soil: 0,1% w.w Releases to water: 2% w.w TOTAL: 7.1% w.w	Applied the standard ERC for mixtures.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Life cycle phase	ERC	Applicable PFAS	Total release into the environment	Comments
User phase				
Indoor use – frequent cleaning/ wetting, washing for a higher potential of release. Assume 100% used indoors with high release.	ERC 11b widespread use of articles with high or intended release (indoor) to all PFAS.	Non-polymeric PFAS (PFAA C2-C3 and PFAA $\geq$ C4) and Side-chain fluorinated polymers.	Emissions to air: 50% Emissions to soil: n.a. Releases to wastewater: 50% TOTAL: 100% w.w	Used the ERC from the Commission study but amended for fluoropolymers. 100% release for fluoropolymers is highly unlikely.
Indoor use – infrequent cleaning /wetting. Assume 100% indoor use with low release.	ERC 11a Widespread use of articles with low release (indoor).	Fluoropolymers and PFPE.	Emissions to air: 0.05% Emissions to soil: n.a. Releases to wastewater: 0.05% TOTAL: 0.1% w.w	Used the ERC used in the Commission study.
Outdoor use – low release- This could include for example outdoor wear. Assume 100% outdoor use.	ERC 10a Widespread use of articles with low release (outdoor).	All PFAS: Fluoropolymers and side chain fluorinated polymers and non-polymeric PFAS (PFAA C2-C3 and PFAA $\geq$ C4) and PFPE.	Emissions to air: 0.05% Emissions to soil: 3.2% Emissions to surface water: 3.2% TOTAL: 6.45% w.w	Used the ERC used in the Commission study.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Note	No	ERC	Default worst-case release factors resulting from the conditions of use described in the ERCs.		
			to air	to water (before STP)	to soil
1,7	1	Manufacture of the substance	5%	6%	0.01%
2,7	2	Formulation into a mixture	2.5%	2%	0.01%
2,7	3	Formulation into a solid matrix	30%	0.2%	0.1%
3, 7	4	Use of non-reactive processing aid at industrial site (no inclusion into or onto article)	100%	100%	5%
4,7	5	Use at industrial site leading to inclusion into/onto article	50%	50%	1%.
5,7	6A	Use of intermediate	5%	2%	0.1%
5,7	6B	Use of reactive processing aid at industrial site (no inclusion into or onto article)	0.10%	5%	0.025 %
5,7	6C	Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)	5%	5%	0%
5,7	6D	Use of reactive process regulators in polymerisation processes at industrial site; (inclusion or not into/onto article)	35%	0.005%	0.025 %
6,7	7	Use of functional fluid at industrial site	5%	5%	5%
3,7	8A	Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)	100%	100%	n.a.
5,7	8B	Widespread use of reactive processing aid (no inclusion into or onto article indoor)	0.10%	2%	n.a.
4,7	8C	Widespread use leading to inclusion into/onto article (indoor)	15%	30% ⁴²	n.a.
3,7,8	8D	Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor)	100%	100%	20%
4,7	8E	Widespread use of reactive processing aid (no inclusion into or onto article outdoor)	0.10%	2%	1%
4,7	8F	Widespread use leading to inclusion into/onto article (outdoor)	15%	5%	0.5%
6,7	9A	Widespread use of functional fluid (indoor)	5%	5%	n.a.
6,7	9B	Widespread use of functional fluid (outdoor)	5%	5%	5%
8	10A	Widespread use of articles with low release (outdoor)	0.05%	3.2.%	3.2%
9,10	10B	Widespread use of articles with high or intended release (outdoor)	100%	100%	100%
8	11A	Widespread use of articles with low release (indoor)	0.05%	0.05%	n.a.
9,10	11B	Widespread use of articles with high or intended release (indoor)	100%	100%	n.a.
10	12A	Processing of articles at industrial with low release	2.5%	2.5%	2.5%
10	12B	Processing of articles at industrial processing with high release	20%	20%	20%
8	12C	Use of articles at industrial sites with low release	0.05%	0.05%	n.a.

Figure B.80. Default worst-case release factors.

Table B.98. Assumptions for backward facing usage rates.

PFAS substances	General rules	1990-2002	2003-2015	2015-2020
Non-polymeric C2 – C3 substances	No usage identified for medical or 'other' textiles. Assume usage rate is zero for all years.	Assume a steady growth rate of 2% annually for home textiles, consumer apparel and technical textiles.	The oil repellence properties of ultra-short chain PFAS is considerably weaker than C8 chemistries. Assume that while the phase-out of PFOS sparked an uptake in C4, C5, and C6 PFAS. C2-C3 was unchanged and continued to grow at 2% per annum.	Assume that while regulatory pressure applied on C6 technologies may slow growth in C4 and above, the demand for PFAS substances and difference performance profile of C2 and C3, means ultra-short-chain is unaffected. Continues to grow at 2% per annum.
Non-polymeric C4 substances	No usage identified in professional apparel; medical textiles; or 'other' textiles. Assume usage rate is zero for all years.	Assume a steady growth rate of 2% annually for home textiles, consumer apparel and technical textiles.	Assume that the voluntary phase-out of PFOS accelerates uptake for short-chain in home textiles and consumer apparel. Growth rate of 4% annually between 2003 and 2012, after which assume growth becomes static due to continued tightening of regulation. For technical textiles, assume growth rate remains steady at 2% annually due to more limited application for oil repellence.	Assume growth rates for home textiles, consumer apparel and technical textiles become static (i.e., no further growth after 2012). This is expected where tightening regulations on PFAS suppress the market and drive uptake of non-fluorine alternatives.
Non-polymeric C5 substances	No usage identified for professional apparel, medical textiles, or 'other' textiles. Assume usage rate is zero for all years.	Assume a steady growth rate of 2% annually for home textiles, consumer apparel and technical textiles.	Assume the same rules apply as C4	Assume the same rules apply as C4
Non-polymeric C6 substances	No usage in medical textiles, assume usage rate	Assume steady 2% annual growth for home textiles, consumer	Assume that the voluntary phase-out of PFOS accelerates uptake of short-chain alternatives. Unlike C4	Growth for use in home textiles, professional apparel, technical textiles, and other

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

PFAS substances	General rules	1990-2002	2003-2015	2015-2020
	is zero for all years.	apparel, professional apparel, technical textiles, and other textiles.	assume that C6 has greater application in professional and technical textiles. Therefore, assume all uses grow by 4% annually year on year from 2003 – 2012, after which regulations tighten further. Assume from 2012 growth in all except consumer apparel continues at 2% annually. CfE suggested demand for C6 in home textiles has been strong throughout. For consumer apparel growing use of fluoropolymer means C6 use becomes static.	textiles continues at 2% per annum. Use for consumer apparel remains static, i.e., no annual growth in use of C6 PFAS (but also no decline).
Non-polymeric C9-C14 substances	No usage identified in professional apparel or medical textiles. Assume usage rate is zero for all years.	The information from TUV suggests that C98-C14 may be impurities present as an impurity within other PFAS mixtures, particularly fluoropolymers. But lack of further evidence in the CfE to that affect. Therefore, the standard growth rate of 2% per annum, is applied for the whole backward-looking time-series.	Assume steady 2% annual growth year on year.	Assume steady 2% annual growth year on year.
Other non-polymeric	No usage in medical	Assume steady 2% annual	As with the above assume the voluntary	Applied a standard 2% growth rate per

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

PFAS substances	General rules	1990-2002	2003-2015	2015-2020
PFAS	textiles, assume usage rate is zero for all years.	growth across all application sectors.	phase-out of PFOS drives diversification. Home textiles and consumer apparel use of other PFAS substances assumed to grow at 4% per annum year on year to 2012, and 2% per annum thereafter. Assume professional apparel, technical textiles and other textiles are more specialist, growth assumed to be 2% per annum year on year.	annum to all application sectors.
All fluoropolymers aggregated	Use in all application sectors identified.	In lieu of better data assume a standard 2% growth annually year on year to all application sectors.	Use of fluoropolymers was already ongoing before the voluntary phase-out of PFOS. It is assumed that the selection of non-polymeric/polymeric is driven by the specific application and production processes. Therefore, it is assumed that other non-polymeric PFAS substances would be more likely to replace PFOS than a fluoropolymer substitute, at least in the short to medium term. Therefore, while C4, C6 and other non-polymeric increase during this phase, assume the use of fluoropolymer continues to grow at a steady 2% per annum year on year.	More recently the demand for fluoropolymer has started to accelerate, particularly PTFE and PVDF (EEA, 2020 report). Market data ⁵⁹ suggests between 2019 and 2025 annual growth rates of 5 – 8%. Therefore, assume demand for all fluoropolymers in the third movement phase (2015 – 2030) is a minimum of 5% annually year on year.
Side-chain fluorinated polymers	No usage for home textiles, technical textiles, or medical	Assume that growth for consumer apparel, professional apparel and	As with fluoro-polymers, assume that the use of non-polymeric/polymeric is driven by the specific application and	Assume that due to the growing awareness and concerns around side-chain fluorinated

⁵⁹ <https://www.statista.com/statistics/732029/ethylene-tetrafluoroethylene-market-volume-worldwide/>, date of access: 2022-12-21.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

PFAS substances	General rules	1990-2002	2003-2015	2015-2020
	textiles. Assume usage for these applications is zero, throughout.	other textiles is a standard 2% annually.	desired physical properties, along with compatibility with the existing production processes. Assume therefore that other non-polymeric PFAS are more likely to replace PFOS than a fluoropolymer. At least in the short to medium term. Therefore, assume growth continues at a standard 2% per annum year on year.	polymers as a source of non-polymeric PFAS emissions, that growth becomes static. I.e., no further increase or decline based on the 2015 year.

Appendix B.9.4. Food contact materials and packaging

Manufacturing emissions:

Paper and board packaging

Very limited data have been identified that enable a comprehensive estimation of the emissions of PFAS from the manufacturing of products. However, some data have been identified that has allowed an estimation of emissions from a representative use, namely the manufacture of paper and board packaging to be used in contact with food and feed. For the manufacturing of the other uses not sufficient data was available

Quantities of PFAS (Surfactant) used in paper and board Packaging in 2019 were between 827 and 6 036 t.

Various environmental assessments produced for the purposes of US FCS Notifications have estimated releases to the various environmental compartments for paper and board-making processes (FDA-US, 2021). These assessments have been done for different PFAS and for different manufacturers in the same way and using the same assumptions. The assumptions are as follows:

- Proportion of copolymer fluorochemicals going to wastewater for treatment is 12% (with 88% incorporated into the finished P&B product)
- At least 90% of the copolymer going to the wastewater is expected to be retained in either the filtered solids or sludges during wastewater treatment i.e. recovered from the wastewater
- Up to 10% of the copolymer will remain in the wastewater and be released to the environment.

These assumptions are reported to be based upon substantial experience (FDA-US, 2021).

An estimate of the total amount of PFAS used by EEA P&B manufacturers in 2019 was derived as follows (assuming that the US data applies in the EEA).

If 88% of PFAS are incorporated into the finished P&B product, then total starting quantity of PFAS is derived by $100/88 \times$ quantity of PFAS are incorporated into the finished P&B product

$$= 1.14 \times 827 \text{ to } 1.14 \times 6,036 = 943 \text{ to } 6\,881 \text{ t}$$

i.e. Total quantity of PFAS used by Paper-making mills in 2019 was between 943 – 6 881 t

Consumer and industrial cookware and food and feed manufacturing equipment

Insufficient information has been obtained to allow a quantitative estimation of the emissions during the manufacture of domestic and industrial cookware in which fluoropolymers are used either as a coating for cookware such as baking tins or frying pans, fluoropolymer conveyor belts or used in components for industrial food processing equipment. To further refine qualitative estimations presented more detailed information would be required for each manufacturing process. Because of the absence of such information, even a default calculation by the REACH methodology has not been possible.

Service life emissions:

- ERC 10a: widespread use of articles outdoors with a low release. This was chosen as the best fit ERC to reflect the service-life for paper and board packaging and for

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

uses of fluoropolymers and side-chain fluorinated polymers for example in consumer or industrial cookware in which the release of the PFASs is not intended.

- ERC 11a: widespread use of articles with low release (indoors). This was chosen as the best fit ERC to reflect the service life for paper and board packaging and fluoropolymer and side-chain fluorinated polymer uses indoors in which the release of the PFASs is not intended.

The default release factors (ERFs) associated with ERCs 10a and 11a are shown below (Table B.99 and Table B.100).

Table B.99. Default ERFs for ERCs 10a and 11a.

Release to Environmental Compartment	Environmental Release Factors (%)	
	ERC 10a	ERC 11a
To air	0.05	0.05
To water	3.2	0.05
To soil	3.2	Not applicable*

* Emissions to soil indoors are not considered relevant for soil in this ERC (ECHA, 2016a).

The annual release is driven by the stock of an article in use. The annual release is derived from the ERF divided by the service-life (T_{service}) of the article. To be representative of the uses in the scope a 1-year life for paper and board packaging was assumed and a 3 year life for fluoropolymer applications (consumer and industrial cookware, and industrial food and feed production equipment).

- One year service-life ERF = ERF(air/water/soil) default x 1/20
- Three year service-life ERF = ERF(air/water/soil) default x 3/20

Other uses: Lacquers & ink, beverage can coating and car wrapping

Tonnages have been multiplied by Adjusted Environmental Release Factors (ERFs) for ERCs 10a and 11a. (The ERF is an ERC corrected for the lifespan of the article). Emissions were finally based on outdoor use, ERC10a, because of a precautionary principle.

Table B.100. Emission factors for "Other uses" during service life.

Type of Use	Generic plastic packaging (processing aids)	Residues in packaging #	Lacquers and ink	Car wrapping (protective sheet during transport)	Drinking and beverage	Drinking can lubricant coating (PTFE wax/micro-powder PTFE)
Service life stage / Type of PFAS	non-polymeric PFAS	non-polymeric PFAS	non-polymeric PFAS	Fluoropolymers	Fluoropolymers	Fluoropolymers
Service life /outdoor	ERC10b	ERC10a	ERC10a	ERC10a	ERC10a	ERC10a

Appendix B.9.8. Ski wax

Table B.101. Summary of assumptions and factors applied to (emission) data.

Component	Value	Assumption and justification
Import/export	Imports = 0 t/y.	Assumption: There is reasonable market data to suggest that 60% of global manufacture of ski-wax occurs within the European Union. However, data on imports/exports has not been identified.
	Exports = 0 t/y. All manufacture remains for use in the EU.	Justification: The justification is that the EU is a primary location for manufacture of ski-wax and can be largely assumed to meet all EU demand. Therefore, the Dossier Submitters do not expect any imports. It is possible that the EU is a net exporter but data on exports has not been identified. It is therefore assumed all manufacture and use remains inside the European Union.
Working concentrations of PFAS in ski-wax	Average concentration of 7.6% w.w	Assumption: Industry responses indicate working concentrations for PFAS between 0.2 – 15% w.w in ski-wax. However, specific concentrations may vary further (for example the call for reference makes comment on 'pure fluoro' waxes which are 100% PFAS mixtures). Based on the range, a middle value of 7.6% w.w has been used to calculate total quantities of all PFAS (which includes both fluoropolymers and non-polymeric PFAS) in use for ski-waxes in the European Union.
		Justification: The range provided by industry is relatively broad. In lieu of better data it is possible to justify the use of a middle value recognising the potential high uncertainty in the final outputs.
Emission factors during formulation of ski-wax	Use ERC emission scenario for 'formulation into a mixture' 2.5% w.w to air; 2% w.w to wastewater; and 0.01% to soil. Furthermore assume 0.5% w.w as solid waste residue for waste management.	Assumption: Data on monitoring of emissions for formulation of ski-wax has not been identified. The production of ski-wax is expected to be completed at elevated temperature using both liquid and solid processes. Therefore, emissions to air (from thermal processes), wastewater (from liquid processes) and generation of solid waste residues (liquid and solid processes) are expected. Trace amounts of PFAS are expected in these wastes. In lieu of better data values from the ERC for formulation of mixtures have been used (see ERC No2).
		Justification: Potential emission pathways can be readily identified, however assigning emission factors is more challenging. For consistency against other PFAS-based Annex XV dossiers the current values have been assigned from the ERC.
Losses during storage.	Assume 0% from spillages/accidents. Assume 0% from volatilisation to air.	Assumptions: Storage is a potentially important life-cycle stage for other sectors and so has been included within the emission model. Industry feedback suggests that storage may cover a period of up to 2 years (including both warehousing and stocking within retail outlets). The product is sold as both a solid (wax) and liquid formulation. Therefore, accidental release is possible but

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Component	Value	Assumption and justification
		perhaps less likely. In lieu of better data releases are assumed to be zero in this life-cycle phase. Justification: For completeness, this life-cycle has been included within the model. Potential accidental losses could be assumed to be very low and therefore to avoid increasing the uncertainty in the estimates and simplicity of the model the emissions calculated to be zero.
In use emissions (application)	Assume 80% is lost during application. However, feedback from industry and NEA is that application sites are typically well maintained and lost material may be recaptured (e.g. through vacuuming/sweeping) and consigned to waste (typically thermal destruction/landfill). In lieu of better data assume 50% of the lost material is recaptured, and 50% genuinely lost to environment. The lost fraction is then evenly split between water and land. This gives the following fractions: Recaptured and consigned to waste = 40% Lost to land (true emission) = 20% Lost to water (true emission) = 20% Retained on the skis/snowboard and pass to next life-cycle stage = 20%	Assumption: The in-use phase is split in two, with application the first sub-phase. The interview notes from the consultation (see Annex E.2.7.) comment that application efficiency can be quite poor with a range of values quoted. The average of these values is 80% loss. The interviewees also commented that application can take place directly over snow or indoors. Further feedback suggests a significant proportion of lost material may be recaptured and consigned to waste (e.g. vacuuming). Therefore, it is assumed that 80% is initially lost, with 40% (half) recaptured and consigned to waste and 40% (half) truly lost to the environment, with an equal split between water and land. Justification: The consultation interviews with industry provided good data on the application efficiency which allows estimates to be made. Realistically application will occur indoors and outdoors. As a worst case assume 100% occurs outdoors but recognise that this may overestimate direct environmental losses (note even losses indoors will reach environment either through tracking on footfall or washing to wastewater).
In use emissions (service life)	90% over the course of active use. Split: 50% to water 50% to land	Assumption: Emission rates for the active use of ski-wax during skiing have not been identified. Where wax is applied to the underside of skis or snowboards and is eroded during use (requiring further application) it is assumed 100% of the wax used is emitted to environment. In lieu of better data it is assumed 10% of the wax purchased is not used and enters the waste cycle (this is where

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Component	Value	Assumption and justification
		the ski-wax bars are worn particularly thin, or liquid products are residue amounts in containers). Emission will be directly to snow/ice. Assumptions about melted ice and run-off to rivers would require significant data and is a high complex process. Therefore, for high level estimates an assumption is made that equal amounts reach surface water and soil, respectively. Justification: Upon use of ski-wax the emission to environment is absolute. i.e., the function of use causes the wax to be emitted. It is possible that close to 100% of the ski-wax purchased is used, however, where winter sports are seasonal, it is more likely that some remaining product does enter the waste cycle (i.e., end of season/end of vacation, end of life of ski, etc). An expert judgement of 10% has been applied for remaining fraction to waste.
Landfill/ incineration.	100% of formulation wastes are incinerated. Recaptured waste from application and from in-use phase (left overs) is discarded in general waste. 50% of general waste goes to landfill 50% of general waste in-use goes to incineration.	Assumption: Data on wastes for ski-wax has not been identified. Feedback from industry suggests that it should be incinerated, but what happens in practice is less clear. It is assumed that manufacturers will have greater control over the formulation of ski-wax, so all solid wastes from this life-cycle stage will be incinerated. The 'in-use' phase covers a wide set of activities, with the most likely pathway being disposal to public bins or household waste. It is assumed that equal portions are landfilled and incinerated Justification: Data on waste has not been identified and is a very challenging element of the model. Feedback from industry does suggest incineration would be preferred. It can be justified that manufacturers have greater control over wastes from formulation. Wastes from in-use phases, are more likely to be typical of other wastes discarded to public bins or household refuse.

Appendix B.9.11. Transport

Table B.102. Annual emissions to air, water and soil, calculated using ERC and release % as shown below.

Tonnage [t] (0.35 kg/ vehicle):	Tonnage [t] (0.8 per vehicle):	ERC	service life [a] ^a	Environmental release [%]		
				air	water	soil
min	max					
48 607.94	111 103.87	10a	11.95	0.05	3.2	3.2
48 607.94	111 103.87	11a	11.95	0.05	0.05	

^a Average age of a vehicle in Europe (ACEA, 2021)

Emissions were calculated using:

Fluoropolymers used in 2019 (t) x compartment specific release factor from ERC (%) / service life (y)

- 50% of the fluoropolymer volume was multiplied with each compartment specific release factors from ERC 10a (Widespread use of articles with low release (outdoor))
- 50% of the fluoropolymer volume was multiplied with the compartment specific release factors from ERC 11a (Widespread use of articles with low release (indoor)).

Appendix B.9.12. Electronics and semiconductors

In Table B.103 the selected ERC are included. In Table B.104, the release factors per ERC are included (ECHA, 2016a).

As the data made available for electronics and semiconductor industry is limited to a single section in the production, it is not possible to differentiate between ERC based on, if it is the formulation or industrial use. The ERC in Table B.103 describes the production (industrial use) and the use stage.

Table B.103. Selected Environmental Release Categories (ERC).

	Production	Use
Fluoropolymers	3	11A
Perfluoropolyethers	5	11A
Side-chain fluorinated polymers	5	11A
Fluorinated gases	4	9A
Ionic non-polymeric PFAS	5	11A
Non-ionic non-polymeric PFAS	4	9A

Table B.104. Calculated one compartment based on default release factors (%) per ERC.

ERC no	ERC description	One compartment (%)
3 ^a	Formulation into a solid matrix	1.3
4	Use of non-reactive processing aid at industrial site (no inclusion into or onto article)	100
5	Use at industrial site leading to inclusion into/onto article)	50
9A ^b	Widespread use of functional fluid (indoor)	10
11A	Widespread use of articles with low release (indoor)	0.1

^aERC 3 one compartment has been amended in the use for fluoropolymers, as emission to air is not relevant. The amended ERC 3 is 0.3%. ^bERC 9A one compartment has been amended in the use for non-ionic non-polymers and fluorinated gases, as emission to soil is not relevant. The amended ERC 9A is 5%

A study by the Beu and Raoux (2019), on greenhouse gases in the electronics industry, indicates that 89% to 99% of fluorinated gases is captured, and 1% and 11% is emitted. Based on these results, a calculation factor of 0.05 (5% will be emitted, 95% captured) is used to estimate the total emissions of PFASs used for cleaning or as solvents (non-ionic non-polymers and fluorinated gases). It is likely that larger emissions happen during production of day-to-day electronics than for semiconductors, hence the emission results for these sub-categories may likely be an underestimation of the emissions.

Other groups have a calculation factor of 1 (100%) as all tonnages not emitted are expected to remain in the products until the use stage.

In Table B.105, emission factors for each PFAS group in production and use stages are included. The values are a result of combining Table B.103 with Table B.104.

Table B.105. Emission factors (%) to the environment based on a one compartment model, corresponding with emissions scenarios from ERC.

	Production (%)	Use (%)
Fluoropolymers:	0.3	0.1
Perfluoropolyethers	50	0.1
Side-chain fluoropolymers	50	0.1
Fluorinated gases	100	5

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

	Production (%)	Use (%)
Ionic non-polymer	50	0.1
Non-ionic non-polymers	100	5

^aFor fluorinated gases and non-ionic non-polymers a combined release factor for production and use was used.

Appendix B.9.13. Energy

In Table B.106, the ERC are included. In Table B.107 the release factors per ERC are included (ECHA, 2016a).

As the data made available for the energy industry is limited to a single section in the production, it is not possible to differentiate between ERC based on, if it is the formulation or industrial use. The ERC in Table B.106 describes the production (industrial use) and the use stage.

Table B.106. Selected Environmental Release Categories (ERC).

	Production	Use
Fluoropolymers	3	11A
Perfluoropolyethers	5	11A
Side-chain fluorinated polymers	5	11A
Ionic non-polymeric PFAS	5	11A
Non-ionic non-polymeric PFAS	4	9A

^aFor fluorinated gases and non-ionic non-polymers a combined release factor for production and use was used.

Table B.107. Calculated one compartment based on default release factors (%) per ERC.

ERC no	ERC description	One compartment (%)
3 ^a	Formulation into a solid matrix	1.3
4	Use of non-reactive processing aid at industrial site (no inclusion into or onto article)	100
5	Use at industrial site leading to inclusion into/onto article)	50
9A ^b	Widespread use of functional fluid (indoor)	10
11A	Widespread use of articles with low release (indoor)	0.1

^aERC 3 one compartment has been amended in the use for fluoropolymers, as emission to air is not relevant. The amended ERC 3 is 0.3%.

^bERC 9A one compartment has been amended in the use for non-ionic non-polymers and fluorinated gases, as emission to soil is not relevant. The amended ERC 9A is 5%.

A study by the Beu and Raoux (2019), on greenhouse gases in the electronics industry indicates that 89% to 99% of fluorinated gases is captured, and 1% and 11% is emitted. Based on these results, a calculation factor of 0.05 (5% will be emitted, 95% captured) is used for the total emissions of PFASs used for cleaning or as solvents (non-ionic non-polymers) in the energy sector as these short chain substances have similar properties to fluorinated gases or degrade to such gases. Limited information on emissions was received from stakeholders, and therefore the emissions are based on the electronics and semiconductor sector. It is likely that production of specialised energy equipment such as fuel cells occurs under similar conditions to specialised electronics (e.g. semiconductors). It is likely that these emission scenarios will lead to an underestimation of emissions from the energy sector, as some production may occur under less controlled environments.

All other PFASs groups have a calculation factor of 1 (100%) as all tonnages not emitted are expected to remain in the products until the use stage.

In

Table B.108, emission factors for each PFAS group in production and use stages are included. The values are a result of combining Table B.106 with Table B.107. Emission factors (%) to the environment based on a one compartment model, corresponding with

emissions scenarios from ERC.

Table B.108. Emission factors (%) to the environment based on a one compartment model, corresponding with emissions scenarios from ERC.

	Production (%)	Use (%)
Fluoropolymers:	0.3	0.1
Perfluoropolyethers	50	0.1
Side-chain fluoropolymers	50	0.1
Ionic non-polymer	50	0.1
Non-ionic non-polymers	100	5

$Emission_{production} = Volume_{production} \times \text{Calculation factor}$

$Emission_{use} = Volume_{use} \times \text{Calculation factor}$

With: $Volume_{production}$ = the volumes in section A.3.13.2.

Appendix B.9.14. Construction products

Assumptions for the assignment of ERC and release factors

Split of volume between articles and construction mixtures. Based on the categories 'Building and construction' and 'Coating and paints' in Glüge et al. (2020) for fluoropolymers a split of 19%/81% in articles/construction mixtures is estimated. For non-polymeric PFASs a split into articles/construction mixtures is estimated to 81%/19%. All side-chain fluorinated polymers is assumed to be used in construction mixtures

Processing aids Based on feedback from one stakeholder the use of processing aids in the production of construction products the processing aid is captured within closed systems and 99.9% re-used.

Application. A 50:50 split between outdoor and indoor applications is assumed in lieu of better data

In Table B.109, the selected ERC for the total release to the environment are presented.

Table B.109. ERC for the total release to the environment.

Life-cycle stage	ERCs	Total release to the environment
Formulation (coatings)	2	4.51%
Formulation (articles)	3	1.3%
Processing aids*	4	100%
Application (coatings)	5	50%
Use (outdoors)	10A	3.25%
Use (Indoors)	11A	0.1%

*99.9% is considered by industry to be recycled.

As can be seen from Table B.109, the same ERCs are used across the different PFAS-groups.

Appendix B.9.15. Lubricants

In Table B.110, the selected ERC for the total release to the environment are presented.

Table B.110. ERC for the total release to the environment.

Life-cycle stage		Assumed splits	ERCs	Total release to the environment	Other assumptions
Formulation stage	Closed/sealed	95%	2	4.51%	
	Open	5%			
Use Stage-Sealed equipment	Indoor	70%	9A	10%	
	Outdoor	30%	9B	10%	
Use Stage-open application	Indoor	70%	8A	90%	ERC8A and 8D with amendment. Assume 10% remains as residue on the article
	Outdoor	30%	8D	90%	
Pre-use stage (use of cleaning agents)	Indoor	50%	8A	90%	ERC8A with amendment. Assume emission control technology is in place for 10%
	Outdoor	50%	8D	100%	

Appendix B.9.16. Petroleum and mining

Flow diagrams for estimated emissions from tracer products, anti-foaming agent products and fluoropolymer products (low and high scenarios) can be found in Baseline year: **2020**

Notes on ranges of data: [1] Scenario 3; [2] Scenario 1; [3] Scenario 1 and 2;

For a full description of each scenario, see NEA (2021).

* Calculated using Environmental Release Category (ERC) emission scenario no.2 for 'formulation into a mixture' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 2.5% w.w to air; 2% w.w to wastewater and 0.01% w.w to soil.

Figure B.81 and Baseline year: **2020**

Notes on ranges of data: [1] Scenario 3; [2] Scenario 1; [3] Scenario 2 and 3;

For a full description of each scenario see NEA (2021).

* Calculated using Environmental Release Category (ERC) emission scenario no.2 for 'formulation into a mixture' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 2.5% w.w to air; 2% w.w to wastewater and 0.01% w.w to soil.

Figure B.82. A source flow diagram for estimated emissions from fluoropolymer products (low scenario) is given in Baseline year: **2020**

[1] Calculated using the total calculated residual monomeric PFAS content of the fluoropolymer and the total emissions across all use stages

* Calculated using Environmental Release Category (ERC) emission scenario no.3 for 'Formulation into a solid matrix' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 30% w.w to air; 0.2% w.w to water (before STP) and 0.1% w.w to soil.

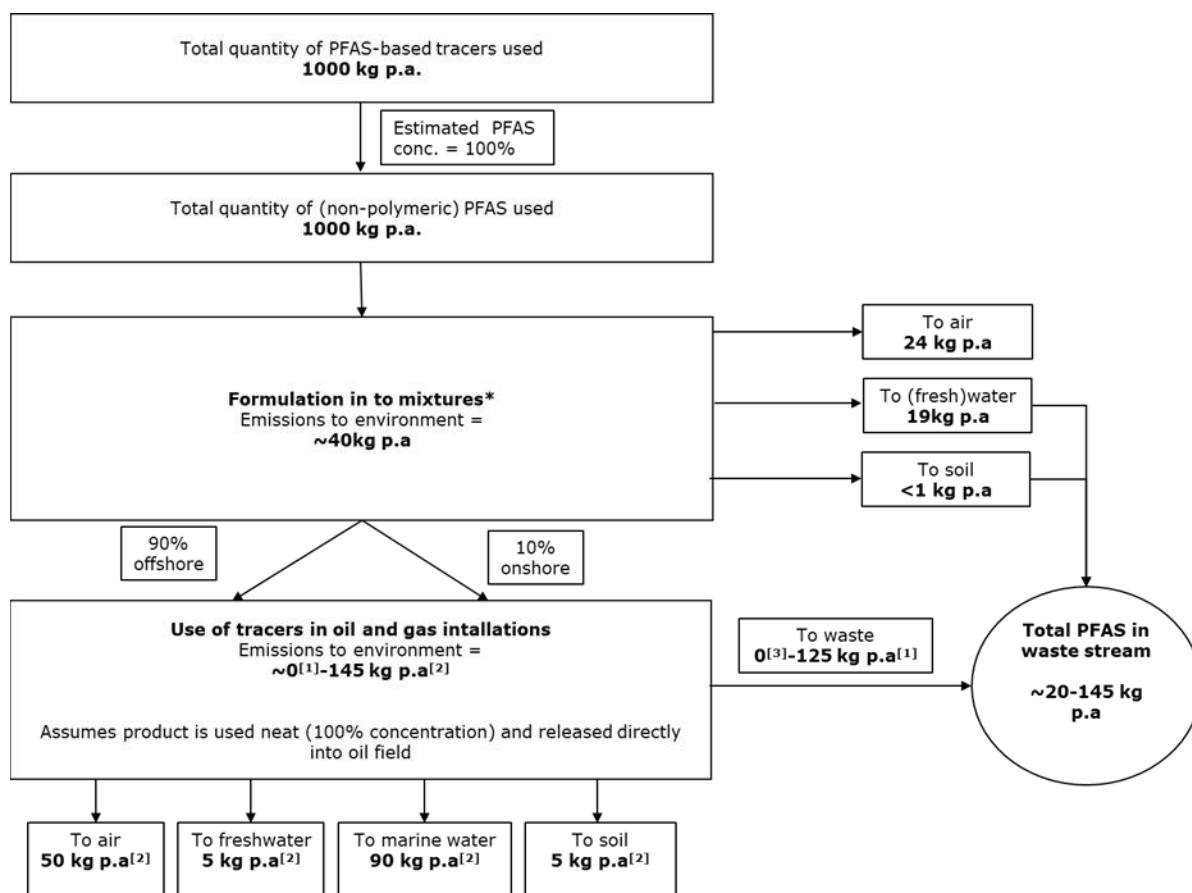
Figure B.83. The high scenario picture for emissions from fluoropolymer products is given in Baseline year: **2020**

[1] Calculated using the total calculated residual monomeric PFAS content of the fluoropolymer and the total emissions across all use stages

* Calculated using Environmental Release Category (ERC) emission scenario no.3 for 'Formulation into a solid matrix' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 30% w.w to air; 0.2% w.w to water (before STP) and 0.1% w.w to soil.

Figure B.84.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)



Baseline year: 2020

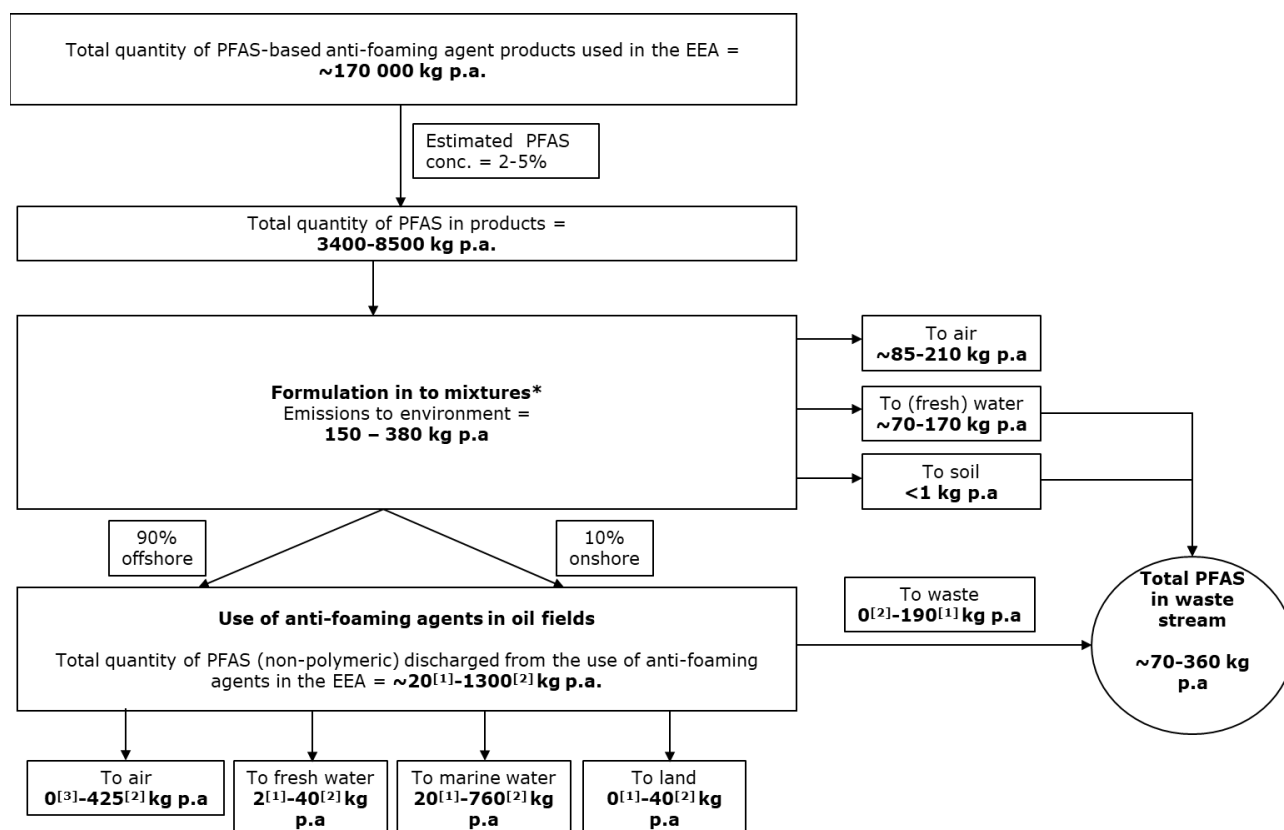
Notes on ranges of data: [1] Scenario 3; [2] Scenario 1; [3] Scenario 1 and 2;

For a full description of each scenario, see NEA (2021).

* Calculated using Environmental Release Category (ERC) emission scenario no.2 for 'formulation into a mixture' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 2.5% w.w to air; 2% w.w to wastewater and 0.01% w.w to soil.

Figure B.81. Source flow diagram for estimated emissions from tracer products.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)



Baseline year: 2020

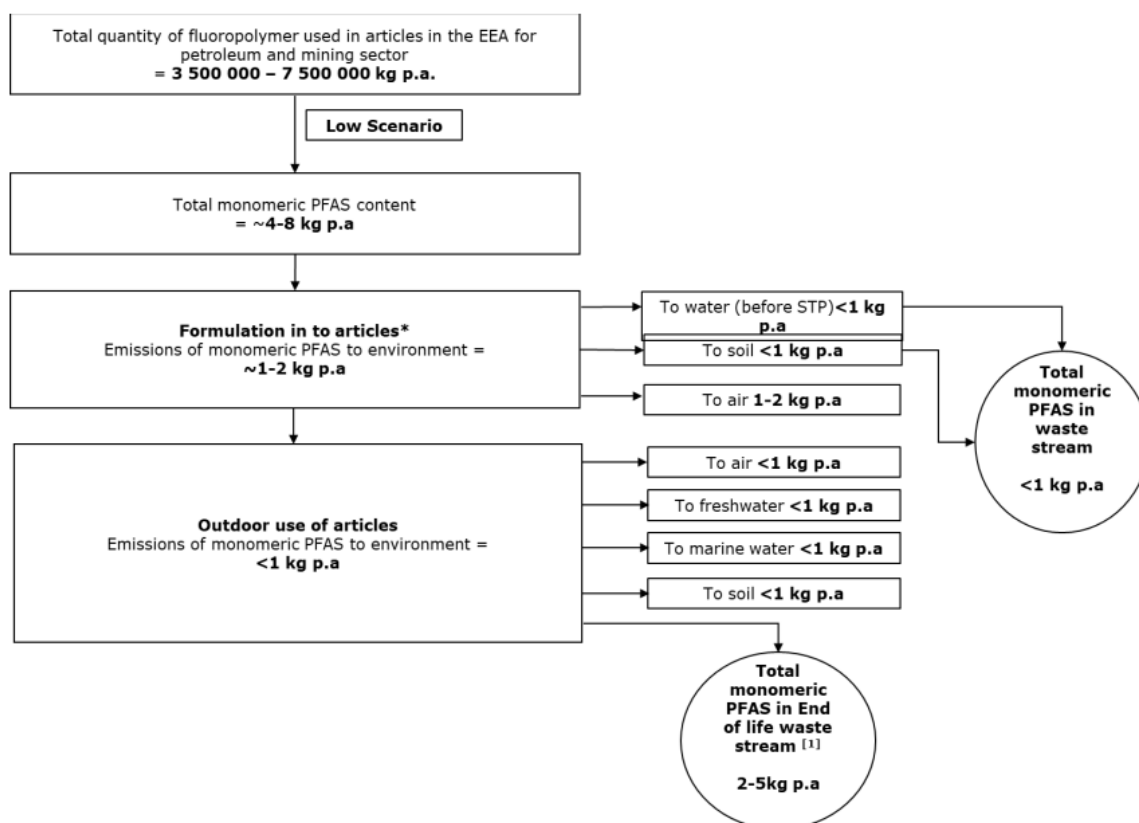
Notes on ranges of data: [1] Scenario 3; [2] Scenario 1; [3] Scenario 2 and 3;

For a full description of each scenario see NEA (2021).

* Calculated using Environmental Release Category (ERC) emission scenario no.2 for 'formulation into a mixture' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 2.5% w.w to air; 2% w.w to wastewater and 0.01% w.w to soil.

Figure B.82. Source flow diagram for estimated emissions from anti-foaming agents products.

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)



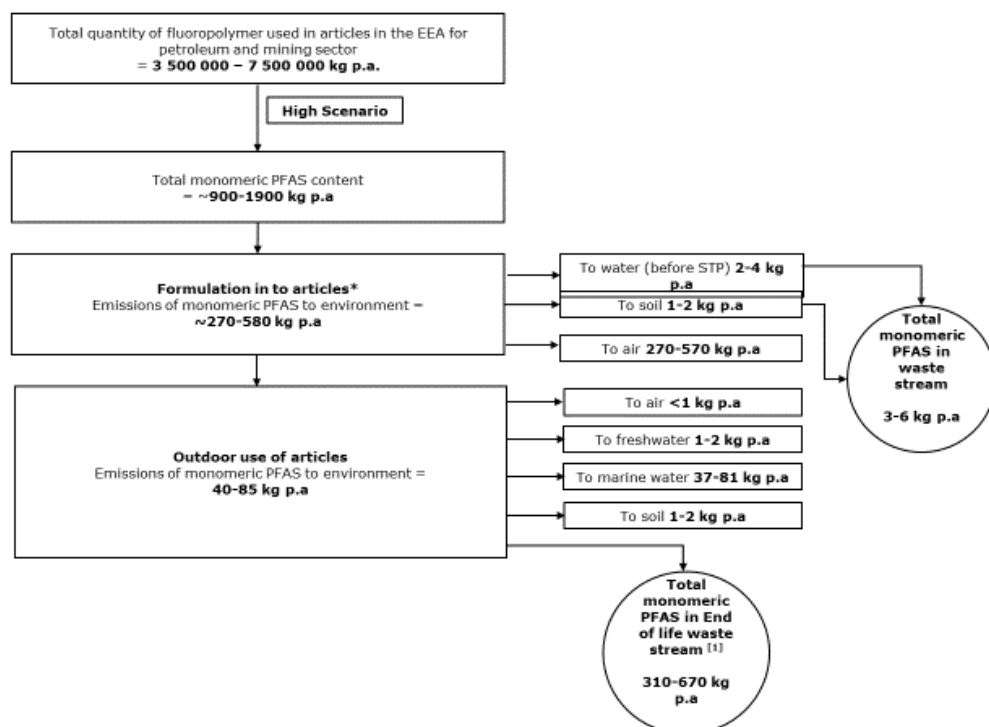
Baseline year: 2020

[1] Calculated using the total calculated residual monomeric PFAS content of the fluoropolymer and the total emissions across all use stages

* Calculated using Environmental Release Category (ERC) emission scenario no.3 for 'Formulation into a solid matrix' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 30% w.w to air; 0.2% w.w to water (before STP) and 0.1% w.w to soil.

Figure B.83. Source flow diagram for estimated emissions (low scenario) from FP products (fluoropolymer products).

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)



Baseline year: 2020

[1] Calculated using the total calculated residual monomeric PFAS content of the fluoropolymer and the total emissions across all use stages

* Calculated using Environmental Release Category (ERC) emission scenario no.3 for 'Formulation into a solid matrix' from ECHA (2016) Guidance on information requirements and Chemical Safety Assessment, Chapter R.16: Environmental exposure assessment. 30% w.w to air; 0.2% w.w to water (before STP) and 0.1% w.w to soil.

Figure B.84. Source flow diagram for estimates emissions (high scenario) from FP products (fluoropolymer products).

Appendix B.9.21. Human exposure

Table B.111 and Table B.112 summarise concentrations of PFASs in indoor air and dust and include all measured PFASs, including precursors and PFAAs covered by existing and/or proposed restrictions.

Table B.111. Concentration of PFAS in indoor air (pg/m³) described by detection frequency (% or x/xx), median in bold and range within brackets.

Site (N)	Country, year	PFCAs	PFSAs	FTOHs	FOSAs	FOSEs	FTACs	6:2 FTMA C	Reference
Homes (10)	Spain, Catalonia 2009			6:2FTOH: 100% (2.0-47) 8:2FTOH: 100% 42 (7.5-170) 10:2FTOH: 80% (<0.6-47) ΣFTOHs: 100% (13-234)	ΣFOSE/FOSAs: (<LOQ-23) MeFOSA: 65% (<1.2-14)				(Ericson Jogsten et al., 2012)
Schools (14)	Germany Munich 2014			4:2FTOH: 0% 6:2FTOH: 100% 3 342 (1 428-46 867) 8:2FTOH: 100% 4 435 (2 480-13 888) 10:2FTOH: 100% 1 807 (1 166-4 774)	MeFOSA: 0% EtFOSA: 57% 243 (<LOD-692)	MeFOSE: 21% (<LOD-156) EtFOSE: 0%	6:2FTACs: 14% (<LOD-2 604) 8:2FTAC: 79% 448 (<LOD-47 739) 10:2FTAC: 57% 307 (<LOD-17 360)		(Fromme et al., 2015)
Homes (13)				4:2FTOH: 0% 6:2FTOH: 100% 1 808 (289-5 424) 8:2FTOH: 100% 8 679 (4 702-21 698) 10:2FTOH: 100% 2 531 (759-10 306)	MeFOSA: 38% (<LOD-166) EtFOSA: 23% (<LOD-119)	MeFOSE: 92% (<LOD-3 796) EtFOSE: 62% 66 (<LOD-155)	6:2FTAC: 0% 8:2FTAC: 100% 271 (58-1 040) 10:2 FTAC: 85% 123 (<LOD-		

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Site (N)	Countr y, year	PFCAs	PFSAs	FTOHs		FOSAs	FOSEs	FTACs	6:2 FTMA C	Refere nce
								560)		
Homes (40)	Norway, Oslo 2008			4:2FTOH: 17% (<LOQ-38) 6:2FTOH: 100% 933 (63-9414) 8:2FTOH: 100% 5 173 (921-25 323) 10:2FTOH: 100% 2 822 (377-28 898)		MeFOSA: 67% 8.3 (<LOQ-70) EtFOSA: 40% (<LOQ-95)	MeFOSE:100% 265 (63-1 433) EtFOSE: 100% 78 (3.7-338)			(Haug et al., 2011b)
Homes (6)	Norway, Tromsø 2007-08			4:2FTOH: 4/6 21 (<16-34) 6:2FTOH: 100% 42 (16-332) 8:2FTOH: 100% 10 005 (3 373-11 109) 10:2FTOH: 100% 3 405 (1 231-5 901)		NMeFOSA: 100% 27 (9.2-224) NEtFOSA: 100% 29 (7.4-104)	NMeFOSE: 100% 846 (222-1 288) NetFOSE: 100% 156 (65-333)			(Huber et al., 2011)
Homes (61)	Norway, Oslo 2013-14			6:2FTOH: 100% 2 970 (604-101 000) 8:2FTOH: 100% 10 400 (1 220-446 000) 10:2FTOH: 100% 3120 (697-255 000)		MeFOSA: 13% (<35-78 300) EtFOSA: 7% (<35-1 350)	MeFOSE:70% 134 (<71-38 800) EtFOSE: 49% (<50-13 200)			(Padilla - Sanchez et al., 2017)
Personal air (24h) (15)				6:2FTOH: 100% 1 970 (543-37 000) 8:2FTOH: 100% 7 170 (2690-57 800) 10:2FTOH: 100% 1 590 (170-9 000)		MeFOSA: 7% (<70-225) EtFOSA: 0% (<70)	MeFOSE:20% (<350-1 105) EtFOSE: 0% (<350)			
Offices (2)	German y			4:2FTOH: <LOD 6:2FTOH: (150-650)	8:2FTOH: (250-830) 10:2FTOH : (110-				(Schlummer et al., 2013)	

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Site (N)	Country, year	PFCAs	PFASs	FTOHs		FOSAs	FOSEs	FTACs	6:2 FTMA C	Reference
					290)					
Commercial kitchen (1)				4:2FTOH: <LOD 6:2FTOH: 240	8:2FTOH: 270 10:2FTOH: 110					
Metal workplace (1)				4:2FTOH: <LOD 6:2FTOH: 280	8:2FTOH: 360 10:2FTOH: 160					
Car lacquering (1)				4:2FTOH: <LOD 6:2FTOH: 910	8:2FTOH: 1890 10:2FTOH: 800					
Sport shops (2)				4:2FTOH: <LOD 6:2FTOH: 1070-6180	8:2FTOH: 12450-17980 10:2FTOH: 3620-5150					
Carpet shop (1)				4:2FTOH: <LOD 6:2FTOH: 35960	8:2FTOH: 26150 10:2FTOH: 9640					
Homes (57)	Finland, Kuopio 2014-15	PFBS: 47% (<1.0-15) PFHxA: 68% 9.0 (<6.0-144) PFHpA: 44% (<2.1-13) lin-PFOA:	br-PFHxS: 2% (<0.2-0.3) lin-PFHxS: 16% (<0.5-1.6) br-PFOS: 93%	6:2FTOH: 98% 1310 (<290-8060) 8:2FTOH: 100% 3570 (1290-13500) 10:2FTOH: 100% 928 (210-8950)		MeFOSA: 21% (<8-20) EtFOSA: 33% (<8-340)	MeFOSE: 95% 56 (<8-394) EtFOSE: 68% 17 (<8-132)	6:2FTAC: 28% (<9.6-61)	58% 21 (<11-13000)	(Winckens et al., 2017a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Site (N)	Country, year	PFCAs	PFSA	FTOHs	FOSA	FOSE	FTAC	6:2 FTMA C	Reference
		98% 15 (<4.5-100) PFNA : 100% 2.4 (0.9-16) PFDA : 100% 4.2 (1.3-30) PFUnDA : 98% 0.7 (<0.3-8.2) PFDoDA : 96% 0.8 (<0.3-5.6) PFTTrDA : 21% (<0.3-2.2) PFTeDA : 63% 0.3 (<0.3-1.8) PFPeDA : 7% (<0.4-1.1)	0.7 (<0.2-2.9) lin-PFOS : 88% 1.2 (<0.5-5.0)						
Homes (59)	Canada, Vancouver 2007	PFHxA : 94% 10 (<0.02-205) PFHpA : 90% 5.4 (<0.3-69) PFOA : 100% 21 (3.4-2 570) PFNA : 62% (<0.02-2 166) PFDA : 97% 7.9 (<0.02-977) PFUA : 23% (0.02-79) PFDoA : 28% (>0.02-263) PFTA : 5%	PFOS : 0% (<0.02)	6:2FTOH : 97% 1 040 (<7-22 890) 8:2FTOH : 100% 2 720 (660-16 080) 10:2FTOH : 100% 980 (220-8 160)	MeFOSA : 98% 21 (<1.4-812) EtFOSA : 100% 19 (3.1-910)	MeFOSE : 100% 320 (54-9 520) EtFOSE : 97% 56 (<0.9-1 000)			(Shoeib et al., 2011)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Site (N)	Country, year	PFCAs	PFASs	FTOHs	FOSAs	FOSEs	FTACs	6:2 FTMA C	Reference
		(<0.03-3.7)							

Table B.112. Concentrations (ng/g) of PFASs in indoor dust described by median in bold and range within brackets. DCC=daycare centers, CR=classrooms.

Location (N)	Country Year	PFASs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
DCC & CR (42)	UK 2007-08	PFHxS: 700 (16-34 000) PFOS: 840 (22-3700)	PFOA: 240 (18-1 700)						FOSA: (<0.02-750) MeFOSA: ND (<0.1) EFOSA: 30 (<0.07-640)	MeFOSE: 660 (<0.02-8400) EtFOSE: 370 (<0.12-13 000)			(Goosey and Harrad, 2011)
Homes (10)	France 2007-09	PFHxS: 77 (54-320) PFOS: 160 (54-1700)	PFOA: 31 (15-220)						FOSA: 3.0 (<0.02-300) MeFOSA: (<0.1-31) EtFOSA: 130 (23-320)	MeFOSE: 130 (<0.22-610) EtFOSE: 140 (<0.12-550)			
Homes (10)	Germany 2007-09	PFHxS: 150 (16-790) PFOS: 170 (47-1000)	PFOA: 300 (19-730)						FOSA: 47 (<0.02-130) MeFOSA: <0.1 (<0.1-16) EtFOSA:	MeFOSE: 38 (<0.22-700) EtFOSE: 120 (11-180)			

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
									120 (36-730)				
Home s (45)	UK 2007-09	PFHxS: 210 (7.6-6100) PFOS: 140 (3.5-7400)	PFOA: 190 (<0.98-4100)						FOSA: 20 (<0.02-300) MeFOSA: <0.1 (<0.1-110) EtFOSA: 40 (<0.07-840)	MeFOSE: 93 (0.22-2 500) EtFOSE: 34 (<0.12-3900)			
Home s (41)	Norway 2008	PFBS: 0.40 (0.17-9.8) PFHxS: 0.60 (0.21-142) PFHpS: 0.19 (0.10-2.1) PFOS: 3.1 (1.2-94) PFDS: 1.1 (0.15-42)	PFBA: ND PFPeA: 3.0 (1.5-29) PFHxA: 28 (4.3-96) PFHpA: 9.4 (4.5-28) PFOA: 18 (6.2-56) PFNA: 23 (3.9-92) PFDA: 4.1 (1.1-12) PFUnDA: ND PFDoDA: 19 (1.4-			6:2FTU CA: 10 (4.3-301) 8:2FTU CA: 3.6 (1.0-78)	6:2FTS: 4.8 (2.2-53) 8:2FTS: 5.3 (2.2-99)		MeFOSA: 0.51 (0.27-1.1) EtFOSA: 0.61 (0.26-33)	MeFOSE: 9.0 (3.5-90) EtFOSE: ND		PFOSA: 0.45 (0.22-41)	(Haug et al., 2011b)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			78) PFTTrDA: 6.8 (1.1-46) PFTTeDA: 3.3 (1.1-35)										
Home s (31)	Germany 2008-09	PFOS: 20 (3.3-1046)	PFOA: 39 (6.1-676)					ΣFTOHs: 26 (4.8-734) 4:2FTOH: ND 6:2FTOH: 3.7 (<LOD-246) 8:2FTOH: 13 (2.4-256) 10:2FTOH: 6.6 (1.0-232)					(Xu et al., 2013)
Home s (10)	Spain 2009	PFBS: 0.36 (<0.001-6.5) PFHxS: 0.44 (0.17-5.3) PFOS:2.4 (1.1-12)	PFBA: 19 (7.2-25) PFPeA: 0.36 (<0.013-0.93) PFHxA: 1.0 (0.40-2.9) PFHpA: 1.2 (0.46-			6:2FTUCA: (<0.002-0.08) 8:2FTUCA: (<0.002-0.08)		6:2FTOH: 0.029 (<0.001-6.5) 8:2FTOH: 0.35 (<0.05-1.3) 10:2FTOH: (<0.04-0.39)		MeFOSE: (<0.12-0/<51) EtFOSE: 0.15 (<0.07-1.9)			(Ericson Jogsten et al., 2012)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPAPs	DiPAPs	FTCA/FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			4.0) PFOA: 4.2 (1.5-36) PFNA: 0.87 (0.4-37) PFDA: 1.4 (0.75-41) PDUnDA: 0.6 (<0.06-15) PFDODA: 0.93 (<0.01-17) PFTTrDA: 0.16 (0.05-77)										
Homes (10)	Spain 2009	PFBS: 1.4 (<0.39-3.9) PFHxS: 0.39 (<0.09-1.0) PFOS: 5.3 (2.1-7.2) PFDS: (<0.01-0.02)	PFBA: (<2.0-3.5) PFPeA: 0.37 (<0.36-2.1) PFHxA: 3.4 (<3.2-5.4) PFHpA: 0.90 (<1.2-5.9) PFOA: 8.8 (<7.0-40) PFNA: 1.7 (<0.96-43)	ΣmPAPs: 15 (<LOD-213)	ΣdiPAPs: 14 (7.8-100)	FTCA/FTUCA: 1.0 (<LOD-26)	6:2FTSA: 2.6 (<LOD-12)		FOSA/FOSE: 6.2 (<LOD-66)			PFOSA: (<LOD-1.6)	(Eriksson and Kärrman, 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			PFDA: 3.7 (2.1-81) PFUnDA: 1.1 (<0.42-33) PFDoDA: 2.0 (1.0-60) PFTTrDA: 0.72 (0.36-13) PFTeDA: 1.1 (0.02-15) PFHxDA: 0.69 (<0.03-12) PFOcDA: (<0.05-0.82)										
Public indoor areas (20)	Greece, 2012	PFBS: (<LOD-99) PFHxS: (<LOD-40) PFOS: (<LOD-227) PFDS: 0.93 (<LOD-12)	PFBA: (<LOD-164) PFPeA: (<LOD-11) PFHxA: 3.6 (<LOD-72) PFHpA: (<LOD-117) PFOA: 10 (<LOD-653)						FOSA: (<LOD-854)				(Besis et al., 2019)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			PFNA: 2.1 (<LOD-11) PFDA: 3.2 (<LOD-7.4) PFUnDA: 1.4 (<LOD-3.7) PFDoDA: 3.8 (<LOD-13)										
Homes (12)	Czech Republic 2013	PFBS: (ND-14) PFHxS: 2.0 (<LOQ-9.3) PFHpS: (ND-4.6) PFOS: 10 (4.8-118) PFDS: 0.8 (ND-6.6)	PFPeA: (ND-6.3) PFHxA: 3.8 (1.4-69) PFHpA: 1.8 (<LOQ-7.8) PFOA: 2.0 (<LOQ-27) PFNA: (ND-11) PFDA: (ND-17) PFUnDA: (ND-4.3) PFDoDA: 0.5 (ND-13) PFTTrDA: (ND-3.5) PFTeDA: (ND-15)							NMeFOS E: (ND-16) NEtFOSE: (ND-6.4)			(Karásková et al., 2016)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPAPs	DiPAPs	FTCA/FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
Home s (10)	Faroe Islands 2013-14	PFBS: 1.9 (<0.39-10) PFHxS: 0.37 (<0.09-11) PFOS: 5.7 (2.6-149) PFDS: (<0.01-0.54)	PFBA: (<2.0-7.0) PFPeA: 0.74 (<0.36-14) PFHxA: 8.0 (2.6-73) PFHpA: 2.3 (1.3-28) PFOA: 15 (<7.0-192) PFNA: 2.4 (1.0-11) PFDA: 4.8 (2.1-13) PFUnDA: 1.4 (0.73-5.2) PFDoDA: 4.1 (1.5-7.8) PFTTrDA: 0.58 (<0.02-2.7) PFTeDA: 1.2 (<0.02-3.7) PFHxDA:1.6 (<0.03-	ΣmPAPs: 451 (162-1691)	ΣdiPAPs: 450 (130-1830)	FTCAs/FTUCA s: 0.2 (<LOD-7.7)	6:2FTSA: 11 (<LOD-15)					PFOSA: (<LOD-2.4)	(Eriksson and Kärrman, 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPAPs	DiPAPs	FTCA/FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			2.6) PFOcDA: (<0.05-0.43)										
Homes (10)	Sweden 2013-14	PFBS: 1.2 (<0.39-2.5) PFHxS: 0.15 (<0.09-3.6) PFOS: 2.8 (<0.68-9.7) PFDS: 0.01 (<0.01-0.44)	PFBA: (<2.0-6.3) PFPeA: (<0.36-5.3) PFHxA: 7.0 (<3.2-40) PFHpA: 1.5 (<1.2-8.8) PFOA: 14 (<7.0-49) PFNA: 2.0 (<0.96-8.5) PFDA: 3.7 (<1.8-35) PFUnDA: 0.94 (<0.42-6.1) PFDODA:	ΣmPAPs: 105 (<LOD-193)	ΣdiPAPs: 62 (12-899)	FTCA/FTUCA: 0.1 (<LOD-20)	6:2FTSA: 1.5 (<LOD-16)		FOSA/FOSE: (<LOD-70)			PFOSA: (<LOD-1.5)	(Eriksson and Kärrman, 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPAPs	DiPAPs	FTCA/FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			3.4 (0.58-17) PFTTrDA: 0.29 (<0.02-3.4) PFTeDA: 0.33 (<0.02-13) PFHxDA: (<0.03-2.2) PFOcDA: (<0.05-0.28)										
Homes (7)	Greece 2013-14	PFBS: 1.2 (<0.39-2.7) PFHxS: 0.41 (0.26-11) PFOS: 7.2 (2.8-81) PFDS: (<0.01-0.43)	PFBA: (<2.0-7.1) PFPeA: (<0.36-8.7) PFHxA: 3.8 (<3.2-26) PFHpA: (<1.2-30) PFOA: 13 (<7.0-129) PFNA: 3.5 (<0.96-18) PFDA: 5.4 (<1.8-21) PFUnDA: 2.9 (0.72-	ΣmPAPs : 6 (<LOD-134)	ΣdiPAPs: 25 (8.8-213)	FTCA/FTUCA: 0.2 (<LOD-3.0)	6:2FTSA: 2.2 (<LOD-3.9)		FOSA/FOSE: (<LOD-17)			PFOSA: (<LOD-12)	(Eriksson and Kärrman, 2015)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPAPs	DiPAPs	FTCA/FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			7.9) PFDoDA: 3.6 (1.1-8.0) PFTTrDA: 1.1 (0.60-3.0) PFTeDA: 1.2 (0.55-6.3) PFHxDA:1.4 (<0.03-4.7) PFOcDA: (<0.05-0.55)										
Homes (46 from 17 homes)	Sweden 2013-14	PFBS: (<LOD-8.7) PFHxS: (<LOD-8.1) PFOS: 13 (<LOQ-220)	PFBA: (<LOD-23) PFPeA: (<LOD-23) PFHxA: 6.4 (<LOD-99) PFHpA: 2.2 (<LOD-95) PFOA: 9.0 (<LOQ-650) PFNA: 3.4 (<LOD-44) PFDA: 3.2 (<LOD-	6:2mPA P: 31 (<LOQ-460) 8:2mPA P: 22 (<LOQ-360)	6:2diPAP : 65 (11-1 300) 8:2diPAP : 49 (7-920)		8:2FTS: 1.8 (<LOD-220)		FOSA: <LOD			6:6PFPI A: (<LOD-16) 6:8PFPI A: (<LOD-27) 8:8PFPI A: 0.10 (<LOD-11) PFHxPA: (<LOD-31) PFOPA: 3.3	(Weiss et al., 2021)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPAs	DiPAPs	FTCA/FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			100) PFUnDA: 1.0 (<LOD-22) PFDoDA: (<LOD-110) PFTTrDA: (<LOD-9.1) PFTTeDA: (<LOD-56)									(<LOD-1800) PFDPA: (<LOD-70)	
Homes (65)	Finland 2014-15	PFBS: (<MDL-13) PFHxS: (<MDL-37) L-PFOS: 0.95 (<MDL-11) Br-PFOS: (<MDL-4.6) PFDS: (<MDL-34)	PFBA: (<MDL-14) PFPeA: (<MDL-5.1) PFHxA: 2.3 (<MDL-54) PFHpA: (<MDL-19) L-PFOA: 5.3 (<MDL-83) Br-PFOA: (<MDL-3.8) PFNA: 1.0 (<MDL-15) PFDA: 1.6 (<MDL-67) PFUnDA: (<MDL-4.6) PFDoDA: 0.78	6:2mPA P: 15 (<MDL-369) 8:2mPA P: (<MDL-76) 10:2mP AP: (<MDL-830)	4:2/6:2d i-PAP: (<MDL-1.3) 6:2diPAP: 54 (1.9-1 360) 6:2/8:2d i-PAP: 11 (<MDL-298) 6:2/10:2 di-PAP: 3.2 (<MDL.154) 6:2/12:2 di-PAP: 1.1 (<MDL-66)		6:2FTSA: (<MDL-92) 8:2FTSA: 3.1 (<MDL-348)	4:2FTOH: ND 6:2FTOH: 28 (<MDL-288) 8:2FTOH: 46 (<MDL-298) 10:2FTOH: 16 (<MDL-138)	FOSA: (<MDL-0.23) MeFOSA: (<MDL-9.2) EtFOSA: ND	MeFOSE: (<MDL-158) EtFOSE: 10 (<MDL-514)	FOSAA: (<MDL-0.27) NMeFOSAA: (<MDL-1.0) NEtFOSAA: 3.0 (0.21-422)	6:2FTMAC: (MDL-50) 6:2Cl-PFESA: (<MDL-0.69) 8:2Cl-PFESA: ND ADONA: ND	(Winkens et al., 2018)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			(<MDL-44) PFTTrDA: (<MDL-4.2) PFTeDA: (<MDL-14) PFPeDA: (<MDL-0.64)		6:2/14:2 di-PAP: 5.5 (<MDL-292) 8:2diPAP : 3.5 (<MDL-118) 8:2/10:2 di-PAP: 0.88 (<MDL-38) 8:2/12:2 di-PAP: 8.0 (<MDL-384) 10:2diPA P: 6.6 (<MDL-322)								
Homes (65)	Belgium, Italy, Spain 2016-17	PFBS: 0.40 (nd-57) PFHxS: 0.13 (nd-11) PFOS: 0.28 (nd-60)	PFBA: 0.11 (nd-21) PFPeA: 0.02 (nd-21) PFHxA: 0.31 (nd-28) PFHpA:						FOSA: 0.01 (nd-1.0)				(de la Torre et al., 2019)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFSAs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			1.0 (nd-105) PFOA: 1.4 (0.21-53) PFNA: 0.04 (nd-9.0) PFDA: 0.49 (nd-26) PFUnDA: 0.17 (nd-7.7) PFDoDA: 0.28 (nd-20) PFTTrDA: 0.23 (nd-11) PFTeDA: 1.1 (nd-38) PFHxDA: 0.75 (nd-15) PFOcDA: 0.46 (nd-5.0)										
Homes (102)	Canada 2007-08				Σ diPAPs: 2214 (NR-185 267)							Σ PFPIAs: 2.3 (NR-2 044) Σ PFPAAs: 2.3 (NR-	(De Silva et al., 2012)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
												1 289)	
Home s (40)	China 2015-18	PFBS: 18 PFHxS: 0.68 L-PFHps: <LOQ (median) PFOS: 4.2 PFDS: <LOQ (median)	PFBA: ND PFPeA: ND PFHxA: ND PFHpA: <LOQ (median) L-PFOA: <LOQ (median) PFNA: <LOQ (median) PFDA: 1.2 PFUnDA: 1.2 PFDoDA: 0.67 PFTTrDA: <LOQ (median) PFTeDA: 0.24	6:2mPA P: <LOQ (median) 8:2mPA P: <LOQ (median)	6:2diPAP : 3.4 8:2diPAP : <LOQ (median)		4:2FTS: ND 6:2FTS: <LOQ (median) 8:2FTS: <LOQ (median)		FOSA: 0.25 NMeFOSA: ND NetFOSA: <LOQ (median)	NMeFOS E: ND NEtFOSE : ND		PFHxPA: ND PFOPA: ND PFDDPA: ND 6:2CI-PFESA: 1.1 8:2CI-PFESA: 0.08	(Xu et al., 2021a)
Home s (13) industrial area	China 2018	PFBS: 113 (<0.03-603) PFHxS: 0.59 (<0.03-62) PFOS: 12	PFBA: 13 (7.0-30) PFPeA: 1.9 (0.95-5.8) PFHxA: 2.8 (1.2-3.6) PFHpA:			6:2FTUCA: 3.1 (<0.08-39) 8:2FTUCA: 0.61 (<0.09-1.3)	6:2FTSA: (<0.03-11)		FOSA: ND			6:2CI-PFESA: 7.4 (1.2-53) 8:2CI-PFESA: 1.2 (0.56-4.4)	(Zhang et al., 2020a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
		(0.33-108) PFDS: (<0.10-1.0)	0.21 (<0.03-3.0) PFOA: 11 (5.1-19) PFNA: 2.1 (0.90-4.8) PFDA: 2.8 (2.2-4.1) PFUnDA: 1.9 (1.1-3.3) PFDODA: 1.7 (1.2-2.7)									ADONA: ND HFPO-DA: ND	
Homes (12) urban area	China, 2019	PFBS: 108 (51-264) PFHxS: (<0.03-24) PFOS: 22 (14-146) PFDS: (<0.1-14)	PFBA: 7.0 (3.6-17) PFPeA: 2.4 (0.40-3.6) PFHxA: 6.0 (3.0-8.7) PFHpA: 3.4 (1.9-4.9) PFOA: 20 (11-133) PFNA: 2.6 (1.1-4.1) PFDA: 2.5 (1.1-5.9) PFUnDA:			6:2FTUCA: 1.3 (<0.08-4.1) 8:2FTUCA: 0.39 (<0.09-1.9)	8:2FTSA: 0.19 (<0.03-1.9)		FOSA: (<0.02-6.2)			6:2Cl-PFESA: 5.2 (2.3-8.7) 8:2Cl-PFESA: 2.9 (1.4-9.2) ADONA: ND HFPO-DA: ND	(Zhang et al., 2020a)

ANNEX XV RESTRICTION REPORT – Per- and polyfluoroalkyl substances (PFASs)

Location (N)	Country Year	PFASs	PFCAs	MonoPA Ps	DiPAPs	FTCA/ FTUCA	FTSAs	FTOH	FOSA	FOSE	FOSAA	Other PFASs	Reference
			1.7 (0.96-5.7) PFDODA: 1.9 (<0.6-6.7)										

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