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A modeling assessment of the physicochemical properties and environmental fate of emerging and novel per- and polyfluoroalkyl substances

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HIGHLIGHTS

- COSMOtherm and SPARC are used to estimate physicochemical properties.
- The properties of PFECAs and PFESAs are similar to PFCAs and PFSAs, respectively.
- The OECD Tool is used to estimate the environmental fate.
- Many fluorinated alternatives have similar environmental fate to legacy PFASs.
- Urgently needed experimental studies are highlighted.

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ABSTRACT

Long-chain perfluoroalkyl carboxylic acids (PFCAs) and perfluoroalkane sulfonic acids (PFSAs) are persistent, bioaccumulative, and toxic contaminants that are globally present in the environment, wildlife and humans. Phase-out actions and use restrictions to reduce the environmental release of long-chain PFCAs, PFSAs and their precursors have been taken since 2000. In particular, long-chain poly- and perfluoroalkyl substances (PFASs) are being replaced with shorter-chain homologues or other fluorinated or non-fluorinated alternatives. A key question is: are these alternatives, particularly the structurally similar fluorinated alternatives, less hazardous to humans and the environment than the substances they replace? Several fluorinated alternatives including perfluoroether carboxylic acids (PFECAs) and perfluoroether sulfonic acids (PFESAs) have been recently identified. However, the scarcity of experimental data prevents hazard and risk assessments for these substances. In this study, we use state-of-the-art in silico tools to estimate key properties of these newly identified fluorinated alternatives. [i] COSMOtherm and SPARC are used to estimate physicochemical properties. The US EPA EPISuite software package is used to predict degradation half-lives in air, water and soil. [ii] In combination with estimated chemical properties, a fugacity-based multimedia mass-balance unit-world model – the OECD Overall Persistence (P_{OV}) and Long-Range Transport Potential (LRTP) Screening Tool – is used to assess the likely environmental fate of these alternatives. Even though the fluorinated alternatives contain some structural differences, their physicochemical properties are not significantly different from those of their predecessors. Furthermore, most of the alternatives are estimated to be similarly persistent and mobile in the environment as the long-chain PFASs. The models therefore predict that the fluorinated alternatives will become globally distributed in the environment similar to their predecessors. Although such in silico methods are coupled with uncertainties, this preliminary assessment provides enough cause for concern to warrant experimental work to better determine the properties of these fluorinated alternatives.

1. Introduction

In the last decade, perfluoroalkyl carboxylic acids (PFCAs) and perfluoroalkane sulfonic acids (PFSAs) were recognized as persistent (Remde and Debus, 1996; Key et al., 1998) and those with "long" perfluoroalkyl chains were shown to be bioaccumulative (Houde et al., 2006) and toxic (Kennedy et al., 2004; Borg et al., 2013). Our definition of "long" chain refers to PFCAs with 7 or more fluorinated carbons (including PFOA, which is designated as bioaccumulative under REACH; ECHA, 2013) and their precursors as well as PFSAs with 6 or more fluorinated carbons alnd their precursors (Buck et al. 2011).

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Long-chain PFCAs and PFSAs are globally present, including in the abiotic environment (Yamashita et al., 2005; Young et al., 2007) and wildlife (Kannan et al., 2002) in remote regions, indicating the long-range transport potential of these substances. Furthermore, humans in industrialized countries contain relatively high levels of long-chain PFCAs and PFSAs in their serum (Kannan et al., 2004; Olsen et al., 2003), suggested to be due to the historical presence of these substances and their precursors in a wide range of consumer products (Vestergren and Cousins, 2009). Due to concern regarding their hazardous properties, there have been a number of actions by industry and regulatory authorities to reduce the environmental release of long-chain PFCAs, PFSAs and their precursors. In the period 2000–2002, 3M phased out its global production of perfluorooctane sulfonic acid (PFOS) and related chemicals derived from perfluorooctane sulfonyl fluoride (POSF, C_8; i.e., POSF-based chemicals) and replaced their use in certain key products with perfluorobutane sulfonyl fluoride (PBSF, C_4)-based chemicals. In 2009, PFOS and related POSF-based chemicals were added to Annex B (restriction of production and use) of the Stockholm Convention on Persistent Organic Pollutants (UNEP, 2009). Similar actions have also taken place for perfluorooctanoic acid (PFOA) and other long-chain PFCA homologues. For example, the US Environmental Protection Agency (US EPA) and eight major global fluoropolymer and fluorotelomer manufacturers have agreed to work toward the elimination of long-chain PFCAs and their precursors from point-source emissions and products by 2015 (US EPA, 2006). In addition, PFOA and its ammonium salt (APFO) as well as C_{11}–C_{14} PFCAs have been listed in the Candidate List of Substances of Very High Concern under the European chemicals regulation, REACH (ECHA, 2013).

A common feature of all the above actions is an on-going industrial transition to replace long-chain PFCAs, PFSAs and their precursors with alternatives, particularly other poly- and perfluoroalkyl substances (PFASs) such as shorter-chain homologues and functionalized perfluoropolyethers (PFPEs) in applications where extremely low surface tension and/or durable oil- and water-repellency is needed (Holt, 2011). Although the identity of fluorinated substances used in industrial processes and consumer products is often claimed as "confidential business information" (CBI) by the manufacturers, a number of fluorinated alternatives used in different industrial branches and consumer products were identified by Wang et al. (2013). A key question is: are these fluorinated alternatives less hazardous for humans and the environment than their predecessors? There have been other historical examples showing the problems associated with removing a chemical from the market and replacing it with other structurally similar chemicals from the same class of substances (Strempel et al., 2012; Goldstein et al., 2013). Wang et al. (2013) reviewed available knowledge on the identified fluorinated alternatives and highlighted the scarcity of information on their production volumes, emissions, (bio) degradability, bioaccumulative potential and (eco)toxicity. Conducting experiments to generate missing data for all these fluorinated alternatives is expensive and time-consuming. However, a preliminary assessment using in silico methods including quantitative structure–property/activity relationships (QSPRs/QSARs) can provide valuable insights and help to prioritize future research needs (Strempel et al., 2012, Gawor and Wania, 2013; Howard and Muir, 2010).

The aim of this work is to provide a preliminary assessment of emerging and novel fluorinated alternatives with state-of-the-art in silico tools. We use the terminology of "emerging" and "novel" that has previously been applied to brominated flame retardants (Bergman et al., 2012). Emerging fluorinated alternatives are defined as alternatives have been recently identified in the environment, wildlife, food or humans (e.g. Adona). Most of the alternatives included in this study are novel alternatives, i.e. those are known to be present in manufacturing processes, materials and products but have not yet been identified in environmental samples, wildlife, food or humans. First, COSMOtherm and SPARC are used to predict physicochemical properties and EPISuite is used to predict degradation half-lives in air, water and soil. COSMOtherm and SPARC were previously used to estimate the physicochemical properties of long-chain PFASs, including partition coefficients (Arp et al., 2006; Wang et al., 2011) and acid dissociation constants (pK_as) (Goss, 2008). The US EPA EPISuite software package is a well-established QSPR/QSAR tool used to estimate physicochemical properties and degradation half-lives in hazard assessments (Strempel et al., 2012; Zarfl et al., 2012). It has, however, been shown to be inaccurate for estimating the physicochemical properties of PFASs (Arp et al., 2006) and is therefore only used here for estimating the environmental degradation half-lives. The structural differences of the fluorinated alternatives and their estimated physicochemical properties are analyzed to provide insights into the impact of structural changes on physicochemical properties. Second, based on the estimated physicochemical properties and degradation half-lives, the environmental fate of the fluorinated alternatives, more specifically the overall persistence (P_{OV}) and long-range transport potential (LRTP), is assessed by using the OECD Overall Persistence and Long-Range Transport Potential Screening Tool (hereafter "the OECD Tool"). The OECD Tool was developed as a "consensus model" combining the essential aspects of nine multimedia fate and transport models (Wegmann et al., 2009). It should be noted that this study focuses on the physicochemical properties and possible environmental fate (POV and LRTP) of the selected fluorinated alternatives. The prediction of bioaccumulation potential (B) and (eco)toxicity (T) is not included in this study because there is a lack of mechanistic understanding about the possible oleo- and proteinophilic bioaccumulation behavior as well as the toxic mode-of-action of these fluorinated alternatives. However, a discussion of possible strategies for assessing B is included in the Discussion section.

2. Methods

2.1. Selected fluorinated alternatives

A total of 16 emerging and novel fluorinated alternatives were investigated, including five perfluoroether carboxylic acids (PFECAs) and two perfluoroether sulfonic acids (PFESAs) identified by Wang et al. (2013) and for which the chemical structures were known (see Table 1). The selection of the fluorinated alternatives for this study was limited by the large amount of unknown fluorinated chemical structures in the products identified by Wang et al. (2013). Furthermore, some fluorinated alternatives (namely "$CF_2{=}CFOCF_2CF(CF_3)CF_2CF_2SO_2F$ (CAS no. 16090-14-5) and $CF_3OCF(CF_3)COF$") were not considered due to their use in closed industrial processes. These substances are likely used as intermediates to produce monomers for certain polymer. they are not expected to be present in significant quantities in the environment because they are chemically bound on the polymers resulting in a limited fraction of them in industrial waste streams (US EPA, 2012). The plausible degradation products of two alternatives were, on the other hand, included in the analysis, since they could possibly be long-lived chemicals and more toxic than their parent compounds, as observed for other contaminants (Farré et al., 2008).

The 16 fluorinated alternatives and 6 degradation products were divided into four groups: 1) fluorinated alternatives replacing PFOA; 2) fluorinated alternatives replacing PFOS; 3) fluorinated alternatives replacing 8:2 fluorotelomer alcohol (8:2 FTOH); and 4) fluorinated alternatives replacing certain POSF- and/or fluorotelomer-based substances.

For practical purposes, each compound was renamed with a specific abbreviation (based on its acronym, commercial name, etc.) as indicated in Table 1 and will be referred to by this abbreviation throughout the paper.

2.2. Estimation of physicochemical properties

For fluorinated alternatives and their predecessors (PFOA, PFOS and 8:2 FTOH), physicochemical properties were predicted using

COSMOtherm and SPARC. COSMOtherm (v. C3.0 release 01.13, COSMOlogic GmbH & Co. KG) is a quantum-chemistry-based model that was developed according to the 'Conductor-like Screening Model for Real Solvents' (COSMO-RS) theory; details about the model and background theory can be found in the review by Klamt (2003). Detailed property estimation work has been described by Wang et al. (2011), who reported results for physicochemical properties of legacy PFASs. In brief, the estimation of physicochemical properties using COSMOtherm follows several steps: 1) COSMOconf (v. 2.1, COSMOlogic GmbH & Co. KG) is used to search for the lowest energy conformer(s) of the compound of interest in the gas phase, which includes geometry optimization on the quantum chemistry level, calculation of the surface charge density of the molecule and cluster analysis; 2) the surface-charge density of the conformer is further converted into the chemical potential of the molecule in solutions of water and octanol as well as in the gas and pure liquid phases based on statistical thermodynamic equations that are built in COSMOtherm (Buggert et al., 2009). The physicochemical properties of each conformer are then estimated from its chemical potential in the given phase(s); 3) the final physicochemical properties of each chemical are the weighted average, based on the Boltzmann distribution, of the properties of individual conformers. The conformers that require higher energy costs for formation have a lower probability of occurrence and thus these conformers have a smaller contribution to the final averaged property than the energetically more favorable conformers. The following properties were predicted by using COSMOtherm: the air–water, octanol–water, and octanol–air partition coefficients (K_{AW}, K_{OW} and K_{OA}), the sub-cooled liquid phase vapor pressure (P_L), and the solubilities in water (S_W) and octanol (S_O). Due to the absence of experimental data, external comparison of estimated properties was not feasible. Internal consistency among estimated properties was controlled by using the "three solubility" approach proposed by Cole and Mackay (2000).

The acid-dissociation constants (pK_as) of acidic fluorinated alternatives (e.g., PFECAs and PFESAs) were predicted using SPARC (October 2011, release w4.6.1691-s4.6.1687). Briefly, SPARC is a linear free energy (LFER)-based model that adjusts the experimental pK_a value of the ionizable moiety in the molecule as a function of the perturbation exerted by the rest of the structure (Hilal et al., 1996). Hilal et al. (1995) used SPARC to estimate the pK_a for 3685 organic compounds (detailed list not provided by the authors) and SPARC has also been used to estimate the pK_a of PFOA and other fluorinated carboxylic acids (Goss, 2008) and in another study C_2–C_9 PFCAs and C_1–C_8 PFSAs (Rayne and Forest, 2009).

2.3. Estimation of degradation half-lives in air ($t_{1/2,A}$), water ($t_{1/2,W}$), and soil ($t_{1/2,S}$)

The US EPA EPISuite (version 4.11) was used to estimate the degradation half-lives in air, water and soil. The degradation half-life in air ($t_{1/2,A}$) was predicted by AOPWIN. AOPWIN considers only reactions with hydroxyl (OH) radicals and does not consider other processes such as direct photolysis. It predicts a second-order rate constant that can be converted to a pseudo first-order rate constant by multiplying the second-order rate constant with the atmospheric OH radical concentration (i.e. 1.5·10^6 molecules/cm^3). The biodegradation half-lives in water and soil ($t_{1/2,W}$ and $t_{1/2,S}$) under aerobic conditions were predicted using BIOWIN3. The BIOWIN3 model is built on estimated scores of the biodegradability of 200 substances for which the molecular structures are divided into fragment descriptors. The model analyzes the occurrence of certain fragments in the molecular structure of a chemical and then uses the corresponding descriptors to estimate the likely biodegradation half-lives with a score system (i.e. 5 = hours; 4 = days; 3 = weeks; 2 = months; 1 = years). BIOWIN3 outputs were converted into half-lives (in hours) with the conversion scheme proposed by Aronson et al. (2006). Degradation half-lives from AOPWIN and BIOWIN3 were estimated for the substances in their neutral form. Experimental half-lives, whenever available, were preferred over EPISuite estimates. For example, the experimental OH radical reaction rate constants of 3:1 FTOH (Bravo et al., 2010) and 5:1 FTOH (Hurley et al., 2004) were used instead of AOPWIN estimates.

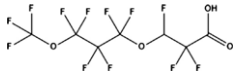
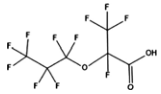
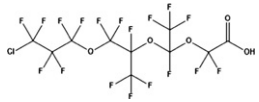
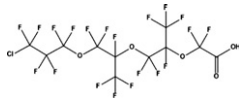
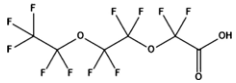
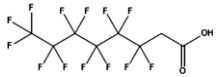
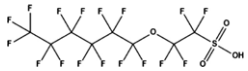
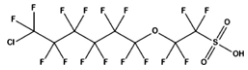
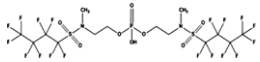
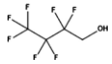
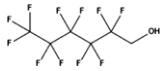
2.4. Structure–property relationships: comparison with PFOS, PFOA and 8:2 FTOH and non-fluorinated analogues

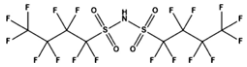
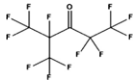
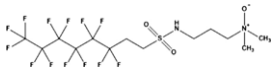
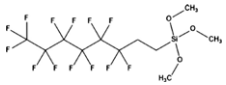
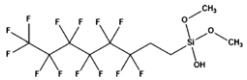
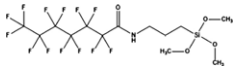
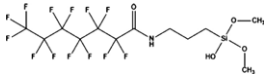
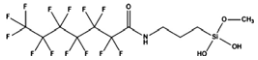
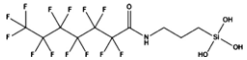
The chemical partition space defined by log K_{OW} and log K_{AW} was used to assess the impact of structural differences, such as the insertion of ether linkages into perfluoroalkyl chains, between PFOS, PFOA and 8:2 FTOH and their respective alternatives (i.e., PFESAs, PFECAs and n:1 FTOHs) on physicochemical properties. Even though PFBSaPA is an alternative to PFOS in metal plating, this compound was not considered at this stage of the analysis since its chemical structure shared few similarities with PFOS. In addition, we conducted comparisons between estimated properties of the PFECAs, PFESAs and PFOS, as a reference for the fully fluorinated carbon chain, and their corresponding hypothetical non-fluorinated analogues (i.e., all fluorine atoms in these fluorinated alternatives were replaced with hydrogen atoms), to gain insight into how (per)fluorination of the molecules influences their physicochemical properties. In order to verify the molecular viability of the non-fluorinated analogues, the experimental information on non-fluorinated analogues of PFECAs and PFESAs was collected; whenever the non-fluorinated compound was not found in the ChemSpider database (i.e., non-fluorinated analogues of PFTECA$_1$, PFTECA$_2$, F-53, F-53B), EPISuite and COSMOtherm were used to assess the likely degradability of the structure and to identify potential reaction centers (i.e., polar moieties). For acidic compounds (such as PFOS, PFOA, PFECAs and PFESAs), the properties of the substances in their neutral form were compared.

2.5. Prediction of environmental fate

The OECD Tool (version 2.2), available for free for download at http://www.oecd.org/env/ehs/risk-assessment/oecdpovandlrtpscreeningtool.htm, was used to assess the environmental fate of the 16 fluorinated alternatives and 6 degradation products. The environmental fate of PFOS, PFOA and 8:2 FTOH was also estimated for comparison. The OECD Tool is a fugacity-based multimedia mass balance unit-world model, containing three bulk compartments representing soil surface layer, seawater surface layer, and the troposphere (Wegmann et al., 2009). Details on the technical background and design of the model are provided by Wegmann et al. (2009). The model input parameters are log K_{AW}, log K_{OW}, $t_{1/2,A}$, $t_{1/2,W}$, and $t_{1/2,S}$. It should be noted that in this study the physicochemical properties were estimated for the neutral form of the substances. Because anionic species have substantially different environmental fate and behavior from neutral species (e.g., anionic species partition much more into aqueous phases rather than into air and/or lipid phases, in comparison to neutral species), it is necessary to account for the extent of dissociation and make adjustments in the modeling. Therefore, we made the following assumptions and adjustment of estimated physicochemical properties: if SPARC predicted the pK_a value to be higher than 6, a substance was assumed to be mainly in the neutral form under assumed environmental pH conditions and the estimated log K_{OW} and log K_{AW} were directly used as input parameters for the model; for substances with a predicted pK_a lower than 6, the estimated log K_{OW} and log K_{AW} were corrected according to the ionized fraction of the chemical. To this end, the air–water and octanol–water distribution ratios, D_{AW} and D_{OW}, as suggested by Wang et al. (2011), were calculated as follows

Table 1
List of the 16 fluorinated alternatives and 6 degradation products chosen in this study, together with their commercial name (whenever available), abbreviation, CAS number, structure and industrial application (whenever available). Strong acids are indicated in bold.

Commercial name	Abbreviation	CAS number	Structure	Industrial application
Fluorinated alternatives replacing PFOA				
Adona	**Adona**	958445-44-8		Fluoropolymer processing aids
GenX	**GenX**	62037-80-3		Fluoropolymer processing aids
Unknown	**PFTECA$_1$** (i.e. perfluoro triether carboxylic acid)	329238-24-6		Fluoropolymer processing aids
Unknown	**PFTECA$_2$** (i.e. perfluoro triether carboxylic acid)			Fluoropolymer processing aids
EEA	**EEA**	908020-52-0		Fluoropolymer processing aids
6:2 FTCA	**6:2 FTCA**	53826-12-3		Fluoropolymer processing aids
Fluorinated alternatives replacing PFOS				
F-53	**F-53**	754925-54-7		Metal plating
F-53B	**F-53B**	73606-19-6		Metal plating
Unknown	**PFBSaPA** (i.e. perfluorobutane sulfonamide w/phosphoric acid)	120945-47-3		Metal plating
Fluorinated alternatives replacing 8:2 FTOH				
RM610	3:1 FTOH	375-01-9		"Building blocks" for substances to be used in surface treatment of textile, leather and carpets
RM620	5:1 FTOH	423-46-1		"Building blocks" for substances to be used in surface treatment of textile, leather and carpets

Fluorinated alternatives replacing certain POSF- and/or fluorotelomer-based substances				
EF-N441S-30	**EF-N**	39847-39-7		Raw material for ionic liquids
Novec 1230	Novec	756-13-8		Fire suppression agent
Forafac 1183	Forafac	80475-32-7		Fluorinated surfactants used in AFFFs
Unknown	PFOTSi (i.e. perfluorooctyltrimethoxysilane)	85857-16-5		Unknown
	PFOTSi-(OH)	Degradation product		
	PFOTSi-$(OH)_2$	Degradation product		
	PFOTSi-$(OH)_3$	Degradation product		
RM720	RM720	154380-34-4		Surface treatment for glasses, natural stones, metals, wood, cellulose, cotton, leather and ceramics
	RM720-(OH)	Degradation product		
	RM720-$(OH)_2$	Degradation product		
	RM720-$(OH)_3$	Degradation product		

(Schwarzenbach et al., 2005) and used as input parameters:

$$D_{AW\ (or\ OW)} = \frac{1}{1 + 10^{(pH - pK_a)}} * K_{AW\ (or\ OW)}. \quad (1)$$

In Eq. (1), partition coefficients and pK_a values estimated by COSMOtherm and SPARC were used and the environmental pH value was assumed to be 7. The pK_a values used for the calculation of D_{AW} and D_{OW} for PFOA and PFOS were 0.5 (Vierke et al., 2013b) and −3.27 (Brooke et al., 2004), respectively. While it is possible to convert partition coefficients of neutral species to distribution ratios of both charged and neutral species, a similar adjustment cannot be carried out for the degradation half-lives, as there is little empirical information available on the impact of ionization on degradation. Because the anionic species of acidic organic chemicals (Tülp et al., 2009) including PFOS and PFOA (Higgins and Luthy, 2006) sorb to organic matter, the hypothetical organic carbon–water partition coefficient (K_{OC}), which is a well-established parameter to quantify sorption to sediments, soil and suspended/volatile particles, was calculated for each of the anionic fluorinated alternatives and specified in the OECD Tool's code. The details of the calculations are presented below Table A2 of the Supplementary data.

Three emission scenarios were considered, in which emissions occur either to air, water or soil, respectively. For each emission scenario, the OECD Tool calculates 1) the overall persistence (P_{OV}) in days; 2) the characteristic travel distance (CTD) in kilometers (km); and 3) the transfer efficiency (TE) in percent. P_{OV} describes the overall lifetime of a chemical in a multi-compartment environment consisting of air, water, and soil. CTD and TE are both LRTP indicators. CTD represents the distance in km at which the initial chemical concentration at the source point has dropped to 1/e (i.e., 37%) (Bennett et al, 1998). It should be noted that in the CTD calculations water and air compartments are considered to be mobile. TE quantifies the transfer of the chemical from the atmosphere into the soil or water compartment in a target region (MacLeod and Mackay, 2004). The final outputs of the OECD Tool are the highest P_{OV}, CTD and TE from the three emission scenarios and are shown in two graphs with LRTP indicators versus P_{OV}, respectively. A Monte Carlo analysis was carried out for each chemical in order to identify the influence of the variability and uncertainty of each input parameter on the key model outputs.

3. Results

3.1. Physicochemical properties of fluorinated alternatives

Fig. 1A shows estimated log K_{AW} and log K_{OW} for PFOS, PFOA and 8:2 FTOH together with PFECAs, PFESAs, 6:2 FTCA and n:1 FTOHs that are replacing these substances. Estimated values of log K_{AW} and log K_{OW} for the fluorinated alternatives replacing certain POSF- and/or fluorotelomer-based substances (i.e., Forafac, PFBSaPA, EF-N, Novec, PFOTSi, RM720) and the six degradation products are presented in Table A2 of the Supplementary data.

Log K_{OW} and log K_{AW} of the two PFESAs (i.e., F-53 and F-53B) are similar to those of PFOS, differing by less than one log unit. Concerning the fluorinated alternatives to PFOA, these display similar log K_{AW} values (i.e., <2 log unit range) as their common predecessor. Their log K_{OW} values, however, are more variable (i.e., lie within a range of ~4 log units). On the log K_{OW} axis, two distinct groups are differentiated, with EEA, GenX, 6:2 FTCA and Adona on one side and PFTECAs, F-53 and F-53B together with PFOS on the other side. 8:2 FTOH is more hydrophobic (higher log K_{OW}) than its replacements, 3:1 and 5:1 FTOHs. Furthermore, 5:1 FTOH has a higher log K_{AW} and log K_{OW} than 3:1 FTOH. Compared to PFOA and PFOS, their respective fluorinated alternatives presented in Fig. 1A have almost identical polarization surface charge densities, σ (see σ-profiles in Figure A7 of the Supplementary data).

PFECAs, PFESAs and PFOS are more hydrophobic than their hypothetical non-fluorinated analogues, with log K_{OW} and log K_{AW} values that are lower by 3–5 and 2–6 log units, respectively (Fig. 1B). In addition, Adona and EEA, which have one and two ether linkages between perfluoroalkyl chains, display similar log K_{AW} with 0.13 log unit difference, whereas their corresponding non-fluorinated analogues have log K_{AW} values that differ by 2.6 log units.

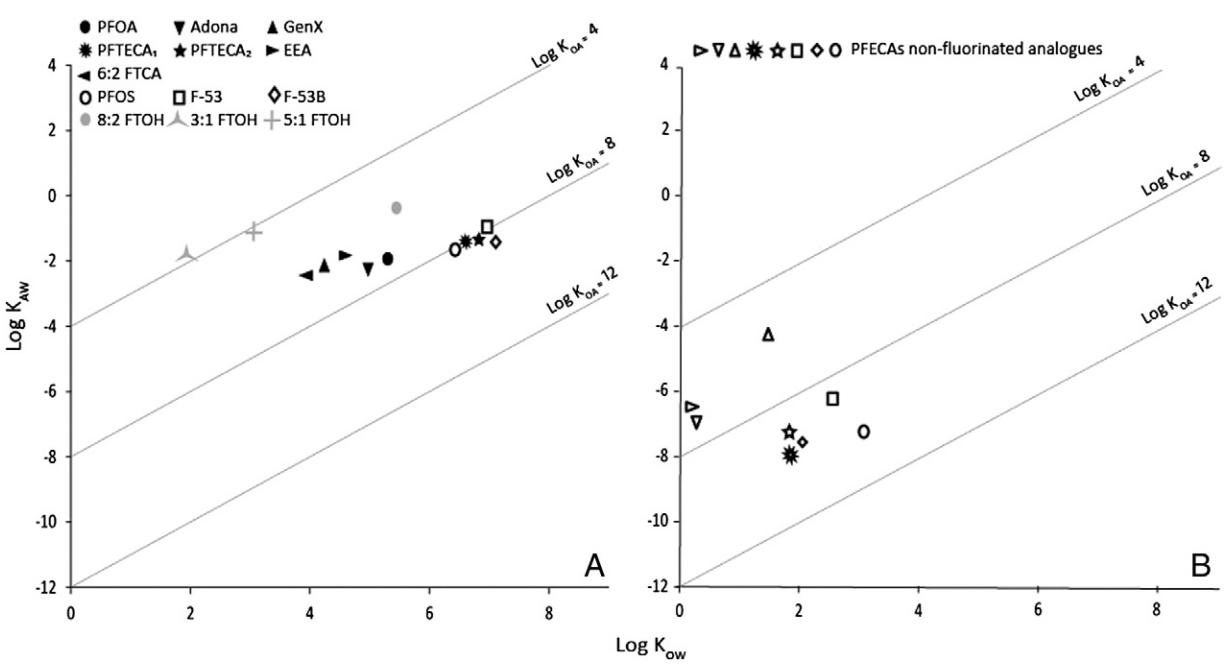


Fig. 1. Chemical space map depicting log K_{AW} versus log K_{OW} for A) fluorinated alternatives to PFOA, PFOS and 8:2 FTOH and B) hypothetical non-fluorinated analogues of PFECAs, PFESAs and PFOS. Diagonal lines correspond to log K_{OA}. The fluorinated alternatives and their corresponding non-fluorinated analogues are indicated by the same symbols.

3.2. Persistence and long-range transport potential

In Fig. 2A, estimated P_{OV} and CTD for PFOS, PFOA and 8:2 FTOH and their fluorinated alternatives are presented. Besides Adona and EEA, which have a CTD and P_{OV} of 592 km and 346 days, respectively, the alternatives to PFOS and PFOA are estimated to be similarly persistent as their predecessors with a common estimated residence time of 1038 days in the whole model environmental system and similar CTDs between 1736 and 1745 km. Furthermore, even though their persistence is less than 300 days, 3:1 and 5:1 FTOHs have CTDs (>40 000 km) more than six times longer than the CTD of 8:2 FTOH. Fig. 2B shows the estimated P_{OV} and CTD of fluorinated alternatives replacing certain POSF- and/or fluorotelomer-based substances. Five of these alternatives are estimated to be less persistent than most of the alternatives as well as the legacy PFASs presented in Fig. 2A, with an average P_{OV} of 326 days for PFOTSi-$(OH)_2$ and RM720, and 131 days for Novec, PFOTSi and PFOTSi-(OH). The averaged CTD of PFOTSi-$(OH)_2$ and RM720 is 800 km, while for PFOTSi and Novec, the CTDs are 1.3 and 2.8 times higher than for PFOS and PFOA, respectively. Forafac, EF-N, PFOTSi-(OH), PFOTSi-$(OH)_3$ and the other degradation products have similar CTDs as PFOA and PFOS. Except for 3:1 FTOH and 5:1 FTOH, which display values exceeding 90% and 100%, respectively, the TE values for the other substances in Fig. 2C and D vary from below 0.001% to 0.87%, depending on the transport media (i.e., air or water) and log K_{OA}. The majority of the fluorinated alternatives have a higher TE compared to the substances they replace.

The contribution of each input parameter to the model outputs is assessed through a Monte Carlo uncertainty analysis (results are provided in Figure A6 of the Supplementary data). Three different cases are observed: [i] for all ionic and for highly hydrophilic (i.e., log $K_{AW} < -8$; log $K_{OA} > 9$) neutral alternatives, the degradation half-life in water is the parameter contributing the most to the output variance of both CTD and P_{OV}, since ions and hydrophilic compounds are mainly distributed in the water phase. Partition coefficients are the most influential input parameters affecting the value of TE. An exception is PFBSaPA, for which CTD and P_{OV} are sensitive to both log K_{AW} and degradation half-life in water while TE is mainly affected by half-life in air. [ii] For (semi-)volatile alternatives (i.e., log $K_{AW} > -3.5$; log $K_{OA} < 7.5$), P_{OV} is sensitive to the degradation half-lives in water, air or soil, while the degradation half-life in air affects the values of CTD and TE. [iii] For alternatives with moderate hydrophilicity (i.e., log $K_{AW} < -3.5$ and log $K_{OA} > 7.5$), P_{OV} and CTD are affected by the degradation half-life in water and TE is sensitive to degradation half-life in air.

4. Discussion

4.1. Influence of structural variability on physicochemical properties

This study provides a preliminary assessment of emerging and novel fluorinated alternatives that replace long-chain perfluoroalkyl acids and their precursors. Even though PFECAs and PFESAs, which are alternatives to PFOA and PFOS, respectively, contain some structural differences such as ether linkage(s) between perfluorinated carbon chains and replacement of fluorine atom with chlorine atom at the end of perfluoroether chain, their physicochemical properties are not significantly changed compared to those of the predecessors. Among PFECAs, the differences in physicochemical properties can likely be explained by different molecular sizes (i.e., PFTECAs versus EEA, Adona and GenX, which have similar σ-profiles but different molecular sizes). Also, while the insertion of ether linkage(s) does not significantly affect the electron withdrawing effects of the perfluorinated carbon chain on the acidic functional group at the other end of the carbon chain, the presence of a methyl

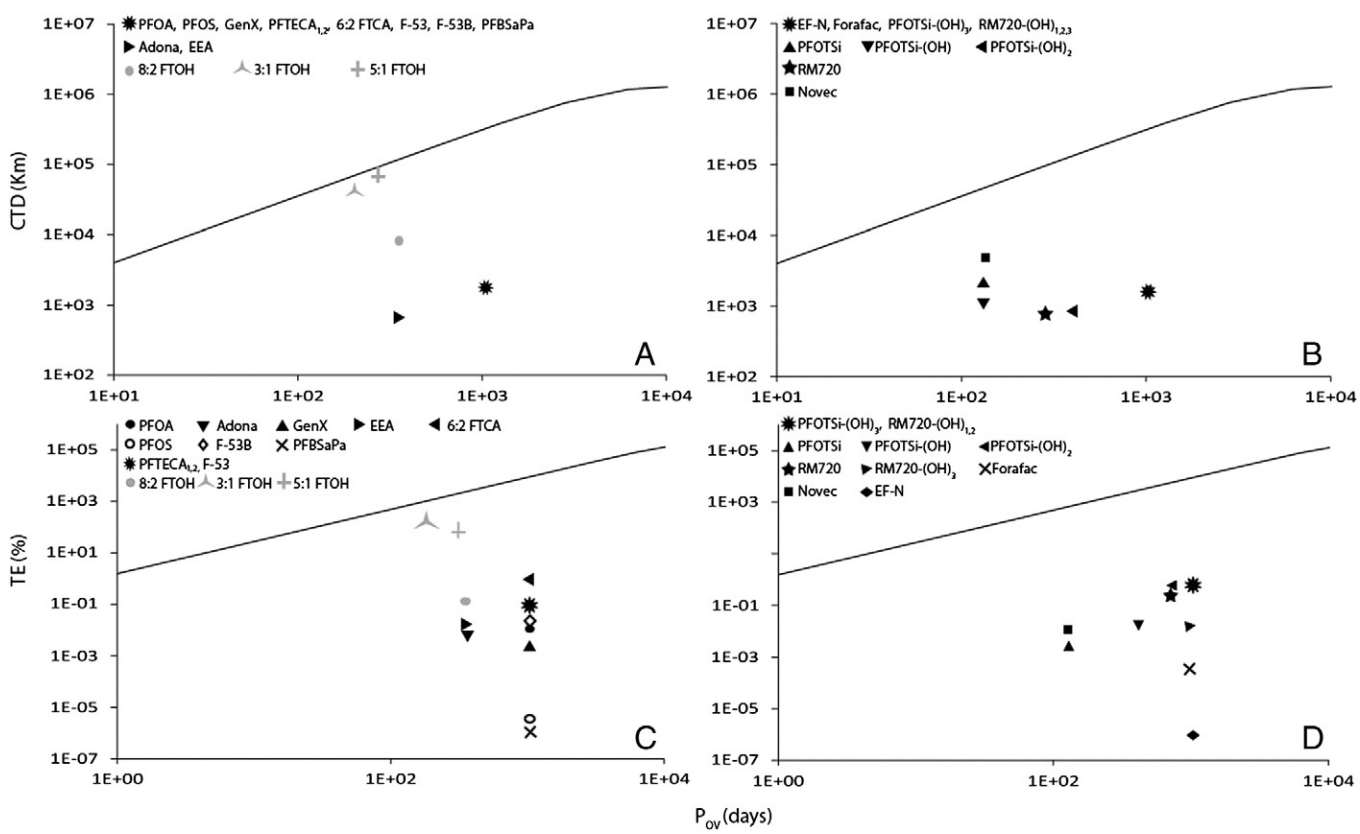


Fig. 2. LRTP indicators – characteristic travel distance (CTD) in km and transfer efficiency (TE) in % – as a function of overall persistence (P_{OV}) in days for fluorinated alternatives to PFOA, PFOS and 8:2 FTOHs (A and C, respectively) and fluorinated alternatives replacing certain POSF- and/or fluorotelomer-based substances (B and D, respectively). The black line represents the maximum CTD or TE for a given P_{OV}.

moiety separating the acid group from the perfluorinated carbon chain (i.e., in the case of 6:2 FTCA) or a partially fluorinated carbon (i.e., Adona) enhances the polarity of the carboxylic group, as depicted in the σ-profiles (see Figure A7 of the Supplementary data). Furthermore, while the substitution of rigid $–CF_2–$ groups with ether groups decreases the molecular size of PFECAs compared to the compounds they replace for a similar chain length, the addition of a chlorine atom increases the molecular size (see Adona, EEA and PFOA for ether and F-53 and F-53B for chlorine in the Supplementary data, Table A2). A smaller molecular size requires less energy to create a cavity among strongly-bonded water molecules. For example, Adona and GenX, which have a similar polarity as PFOA, but a smaller molecular size than PFOA (see σ-profiles in Figure A7 of the Supplementary data) display a slightly more hydrophilic behavior than PFOA. On the contrary, due to a higher chemical potential in water caused by the higher energy costs of cavity formation, larger molecules such as $PFTECA_1$ and $PFTECA_2$ have a higher K_{AW} than PFOA. The numerous factors involved in controlling K_{OW} make it difficult to accurately assess the thermodynamic origins behind this partition process, which considers the costs of cavity formation of the solute and solute–solvent interactions in both water and octanol phases. Unlike in air, the solute can have Van-der-Waals and H-bond interactions with octanol, as it is, to a lesser extent than water, a bipolar solvent.

Replacing hydrogen with fluorine clearly homogenizes the structural variability among different molecules by delocalizing the polarity of the acidic functional group (see σ-profiles, Figure A7 in the Supplementary data). Unlike hydrogen, the strongly electronegative fluorine atoms minimize the global polarity of the molecule by pulling the electrons of partially charged poles toward the fluorinated carbon chain. As a consequence, the presence of ether-linkage(s) and chlorine atom in the molecule increases the polarity of the non-fluorinated analogues more strongly than for the PFECAs and PFESAs. In addition, all conformers of the non-fluorinated analogues contain intramolecular H-bond interactions, whereas no intramolecular H-bonding is observed for conformers of PFECAs and PFESAs. Intramolecular H-bonding competes with intermolecular H-bond interaction resulting in a decrease of polarity of the compound and increase of its chemical potential within polar solvents (Wang et al., 2011). A lower K_{AW} and K_{OW} would therefore be observed without such internal H-bonds. The rigidity of the skeletal structure of PFECAs and PFESAs, which impedes intramolecular interaction, is induced by the presence of fluorine atoms. In addition, the molecular volume of PFECAs and PFESAs is 30% larger than that of the non-fluorinated analogues (see Table A2 in the Supplementary data) and size variability among PFECAs and PFESAs is higher (i.e., 240 Å for PFECAs and PFESAs versus 150 Å for non-fluorinated analogues). Together, these factors can likely explain the higher variability of K_{AW}, respectively, among the non-fluorinated analogues than the PFECAs, PFESAs and their predecessors.

4.2. Assessment of the environmental fate of alternatives

Both P_{OV} and LRTP reflect the overall fate and behavior of the chemical in the environment that results from the combination of degradation processes in different media, intermediate exchange and thermodynamic force-driven phase partitioning. According to our study, the P_{OV} and LRTP of the fluorinated alternatives to PFOA and PFOS are similar to those of their predecessors. Moreover, some of the fluorinated alternatives replacing certain POSF- and/or fluorotelomer-based substances are as persistent and mobile as PFOS and PFOA. It is, therefore, likely that these alternatives can be globally distributed in the environment and reach remote regions far from the primary emission sources, similarly to the legacy PFASs (MacDonald et al., 2000; Wania, 2007; Stock et al., 2007). The 16 fluorinated alternatives and 6 degradation products presented in this study can likely be considered as very persistent under the EU REACH guidelines, since their estimated degradation half-lives in water and soil are >60 days and >180 days, respectively (ECHA, 2012). In addition, the extremely persistent perfluorinated fractions (the C–F bond is the strongest bond in chemistry; Krafft, 2001) may well be the ultimate degradation products of the fluorinated alternatives and accumulate in the environment. Transfer from the atmosphere to the Earth's surface, depicted by TE, is estimated to be more efficient for $PFTECA_1$, $PFTECA_2$, 6:2 FTCA, F-53, F-53B, 3:1 FTOH and 5:1 FTOH compared to the compounds they replace and also for most of the fluorinated alternatives replacing certain POSF- and/or fluorotelomer-based substances. However, although TE estimates are higher for these alternatives than for PFOS and PFOA, the absolute values are still low and do not necessarily imply enhanced atmospheric transport. Hydrophilic alternatives display low TE and will mostly reach remote regions via ocean currents (Zarfl et al., 2012) rather than by atmospheric transport. Furthermore, a high TE value (≥100%) indicates that the compound (e.g., alternatives to 8:2 FTOH) cycles several times between soil and air due to its relatively long degradation half-life in air, high vapor pressure and low hydrophobicity (Wegmann et al., 2009).

4.3. Assessment of bioaccumulation potential

One well-established assessment of the bioaccumulative potential of chemicals is by means of K_{OW} as an indicator of the ability of a neutral compound to partition from water into lipid-rich tissues within an organism. According to this screening criterion that has been adopted by the REACH guidelines (ECHA, 2012), some of the alternatives such as Novec and PFOTSi are likely bioaccumulative, since their estimated log K_{OW} is above 4.5. Furthermore, neutral alternatives with intermediary log K_{OW} and high log K_{OA} (>5) may have the tendency to biomagnify in air-breathing animals (Kelly et al. 2007). Recently, the membrane–water partition coefficient (K_{lipw}) has been proposed to be a more accurate descriptor of bioaccumulation than K_{OW} for conventional organic substances (Gobas et al., 1998), more specifically for H-bond donor compounds and undissociated acids (Endo et al., 2011). A first approximation of K_{lipw} using the simple regression equation proposed in Endo et al. (2011) shows that the difference between K_{lipw} and K_{OW} for the neutral alternatives and the protonated species of the acidic alternatives is not significant (<0.2 log units) (see Table A2 in the Supplementary data). It should be noted that for highly acidic PFCAs and PFSAs, the ionic species is likely predominant except at very low pH values (<2) (Vierke et al., 2013a). The ionic state of PFAAs prevents them from accumulating in adipose tissues and induces rather a proteinophilic behavior, especially with plasma albumin (Jones et al., 2003, Chen and Guo, 2009; Hebert and MacManus-Spencer, 2010). As a result of the structural similarities to PFCAs and PFASs, it is possible that many PFECAs and PFESAs might also have high affinity to proteins. Therefore, assessing the bioaccumulation of these acidic fluorinated alternatives with a $pK_a < 6$ (Conder et al., 2008) according to the regulatory criteria that are solely based on K_{OW} or K_{lipw} (i.e., chemical partitions into adipose tissues) could possibly result in significant underestimation. Therefore, in order to assess the bioaccumulation potential of these acidic fluorinated alternatives, much of the empirical work to understand the protein-binding mechanisms and kinetics of PFAAs and their alternatives is still needed (Ng and Hungerbuhler, 2013).

4.4. Evaluation and uncertainties

For a preliminary assessment of the environmental fate of fluorinated alternatives (on a global scale), the OECD Tool is likely sufficient. However, the accuracy of estimated results depends strongly on 1) the consistency and accuracy of input parameters and 2) the environmental processes considered in the model.

4.4.1. Uncertainties in the input parameter estimation

For physicochemical properties, the applicability of COSMOtherm for PFASs in their neutral form has been demonstrated in two studies

(Wang et al., 2011; Arp et al., 2006), whereas the applicability of HENRYWIN, KOWWIN and MPBPWIN in the EPISuite package, which predict K_{AW}, K_{OW} and P_L, respectively, is questionable for PFASs, given that they performed poorly for legacy PFASs as shown in a previous study (Arp et al., 2006). SPARC is a well-established tool that has been extensively used by regulators and scientists to predict the pK_a of chemicals (US EPA, 2003). However, the pK_as of fluorinated alternatives are likely underestimated by SPARC. As shown in the case of GenX, its experimental pK_a of 3.8 (ECHA, 2013) is much higher than the estimated one (−0.06). There are large uncertainties regarding the pK_as of the fluorinated alternatives, which was also true for the PFCAs (Goss, 2008) due to difficulties in measuring pK_a for highly fluorinated substances. For some acidic alternatives, the value of pK_a used in calculations of P_{OV} and LRTP can have a large impact on the results of CTD and TE as shown in Table A8 of the Supplementary data. Reducing the uncertainty in pK_as of fluorinated alternatives that have pK_a values in the environmental pH range is therefore a research priority.

For degradation half-lives, the EPISuite models used, AOPWIN and BIOWIN, apply QSPR methods (Kwok and Atkinson, 1995; Boethling et al., 1994). Evaluating the predictive power of these QSPRs for fluorinated compounds is limited by the scarcity of empirical values. Some studies already corroborate the accuracy of AOPWIN predictions when it comes to reaction of organic chemicals with OH radicals in the atmosphere (Güsten et al., 1995; Sabljic and Peijnenburg, 2001). Measured second-order rate constants for atmospheric OH radical-mediated degradation are available for three fluorinated alternatives and four legacy PFASs, allowing a limited evaluation of AOPWIN (see Table A4 of the Supplementary data). Even though its training and test sets contain several fluorinated substances, AOPWIN has a tendency to overpredict second-order rate constants. For example, the predicted rate constant of N-ethyl perfluorobutane sulfonamide (EtFBSA) is 24 times higher than the experimental one (Martin et al., 2006). In addition, AOPWIN slightly overpredicts the second-order rate constants by less than a factor of 2 for 3:1 FTOH (Bravo et al., 2010) and 5:1 FTOH (Hurley et al., 2004), by a factor of 3 for N-methyl perfluorobutane sulfonamidoethanol (MeFBSE) (D'Eon et al., 2006) and by a factor of 4 for 8:2 FTOH (Ellis et al., 2003) and PFOA (Hurley et al., 2004). As a consequence, the fluorinated alternatives presented in this work are likely to be even more persistent in air (and have greater CTD) than shown in Fig. 2. In addition, it is noted that AOPWIN, which only encompasses reaction with OH radicals (i.e., indirect photolysis), recognizes when a molecule cannot undergo indirect photolysis. For instance, the half-life of Novec could not be predicted, since this molecule is degraded through direct photolysis only (Jackson et al., 2011, Taniguchi et al., 2003).

Several studies evaluated the accuracy of the BIOWIN program for organic compounds. While it is an effective tool for binary classification of chemicals (i.e., readily biodegradable or not), BIOWIN has limited, quantitative predictive power (Gouin et al., 2004, Aronson et al., 2006, Kühne et al., 2007, Lim and Fox, 2012). Due to the lack of experimental data on ultimate microbial degradation of fluorinated alternatives, assessing the accuracy of BIOWIN3 estimated for these compounds is currently not possible. Nevertheless, experimental primary biodegradation half-lives of several fluorotelomer-based substances (Liu and Mejia Avendaño, 2013) allow an assessment of BIOWIN4, which is an expert survey module based on the same estimation method as BIOWIN3 but designated for primary rather than ultimate degradation. Assessing BIOWIN4 can thus provide insight into the predictive power of BIOWIN3. BIOWIN4 underestimates the primary degradation half-life of 6:2 fluorotelomer sulfonic acid (6:2 FTSA) by a factor of more than 2.5 and overestimates the primary degradation half-life of 8:2 FTOH into PFOA by up to 17 times. The poor predictive power of BIOWIN 4 indicates that the estimations of BIOWIN3 are also inaccurate. As a consequence, the predictive power of BIOWIN3 for PFASs is expected to be limited.

4.4.2. Environmental fate model and output parameters

The Monte Carlo analysis revealed that the degradation half-lives in water and air are the major contributors to the uncertainty of P_{OV} and CTD. Both estimated input parameters also depend on the environmental processes considered in the OECD Tool's calculations. Some possibly significant processes that may influence the P_{OV} and LRTP of fluorinated alternatives are not represented in the OECD Tool. Among them is the possible transfer of fluorinated alternatives from the seawater surface to the atmosphere via marine aerosol generation, due to their surfactant-like properties. This phenomenon is already rather well documented for PFO/PFOA (Webster and Ellis, 2010, Reth et al., 2011, McMurdo et al., 2008) as well as for other long-chain PFCAs and PFSAs (Reth et al., 2011). Briefly, the strong surfactant-like properties of long-chain PFCAs and PFSAs cause them to accumulate in the surface microlayer of the ocean and thus also in the marine aerosols formed from the microlayer of ocean surface water caused by the waves. The pH of marine aerosols is between 3.7 and 5.4 (Pszenny et al., 2004) on average. Thus, if a fluorinated alternative has a pK_a in this pH range, a large fraction of protonated form of the substance may well be present in the marine aerosols. In this case, if the protonated fluorinated alternatives have a high vapor pressure, a significant amount of protonated species may volatilize from the marine aerosol into the atmosphere and thus be transported long distances. Since such environmental processes are not included in the OECD Tool, the CTD outputs might be underestimated for some of the fluorinated alternatives.

5. Outlook

To date, the absence of experimental data on degradation half-lives and physicochemical properties is a major drawback for carrying out hazard and risk assessments of emerging chemicals such as fluorinated alternatives. At this stage, the use of in silico methods remains the only time- and resource-saving tool for the identification of potential hazardous chemicals. Despite the inherent uncertainties, our study provides qualitative evidence that most of the alternatives do not differ significantly from PFOA, PFOS and their precursors regarding the physicochemical properties and likely environmental fate. These alternatives are GenX, $PFTECA_1$, $PFTECA_2$, 6:2 FTCA (alternatives to PFOA) F-53, F-53B, PFBSaPa (alternatives to PFOS), 5:1, 3:1 FTOHs (alternatives to 8:2 FTOH), Forafac, EF-N, Novec, the degradation products of RM720, PFOTSi and its degradation products (alternatives to certain POSF- and/or fluorotelomer-based substances) and further investigations should focus on them. Furthermore, improvement of the data quality and information on production volumes and environmental emission estimates are required for further, more quantitative risk assessment. The experiments that are urgently needed to improve the hazard assessment of the aforelisted fluorinated alternatives and to determine if they are safe for humans and biota are: 1) (bio)degradation experiments in relevant environmental media for individual substances; 2) pK_a measurements of the acidic fluorinated alternatives, in particular PFECAs and PFESAs; 3) bioaccumulation experiments, including protein-binding experiments for the acidic fluorinated alternatives and K_{OW} experiments for the neutral ones; and 4) toxicity tests to identify their mode-of-action and toxicity, which can be further used to develop QSAR models that can be reliably used to predict the toxicity of PFASs. A summary table showing a comparison of fluorinated alternatives to legacy PFASs and highlighting experimental priorities for each fluorinated alternatives is available in Table A9 of the Supplementary data.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.scitotenv.2014.10.062.

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