Substance Name: Perfluoroheptanoic acid and its salts

EC Number: -

CAS Number: -

MEMBER STATE COMMITTEE SUPPORT DOCUMENT FOR IDENTIFICATION OF

PERFLUOROHEPTANOIC ACID AND ITS SALTS

AS A SUBSTANCE OF VERY HIGH CONCERN BECAUSE OF ITS TOXIC FOR REPRODUCTION (ARTICLE 57C),PBT (ARTICLE 57D),VPVB (ARTICLE 57E),EQUIVALENT LEVEL OF CONCERN HAVING PROBABLE SERIOUS EFFECTS TO HUMAN HEALTH (ARTICLE 57(F) - HUMAN HEALTH),EQUIVALENT LEVEL OF CONCERN HAVING PROBABLE SERIOUS EFFECTS TO THE ENVIRONMENT (ARTICLE 57(F) - ENVIRONMENT) PROPERTIES

Adopted on 28 November 2022

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ABBREVIATIONS

APFO	Ammonium pentadecafluorooctanoate
B	Bioaccumulative
BAC	Biological Activated Carbon
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
CAS	Chemical Abstracts Services
CLP	Classification Labelling and Packaging regulation
CMR	Carcinogenicity, Mutagenicity and/or Reproductive toxicity
CTD	Characteristic Travel Distance
diPAP	perfluoroalkyl phosphate diester
DT50	Degradation Time to reach 50%
dw	dry weight
EC	European Community
ECHA	European Chemicals Agency
EDTA	Ethylenediaminetetraacetic acid
ELoC	Equivalent Level of Concern
FTCA	Fluorotelomer carboxylic acid
FTOH	Fluorotelomer alcohol
6:2 FTSA	6:2-fluorotelomer sulfonate
FTUCA	Fluorotelomer unsaturated carboxylic acid
GAC	Granular Activated Carbon
GenX	PFPrOPrA; HFPO-DA; PerfluoroPropane Oxide Propionic Acid
GHS	Globally Harmonized System of classification and labelling of chemicals
HCB	Hexachlorobenzene
HCH	Hexachloro-cycloxexane
HFPO-DA	GenX; PFPrOPrA; Hexafluoro propylene oxide – dimer acid
HPLC	High-performance liquid chromatography
HLC	Henry's Law Constant
IUPAC	International Union of Pure and Applied Chemistry
LC	Liquid chromatography, or Long Chain
LOD	Limit of Detection
LOQ	Limit of Quantification
LRTP	Long-Range Transport Potential
monoPAP	perfluoroalkyl phosphate monoester
MS	Mass spectrometry
MS/MS	Tandem mass spectrometry
NaPFO	Sodium pentadecafluorooctanoate
OC	Organic Carbon
OECD	Organisation for Economic Co-operation and Development
P	Persistent
PAC	Powdered Activated Carbon
PBT	Persistent Bioaccumulative and Toxic
PCB	Polychlorinated Biphenyls
PFAA	Perfluoro Alkyl Acids
PFAS	Per- and polyfluoroalkyl substance
PFBA	Perfluorobutanoic acid
PFBS	Perfluorobutane sulfonic acid
PFCA	Perfluoroalkyl carboxylic acid/ perfluoroalkyl carboxylate
PFDA	Perfluorodecanoic acid
PFDoDA	Perfluorododecanoic acid
PFECA	Perfluoro Ether Carboxylic Acids
PFHpA	Perfluoroheptanoic acid
PFHp	Perfluoroheptanoate
PFHp-A	Ammonium perfluoroheptanoate

PFHp-K	Potassium perfluoroheptanoate
PFHp-Na	Sodium perfluoroheptanoate
PFHpS	Perfluoroheptane sulfonic acid
PFHxA	Perfluorohexanoic acid
PFHxS	Perfluorohexane sulfonic acid
PFMOAA	Perfluoro-2-methoxyacetic acid
PFMOPrA	Perfluoro-2-methoxypropanoic acid
PFNA	Perfluorononanoic acid
PFO2HxA	Perfluoro(3,5-dioxahexanoic) acid
PFO3OA	Perfluoro(3,5,7-trioxaoctanoic) acid
PFO4DA	Perfluoro(3,5,7,9-tetraoxadecanoic) acid
PFOA	Perfluorooctanoic acid
PFMOBA	Perfluoro-4-methoxybutanoic acid
PFOS	Perfluorooctane sulfonic acid
PFOSA	Perfluorooctane sulfonamide
PFPeA	Perfluoropentanoic acid
PFPeS	Perfluoropentane sulfonic acid
PFPrOPrA	GenX; HFPO-DA; PerfluoroPropaneOxide Propionic acid.
PFSA	Perfluoroalkane sulfonic acid
PFUnDA	Perfluoroundecanoic acid
PFTeDA	Perfluorotetradecanoic acid
PFTrDA	Perfluorotridecanoic acid
POP	Persistent Organic Pollutant
Pov	overall Persistence
ppb	parts per billion
ppm	parts per million
(Q)SAR	(Quantitative) Structure-Activity Relationship
RAC	Risk Assessment Committee
REACH	Registration, Evaluation and Authorisation of CHemicals
SC	Short Chain
STOT RE	Specific Target Organ Toxicity – Repeated Exposure
SVHC	Substance of very high concern
TFA	TriFluoro Acetic acid
ThOD	Theoretical Oxygen Demand
TMF	Trophic magnification factor
UPLC	Ultra high performance liquid chromatography
vB	very Bioaccumulative
vP	very Persistent
vPvB	Very Persistent and very Bioaccumulative
ww	wet weight
WWTP	Waste Water Treatment Plant

IDENTIFICATION OF SUBSTANCES OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name: Perfluoroheptanoic acid and its salts

EC Numbers: -

CAS Numbers: -

- The substances are identified as substances meeting the criteria of Article 57 (c) of Regulation (EC) No 1907/2006 (REACH) owing to their classification in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child').
- The substances are identified as persistent, bioaccumulative and toxic (PBT) according to Article 57 (d) of Regulation (EC) No 1907/2006 (REACH).
- The substances are identified as very persistent and very bioaccumulative (vPvB) according to Article 57 (e) of Regulation (EC) No 1907/2006 (REACH).
- The substances are also identified as equivalent level of concern to those of other substances listed in points (a) to (e) of Article 57 of Regulation (EC) No 1907/2006 (REACH) according to Article 57(f) of REACH Regulation.

Summary of how the substance meets the criteria set out in Article 57 of the REACH Regulation

Perfluoroheptanoic acid (PFHpA) and its salts are identified as substances of very high concern in accordance with Article 57(c), (d), (e) and (f) of Regulation (EC) 1907/2006 (REACH) because in water under environmental conditions and in the human body these substances exist in the (dissociated) form of perfluoroheptanoate, for which there is scientific evidence of reprotoxic effects as well as PBT and vPvB properties and of probable serious effects to the environment and human health which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e) of Article 57 of REACH.

Toxicity for reproduction:

PFHpA is covered by index number 607-761-00-3 of Regulation (EC) No 1272/2008. Pursuant to Commission Delegated Regulation (EU) 2022/692 of 16 February 2022, PFHpA will be classified in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child') as well as Specific target organ toxicity — repeated exposure category 1, STOT RE 1 (H372 (liver))[1]. Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that PFHpA and its salts meet the criteria for classification in the hazard class:

- Toxic for reproduction category 1B in accordance with Article 57 (c) of REACH.

[1] Commission Delegated Regulation (EU) 2022/692 of 16 February 2022 amending, for the purposes of its adaptation to technical and scientific progress, Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the 18th ATP to CLP). Pursuant to the second paragraph of Article 2 of this Regulation, this new harmonised classification applies from 23 November 2023. However, pursuant to the third paragraph of that provision substances and mixtures may already be classified, labelled and packaged in accordance with this classification.

PBT and vPvB:

A weight-of-evidence determination according to the provisions of Annex XIII of REACH has been used to identify the substances as PBT and vPvB. Available relevant information, such as the results of standard tests, monitoring and modelling, information from the application of the category and analogue approach (grouping, read-across) and (Q)SAR results, was considered together in a weight-of-evidence approach.

Persistence:

In general, the persistence of PFHpA and its salts can be explained by the shielding effect of the fluorine atoms, blocking *e.g.,* nucleophilic attacks to the carbon chain. High electronegativity, low polarisability and high bond energies make highly fluorinated alkanes one of the most stable organic compounds. It is not expected that the carboxylic group in perfluorinated carboxylic acids (PFCAs) or their salts alters the persistence of the perfluorinated carbon chain.

The persistence (P and vP) of seven long-chain PFCAs (PFOA/APFO (C_8-PFCA), PFNA (C_9-PFCA), PFDA (C_{10}-PFCA), and C_{11}-C_{14} PFCAs) and a short-chain PFCA (HFPO-DA (C_6-PFCA where two chains of three carbon atoms are joined by an ether bond)) has already been confirmed by the Member State Committee prior to their inclusion into the Candidate List. In the RAC opinion on the PFHxA (C_6-PFCA) restriction proposal it was concluded that PFHxA exceeds by far the trigger of being very persistent and clearly exceeds the threshold values for being "very persistent" (vP) as defined in REACH Annex XIII.

Considering the stability of the C-F bond and the read-across approach with PFHxA, HFPO-DA, PFOA, PFNA, PFDA and C_{11}-C_{14} PFCAs, it can be concluded that PFHpA and its salts will undergo, no or extremely limited, degradation in the environment.

Monitoring data support the above conclusion. The detection and/or quantification of PFHpA in remote areas such as the Arctic (in air, snow, fresh- and marine water (including sediments) and soil) and the Antarctic (snow), in locations far away from point sources, point towards persistence of PFHpA.

Based on a weight-of-evidence approach, it is concluded that PFHpA and its salts are very persistent. Annex XIII, point 3.2.1.(d) of the REACH Regulation requires that any relevant information for the assessment of the persistence of the substance be considered. Therefore, it is concluded that PFHpA and its salts fulfil the P- and vP- criteria in accordance with the criteria and provisions set out in Annex XIII of REACH.

Bioaccumulation:

Based on a direct comparison with the bioaccumulation criteria for aquatic organisms, PFHpA and its salts do not seem to be bioaccumulative in water-breathing organisms.

In air-breathing organisms results appear to differ between species. In rats, the elimination half-life for both males and females is less than 1 day. In pigs, however, much longer elimination half-lives have been reported with the highest values being in the order of 500 days. There was considerable variation between individual pigs though, resulting in a geometric mean elimination half-life of 74 days. The latter value corresponds to a biomagnification factor of 2.7, showing that PFHpA and its salts have the potential to biomagnify in pigs. Therefore, PFHpA and its salts should be considered very bioaccumulative (vB) in at least some air-breathing species such as the pig. The elimination half-life of PFHpA of 74 days fits well between values derived for PFOA (236 days) and PFHxA (4.1 days) that are the closest structural

analogues differing only by one perfluorinated carbon in chain length.

Several studies in humans point to high elimination half-lives with the highest value being 3.3 years. As seen for other mammalian species, there is considerable variation between individuals, resulting in an average elimination half-life in humans that is at least 76 days. This value exceeds the range of guiding values for biomagnification of substances in humans that are considered to be in the range of 30 to at most 70 days and thus, the half-lives observed for PFHpA are high enough to reach higher concentration of PFHpA in the human body than in the food consumed. Further supporting high bioaccumulation potential of PFHpA and its salts in humans is the observed build up over the years in humans. Therefore, PFHpA and its salts are considered very bioaccumulative in humans.

This is in line with the close structural analogue PFOA that is one perfluorinated carbon in chain length longer than PFHpA. Although PFOA was not proposed and identified as a vPvB substance under REACH in 2013, the Persistent Organic Pollutants Review Committee (POPRC) concluded at its twelfth meeting in September 2016 that PFOA is persistent, bioaccumulative and toxic to animals including humans (UNEP/POPS/POPRC.12/11/Add.2). Under the POP regulation the B criterion for aquatic organisms is defined as 5000 L/kg, which equals the vB criterion under REACH. The POPRC thus concluded that the half-life in humans is of similar concern as the vB criterion for aquatic organisms.

Overall, taking all available information together in a weight-of-evidence approach, thereby giving the data from pigs and humans a high weight, a high bioaccumulation potential of PFHpA and its salts in humans and at least some other air-breathing mammalian species has been identified. Annex XIII, point 3.2.2.(b) of the REACH Regulation requires that data from the toxicokinetic behaviour of the substance be considered. Therefore, it is concluded that the vB criterion of REACH Annex XIII is fulfilled.

Toxicity:

PFHpA is covered by index number 607-761-00-3 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3 (the list of harmonised classification and labelling of hazardous substances) and it is classified in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child') and STOT RE 1 (H373) (liver)[2]. Therefore, the toxicity criterion of REACH Annex XIII is fulfilled. It is therefore concluded that PFHpA and its salts meet the toxicity criterion (T) in accordance with Annex XIII, points 1.1.3 (b) and (c), of the REACH Regulation.

Conclusion on the P, B and T properties
In conclusion, PFHpA and its salts meet the criteria for PBT and vPvB substances according to Article 57 (d) and (e) of the REACH Regulation.

Equivalent level of concern:

Based on the following assessment it is also concluded that PFHpA, should be regarded as "substances for which there is scientific evidence of probable serious effects to human health and the environment which give rise to an equivalent level of concern to those of other substances listed in Article 57 points (a) to (e) of the REACH Regulation".

Intrinsic properties of PFHpA and its salts

[2] Commission Delegated Regulation (EU) 2022/692 of 16 February 2022 amending, for the purposes of its adaptation to technical and scientific progress, Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the 18th ATP to CLP). Pursuant to the second paragraph of Article 2 of this Regulation, this new harmonised classification applies from 23 November 2023. However, pursuant to the third paragraph of that provision substances and mixtures may already be classified, labelled and packaged in accordance with this classification.

Persistency:

PFHpA and its salts is expected to undergo extremely limited degradation in the environment and thus fulfils the P- and vP- criteria in accordance with the criteria and provisions set out in Annex XIII of REACH.

Mobility:

Due to its low to very low adsorption potential (log K_{oc} 1.63-1.7), high water solubility (salts and dissociated form of PFHpA >1000 mg/L) and low tendency to volatise from water to air (Henry's Law constant of 6.38 $Pa \cdot m^3/mol$ for the ammonium salt) PFHpA and its salts predominantly resides in the aquatic compartment. These properties make PFHpA and its salts very mobile in the aquatic environment. Once PFHpA has entered the aquatic environment, e.g., surface waters, there are limited fate processes that would prevent it from being distributed to groundwater and to the marine environment. Monitoring data show that PFHpA or its salts has been detected in tap water, bottled drinking water and groundwater which supports the conclusion that PFHpA and its salts are mobile in water.

Removal from the environment and drinking water:

Since PFHpA and its salts have a preference for the aqueous phase in the environment, the most important compartment for removal of PFHpA and its salts is water. The same properties that make PFHpA and its salts mobile in the environment are also the reason why their removal is challenging. Due to the high aqueous solubility and the low sorption potential, PFHpA and its salts will only bind to a low extent to adsorption materials and will rather remain in the water phase during the purification process.

PFHpA is not readily removed with conventional or advanced surface water treatment processes. The methods available today to remove PFHpA from drinking water and lower the human exposure are expensive and not commonplace. The presence of PFHpA precursors may complicate water treatment processes even further as the precursors may behave differently through the purification steps and may break down to PFHpA and its salts either during or after purification.

Long-range transport:

Modelling and monitoring data indicate that the combination of extreme persistence and mobility lead to a high potential for long-range transport in the environment, which takes place via the atmosphere and oceanic currents. This may also apply to PFHpA-precursor substances to varying degrees. Occurrence of PFHpA in remote regions such as Arctic, Antarctic and high altitude remote areas in the European Alps has been confirmed by measurements in snow. PFHpA is detected in practically all compartments of the polar regions. Thus, vulnerable remote ecosystems are currently exposed to PFHpA.

Bioaccumulation and bioavailability:

PFHpA is very bioaccumulative in humans and in at least some other air-breathing mammalian species. Overall, taking all available information together in a weight- of- evidence approach, it is concluded that the vB criterion of REACH Annex XIII is fulfilled.

Enrichment in plants:

Studies have demonstrated the uptake of PFHpA in crops including lettuce, tomato, carrots, corn, radish and soybeans. From the plants PFASs can transfer to humans and wildlife through

the food chain. Due to the uptake observed in crops, consumption of these by humans and wildlife will lead to inevitable exposure to PFHpA and its salts.

Toxicity:

PFHpA is classified in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child') and STOT RE 1 (H373) (liver) and therefore, the toxicity criterion of REACH Annex XIII is fulfilled.

Environmental toxicity and secondary poisoning:

The direct toxicity of PFHpA to aquatic and terrestrial species, such as algae, daphnids, fish, earthworms and plants, is assumed to be low and was not considered as the highest concern in the context of the present equivalent level of concern assessment. However, concern for secondary poisoning may be significant, as mammals show more toxic effects of PFHpA than organisms from lower trophic levels. Relatively stringent safety levels may result from the fact that a particular food item such as terrestrial plants and fish are often the sole energy source for a specific mammalian species, leading to a relatively high PFHpA intake. Hence, PFHpA exposure may be of concern to wildlife. Secondary poisoning is therefore considered a relevant endpoint for the equivalent level of concern assessment.

Concerns arising from the substance properties

Several concerns are caused by these intrinsic properties of PFHpA and its salts. Overall, they have a very high potential to cause effects in wildlife and in humans exposed via environment, due to their persistence, mobility, potential for long-range transport, and toxicity. The very high persistence together with low adsorption potential and high mobility imply a very high potential for increasing pollution stock in the environment and for irreversible and increasing exposure of both wildlife and humans exposed via the environment. Also, their low adsorption potential and high water solubility imply that PFHpA and its salts are highly bioavailable for uptake via water. Together, these elements of concern lead to a very high potential for irreversible effects once effect levels have been reached, as well as an increasing seriousness of effects while exposures keep increasing.

Its properties make PFHpA (very) mobile in the aquatic environment and very difficult to remove from (contaminated) aqueous sites e.g., for drinking water remediation or groundwater clean-up. The usually applied techniques in wastewater treatment plants are not capable of removing PFHpA from the environment. Also for water treatment plants different studies show that even though different techniques are applied they do not effectively remove PFHpA from the water. But also studies investigating more advanced treatment techniques show a lack of removal of PFHpA. Once PFHpA has entered the aquatic environment, e.g., surface waters, there are limited fate processes that would prevent it from being distributed to groundwater and to the marine environment.

Due to its mobility and persistence, PFHpA is found in surface waters, groundwater, tap water and bottled water. Decontamination can only be achieved at high societal costs. Furthermore, PFHpA is classified as Repro 1b and STOT RE 1 (liver) and humans will be exposed via consumption and use of drinking water. Water is used for drinking and cooking each day and it is the basis of all food over the whole life of humans. That is why its presence in drinking water is of high concern. Consequently, there is societal concern for the presence of PFHpA in drinking water that requires immediate action.

Due to the extreme persistence of PFHpA and its very long presence in the environment, results of toxicity studies may be of limited value as they do not regard cross generational effects. Additionally, PFASs are continuously introduced into aquatic ecosystems and are ubiquitously present in complex mixtures which is not covered by a single substance test. PFHpA has been

measured in different species of wildlife, including polar bears which are listed on the IUCN red list of threatened species. Monitoring data indicates that birds and mammals show a concern for uptake via fish/plants contaminated with PFHpA. For these reasons also a safe concentration cannot be derived and a quantitative risk assessment cannot be performed.

Monitoring data indicate that often more than one PFAS can be identified in environmental samples suggesting that PFASs are likely to co-occur as contamination in soil, groundwater or drinking water. Literature indicates that different PFAS have similar, additive, effects, increasing the concern for serious effects in the environment.

Equivalent level of concern

The level of concern is considered very high due to the combination of the following concern elements:

- high potential for irreversible exposure due to very high persistence and, in the case of human exposures via environment, the difficulty to decontaminate the drinking water,
- high potential for increasing contamination and increasing fully bioavailable exposures, and the intrinsic properties cause difficulties to remove the substance after release,
- high potential for rapid and wide geographic scale contamination,
- high potential for causing serious effects (PFHpA fulfills the criteria for classification as Reprotoxic cat.1B and STOT-RE),
- potential to cause combined effects with other PFAS
- potential for inter-generational effects,
- high societal concerns.

The irreversibility of exposure to PFHpA due to its persistence adds to the concern. Furthermore, it may be difficult in practice to control exposure due to the high mobility of PFHpA (and its salts) and the fact that exposure may take place at a different location than where releases occurred and at a different moment in time. Furthermore, the high persistence and high mobility of PFHpA (and its salts) lead to a concern for co-exposure with other contaminants with similar health effects. Co-exposure may eventually occur and may last for a very long time, because natural degradation processes for these substances are slow or negligible. This is brought into the weight-of-evidence as supportive information.

Limitations of the available remediation techniques raise a concern that the removal of PFHpA and its salts from drinking water as well as wastewater and, may only be possible with high societal costs. Remediation of environmental pollution may be practically impossible due to PFHpA's (and its salts) high solubility in water, its low adsorption potential and its high mobility. Remediation is also difficult because PFHpA (and its salts) will quickly diffuse from contaminated sites.

Therefore, the substances are also identified as substances of equivalent level of concern having probable serious effects to the environment and human health to those of other substances listed in points (a) to (e) of Article 57 of Regulation (EC) No 1907/2006 (REACH) according to Article 57(f) of REACH Regulation.

In conclusion:

In conclusion, perfluoroheptanoic acid and its salts meet the criteria for Reproductive toxicity according to Article 57(c) and PBT and vPvB substances according to Articles 57(d) and (e). The combined intrinsic properties which demonstrate scientific evidence of probable serious effects to human health and the environment and which give rise to an equivalent level of concern according to Article 57(f) are the following: very high persistence, high mobility in water, potential for being transported in the water phase over long distances, difficulty of remediation and water purification. The observed probable serious effects for human health and the environment are reproductive toxicity. However, the combination of substance

properties may also lead to yet unknown environmental effects that are not detectable in standard toxicity tests and that may only emerge after life-long exposure. Together, these elements lead to a very high potential for irreversible effects.

Registration dossiers submitted for the substance: None

Justification

1. Identity of the substance and physical and chemical properties

Perfluoroheptanoic acid (PFHpA) and its salts dissociate at all relevant environmental pH's (4-10) to perfluoroheptanoate (PFHp), the conjugate base, in aqueous media in the environment and in organisms. The physico-chemical properties of PFHpA and PFHp are different.

The sodium (PFHp-Na), ammonium (PFHp-A) and potassium (PFHp-K) salts are very soluble in water. In aqueous solution at environmentally relevant pHs, they will be present as the anion PFHp and, respectively, the sodium, the ammonium or the potassium cation.

For clarity, it is usually referred to PFHpA in the discussions and conclusions on health and environmental effects in this document. However, based on the reasoning above, the conclusions are considered equally valid for any PFHpA salt as well. As the scope of the present SVHC dossier we have selected PFHpA and any/all of its salts. These entities are indistinguishable in the environment and will all contribute to the PFHpA levels. It should be noted that the sodium-, ammonium- and potassium-salts are the most widely manufactured, used and studied among the PFHpA salts. In the literature, the concentration reported in environmental and monitoring studies refer to both PFHpA and PFHp. No differentiation is made between the two species, because they are in equilibrium with each other. In the following, PFHpA refers to the acid (PFHpA) as well as to its conjugate base PFHp. Only in cases where it is important to distinguish between both species and where species specific knowledge is available, it is clearly indicated that either the acid PFHpA or the conjugate base PFHp is meant.

For simplicity, in the discussions and conclusions in this document, PFHpA is usually referred to. Based on the reasoning above, the conclusions are, however, considered valid for PFHpA and its salts, like PFHp-Na, PFHp-A and PFHp-K.

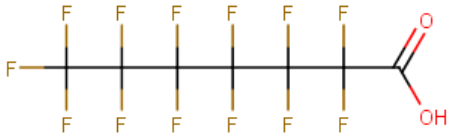
1.1 Name and other identifiers of the substance

Table 1. Substance identity of PFHpA and its salts

EC number:	206-798-9 [1], 243-518-4 [2], 228-098-2 [3], Not applicable [4]
EC name:	Perfluoroheptanoic acid [1] Sodium perfluoroheptanoate [2] Ammonium perfluoroheptanoate [3] Not applicable [4]
CAS number (in the EC inventory):	375-85-9 [1], 20109-59-5 [2], 6130-43-4 [3], Not applicable [4]
CAS number:	375-85-9 [1], 20109-59-5 [2], 6130-43-4 [3], 21049-36-5 [4]
CAS name:	Heptanoic acid, 2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro- [1] Heptanoic acid, 2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-, sodium salt (1:1) [2] Heptanoic acid, 2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-, ammonium salt (1:1) [3] Heptanoic acid, 2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-, potassium salt (1:1) [4]
IUPAC name:	Tridecafluoroheptanoic acid [1] Sodium tridecafluoroheptanoate [2] Ammonium tridecafluoroheptanoate [3] Potassium tridecafluoroheptanoate [4]
Index number in Annex VI of the CLP Regulation	607-761-00-3
Molecular formula:	$C_7HF_{13}O_2$ [1] $C_7F_{13}NaO_2$ [2] $C_7H_4F_{13}NO_2$ [3] $C_7F_{13}KO_2$ [4]
Molecular weight range:	364.06 g/mol [1] 386.04 g/mol [2] 381.09 g/mol [3] 402.15 g/mol [4]
Synonyms:	PFHpA C_7-PFCA Perfluoroenanthic acid Perfluoro-n-heptanoic acid

Structural formula:

[1]



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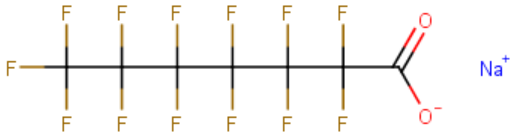

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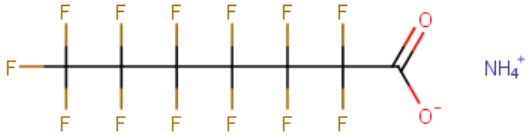

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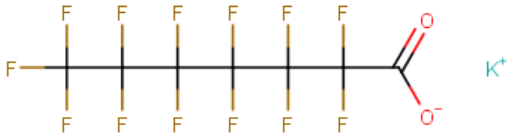

1.2 Composition of the substance

Name: Perfluoroheptanoic acid (PFHpA) and its salts

Description: -

Substance type: not applicable

Perfluoroheptanoic acid (PFHpA) is a mono-constituent substance. Depending on the chemical nature of the counterion(s) in the substance, the substances covered by this proposal may refer to mono-constituent, multi-constituent or UVCB substances. The identification as SVHC is based on the properties of the acid (PFHpA) and the dissociated equivalent (PFHp). Therefore, in this case, the rest of the composition, including also other possible constituents or impurities in the substances, were not considered for the identification as SVHC.

1.3 Identity and composition of structurally related substances (used in a grouping or read-across approach) and precursors

PFHpA is not registered for production or import and does not seem to have a commercial application. There are no natural sources known for PFHpA and the substance is considered anthropogenic, without any natural background concentration at all. Although PFHpA is not commercially produced, the substance is present in environmental compartments all over the Earth. This ubiquitous presence is considered to be the result of environmental transformation of (longer chain) PFAS in general. PFHpA is thought to be a (minor) degradation products of all kinds of PFAS with a fluorinated carbon chain of 7 carbon atoms *or longer.* Analogous to the

precursors of PFOA (ECHA, 2013a, b) it can be expected that any substance containing a (linear) carbon chain of 8 carbon atoms where 7 are perfluorinated will eventually (environmentally) transform into the carboxylic acid, i.e. PFHpA. However, commercial PFAS precursors containing a perfluorinated carbon chain of exactly 7 carbon atoms are also not known. In the degradation pathway of longer chain PFAS precursors, such as e.g. 8:2-fluorotelomer alcohol (FTOH) – a well-known PFOA precursor – one perfluorinated carbon atom is actually de-fluorinated, as PFOA contains only 7 perfluorinated carbon atoms of the total carbon chain length of 8. PFOA is however known to be not the only stable degradation product of 8:2-FTOH, but also shorter chain length PFCAs are produced, like PFHpA (6 perfluoro carbon atoms), PFHxA (5 perfluoro carbon atoms, etc. (Liu & Avendano 2013) The type and length of the non-perfluorinated part of the PFAS precursor molecule is directly influencing the yield of different carbon chain length PFCAs. Where PFHpA is only a minor metabolite in the degradation of 8:2-FTOH, it can be a more prominent metabolite from other PFAS-precursors, e.g. 6:2 FTOH, 7:3-FTOH, or any other telomer precursor. In fact, any PFAS with a perfluorinated carbon chain of 7 *or longer* can potentially produce PFHpA as the stable end-product of environmental degradation processes, and thereby contribute to the presence, and build-up of PFHpA concentrations in the environment (Liu & Avendano, 2013). Lee *et al.* (2010) showed that aerobic biodegradation of 6:2 polyfluoroalkyl phosphonic acids (PAPs and diPAPs) in a mixture of raw wastewater, sewage sludge and phosphate-free mineral medium for 92 days yielded 6:2 FTOH, which was further oxidised via transient transformation products, i.e. 6:2 FTCA and 6:2 FTUCA, to primarily PFHpA and in lesser amounts to PFHxA, PFPeA and 5:3 Acid. Atmospheric degradation of 4:2, 6:2 and 8:2 FTOHs was investigated by Ellis et al. (2004; Reliability 2) and showed that oxidation of 8:2 FTOH yields PFNA (1.6%), PFOA (1.5%), PFHpA (0.32%), PFHxA (0.24%), PFPeA (0.10%), PFBA (<0.1%), PFPrA (<0.1%), TFA (<0.1%). Oxidation of 6:2 FTOH produced PFHpA, PFHxA, PFPeA, PFBA, PFPrA, TFA, 6:2 FTCA, 6:2 FTAL, PFHxAL and 6:1 FTOH (yields not given).

PFHpA belongs to the chemical group of short-chain PFCAs. As such PFHpA and its salts can be expected to have properties similar to those of the short-chain PFCAs. PFHpA is, however, the longest possible short-chained PFCA with a chain of 6 perfluorinated carbon atoms and a total carbon chain length of 7. This is one perfluorinated carbon atom less than the shortest of the long-chain PFCAs. Therefore, PFHpA and its salts are also expected to have properties similar to those for the shortest of the long-chain PFCAs[3]. The long and short chain PFCAs all have a highly similar chemical structure: a chain of perfluorinated carbon atoms and a carboxylic acid group. They differ only in the length of the perfluorinated carbon chain (the number of CF_2 and CF_3 groups). Based on the experimental and estimated data it can be stated with sufficient reliability that the behaviour of the PFCAs follows a regular pattern: an increase in the chain length results in a decrease in water solubility and an increase in sorption potential.

Seven entries of long-chain PFCAs have already been included into the Candidate List, as well as a short-chain PFCA. These are given in Table 1. The short-chain PFCA is identified as SVHC on the basis of the persistence, mobility, long-range transport and potential for serious adverse effects, where the longer chain PFCAs are identified as PBT, or in the case of the very long ($>C_{11}$) PFCAs, as vPvB substances. In the RAC opinion on the short-chain PFHxA (C_6-PFCA) restriction proposal it was concluded that PFHxA is persistent, mobile, has long-range transport potential and potential for serious adverse effects (RAC, 2021).

[3] According to the definition proposed by OECD (OECD, 2013) long-chain PFCAs consist of >7 perfluorinated carbon atoms, starting with the shortest long-chain PFCA that is perfluoro octanoic acid (PFOA) with a carbon chain length of 8 carbon atoms and 7 perfluorinated carbon atoms.

Table 2. PFCAs already on the Candidate List, or proposed to be on the candidate list

EC number	CAS number	Substance name	carbon chain length	Details on SVHC-identification	Reference
236-236-8 [1]	13252-13-6 [1]	2,3,3,3-tetrafluoro-2-(heptafluoropropoxy) propionic acid [1], its salts and its acyl halides (HFPO-DA)	6*	Persistence, mobility, LRTP, observed adverse effects (Article 57 f)	ECHA (2019b)
223-320-4	3825-26-1	Ammonium pentadecafluoro octanoate (APFO)	8	Toxic for reproduction (Article 57 c); PBT (Article 57 d)	ECHA (2013a)
206-397-9	335-67-1	Pentadecafluoro octanoic acid (PFOA)	8	Toxic for reproduction (Article 57 c); PBT (Article 57 d)	ECHA (2013b)
206-801-3 [1], Not applicable [2], Not applicable [3]	375-95-1 [1], 21049-39-8 [2], 4149-60-4 [3]	Perfluorononan-1-oic acid (PFNA) [1], and its sodium [2], and ammonium salts [3]	9	Toxic for reproduction (Article 57 c); PBT (Article 57 d)	ECHA (2015)
206-400-3 [1], Not applicable [2], 221-470-5 [3]	335-76-2 [1], 3830-45-3 [2], 3108-42-7 [3]	Nonadecafluoro decanoic acid (PFDA) [1], and its sodium [2], and ammonium salts [3]	10	Toxic for reproduction (Article 57 c); PBT (Article 57 d)	ECHA (2016)
218-165-4	2058-94-8	Henicosafluoro undecanoic acid (PFUnDA)	11	vPvB (Article 57e)	ECHA (2012a)
206-203-2	307-55-1	Tricosafluoro dodecanoic acid (PFDoDA)	12	vPvB (Article 57e)	ECHA (2012b)
276-745-2	72629-94-8	Pentacosafluoro tridecanoic acid (PFTrDA)	13	vPvB (Article 57e)	ECHA (2012c)
206-803-4	376-06-7	Heptacosafluoro tetradecanoic acid (PFTeDA)	14	vPvB (Article 57e)	ECHA (2012d)

* the number of carbon atoms in HFPO-DA is six (two chains of 3 carbon atoms, joined by an ether bond), the longest chain length including the ether-bond is 6.

Other structurally related substances would be PFBA and PFPeA, as well as branched isomers of PFHpA. The only chemical difference between PFHpA and those PFCAs is the number of perfluorinated carbon atoms and/or the length of the (linear) perfluoroalkyl chain. A complete list of substances relevant for read across is given in Table 3. However, as very little substance property information is available for branched PFCAs, these are given in grey in Table 3. The chemical structures and substance information of PFCAs relevant for a read-across approach of substance properties are given in Annex I. With a chain length of 7 carbon atoms and 6 perfluorinated carbon atoms, PFHpA (and its salts) is most similar to PFHxA and HFPO-DA

(carbon chain length of 6, containing 5 perfluorinated carbon atoms), as well as to PFOA (carbon chain length of 8, containing 7 perfluorinated carbon atoms). Therefore, PFHpA and its salts can be expected to have very similar properties to PFHxA, HFPO-DA and PFOA, leading to potential PBT/vPvB based on PFOA and potential mobility properties based on PFHxA and HFPO-DA. These most relevant read-across substances are indicated in bold in Table 3.

Please see Annex I for the read across justification and the table of read-across substance properties.

Table 3. PFCAs for a read-across approach

EC name (abbreviation)	**EC number**	**CAS number**	**Nr. of perfluoro-carbon atoms**	**Longest linear carbon atom chain**
Heptafluorobutanoic acid (C_4-PFCA; PFBA)	206-786-3	375-22-4	3	4
Nonafluoropentanoic acid (C_5-PFCA; PFPeA)	220-300-7	2706-90-3	4	5
2,3,3,3-tetrafluoro-2-(heptafluoropropoxy) propionic acid, its salts and its acyl halides (HFPO-DA)	**236-236-8**	**13252-13-6**	**5**	**3, but persistent back bone length is 6 (including ether bond)**
Undecafluorohexanoic acid (C_6-PFCA; PFHxA)	**206-196-6**	**307-24-4**	**5**	**6**
Tridecafluorohexanoic acids, branched C_7-PFCA; PFHpA branched e.g. 5-trifluoromethyl-PFHxA 3,3-bis(trifluoromethyl)PFPeA	240-035-0 -	15899-29-3 558473-70-4	6 6	6 5
Tridecafluorohexanoic acid C_7-PFCA; PFHpA linear	206-798-9	375-85-9	6	7
Pentadecafluorooctanoic acid (C_8-PFCA, PFOA)	**206-397-9**	**335-67-1**	**7**	**8**
Ammonium pentadecafluorooctanoate (C_8-PFCA; APFO)	**223-320-4**	**3825-26-1**	**7**	**8**
Sodium pentadecafluorooctanoate (C_8-PFCA; NaPFO)	**206-404-5**	**335-95-5**	**7**	**8**
Heptadecafluorononanoic acid (C_9-PFCA; PFNA)	206-801-3	375-95-1	8	9
Nonadecafluorodecanoic acid (C_{10}-PFCA,PFDA)	206-400-3	335-76-2	9	10
Henicosafluoroundecanoic acid (C_{11}-PFCA; PFUnDA)	218-165-4	2058-94-8	10	11
Tricosafluorododecanoic acid (C_{12}-PFCA; PFDoDA)	206-203-2	307-55-1	11	12
Pentacosafluorotridecanoic acid (C_{13}-PFCA; PFTrDA)	276-745-2	72629-94-8	12	13
Heptacosafluorotetradecanoic acid (C_{14}-PFCA; PFTeDA)	206-803-4	376-06-7	13	14

1.4 Physicochemical properties

Table 4. Overview of physicochemical properties of perfluoroheptanoic acid.

Property	Description of key information	Value [Unit]	Reference/source of information
Physical state at 20°C and 101.3 kPa	Observed	Beige crystalline solid	Sigma-Aldrich
Melting/freezing point	Measured Measured	31 – 36 °C 30 °C	NICNAS, 2015 Sigma-Aldrich
Boiling point	Measured Measured (at 1 atm)	177 °C 175 °C	NICNAS, 2015 Siegemund (2000)
Vapour pressure	Measured (at 15 °C)	0.133 mmHg (= 17.7 Pa)	US EPA Chemistry Dashboard
Density	Measured (at 20 °C)	1.735 g/cm^3	Siegemund (2000)
Water solubility	Estimated using WSKOW v1.42 of the EPISuite tool*	3.65 mg/L (neutral species) 1936 mg/L (Na salt)	US EPA (2002-2012)
Partition coefficient n-octanol/water (log value)	Estimated using COSMOtherm (for details on the model see Klamt *et al.*, 2010). Estimated using KOWWIN v1.68 of the EPISuite tool PFHpA has surface active properties*.	4.7 4.15	Wang *et al.* (2011) US EPA (2002-2012)
Dissociation constant (pKa)	Estimated Estimated	<1.6 -2.29	Vierke *et al.* (2013) ChemSpider (2015)
Surface activity**	Measured (1mg/L water)	71 mN/m	Lyu et al. (2022)

* As PFHpA (and more specifically the longer chain PFCAs in general) can have surface active properties (at higher concentration in water), measurement of physicochemical properties like water solubility and octanol/water partition coefficient is considered very difficult and likely unreliable. Therefore theoretical values estimated by QSAR are preferred to give indications of the (range of) solubility or partition that is expected. Furthermore, the full dissociation of PFHpA and its salts at environmentally relevant pH's will also strongly influence the solubility and partitioning behaviour of PFHpA. For different purposes it might therefore be necessary to select a different value, e.g. for the fate modelling (section 3.4) the (estimated) log Kow for the sodium salt is considered a better representative of (dissociated) PFHpA partitioning (over environmental compartments) then the log Kow for the neutral PFHpA species presented here. Any adjustment from the values presented in this table will be argumented in the respective sections.

** at the indicated concentration of 1 mg/L the surface activity of PFHpA is not sufficient to consider PFHpA as a surface active substance. In the article by Lyu et al. (2022) the surface activity of PFHpA is considered 0.35 times that of PFOA. The critical reference concentration which indicates the concentration in water above which a substance is considered surface active is given as 30 mg/L for PFHpA.

Physicochemical properties of the read-across substances are provided in Table A.2 in Annex 1.

2. Harmonised classification and labelling

PFHpA is covered by Index number 607-761-00-3 in part 3 of Annex VI to the CLP Regulation. Pursuant to Commission Delegated Regulation (EU) 2022/692 of 16 February 2022, PFHpA will be classified in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child') and Specific target organ toxicity — repeated exposure category 1, STOT RE 1 (H372 (liver))[4]. This is based on a combined 90-day repeated dose toxicity study with reproductive/developmental toxicity screening (OECD TG 408 and 422) in CD1 mice (RAC, 2020).

Table 5. Classification according to the 18th ATP of Regulation (EC) No 1272/2008

Index No	Chemical name	EC No	CAS No	Classification		Labelling			Spec. Conc. Limits, M-factors and ATEs[5]	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s)	Hazard statement code(s)	Suppl. Hazard statement code(s)		
607-761-00-3	Perfluoroheptanoic acid; tridecafluoroheptanoic acid	206-798-9	375-85-9	Repr. 1B STOT RE 1	H360D H372 (liver)	GHS08 Dgr	H360D H372 (liver)			

[4] Commission Delegated Regulation (EU) 2022/692 of 16 February 2022 amending, for the purposes of its adaptation to technical and scientific progress, Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the 18th ATP to CLP). Pursuant to the second paragraph of Article 2 of this Regulation, this new harmonised classification applies from 23 November 2023. However, pursuant to the third paragraph of that provision substances and mixtures may already be classified, labelled and packaged in accordance with this classification.

[5] Acute Toxicity Estimate

3. Environmental fate properties

3.1 Degradation

3.1.1 Abiotic degradation

3.1.1.1 Hydrolysis

There are no studies on the hydrolysis of PFHpA available. Based on the category approach presented in Annex I, results of studies of structurally similar substances of the same chemical group were used to evaluate the hydrolysis of PFHpA.

The analogue PFNA (C_9-PFCA) showed no, or hardly any decomposition after 6 hours in hot water (80°C) with 97% of the initial amounts of PFNA remaining in the aqueous phase (Hori *et al*. 2008; Reliability 2).

The analogue PFOA (C_8-PFCA) is hydrolytically stable under environmental conditions with a hydrolytic half-life greater than 92 years (ECHA, 2013b).

Hence, based on read-across to PFNA and PFOA (Annex I), PFHpA is considered to be hydrolytically stable under environmental conditions. For PFHxA it was concluded in the RAC opinion (RAC 2021) that hydrolysis is not a relevant transformation pathway.

3.1.1.3 Phototransformation/photolysis

3.1.1.3.1 Phototransformation in air

There are no studies on phototransformation in air for PFHpA available.

The QSAR model AOPWIN v1.92 of the EPISuite tool (US EPA, 2002-2012) predicts degradation rates and half-lives for direct and indirect photolytic degradation in the atmosphere. Using the default settings of the model (assuming indirect degradation via OH-radicals, 12 h-day, 1.5e+06 OH radicals per m³), a degradation rate constant of 0.52e-12 cm³/(molec * s) is predicted for PFHpA, which corresponds to an atmospheric half-life of 20.57 days. The same prediction is obtained for PFOA and PFHxA.

For shorter chained PFCA's (C_2-C_5-PFCAs) some experimental data on abiotic degradation in air is available (Hurley *et al.*, 2004; reliability 2). In the respective study, the kinetics of the reactions of OH radicals with the C_2-C_5-PFCAs at an air pressure of 700 Torr and a temperature of 296 ± 2 K was investigated. The length of the perfluorinated carbon chain had no discernible impact on the reactivity of the molecule. Atmospheric lifetimes of TFA (C_2-PFCA) with respect to reaction with OH radicals were estimated to be approximately 230 days, while for the longer chained PFCAs (C_3-C_5-PFCAs) the atmospheric lifetime was estimated to be approximately 130 days. Reaction with OH radicals was considered a minor atmospheric transformation pathway for C_2-C_5-PFCAs (Hurley et al., 2004).

The Hurley *et al.* (2004) study was used to predict the atmospheric lifetime of PFOA as being 130 days (ECHA, 2013b).

3.1.1.3.2 Phototransformation in water

The photochemical decomposition of C_5- to C_7 and C_9-PFCAs in water by use of persulfate ion ($S_2O_8^{2-}$) was examined by Hori *et al.* (2005) (reliability 2). In water and in the absence of $S_2O_8^{2-}$ (direct photolysis) PFHpA decomposition of 18.7% was determined after 12 hours (for comparison decomposition of C_5-,C_6-, and C_9-PFCAs amounted in water to 15.6, 12.0, 64.5%, respectively). In the presence of $S_2O_8^{2-}$ the decomposition increased to 100% for all tested

PFCAs. The reaction products were mainly F- and CO_2. Short chain PFCAs ($C_nF_{2n+1}COOH$; n=1-5) were minor reaction products. Since the conditions in these studies are not relevant for an aqueous environment (wavelength used for irradiation <300 nm), the studies were not described in detail.

PFOA does not undergo direct photodegradation in natural waters. Its estimated half-life for indirect photolysis (Fe_2O_3) is greater than 349 days (ECHA, 2013b).

3.1.1.4 Summary on abiotic degradation

Under environmentally relevant conditions PFCAs are extremely stable. As there are no experimental studies under relevant environmental conditions available for PFHpA, data from similar substances were considered and are discussed below. Based on the category approach presented in Annex 1, results of studies of structurally similar substances of the same chemical group were used to evaluate the abiotic degradation of PFHpA.

The data on PFOA indicate that abiotic degradation in the atmosphere is expected to be slow (atmospheric lifetime = 130 days). Under relevant environmental conditions PFOA is hydrolytically stable (estimated DT50 > 92 years) and does not undergo direct photodegradation in natural waters. Its estimated half-life for indirect photolysis (Fe_2O_3) is greater than 349 days.

Based on the read-across rationale described in Annex 1, data on the chemically similar substance PFOA are used as evidence to conclude that PFHpA is stable under environmental conditions and that the abiotic degradation of PFHpA is expected to be as low as for PFOA.

3.1.2 Biodegradation

3.1.2.1 Biodegradation in aqueous media or aqueous environment

Estimated data

The QSAR model BIOWIN v4.10 of the EPISuite tool (US EPA, 2002-2012) includes several QSARs for estimating intrinsic substance properties and environmental fate and behaviour of chemicals, providing degradation timeframes for primary and ultimate degradation of chemicals. BIOWIN also provides an estimate whether a substance fulfils the criteria of being rated as "readily biodegradable". The outcome of the different BIOWIN QSAR estimates is provided in Table 6.

The combination of these QSARS gives an estimate whether a chemical is potentially persistent in the environment or not. According to REACH guidance document R.11 (ECHA, 2017), the screening criteria below which persistence for PBT assessment is likely are BIOWIN 2 or BIOWIN 6 scores below 0.5 in combination with a BIOWIN 3 value equal to or below 2.25. The values for PFHpA lie well below these screening criteria and thus the QSARs indicate that PFHpA is potentially (very) persistent. As expected, the values obtained for PFHpA lie in between those obtained for PFOA and PFHxA, which are one perfluorinated carbon longer, respectively, shorter than PFHpA.

For evaluation of the BIOWIN prediction it has to be kept in mind that the outcome for perfluorinated hydrocarbons has to be interpreted as a qualitative prediction. This is because the training data set is incompletely implemented for perfluorinated carbon chains. In particular, there is no fragment coefficient for a non-terminal perfluorinated carbon in the BIOWIN models. For example, for PFHpA the perfluorinated carbon chain is contributing to the predicted biodegradability score by five fragments of "carbon with 4 single bonds & no hydrogens".

Table 6. Outcome of the different QSAR estimates on biodegradability of PFHpA, PFHxA and PFOA for comparison

Model	Result (value) PFHpA	Result (value) PFHxA	Result (value) PFOA	Conclusions from the estimate
BIOWIN 1	-0.7932	-0.5854	-1.0009	Does Not Biodegrade Fast
BIOWIN 2	0.0000	0.0000	0.0000	Does Not Biodegrade Fast
BIOWIN 3	1.1857	1.5083	0.8631	Recalcitrant
BIOWIN 4	2.6665	2.892	2.4409	Weeks-Months
BIOWIN 5	0.3742	0.4206	0.3278	Not Readily Degradable
BIOWIN 6	0.0000	0.0000	0.0000	Not Readily Degradable
BIOWIN 7	-0.6483	-0.3141	-0.9825	Does Not Biodegrade Fast
Ready biodegradability prediction	NO	NO	NO	Criteria of BIOWIN predictions are not fulfilled: module BIOWIN 3 should predict "degradation within weeks" or faster AND module BIOWIN5 should result in value ≥ 0.5.

This is complemented in BIOWIN 1-4 with a specific fragment for a trifluoromethyl group, and in BIOWIN 5 and 6 with 13 fragments of fluoride. Remarkedly, the fluoride has a slightly positive influence on biodegradability in BIOWIN 5 but a strongly negative influence on the biodegradability in BIOWIN 6. BIOWIN 7 recognises both additional fragments but has a coefficient of zero in both cases (i.e., no effect on the prediction of degradability). It should also be noted that in BIOWIN 1-4 the trifluoromethyl fragment is based on only one compound in the training set (3'-methyl-4'-chloro-2,2,2-trifluoroacetophenone, CAS 286017-71-8, which is not a perfluorinated alkyl substance).

Nevertheless, the result of BIOWIN modelling provides sufficient evidence that PFHpA will not fulfil the criteria for being rated as "readily biodegradable", and, considering the above, the screening assessment on persistence of PFHpA based on BIOWIN predictions, adds to the weight-of-evidence that PFHpA is "potential P or vP" according to ECHA Guidance on PBT/vPvB assessment (ECHA, 2017).

Screening tests

There are no biodegradability screening studies available for PFHpA. Based on the category approach presented in Annex I, results of studies of structurally similar substances of the same chemical group were used to evaluate the biodegradation potential of PFHpA.

In a biodegradability screening test based on OECD 301 D with modifications, a mixture of PFHxA, PFOA, PFNA and PFOS was tested at a concentration of 4 mg/L for 3.5 months (Sáez *et al.*, 2008) (reliability 2). After 3 weeks degradation amounted to approximately 5, 5 and 10% for PFHxA, PFOA and PFNA, respectively (based on test material analysis). After a prolonged test period of 15 weeks degradation increased to 45% for PFHxA, while it remained low for PFOA and PFNA, with degradation being respectively 0 and 10%. For interpretation of the measured degradation rates, it has to be noted that the inoculum for the test was taken

from a sewage treatment plant that is located in a highly industrialised area of the west harbour of Amsterdam. Therefore, it can be assumed that the sewage treatment plant is predominantly treating industrial wastewater and that the inoculum might have already been subject to (low level) pre-adaption to PFHxA or to structurally similar substances. Nevertheless, these data show that PFHxA, PFOA and PFNA screen as potentially persistent.

In a ready biodegradability test (OECD 301 F) using either 50 mg/L PFOA (27.8 mg/L as ThOD) or 50 mg/L PFNA (28.4 mg/l ThOD) together with 30 mg/L activated sludge and 10 mg/L allylthiourea (to prevent nitrification) no biodegradation was observed for either substance after 28 days (Stasinakis *et al.*, 2008) (Reliability 2).

In a further test the ready biodegradability (OECD 301 C) of PFOA and its ammonium salt was investigated (using 100 mg/L test substance and 30 mg/L activated sludge). Only 5% and 7% degradation was observed by BOD for PFOA and its ammonium salt, respectively (MITI-list, 2002) (Reliability 2).

In summary, based on the read across to PFHxA, PFOA and PFNA, PFHpA is considered to be not readily biodegradable.

Simulation tests in water

For PFHpA no experimental degradation test in water is available. Based on the category approach presented in Annex I, results of studies of structurally similar substances of the same chemical group were used to evaluate the biodegradation potential of PFHpA in water.

Therefore, test results for PFOA and its salts are discussed shortly. There were four studies that investigated the biodegradation of PFOA and its salts, of which one was considered reliable, i.e., Liou *et al*. (2010) (reliability 2).

Liou *et al.* (2010) investigated the anaerobic biodegradability of PFOA respectively its ammonium salt APFO. In a two-phase experiment (preliminary screening, hypothesis refinement) the use of PFOA as a physiological electron acceptor (electron donator: acetate, lactate, ethanol or hydrogen gas) was studied. Additionally, the possibility of co-metabolism of PFOA during reductive dechlorination of trichloroethene and during various physiological conditions (aerobic, nitrate-reducing, iron-reducing, sulfate reducing, and methanogenic) was analysed. Five different inoculums were used (from a municipal waste-water treatment plant, industrial site sediment, an agricultural soil, and soils from two fire training areas). In no combination of the inoculum source, electron donator or physiological conditions a significant percentage of the initial PFOA (100 ppm and 100 ppb) was consumed (half-lives ranging from 110-259 days). In a test with ^{14}C labelled APFO (inoculum = sewage), no loss of APFO was detected, no radiolabelled APFO transformation product was indicated. Co-metabolism of PFOA during reductive dechlorination of trichlorethene was suggested by a drop in PFOA concentration in the 100 ppb treatment after a 65-d incubation period. However, extensive analysis failed to determine corroborating transformation products. Overall, the results show that under the anaerobic conditions examined in this study, PFOA is environmentally persistent.

A study investigating the biodegradation of ^{14}C-labelled AFPO in mixed bacterial culture and activated sludge under aerobic conditions, reported that after 28-days <0.6% of $^{14}CO_2$ was formed (Wang *et al*., 2005). The reliability of the study could not be assessed due to limited reporting (Reliability 4). However, the study was considered as indicating that APFO is not biodegradable within 28 days under aerobic conditions.

In conclusion, one non-standard aerobic degradation simulation study and one non-standard anaerobic degradation simulation study on PFOA demonstrate the high persistence of the compound in water. Based on the read across rationale described in Annex I, data on PFOA can be used as evidence of persistence for PFHpA in water.

Biodegradation in sediment

For PFHpA no simulation degradation test in sediment is available. Based on the category approach presented in Annex I, results of studies of structurally similar substances of the same chemical group were used to evaluate the biodegradation potential of PFHpA in sediment.

The anaerobic biodegradability of the analogues PFOA respectively APFO in industrial site sediment was investigated by Liou *et al.* (2010) (see section 3.1.2.1.3.1). No significant amount of the initial PFOA was dissipated after 259 days.

In conclusion, the one non-standard anaerobic degradation simulation study on PFOA demonstrates the high persistence of the compound in anaerobic sediment. Based on the read across rationale described in Annex I, data on PFOA can be used as evidence of persistence for PFHpA in anaerobic sediment.

Biodegradation in soil

For PFHpA no simulation degradation test in soil is available. Based on the category approach in Annex I, results of studies of structurally similar substances of the same chemical group were used to evaluate the biodegradation potential of PFHpA in soil.

Therefore, test results for PFOA and its salts are discussed shortly.

A number of studies investigated the biodegradation of PFOA and its salts and were previously discussed in the OECD SIDS Initial Assessment Report (OECD, 2006):

Moody and Field (1999) conducted sampling and analysis of samples taken from groundwater 1 to 3 meters below the soil surface in close proximity to two fire-training areas with a history of aqueous film forming foam use. Perfluorooctanoate was detected at maximum concentrations ranging from 116 to 6750 µg/l at the two sites many years after its use at those sites had been discontinued. These results suggest that PFOA can leach to groundwater (Moody and Field, 1999).

Extensive site specific monitoring of soil and ground water concentrations of PFOA and related substances was conducted by 3M, DuPont Daikin and others. PFOA in soil has been shown to persist for decades and to be a long term source of groundwater and surface water contamination (see for example (DuPont Co., 2003; 3M Co., 2005)).

At the DuPont Washington Works site soil contaminated by perfluorochemical waste has been shown to contain ppm levels of PFOA 3 decades after application ceased. The underlying groundwater also contains ppm levels of PFOA (DuPont Co., 1999a).

Extensive field monitoring data generated by 3M at the Decatur, AL site have also shown that PFOA is persistent in soils. Soil samples were collected from a former sludge application area of the 3M Decatur, AL facility also show soil contamination and underlying groundwater contamination up to ppm levels decades after application ceased.

In addition, Moody *et al.* (2003; Reliability 2) investigated groundwater at a former fire-training area that was used between 1950s and 1993 and estimated that perfluorinated surfactants had been in the groundwater for at least five years and possibly for as long as 15 years. This shows that degradation of PFOA was negligible under the environmental conditions at this site (for both soil and groundwater).

Finally, the anaerobic biodegradability of PFOA in soil sampled from two fire training areas was investigated by Liou *et al*. (2010) (see section 3.1.2.1.3.1). No significant amount of the initial PFOA concentration dissipated within 259 days.

In conclusion, the available data on PFOA demonstrate the high persistence of the compound in soil. Based on the read across rationale described in Annex I, data on PFOA can be used as evidence of persistence for PFHpA in soil.

3.1.2.3 Summary and discussion on biodegradation

Screening studies for PFHpA are not available. However, results from screening studies of PFHxA, PFOA and PFNA used in a read-across approach as described in Annex I indicate that PFHpA is not readily biodegradable. This is supported by the BIOWIN predictions.

Results from aerobic and anaerobic non-standard degradation studies with PFOA and field monitoring data on PFOA from contaminates sites, provide good evidence that biodegradation of PFOA does not occur in water, soil or sediment. Since the stability of PFCAs is in general based on the stability of the fluorinated carbon chain it can be concluded using the read-across approach as described in Annex I that also for PFHpA no biodegradation in water, soil or sediment can be expected. Thus, it can be assumed that PFHpA is not biodegradable and persistent.

3.1.3 Summary and discussion of degradation

For PFHpA there is no degradation study under environmental conditions available. Therefore, data from chemically similar substances are considered in a read-across approach (see Annex I for further details). Generally, it is known that the bond between carbon and fluorine is one of the most stable ones in organic chemistry and therefore expected to have a very low susceptibility to degradation by microorganisms occurring in the environment.

A number of studies for the longer chain homologues PFNA and especially PFOA show that these substances are extremely persistent and do not undergo abiotic or biotic degradation at all under environmental conditions. The persistence of PFOA and PFNA was already confirmed by the Member State Committee that identified PFOA and PFNA as SVHC based on their PBT properties (ECHA, 2013b; ECHA 2015).

PFCAs are synthetic compounds which contain a common structural feature: a perfluorinated carbon chain combined with a carboxylic group. The chemical structure of these compounds differs only in the number of perfluorinated carbons in the carbon chain.

The stability of organic fluorine compounds has been described in detail by Siegemund *et al.* (2000). 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 attack. Several other properties of the carbon-fluorine bond contribute to the fact that highly fluorinated alkanes are very stable organic compounds. These include polarisability and high bond energies, which increase with increasing substitution by fluorine. The influence of fluorine is greatest in highly fluorinated and perfluorinated compounds. Properties that are exploited commercially include high thermal and chemical stability.

Based on their molecular properties, it is thus clear that researchers could not measure degradation of PFOA and of PFNA (or of their salts). Considering the organic chemistry of this substance group, it seems very likely that PFHpA, which has a carbon chain being only one CF2-group shorter than PFOA and two CF2-groups shorter than PFNA, is not significantly less persistent than PFOA or PFNA. Therefore, it can be concluded that PFHpA will be resistant to degradation.

In summary, considering the knowledge on the high stability of the C-F bonds and using the described read-across approach, it can be concluded that PFHpA is a very persistent synthetic compound which is resistant to abiotic and biotic degradation. Therefore, based on the knowledge of the stability of the C-F bond and the read-across approach with PFHxA, PFOA,

PFNA, PFDA and C_{11}-C_{14}-PFCAs it is concluded that PFHpA is expected to undergo no or extremely limited degradation in the environment and thus fulfils the P- and vP- criteria in accordance with the criteria and provisions set out in Annex XIII of REACH.

3.2 Environmental distribution

Based on information in the tables entitled "Basic substance information and physical chemical properties relevant to justify read across in the PBT assessment" in the support documents for the SVHC identification of different PFCAs already on the Candidate List (see Table 2), the distribution of PFCAs is influenced by the pH of the environment (e.g., ECHA, 2012a). Based on range of pK_a values for PFCAs, (estimated using ChemAxon software to vary from -5.20 for C_{14}-PFCA to 0.95 for C_1-PFCA (TFA) it is expected that PFHpA (as well as its salts and all other PFCAs) will be completely dissociated at environmentally relevant pH's. The water solubility, the adsorption potential and hence the distribution in the environment exhibit a regular pattern depending on the alkyl chain length of the PFCA.

In RAC's opinion on the PFHxA (C_6-PFCA) restriction proposal it was concluded that PFHxA is considered to be very persistent and mobile in the environment (RAC, 2021). PFHxA has one CF_2- unit less than PFHpA and shows a similar adsorption and volatilisation behaviour as discussed below.

HFPO-DA, which differs from PFCAs due to the presence of an ether bond in the perfluoro chain, has been identified as SVHC under article 57(f) based on its very high persistence, mobility and toxicity (ECHA, 2019b). A read-across between PFHpA and HFPO-DA is considered justifiable. The read-across of properties to PFHpA from HFPO-DA and PFHxA on one hand and PFOA on the other hand has been detailed in the respective background documents. Read-across to PFHxA and HFPO-DA underpins the mobile character of PFHpA.

The environmental distribution of PFHpA especially with respect to a potential for long-range transport is further evaluated in section 3.3.

3.2.1 Adsorption/desorption

For PFHpA no results from studies following one of the standard test guidelines commonly recommended for the REACH Regulation are known at the moment. However, adsorption was tested in different laboratory or semi-natural set-ups. A few studies are available in which different PFASs were analysed in batch equilibrium studies at several concentrations to obtain sorption isotherms similar to the OECD TG 106.

Batch equilibrium studies

Guelfo and Higgins (2013; reliability 2) evaluated the adsorption/desorption of C_{4-11}-PFCAs. Three different soils were used in a batch equilibrium experiment with five different concentrations: a loamy sand soil (OC content 1.7 %, pH 6.1), a loam soil (OC content 4.5 %, pH 7.8) and a sandy clay loam soil (OC content 0.8 %, pH 5.2). All soils were dry sieved (2 mm) prior use. The average log K_{OC} values were 1.88, 1.37, 1.31, 1.63, 1.89, 2.36, 2.96 and 3.56 for PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA and PFUnA, respectively. The log K_{OC} of 1.63 for PFHpA supports low adsorption potential.

Higgins and Luthy (2006; reliability 4) determined an increasing adsorption coefficient in batch equilibrium experiments with 5 sediments with organic carbon contents ranging from 0.56 to 9.66%. Values for log K_{oc} obtained from a regression over 2 to 5 sediments with different organic carbon content ranged from log K_{oc} = 2.11 for PFOA) to 3.47 for PFUnDA. These values were similar as the ones obtained for soil under similar experimental conditions (Guelfo and Higgins, 2013). In both studies a strong correlation between sorption and the organic carbon content was observed. It can be concluded that although PFHpA itself was not measured in this study with sediments, also for sediment the log K_{oc} of PFHpA will be below 2.

Zhang *et al.* (2013a; reliability 2) investigated the sorption of C_{2-15}-PFCAs on thirteen sewage sludges in batch equilibrium experiments. It was concluded that sorption on sludge increases with increasing alkyl chain length for PFCAs with C_5–C_{15}, indicating that hydrophobic interactions play an important role for sorption of these chemicals. For PFHpA the log K_f values range for 1.00-1.88, and for PFPeA 0.81-1.49, PFHxA 0.86-1.66, PFOA to 1.13-2.28, and PFNA 1.33 – 3.21. From the study, an average K_{oc} value for PFHpA of 1.80 ± 0.20 can be derived from the presented Kf values and fraction total organic carbon reported for the thirteen sludges. This represents the log K_{oc} at 1 pmol/L, i.e., less than a factor of 10 lower than the lowest tested concentrations. The coefficients of the Freundlich isotherms are close to 1, indicating almost linear sorption isotherms, but at higher concentrations the K_{oc} value will be even lower if non-linear sorption is observed.

Campos Pereira et al. (2018; reliability 2) investigated the effect of cation composition and pH on the sorption of $C_{4-12,14}$-PFCAs to an organic soil horizon. For this study a mono layer soil sample with pH 4.8, containing 45 % C, 1.3 % N and 3.4 % ash content on a dry weight basis was used. The sample was sieved <2 mm prior to homogenisation, and then stored at 5 °C in its field-moist state with 69 % water content until further use. The sorption was investigated regarding dependence from pH and added concentrations of aluminium (Al3+), calcium (Ca2+) and sodium (Na+) ions. For PFHpA the averaged adsorption coefficient was approximately log K_{OC} = 1.7 from all values for the different pH-values and cations added. Log K_{OC} values amounted to approximately 0.7, 1.2, 1.3, 1.7, 2.2, 3.1, 4.4, 4.7,4.3 and 4.3 for PFBA, PFPeA , PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDa, and PFTeDA, respectively.

Column leaching studies

Vierke *et al.* (2014; reliability 3) investigated the transport of C_{4-10}-PFCAs and $C_{4,6-8}$-PFSAs in a water-saturated sediment system representing a riverbank filtration scenario and determined sorption parameters for the investigated PFASs. The column was embedded in a natural slow sand filter basin and fed by the surrounding surface water. The column is supposed to represent river bank filtration and therefore was water saturated The water, which was checked daily, was pumped through the sediment at a filter velocity of 1.1 m/d. The column was filled with coarse-grained medium sand, followed by 30 cm gravel. The sand had a content of 0.02 % nitrogen (N), 0.07 % organic carbon (OC), 0.3 % carbonate C and a C/N-ratio of 16.1. The PFASs were spiked as one initial pulse in the supernatant of the column. Concentration of PFASs was determined in samples from the supernatant, but also in depths of 40 cm and 80 cm in the column over a period of two weeks. The pH value of the water samples ranged from 7.4 to 7.9. The test substances were mixed with a tracer (here 25 % sodium chloride (NaCl) solution) to quantify the sorption process for every analyte.

Unfortunately, the concentrations in the blank samples of PFHpA and PFOS were too high and these two PFAS were excluded from further evaluation. A distribution coefficient was presented for PFBA, PFPA, PFHxA, PFOA and PFNA. Based on these data it can be expected that PFHpA values will be in between those reported for PFHxA (log K_d = -0.18/0.46 (in 40 cm/80 cm) and PFOA (log d = 0.82/0.69 (in 40 cm/80 cm)). Leaching of PFHxA through the column was faster than for PFOA and PFNA. Given the very low organic carbon content of the soil (0.07%), the log K_{oc} values from this study (3.0/3.6 (in 40 cm/80 cm) for PFHxA and 4.0/3.9 (in 40 cm/80 cm) for PFOA) cannot be considered reliable.

Gellrich *et al.* (2012; reliability 4) also performed a column study with amongst others $C_{4-12,13}$-PFCAs. The columns were 60 cm long and 5 cm in diameter filled with loamy sand (LUFA standard soil no. 2.2; soil parameters: OC concentration 2.16 %, 13.9 % of the particles < 0.02 mm, pH-value 5.4, cation exchange capacity 10 meq/100 g) or sewage sludge. However, no distribution coefficients were calculated. In this study PFBA, PFPeA and PFHxA were not retained by the loamy sand and eluted together with the tracer. PFHpA eluted almost completely over a period of 70 weeks with a fast first desorption followed by a slower second desorption. The desorption of PFOA commenced after 33 weeks, while >C_8-PFCAs could not be detected in the percolating water after 140 weeks. In sewage sludge elution of PFBA started

after nine weeks, followed by PFPeA, PFHxA and PFHpA with elution commencing according to their chain length. PFOA started to elute after 1 year, while >C_8- PFCAs were not detected in the percolating water after 120 weeks.

Other laboratory experiments

Sepulvado *et al.* (2011; reliability 2) investigated the fate of amongst others C_{4-12}-PFCAs in soil. They investigated the presence of PFCAs in sewage sludge of several municipal sewage treatment plants together with the occurrence of these PFCAs in agricultural soils on which these sewage sludges were applied over several years. The investigated soil types were a silty clay loam soil (OC content 4.1 %), a fine sand soil (OC content 1.1 %) and a silt loam soil (OC content 4.7 %). In a first stage the presence of PFCAs in the samples was investigated, followed by desorption experiments for C_{6-10}-PFCAs over 14 days to determine the time necessary for the soil-water mixtures to reach equilibrium. From those experiments, the authors calculated the desorption-based K_{OC} values. The log K_{OC} values averaged 1.63-2.35 for PFHxA, 2.22-2.82 for PFHpA, 2.42-2.59 for PFOA, 2.42-2.59 for PFNA, and 3.14-3.32 for PFDA, respectively.

Field studies

In a monitoring study by Ahrens *et al.* (2010; reliability 2) showed that the log K_{oc} of PFCAs in sediment of Tokyo Bay increases with the length of the carbon chain (PFOA: log K_{oc} = 1.9, PFUnDA: log Koc = 4.8). For suspended matter, these values range from 2.9 for PFHpA to 5.1 for PFUnDA. Those findings are supported by the work of Higgins and Luthy (2006; reliability 2), who also determined an increasing adsorption/desorption coefficient from C_8-PFCA (log K_{OC} = 2.06) to C_{11}-PFCA (log K_{OC} = 3.3). For a more detailed overview please see the read-across information in Annex I of this document.

Li *et al.* (2011; reliability 2) investigated perfluorinated compounds present in the Haihe River and Dagu Drainage Canal in Tianjin, China. They found that PFHpA had an average partition coefficient log K_{OC} (sediment and overlapping dissolved phase) in the range of 3.0 – 3.6 (corresponding log K_D of 1.7 – 2.4). For PFHxA the log K_{OC} was 3.1 – 3.7 (corresponding log K_D was 1.8 – 2.5) and for PFOA log K_{OC} was 3.1 – 3.7 (corresponding log K_D was 1.8 – 2.5).

3.2.2 Volatilisation

No experimental data are available for Henry's Law constant (HLC). The QSAR program HenryWin v3.20 of EpiSuite (US EPA, 2002-2012) calculates a HLC by the bond method. This value is for the acid 1.75 x 10^3 Pa·m^3/mol, or 0.71 unitless (m^3 water/m^3 air). Practically the same value is obtained for the sodium salt 1.76 x 10^3 Pa·m^3/mol, or 0.71 unitless. For the ammonium salt a much lower HLC is obtained, i.e., 8.42 x 10^{-6} Pa·m^3/mol, or 3.4 x 10^{-9} unitless.

For the acid a vapour pressure of 17.7 Pa is reported which is high. For the ammonium salt no vapour pressure is available but can be estimated with Mpbpwin v1.43 from EPI Suite 0.064 Pa at 20 °C (Modified Grain Method selected by QSAR). For the acid a vapour pressure of 104 Pa (mean of Antoine and Modified Grain Method selected by QSAR) is predicted. Using these vapour pressure values and the formula "HENRY = VP · MOLW / SOL" from REACH technical guidance R.16, and the physicochemical properties listed in Table 4 (mw = 364.06 g/mol; S_w = 3.65 g/L) the following HLC values are obtained: for the acid a HLC of 1.765 x 10^3 Pa·m^3/mol based on Vp of 17.7 Pa, and a HLC of 1.04 x 10^4 Pa·m^3/mol, for the ammonium salt a HLC of 6.38 Pa·m^3/mol.

Considering that PFHpA is present in the anionic form in the aquatic environment at environmentally relevant conditions, the HLC values calculated for the ammonium salt are considered to show the real potential to volatilise from water. As these values are far below the threshold for volatile substances (HENRY > 250 Pa·m³/mol) from REACH Guidance R.16 (ECHA, 2016a) it can be concluded that PFHpA has a low to moderate tendency to volatilise from water.

3.2.3 Distribution modelling

See section 3.3 on long-range transport.

3.2.4 Field and monitoring data

The studies on field and monitoring data discussed below, do not follow standardised study guidelines as such guidelines are not available for this kind of studies. Furthermore, these studies have generally not been performed under GLP. Their reliability can consequently not exceed Klimisch 2. Studies that are considered to be questionable or unreliable (Klimisch 3) have not been included in the overviews below. If a study is mentioned below, the results are considered reliable enough to include them to evaluate the concern for PFHpA.

PFHpA in surface water

PFHpA is detected in surface waters all over the world. As an illustration some monitoring taken from the EU PFAS-Fire Fighting Foam proposal for Restriction (ECHA, 2022) are given. The overview table of levels of PFASs detected in surface waters, including specific levels of PFHpA in different monitoring programs (Annex B) shows consistently nanogram/Liter levels of PFHpA in surface waters all over Europe: Austria 0-6.6 ng/L (2 studies), Bulgaria 0-1.2 ng/L (n=3), Croatia 0-19 ng/L (n=3), Czech republic 2-2.6 ng/L (river water, n=1), France 0-7 ng/L (river water n=1), Hungary 0-10 ng/L (river water, n=3), Netherland 0-5 ng/L. Italy is showing one of the highest observed surface water concentrations, close to 1 ug/L: 0.3-946 ng/L. Also in sea water PFHpA is routinely detected in the nanogram/L ranges: Georgia 0-0.8 ng/L (n=2), Germany 0.15-0.2 ng/L (n=1),

Although local hotspots seem to occur (Italy) this might be related to local sources of PFHpA precursors, the picture is clearly that PFHpA as degradation product of PFAS precursors and probably due to its high mobility is consistently identified in the nanogram/L ranges in European surface waters.

PFHpA in ground water

In the EU PFAS-Fire Fighting Foam proposal for Restriction (ECHA, 2022) a table presents levels of PFASs detected in groundwater. PFHpA is detected in groundwater monitoring in e.g. France from <LoQ up to 224 ng/L, Germany sees levels of 300 to 540 ng/L detected, for Italy concentrations reach from 0.88 to 761 ng/L in the groundwater, in the Netherlands up to 318 ng/L is detected.

Loos *et al.* (2010) describe (already in 2010) an overview of 164 individual ground-water samples from 23 European Countries which were evaluated for the presence of a.o. PFASs. PFHpA was present in 30% of the samples, with a maximum concentration of 21 ng/L and an average concentration of 1 ng/L. Both the frequency as well as the maximum concentrations are already in 2010 quite high considering that PFHpA was, and still is not produced or manufactured, and therefore all environmental concentrations have to be explained by the transformation of PFHpA precursors to stable. For comparison PFOA was detected in 66% of the groundwater samples with a maximum concentration of 39 ng/L and average concentration of 3 ng/L; and PFHxS was detected in a comparable 35% of the locations with a maximum concentration of 19 ng/L and average concentration of 1 ng/L.

More recently Yan Liu *et al.* (2019 describe the occurrences of 10 PFAS in groundwater in the alluvial-pluvial plain of Hutuo River (APPHR) in the North China Plain (NCP). Total PFAS concentrations ranged from 0.56 ng/L to 13.34 ng/L, with an average value of 2.35 ng/L. In one of the four sampling regions (G1: Fissure and pore water unit in the valley in Gangnan Reservoir and Huangbizhuang Reservoir) the detection frequency of PFHpA was 100% in the 12 ground water sample locations in that area – spread over close to and far away from the Hutuo river. This is a strong indication that PFHpA is not static or correlated to a specific

contamination site but, has the potential to spread out over large (groundwater) areas due to its mobility (and persistence).

Recent measurements of a monitoring site in Colorado (US Department of Energy, 2022) around the former Rocky Flats fire department and associated training area, and a former landfill, surrounded by Rocky Flats National Wildlife Refuge. Eleven locations (six groundwater wells, three treatment plant influent or effluents and two surface water locations were sampled to screen for PFAS contamination including PFHpA. The concentration of the surface water location upstream of the contamination sites was 0.4 ng/L which was the limit of detection. The influent concentration of the fire department and training site was 0.51 ng/L, whereas the groundwater well located ~ 300 meters downstream contained 0.8 ng/L. The influent of the treatment plant processing the former landfill seepage (different location) contained 13 ng/L whereas the effluent of the treated landfill seepage contained up to 24 ng/L PFHpA, a concentration increase after seepage water treatment. In the groundwater wells downstream from both the fire department and the former landfill (approx. 1 kilometre away from the treatment plant of the landfill seepage), and also in the zone ~1 km away from the groundwater well close to the fire department site up to 82 ng/L of PFHpA was measured in the groundwater. In a surface water location in the same creek where the upstream samples were taken ~2 km downstream from both the landfill and the fire department site 2.9-3.1 ng/L of PFHpA was measured in the surface water. These are clear indications that PFHpA is formed as a product of PFAS-precursors, and is highly mobile, moving and contaminating not only the surface water but also easily reaching the (deep) groundwater.

PFHpA in drinking water

A recent global survey found a widespread distribution of SC-PFAAs in drinking water (Kaboré *et al.*, 2018), with PFHpA detected in 42% of bottled water (max. concentration 1.1 ng/L) and in 90% of tap water with mean and max concentrations of 0.33 and 3.2 ng/L.

In the EU PFAS-Fire Fighting Foam-restriction proposal (ECHA, 2022) overviews of detection of PFASs in drinking water are presented (Table 22, Annex X): PFASs have been detected in European drinking waters according to the NORMAN database (https://www.norman-network.com/nds/). In drinking/tap water, the highest concentrations of PFHpA have been measured in Italian drinking/tap water: up to 100 ng/L. In the Netherlands concentrations up to 3.1 ng/L PFHpA have been reported in tap water; PFASs have also been measured in bottled drinking water: e.g., PFHpA up to 12 ng/L in Germany, 19 ng/L in Spain and 22 ng/L in France (ECHA, 2022).

PFHpA in edible crops

PFCAs, including PFHpA, might enter the food chain easily when they are taken up by (edible) crops. The possible routes of exposure of crops are very diverse: from groundwater, surface water, soil, sludge, as well as deposition from air as transformation product from volatile PFHpA precursors.

There is also already a widespread presence of PFCAs including PFHpA precursors in wastewater, and since wastewater treatment sludge can be applied on soil as fertiliser, it is likely that PFHpA as a transformation product will also be able to migrate into (edible) crops via that route (Blaine *et al.*, 2013). Blaine et al. (2013) measured uptake of PFAAs by greenhouse lettuce (Latuca sativa) and tomato (*Lycopersicon lycopersicum*) grown in an industrially impacted biosolids-amended soil, and a municipal biosolids-amended soil. Both biosolids-amended soils had comparatively low levels of the shorter chain carboxylates (PFBA, PFPeA, PFHxA, PFHpA): <12 ng/g dry weight of each in the industrially impacted soil and <3 ng/g dry weight in the municipal biosolids-amended soil. Bioaccumulation factors (BAFs) were calculated by dividing the concentration in the plant tissue on a dry weight basis by the concentration in the soil on a dry weight basis: for the edible portions of both lettuce and tomato. For lettuce the BAF of PFHpA was 3.3 (+/-0.7) in the soil amended with municipal

wastewater treatment solids, and 2.7 (+/-0.5) for soil with industrial WWTsolids. For the tomato on industrial WWTsolids amended soil the BAF was 0.9 (+/-0.2). Although the bioaccumulation factors are small, it shows that PFHpA will enter the food chain through edible crops, as contact with PFHpA (from groundwater, surface water, soil, sludge) becomes inevitable.

An overview of PFCA concentrations in crops from PFAS contaminated sites is provided by Li *et al.* (2022b), showing the presence of (strongly) elevated levels of PFHpA in different crops and vegetables grown in the neighbourhood of contaminated sites. Levels up to 229 ng/g dw in carrots, 249 ng/g dw in corn and radish, and 530 ng/g dw in soybeans near a fluorochemical manufacturing park. This shows the ready uptake of PFHpA (from contaminated sources) in a large diversity of edible crops.

The presence of PFHpA in surface water, ground water, drinking water and the ready uptake in crops will inevitably lead to unavoidable exposure of both humans as well as animals. This gives rise to equivalent levels of concern as CMR substance for both humans as well as the environment due to very long-lasting (very persistent) and inevitable exposure to PFHpA. Due to the persistence the exposures are likely to increase over time if sources of PFHpA continue to be emitted to the environment, which will make (toxicological) effects more likely to occur, even if they are not observed at present.

Biomonitoring data to support the LRTP.

The presence of PFHpA in biota in remote areas delivers a strong argument for its long-range transport potential (LRTP) in combination with the fate modelling (section 3.3), high potential for exposure (conclusion of the section on presence of PFHpA in crops), mobility, and widespread presence in various environmental compartments of PFHpA. The LRTP of (volatile) PFHpA precursors can cause atmospheric deposition of PFHpA in remote areas and as such can contribute to the LRTP of PFHpA. The fact that PFHpA is detected in remote areas is supported by several studies that have detected PFHpA in various (predating) animals in the Arctic as well as in the Antarctic. Routti *et al.* (2017) for example have measured PFHpA (and other PFASs) in artic foxes and polar bears on Svalbard, Norway during 1997-2014. In 99% of the 70 samples in polar bears PFHpA was detected with a mean maximum concentrations of 0.48 and 2.51 ng/g ww blood plasma. The frequency of detection was lower in arctic foxes with 36% (of 70 samples) with concentrations in the liver reaching mean and maximum concentrations of 0.32 and 0.86 ng/g ww PFHpA. This difference in frequency of detection is likely due to differences in diet with polar bears eating more fish or fish eating predators. Concentrations or detection frequency of PFHpA did not change over time (1997-2014).

Schiavone *et al.* (2009) have detected PFHpA in a 2003/2004 monitoring campaign in penguin eggs and in Antarctic fur seals in King George Island and the Livingston Island in the Antarctic Peninsula. The detection frequency in fur seal pup livers was 100% (of 17 seal pups) with a mean PFHpA concentration of 1.0 ng/g ww liver tissue. In Adélie penguin eggs the detection frequency was 54% (n=13), with a mean PFHpA concentration of 2.5 ng/g ww egg. PFHpA was the most dominant PFAS in Adélie penguin eggs together with PFUnDA (2.3 ng/g ww egg). High concentrations of longer-chain PFCAs in eggs suggest oviparous transfer of these compounds. According to Schiavone *et al.* (2009), Antarctic fur seals and Adélie penguins are non-migratory and non-nomadic species breeding in the Antarctic region. As a consequence, the findings of PFHpA in the livers and in the eggs of these species suggest long-range transport of PFHpA from sources outside of Antarctica.

These examples show that PFHpA is present in the food chain in remote areas like the Arctic and Antarctic, supporting the expected Long-Range Transport behaviour predicted by fate modelling based on physico-chemical parameters (section 3.3).

3.2.5. Decontamination and removal from the environment and drinking water

For the proposal for restriction of PFAS in Fire Fighting Foams (FFF) (ECHA, 2022) a summary is given of available clean-up and decontamination techniques for PFAS in general, and the difficulties and costs related to removal of PFAS from the environment and/or (drinking) waters. Most, if not all, of the techniques and related difficulties apply directly to removal, of PFHpA. The conclusions in the FFF-restriction proposal that clean-up is either hardly possible or comes with excessive cost is therefore valid for PFHpA as well. The most relevant (for PFHpA) information is therefore given here.

Clean-up of sites facing a PFAS contamination and remediation of historically contaminated sites can in certain cases potentially mitigate the impact of these pollutions. 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 return on investment in euros spent per mass unit of PFASs removed is largest in the source area. The absolute PFAS mass removed is greater in the source area when comparing to groundwater extraction and subsequent treatments. 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. As PFHpA is a possible stable transformation product of a large number of PFAS-precursors where the non-fluorinated part of the PFAS is transformed. This would mean that not only PFHpA but also all possible precursors have to be removed in the source area, in order to prevent formation of PFHpA in e.g. groundwater. 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. 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 already a concern at very low concentrations.

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 a 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 PFASs).

Hydraulic site control

To eliminate off-site migration of PFAS-contaminated groundwater, impacted groundwater is extracted 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.

"End-of-pipe" treatment

In the event that PFAS contaminated groundwater or surface water is extracted for human use or consumption or for agricultural use, it would need to be treated after extraction. Commercially available treatment technologies to remove PFAS molecules 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 contaminated water sources.

Shorter-chain PFAS like PFHpA can be more resilient to some of these treatment technologies, so that more rigorous (and expensive) 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.

Drinking water treatment

A recent review paper from (Li *et al.*, 2020) on occurrence, impacts and treatment of short-chain PFASs concludes that:

1) short-chain PFASs 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 homologues, and are challenged with poor material regeneration efficiency and disposal of process waste residues;

3) thermolysis and sonolysis can achieve complete mineralisation, 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 short-chain PFASs in drinking water.

Conventional water treatment

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

PFECAs have been detected downstream of a PFASs manufacturer 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.

Water treatment with powdered activated carbon (PAC) filters

- Long chain-PFCAs and -PFSAs can be removed with powdered activated carbon (PAC) filters, with higher removal efficiency for PFSAs compared to PFCAs analogues (Eschauzier *et al.*, 2012, Rahman *et al.*, 2014; Sun *et al.*, 2016).

- Sun et al. 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 ($C_4HF_7O_3$), PFMOBA ($C_5HF_9O_3$), PFPrOPrA (GenX $C_6HF_{11}O_3$) and PFO2HxA ($C_4HF_7O_4$) (Sun et al. 2016). PFHpA would be most comparable to PFPrOPrA (GenX) with respect to chain-length and physico-chemical properties.

- Short chain-PFAAs (and C_7-PFCA, i.e., PFHpA) cannot be effectively removed by granular activated carbon (GAC) or powdered activated carbon (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, it can be assumed that the more hydrophilic SC-PFAAs, 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 like PFHpA) compared to sulfonic acids groups (PFSAs) or phosphonic groups (PFPAs) due to their lower sorption potential and higher water solubility.

Water treatment with ion exchange resins

LC-PFAAs can be removed with ion exchange resins, higher removal efficiency is again achieved for PFSAs compared to PFCAs analogues (Rahman *et al.*, 2014; Appleman *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 C_4-PFSA (81%) and only partially (46%) remove C_7-PFCA (PFHpA) (Appleman *et al.*, 2014)

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 ($\geq C_4$ PFSAs and $\geq C_4$ PFCAs from water) in bench (Appleman *et al.*, 2013; Zhen *et al.*, 2017) and full-scale studies (Thompson *et al.*, 2011, Appleman *et al.*, 2014). 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 such as PFHpA - resulting from the degradation of other PFASs in the environment - are such that water treatment becomes very difficult, 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 3.2.4 for monitoring data) demonstrates the current lack of purification of drinking water. EUREAU (2021) has also assessed the purification methods for water suppliers and concludes that PFASs should be managed at their source due to the large challenges in the water supply.

Wastewater treatment

Several studies showed that conventional wastewater treatments have a limited efficiency in removing short-chain and long-chain PFCAs and PFSAs from aqueous waste streams. SC- and LC-PFCAs and PFSAs accumulate in sludge and are released to receiving waters via WWTP effluents (Bossi *et al.*, 2008; Arvaniti and Stasinakis, 2015; Eriksson *et al.*, 2017).

SC- and LC- PFCAs, including PFHpA, are generally found in higher concentrations in the effluent water than the influent water (Bossi *et al.*, 2008; Sinclair and Kannan, 2006; Eriksson *et al.*, 2017), which indicates that they are hard to remove from water during wastewater

treatment process and that precursors are transformed into extremely stable PFCAs during the wastewater treatment.

Several PFCAs precursors (FTSAs, FTCA/FTUCA, diPAP) were found in lower concentration in the effluent water than in the influent water of three WWTPs in Sweden (Eriksson *et al.*, 2017), 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 PFCAs precursors can potentially be degraded to PFCAs during wastewater treatment process.

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

The adsorption of LC-PFAAs in sludge has been observed to increase with increasing chain length (increase in distribution coefficient between influent water and sludge; Erickson *et al.*, 2017), which can be explained due to the increase of hydrophobicity of the molecules (Zhang *et al.*, 2013a). However, for SC-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).

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

3.2.6 Summary and discussion of environmental distribution

PFHpA predominantly resides in the aquatic compartment due to its low adsorption potential, high water solubility and low to moderate tendency to volatise from water to air. These properties make PFHpA (very) mobile in the aquatic environment and very difficult to remove from (contaminated) aqueous sites e.g., for drinking water remediation or groundwater clean-up. Once PFHpA has entered the aquatic environment, e.g., surface waters, there are limited fate processes that would prevent it from being distributed to groundwater and to the marine environment. Monitoring data from all over the world show that PFHpA is very frequently detected in ground water, surface water, drinking water (both tap and bottled) in or well above the ng/L ranges.

3.3 Data indicating potential for long-range transport

There are no natural sources of PFHpA. PFHpA is formed in the environment as a transformation product of several PFAS precursors, where the perfluorinated part of the PFAS precursors is preserved due to its inherent resistence to (biological) degradation. The number of possible precursors is unknown and the PFHpA yield varies between them. Environmental monitoring data shows that PFHpA is already ubiquitously present in the environment, even in remote areas. Kirchgeorg *et al.* (2013) detected PFHpA in remote area of the European Alps in a 10 m long firn core from Colle Gnifetti in the Monte Rosa Massif (4455 m above sea level) away from human activity. Muir *et al.* (2019) summarised in their review the detection of PFASs in Arctic environmental media up to 2018. Their overview shows that PFHpA has been detected in the atmosphere (air, snow), terrestrial compartment (soil, biota), freshwater compartment (water, sediment) and marine compartment (water, sediment and biota). For examples of biomonitoring data from remote areas (Arctic, Antarctic) see section 3.2.4.

In the European Arctic (Svalbard, Norway), PFHpA has been detected in surface snow and surface water samples (i.e., glacier water, river water, sea water and lake water) collected

from the glacier to the downstream and coastal areas (Kwok *et al.*, 2013). PFHpA has also been detected in the Antarctic. Xie *et al.* (2020) reported that PFOA (358 ± 71 pg/L), PFHxA (358 ± 71 pg/L), PFHpA (358 ± 71 pg/L) and PFPeA (175 ± 105 pg/L) were the dominant PFASs detected in surface snow sampled in 2016 at Dome C on the Antarctic Plateau. These monitoring data far away from any point sources provide a clear indication that PFHpA is subject to long-range transport over vast distances. The transport can take place via the atmosphere or with ocean currents and might not only concern PFHpA, but also precursors such as the volatile substance 6:2 FTOH. Muir *et al.* (2019) showed that 6:2 FTOH is found in atmospheric air, in the Arctic, but unlike the terminal transformation products PFCAs it was not detected in any of the other investigated compartments (atmospheric snow, terrestrial, freshwater or marine compartments). This points towards the likely degradation of 6:2 FTOH to PFCAs, such as PFHpA and PFHxA.

Joerss *et al.* (2020) investigated the spatial distribution of 29 PFASs, including PFHpA, in seawater along a sampling transect from Europe to the Arctic and two transects within Fram Strait, located between Greenland and Svalbard, in the summer of 2018. PFHpA was detected at all sampling locations. The authors referred to Wang et al. 2014 who reported that >74% of PFHpA was released to the environment as degradation products of precursors, whereas >75% of PFNA was emitted from direct sources. The PFHpA/PFNA ratio increased from east of 0°EW (0.95 ± 0.12) to west of 0°EW (1.40 ± 0.22) which was considered an indication that the contribution of atmospheric PFAS sources is higher to Arctic outflow than to Arctic inflow. The PFHpA/PFNA ratio in the North Sea was considerably higher (5.4 ± 1.1). Consequently, the authors expect that the PFHpA/PFNA ratio in both Arctic in- and outflow can be expected to increase within the next years, with a rate that depends on the relative contributions from slow oceanic transport and fast atmospheric transport.

The atmospheric long-range transport of PFHpA to remote regions is slightly more complicated as not necessarily only the properties of the PFHpA determine its' LRTP. Neutral volatile PFASs such as fluorotelomer alcohols (FTOHs) which can be transformed to PFHpA are transported mainly in the gaseous phase and may degrade to less volatile perfluoroalkyl acids (PFAAs) including perfluoroalkyl carboxylic acids (PFCAs) such as PFHpA (Schenker *et al.*, 2008a, Young and Mabury, 2010). Another way of transport would be formation of PFHpA (as a transformation product) in the atmosphere where it can be bound onto particles or dissolved in cloud, rain, or fog droplets (Arp and Goss, 2009). Atmospheric transformation of PFCA precursors due to abiotic processes such as OH-radical can be much faster than biotic transformation. As the potential precursors of PFHpA are numerous and will have very different transformation rates in different media, it is impossible to model all of these potential routes of global transport.

Nevertheless, PFHpA's physical-chemical properties (Section 1.4), very high persistence (Section 3.1), and its estimated atmospheric half-life indicate that the substance itself can be transported to remote areas. Annex D, Section 1 (d) of the Stockholm Convention on Persistent Organic Pollutants (POPs) states the criterion for atmospheric half-life >2 days (48 hours), which is by far exceeded for PFHpA with an estimated atmospheric half-life of 20.57 days by AOPWin v1.92 of EpiSuite (see Section 3.1.1.3.1). This AOPWin estimate is considered a best-case estimate, as in analogy to PFOA, reference can be made to the shorter chained C_3-C_5-PFCAs for which experimentally derived atmospheric lifetimes are available being 130 days. The very long half-life of PFHpA, and PFCAs in general, is explained by the perfluorinated carbon backbone of PFHpA, which does not offer any suitable atomic site where the OH-radical, or ozone, could start oxidation/degradation. The only perceived site of oxidation is the carboxylic acid group, which is already completely oxidised, and therefore not very vulnerable to further oxidation by OH-radicals.

To substantiate the assumed long-range transport which is supported by the confirmed presence of PFHpA in remote areas such as the Arctic as well as the Antarctic (see section 3.2.5), the transport potential of PFHpA was modelled using the OECD tool for estimation of the long-range transport potential [OECD POV and LRTP Tool v2.2; OECD, 2009; Wegmann *et al.*, 2009]. The LRTP Tool is a spreadsheet form based on multimedia fate models. The model

requires molecular mass, air-water (K_{aw}) and octanol-water (K_{ow}) partition coefficients and (estimated) half-lives in air, water and soil as input parameters for the modelling. The tool then estimates a characteristic travel distance (CTD), indicating the distance from a point source at which the chemical's concentration has dropped to 38% of its initial concentration) and an estimated overall environmental persistence (Pov) in the environment (an overall half-life taking into account the estimated volumes of the emission in the different environmental compartments) as well as a so-called Transfer Efficiency. The latter is not discussed as it essentially leads to identical observations and conclusions as the CTD metric. Input parameters that have been used to model the long-range transport potential for PFHpA are summarised in the table below. As PFHpA will be 100% dissociated at relevant environmental pHs, the octanol water partition coefficient should reflect this and ideally the log D (pH dependent log K_{OW}) is used as input for the fate model. The USEPA KOWWIN model can be forced to estimate the log K_{OW} for the dissociated acid by estimating the log K_{OW} for the sodium salt, which triggers a correction factor for sodium salts of carboxylic acid to be applied to the estimation.

Table 7. Input parameters used to model the long range transport potential for PFHpA

Parameter	Value used in the modelling	Comments
log D_{OW} at pH 7	0.33	Estimated using KOWWIN v1.68, for the sodium salt of PFHpA. The neutral PFHpA (undissociated) would yield a log K_{OW} estimate of 4.15 (KOWWIN) or 4.7 using the COSMOtherm QSAR model, (Wang *et al.*, 2011). The estimated ClogP value (Bio-Loom, BioByte corp.) is 3.38 for the neutral acid. Chemaxon log D estimator shows an estimated log D of 0.88 at pH>1.5.
log K_{AW}	-2.2	Estimated using COSMOtherm (Wang et al. 2011)
Atmospheric degradation half-life	130 days (3120 hours)	Read-across to experimental data for C_2-C_5-PFCAs (as was done for PFOA) (Hurley *et al.*, 2004)
Water half-life	60 days (1440 hours) up to 3 years (26280 hours)	the vP criterion for water, and a less optimistic value of 1 and 3 years.
Soil half-life	180 days (4320 hours) up to 3 years (26280 hours)	the vP criterion for soil, and a less optimistic value of 1 and 3 years.
Molecular weight	364.06 g/mol	Neutral acid form of PFHpA

KOWWIN gives an estimated log K_{OW} of 0.33 for the dissociated PFHpA. The ChemAxon log D model estimates the log D to be in the same order of magnitude at 0.88 for pHs>2. The air-water partition coefficient (Kaw) estimates are subject to the same dependence on partitioning behaviour, and depending on the use of log Kow for the neutral or ionic form (simulated by calculating the sodium salt species in KOWWiN for example) higher or lower values of log Kaw will result. The COSMOTherm estimates as published by Wang *et al.* (2011) have been considered the most realistic in the HFPO-DA SVHC support document (ECHA, 2019b) and therefore the COSMOtherm estimate for log Kaw (representing the ionic form of PFHpA in the water phase) is used here as well. The value is in line (correct order of magnitude) with the estimated log D values at neutral pH (see table 7). Using the KOWWIN estimate for log Kow of the sodium salt of PFHpA and the COSMOtherm estimate of log Kaw, with the estimated half-lives as detailed in the table below, results in an estimated of CTD of 26165 km and a Pov of 128 days for PFHpA using as a best case estimate the environmental compartment half-lives reflecting the vP criteria of 60 days (water) and 180 days (soil) in the calculations. The CTD

increases to 41343 km and Pov is raised to 356 days when using water and soil compartment half-lives of one year and increases up to a CTD of 51480 km and a Pov of 533 days using water and soil half-lives of three years.

A characteristic travel distance (CTD) of 26165 km estimated with water and soil half-lives at the vP criterion already indicates that PFHpA can reach any parts of the globe before any significant amount of substance degradation has occurred. The estimated overall persistence of 128 days is reflecting the distribution over the most relevant compartments water (65%) and air (35%). Soil is not the most relevant compartment, because of the high water solubility and limited absorbtion of PFCA substances to soil matrices in general. Only if emissions are to soil only, 3.6% of the mass of emitted PFHpA ends up in the soil. Current fate modelling suggests the water compartment to be the main residence compartment. This confirms the mobile character of the substance. It should be noted that this modelling reflects the remote steady-state, e.g., long after emissions have stopped. In situations where emission is still ongoing, the steady-state concentrations of PFHpA in soil will likely be higher.

The detailed information on the calculations from the OECD LRTP-tool estimations for PFHpA, given in Annex II confirm this. If emissions are only to the water compartment, 74% of the total emission volume is estimated to end up in the water compartment at equilibrium state, while only 0.01% will end up in the soil. When emissions only occur to the soil compartment only 3.6% remains in the soil compartment. With emissions only to the air compartment, 60% remains in the atmosphere, while 40% goes to water. Thus, it can be concluded that regardless of the emission compartment PFHpA will be readily transported over long ranges, even if emissions are to soil or water only.

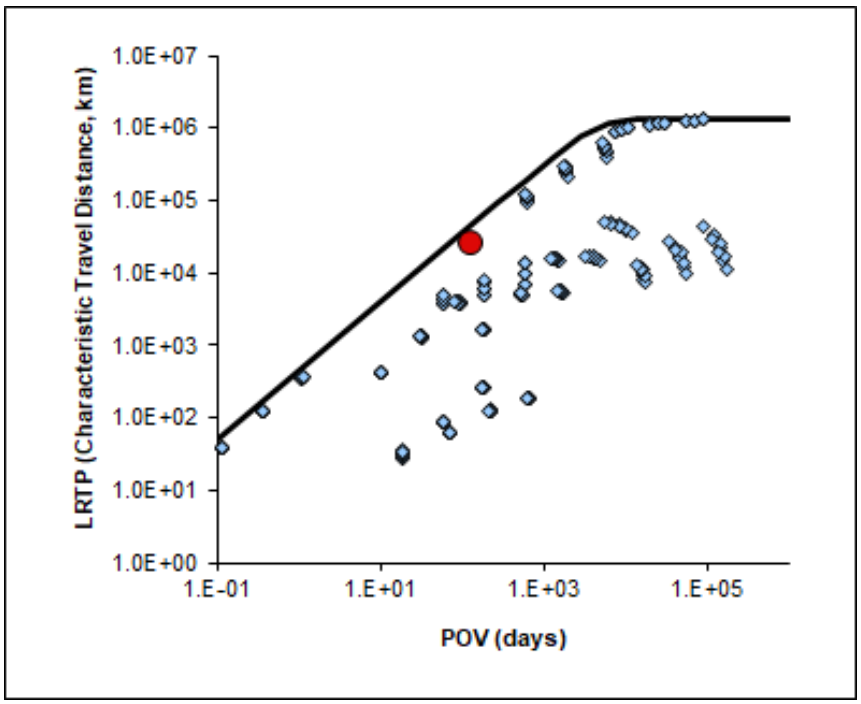

Figure 1. Characteristic Travel Distance (CTD) and overall persistence (Pov) of PFHpA (red dot) using the best case estimated half-lives (table 7). See text for detailed description.

Figure 1 gives the graphical representation of the calculated CTD and Pov for PFHpA (red dot) using the best case estimated environmental half-lives (see table 7) of 130 days (atmosphere), 60 days (water) and 100 days (soil) as input. The calculated Pov and CTD of PFhPA is given in comparison to a set of generic POP substances, which act as reference substances (blue squares). The estimated overall persistence in the environment is in the range of the Pov of a-hexachlorocyclohexane when using the best case water and soil half-lives of 60 and 180 days,

the half-life criterion for very Persistent (vP) substances. The actual half-lives for PFHpA in the environment are expected to well exceed this criterion, leading to higher estimated Pov, and an increase in the CTD as well. The CTD is very close to the maximum CTD and the value (lowest estimate 26165 km) indicates that PFHpA can reach any area on the Earth before any significant degradation has occurred. The presence of PFHpA in the polar regions, as confirmed by multiple monitoring studies (section 3.2.4), is in line with this estimated LRTP. Based on these modelling results it is likely that PFHpA has a capacity for long-range transport in the environment is similar to or exceeding known POP-substances like PCBs, HCH and HCB.

These estimations for PFHpA should be considered with some reservations: the QSAR estimations of the physico-chemical properties for PFHpA in the OECD LRTP tool (K_{AW} and K_{OW}) are known to be difficult to predict using QSAR models. This makes these estimations less reliable. However, measuring a representative value (for fate modelling) will be even more difficult due to the surface activity of perfluoroalkyl acids. Despite these uncertainty, the general trend of the modelling results is clear and not very dependent on the choice of the (boundaries) of the relevant parameters like persistence in the different compartments. Even with lower boundary estimates (vP-criteria) the properties of PFHpA already give rise to clear long range transport potential and perfluoro alkyl acids in general and PFHpA specific is well exceeding the vP-criteria. The presented results therefore have to be considered as best case estimates, and any uncertainty in the physico-chemical and environmental half-lives estimates will only lead to higher Pov en CTD values. The modelling results are nicely in line with the monitoring data that indicate that PFHpA is found in very remote areas from the emission sources (for examples see section 3.2.4 Field and monitoring data). When persistence is increased to more realistic values of several years (in the water and soil compartment) this behaviour becomes only more notable.

Overall, it can be concluded that PFHpA has a clear potential for long-range transport, in line with the confirmed presence of PFHpA in remote areas like the polar regions, in biota, in surface fresh- and marine water, in air as well as in snow.

3.4 Bioaccumulation

3.4.1 General remarks

According to Sections 3.2.2 (b) and (c) of Annex XIII of REACH, not only the numerical bioaccumulation (B) criterion based on bioconcentration factors can be used to assess the bioaccumulation potential of a substance but also other information can be used in a weight of evidence approach. This additional information which includes elevated levels in biota, information on the ability of the substance to biomagnify in the food chain, data from analysis of human body fluids or tissues and assessment of toxicokinetic behaviour of the substance should also be considered for the assessment using a weight-of-evidence approach.

Information on the bioaccumulation potential of PFHpA in laboratory mammals and humans as well as data from analysis of human body fluids is described in section 4.1.

3.4.2 Bioaccumulation in aquatic organisms (pelagic & sediment organisms)

There is one study available that studied the bioconcentration of PFHpA in fish. In this study, rainbow trout (*Oncorhynchus mykiss*) were exposed in a flow-through system for 12 days followed by a depuration time of 33 days in fresh water to determine tissue distribution and bioconcentration (Martin *et al*., 2003; reliability 2). For determination of bioconcentration, juvenile fish (5-10 g) were exposed simultaneously to PFCAs of varying chain length. No adverse effects were observable based on fish mortality, growth, and liver somatic index. The exposure concentration of each PFCA was analytically checked. PFCA concentrations were stable throughout the uptake phase except for an initial decrease that was observed between 0.25 h and 24 h. This initial decrease was considered to be caused by the rapid uptake of PFCAs. For PFHpA the measured concentration in water was 1.6 µg/L with a relative standard deviation of 12%. At 7 occasions during the uptake period and 9 occasions during the depuration phase, three fish from the exposure tank and one fish from the control were removed to analyse the blood, liver and carcass of the fish in order to determine the kinetics of uptake and depuration. The concentration of PFHpA in fish was below the detection limit. This indicated that the bioconcentration factors (BCFs) of PFHpA were lower than that for the analogue PFOA, the latter being 4.0 L/kg for carcass, 27 L/kg for blood and 8.0 L/kg for liver.

3.4.3 Field data

Bioaccumulation factor

There are several field studies that investigated bioaccumulation of PFHpA in the field. These include mostly the lower trophic levels of aquatic foodwebs including phyto- and zooplankton, invertebrates and fish.

Loi *et al.* (2011; Reliability 2) included phytoplankton (n=1), zooplankton (n=2), gastropod (n=3), worm (n=2-3), shrimp (n=2-3), fish (n=2-6), and water bird (n=3). However, those were sampled 5 to 7 years prior to the sampling of the other biotic and abiotic samples.

Xu *et al.* (2014; Reliability 2). investigated a pelagic food web in Taihu Lake (China), including phytoplankton (n=17), zooplankton (n=17), (snail) (n=9), bivalve (n=8), shrimp (n=9), fish (n=4-22), and water bird (n=2). While PFOA was measured in all species except carp, PFHpA was detected in phytoplankton, zooplankton, and several fish species, but not in the water bird.

Fang *et al.* (2014) investigated a food web including phyto- and zooplankton, shrimp, mussels and fish, but no higher trophic levels.

The BAFs that can be derived from these food web studies are all still below 500 L/kg.

Trophic magnification factor
The trophic magnification factor (TMF) is a measure to evaluate biomagnification occurring in food webs, with a TMF greater than one indicating accumulation within the food chain.

Several literature studies investigate trophic magnification in aquatic foodwebs from plankton to fish for PFHpA. The reported TMFs do not point towards any significant biomagnification within these food webs (Kelly *et al.* (2009); Liu *et al* (2018); Penland *et al.* (2020) reviewed by Miranda *et al*. (2022). These studies as summarised and averaged by Miranda et al. do not allow to conclude on magnification in higher trophic levels above fish. Either the higher trophic levels were not present (Liu *et al.*, 2018 and Penland *et al.*, 2020) or PFHpA was not present in detectable levels, in the whole foodchain (Kelly *et al.*, 2009).

In the Kelly *et al.* (2009) study different food webs are compared to show that the TMF for PFOA is below one in the case of piscivorous food webs if air breathing organisms are excluded but becomes larger than one if air breathing organisms are taken into account.

3.4.4 Summary and discussion of bioaccumulation

Based on a direct comparison with the bioaccumulation criteria for aquatic organisms, PFHpA is not bioaccumulative in water-breathing organisms, because the BCF is far below the B criterion of 2000. Also, other endpoints for aquatic organisms do not show a concern for bioaccumulation for those organisms. TMF values from aquatic food web studies do not point at any significant biomagnification in water-breathing organisms.

Annex XIII, point 3.2.2.(b) of the REACH Regulation requires that data from the toxicokinetic behaviour of the substance be considered. Information on air-breathing mammalian top-predators in aquatic food web studies is extremely limited. Based on information available on toxicokinetic studies (section 4.1.1 and 4.1.2) bioaccumulation is likely to occur in some air-breathing mammals, e.g. pigs, and humans.

The data from pigs and humans is given a high weight and indicates that PFHpA bioaccumulates (section 4.1.3). Therefore, it is considered that the vB criterion of REACH Annex XIII is fulfilled.

4. Human health hazard assessment

Information on hazard to human health relevant for the identification of the substance as SVHC in accordance with Article 57 (c) of the REACH Regulation is provided in Section 2 of this report.

The classification as Repr. 1B (H360D: 'May damage the unborn child') and STOT RE 1 (H372 (liver)) are both of relevance for the identification of the substance as SVHC in accordance with article 57(d) of the REACH regulation and the assessment of PFHpA as a substance of very high concern according to Article 57 (f).

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

4.1.1 Non-human information

Half-lives of PFHpA in animals have been determined in several studies which are discussed below. Repr.1B and STOT RE1 (liver) classifications are based on a study in mice.

Mice

In one study with mice, C_6- to C_{14}-PFCAs were administered intravenously (IV) or by gavage (Fujii *et al.*, 2015; reliability 2). Whole blood samples were collected from the tail veins at 0, 1, 3, 6, 12 and 24 hours after IV or gavage administration. An additional collection was made at 0.5 hours for IV administration. After 24 hours, urine and feces were collected in metabolic cages. Mice were euthanized and a portion of the whole blood was collected and centrifuged to isolate the serum. Liver, kidney and brain tissues were collected and weighed. Adipose tissue was collected from the abdominal mesenteric fat and was assumed to be 2.3% of the total body weight of mice. PFCAs were extracted from homogenized samples with a mixture of Milli-Q water/methanol (1:1). Analysis was done by GC-MS.

The ratio of PFCAs between whole blood and serum at 24 hours was used to convert PFCA concentrations in whole blood samples into serum PFCA concentrations. Serum concentration data were analyzed using a two-compartmental model. Mouse urinary and fecal clearances were determined by dividing the total amount excreted in the urine, respectively, feces, during a 24-h period with the area under the curve (AUC) of the serum concentration of each PFCA between 0 to 24 hours.

Following IV administration, for C_7- to C_{14}-PFCAs, but not PFHxA, the serum levels were above the method detection limits. PFHpA disappeared from the serum in a time-dependent manner, while C_8- to C_{14}-PFCAs were slowly eliminated from the serum. Total recoveries for all measured PFCAs were >76% for males and >58% for females. For PFHxA and PFHpA, almost all of the administered doses were recovered in the urine after 24 hours (101 and 99% for males, 66 and 79% for females, respectively), with only a small portion excreted in the feces (5 and 3% for males, 16 and 13% for females, respectively). For PFOA, only a small portion was excreted in the urine (6% for males, 7% for females), and even less was excreted in the feces (<1% for both sexes). For PFOA, the majority was retained in the serum and liver (80% for males, 62% for females). For C_9- to C_{14}-PFCAs the distribution pattern was similar to that of PFOA only excretion in the urine and feces was in both sexes lower. The urinary and faecal clearance did not differ between sexes for the different PFCAs. Average urinary clearance was 276, 11.4, 3.3, 0.9, 0.4, 0.4, 0.4 and 0.4 mL/day/kg for PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA and PFTeDA, respectively. Average faecal clearance was 25.5, 1.5, 1.2, 1.6, 2.7, 4.2, 6.5, and 9.8 mL/day/kg, respectively.

Following gavage administration, similar findings were reported as for IV administration. Again only PFHxA was not detected in the serum. While total recoveries were lower for gavage in comparison to IV administration, the observed pattern was similar: PFHxA and PFHpA were mostly recovered in the urine, while PFOA and higher PFCAs were recovered in the liver and serum. Only small volumes of PFCAs were excreted in feces. The urinary and faecal clearance did not differ between sexes for the different PFCAs. Average urinary clearance was 208, 7.9, 0.9, 0.3, 0.2, 0.2, 0.2, and 0.3 mL/day/kg for PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA and PFTeDA, respectively. Average faecal clearance was 33.6, 3.2, 2.3, 2.7, 4.2, 7.1, 25.4, and 77.3 mL/day/kg, respectively.

It can be concluded that the total clearance (urinary and faecal) of PFHpA in mice is much faster than for PFOA. Urinary clearance decreases with chain length, while faecal clearance appears to be the lowest for C_8- to C_{10}-PFCAs. No clearance could be determined for PFHxA as it was rapidly excreted. These data show that PFHpA clearance from mice is between PFHxA and PFOA which are, respectively, one perfluorinated carbon atom shorter and longer.

Rats

In one study with rats, PFASs were administered intravenously and urine was collected continuously (Ohmori *et al.*, 2003; reliability 2). PFASs were extracted from urine and plasma with a mixture of ethyl acetate and hexane with an added buffer tetrabutylammonium and sodium carbonate (pH=10). The sample was evaporated to dryness and PFASs were derivatised

with 3-bromoacetyl-7-methoxycoumarin in acetone. Analysis was done by HPLC with fluorescence detection.

A two-compartment model was used to fit the data. The half-lives however are reported to have been fitted on the plasma concentrations in the course of time. The half-lives for PFHpA were short and amounted 0.05 days for female and 0.10 days for male rats. The half-life for PFOA in female rats of 0.08 days was comparable to PFHpA, but for male rats it was considerably higher (5.63 days). This difference between female and male rats was also observed for PFNA (2.44 and 29.57 days, respectively) and to a lesser extent for PFDA (39.92 and 58.57 days, respectively). It can be concluded that the half-lives for PFHpA, and PFOA in female rats, are very short in comparison with the other half-lives. These results are in accordance with an earlier study from the same group in which followed the elimination of the PFASs in urine and feces over 120 hours after an intraperitoneal dose (Kudo *et al.*, 2001).

A study with 6 hours exposure to 6:2 FTOH in male and female rats examined the kinetics over 1 day including metabolites, of which PFHpA is one (Russell *et al.*, 2015, reliability 2). A model was constructed in which PFHpA is formed through 6:2 FTCA. The modelled half-life of 6:2 FTOH was very low. PFHpA was formed in low yield (0.3% and 0.7% at 0.5 ppm for females and males respectively and 0.1% for both sexes at 5 ppm). The half-lives were 2.1 and 1.2 hours for females at 0.5 and 5 ppm and 15.4 and 23.3 hours for males at 0.5 and 5 ppm, respectively. With the same yield assumed as in the 1-day study, a half-life of 16.9 hour for PFHpA in male rats was estimated from the final serum concentration in a 31-d inhalation study with 6 hours exposure per day for 5 days per week (23 x 6 hours exposure).

The estimated value for male rats from the second study is remarkably higher than that from the first study. However, in both studies all estimated half-lives for PFHpA in rats are less than 1 day.

Pigs

Numata *et al.* (2014; reliability 2) performed a study in which pigs received food contaminated with a mixture of PFASs for three weeks. The pigs, i.e. 8 gilts, 8 barrows and 8 young boars and 2 of each in a control group, were on average 83 kg at the start of the study and increased in weight to 103 kg at the end of the study. Blood samples were collected 4 days prior to exposure started, on days 4, 8, 11, 15, and 18 during feeding, and on day 22, one day after exposure stopped and before slaughter. The following organs were analysed: kidney, liver, fat, dorsal muscle tissues and ventral muscle tissues. Urine was collected during feeding, weighing, or blood sampling of the pigs. Samples were frozen at -20 °C before analysis. Before analysis formic acid was added to plasma and urine. Feed was extracted with methanol. Tissue samples were hydrolysed with pepsine. Samples were purified with solid-phase extraction before analysis. Analysis was performed with HPLC-MS/MS.

A two-compartment first-order toxicokinetic model was applied to simulate the observed data. The modelled parameters showed an almost instantaneous internal distribution between plasma and the other body parts. Therefore, the kinetics between plasma and the other organs were replaced by equilibrium partitioning, which leaves the modelling to be equivalent to a one-compartment model. The authors further assume that absorption efficiency of PFASs is high, comparable between species (sheep and pigs) and not dependent on the food administered. These assumptions are considered acceptable. The biomagnification factor is thus directly linked to the daily feeding ratio and is thus dependent on the food provided and not a fixed value.

The estimated half-lives and biomagnification factors derived in this study (see below) are dependent on the urinary rate constant kU, and on the mass balance and distribution of the PFASs over the body of the pigs, which are associated with some uncertainties.

Firstly, the urinary rate constant kU is obtained by fitting of the data that do not show a

significant levelling for all PFASs except PFHxA. The accuracy of kU is therefore fully dependent on the mass balance of the PFASs, which is constructed of the sum of the amounts estimated in individual body parts and the estimated amount excreted with urine in time. The amount in each compartment was calculated from the concentrations determined after slaughter and the estimated weights of the individual body parts. Only for plasma concentrations were available for a times series.

Secondly, the considered body compartments are not complete (e.g., head, skin and bones were not taken into consideration). An indication for an incomplete mass balance follows from the volumes of distribution, which can be calculated from the presented data on plasma volume and distribution over the compartments. This volume of distribution is 80-90 mL/kg, except for PFOS for which it is around 180 mL/kg. These values for the PFASs except PFOS are rather low in comparison with the values obtained in other studies. This may have a direct effect on the estimated half-lives, which would be underestimated by a too low volume of distribution.

Finally, the amount excreted with urine was not experimentally determined but calculated from measured concentrations in urine and an assumed daily volume of urine based on literature data on pigs. Also, the non-absorbed part, excreted by faeces, was estimated from literature data on sheep. The applied model assumes that all excretion occurs by urinary excretion. This was justified by the fact that the mass balance was almost complete with urinary excretion as the only important excretion route. PFHpA showed the lowest mass balance of the seven compounds considered, with an overall mass balance of slightly less than 80%.

Despite the above discussed uncertainties the derived half-lives and BMF values are still considered reliable and rather underestimate and not overestimate the bioaccumulation potential of PFHpA in pigs.

The elimination half-lives for PFHpA ranged for individual pigs from around 10 to around 500 days (see figure below). For some pigs there is a start of levelling off of the plasma concentrations and based on those individuals the lower end half-lives still seem realistic and not an artefact. For other pigs the increase in plasma concentration of PFHpA is almost linear and no levelling off is observed during the 21 days of exposure, indicating that the half-life is considerably longer than the time span of the experiment. The geometric mean elimination half-life of PFHpA amounts to 74 days. This elimination half-life of PFHpA of 74 days falls well between the geometric mean half-lives derived for PFOA and PFHxA that are, respectively, 236 and 4.1 days, which are the closest structural analogues differing only by one perfluorinated carbon in chain length. The corresponding biomagnification factors for whole pig for PFOA, PFHpA, and PFHxA are, respectively, 7.9, 2.7, and 0.13. Biomagnification factors based on liver were higher than those for whole pig, those based on meat lower than for whole pig. For PFHpA all these BMF were higher than 1, being 7.0 and 1.8. This clearly indicates bioaccumulation potential for PFHpA in pigs.

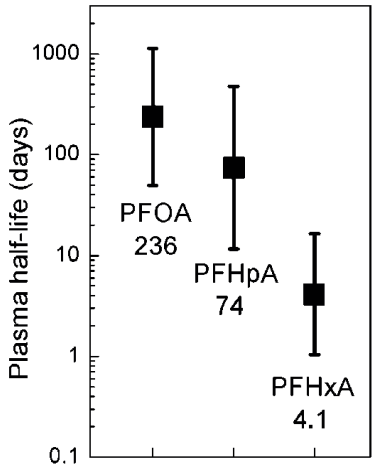

Figure 2. Elimination half-life of PFHxA, PFHpA and PFOA in pigs* (modified from Numata *et al.*, 2014)

*The squares denote the geometric average over up to 24 pigs, and the bars show 95% variability (Student's t statistics). These values reflect both the blood plasma and the edible tissue elimination half-lives, because plasma and edible tissue were found to be in fast equilibrium with each other.

4.1.2 Human information (including bioaccumulation in humans)

Half-lives of PFHpA in humans have been determined in several studies which are discussed below.

First study: Ski waxers (Freberg *et al.*, 2010)

Freberg *et al.* (2010; reliability 2) sampled blood from 13 professional Norwegian ski waxers in March 2008, November 2008 and March 2009. The age of the participants was on average 40.6 years with a range from 28.3 to 52.9 years, and the participants were active as ski waxer for 7 years on average with a range of 2 to 13 years. Blood was collected in 10 mL tubes, stored at room temperature for 45 minutes, then centrifuged at 2300 rpm for 20 minutes. The serum was stored frozen at -20 °C. The serum was extracted by adding methanol (including the internal standards) to precipitate proteins and centrifuged after which formic acid was added for analysis. Analysis was done by HPLC coupled to a triple quadrupole MS. Calibration solutions were prepared of in serum of newborn calves. The LOQ was set at the lowest calibration point of 0.050 ng/mL.

A number of PFASs were analysed, including C_4-C_{14} PFCAs. The percent reduction in serum concentration from the end of the season (March 2008) to the beginning of the new season (November 2008) was expressed graphically for those PFASs for which the concentrations could be measured. These reductions are presented for C_6-C_{14} PFCAs in Table 8. In the 8-month period between seasons (~245 days) no occupational exposure to ski waxes occurred. There is no indication that significant exposure to other PFCAs sources occurred in this period. Using the reductions in serum concentrations, elimination half-lives were calculated assuming a first-order decline. For PFHpA to PFTrDA a significant positive correlation between the serum concentration and the number of years working as a ski waxing technician was observed, implying that these compounds build up over the years.

Table 8. Reduction of C_{4-14}-PFCA concentrations in serum of ski waxers during the period March to November (read from presented figure 1 in Freberg *et al.* 2010).

PFAS	Reported reduction [%]	Standard deviation	Deduced half-life [d]*
PFHxA	79	4	110
PFHpA	53	7	220
PFOA	6	2	2700
PFNA	3	2	5600

PFDA	11	2	1500
PFUnDA	18	5	860
PFDoDA	34	3	410
PFTrDA	34	4	410
PFTeDA	65	3	160

* First-order half-lives are deduced with the assumption of no significant exposure to PFCAs in between seasons.

Second study: Ski waxers (Nilsson *et al.*, 2010a; 2010b; 2013; Russell *et al.*, 2015).

Nilsson *et al*. (2010a; reliability 2) performed a similar study on ski waxers with eight ski waxers working for the national cross-country ski teams of Sweden and the USA. Blood was sampled before (in September 2007), during (from December 2007 to March 2008), and after (from April to August 2008) the exposed period (i.e., the World Cup competitions period). The age of the participants ranged from 27 to 51 years, and the participants were active as ski waxer from 3 to 15 years. Blood samples were stored in tubes containing EDTA and were frozen at -20 °C. A mixture of water and formic acid and the internal standards were added to the blood. After sonification and centrifugation, the samples were extracted by solid-phase extraction with weak anion exchange and extracted with 2% ammonium hydroxide in methanol. Analysis was done by UPLC with ES-MS/MS. A number of PFASs were analysed. In this summary only the data for PFCAs are discussed, i.e. C_4-C_{14}, C_{16} and C_{18} PFCAs.

A significant positive correlation between the age of the technicians and the concentrations in blood was only found PFNA. For PFHpA, PFOA, PFNA, PFDA and PFUnDA a significant positive correlation was found between the number of years in the profession and the concentration in blood (which was not the case for the shorter chained PFCAs: PFBA, PFPeA and PFHxA). The data show that C_7-C_{11} PFCAs were significantly correlated to each other, as were C_4-C_6 PFCAs.

This study indicates that PFCAs with longer chain lengths (PFHpA and higher) are not sufficiently eliminated between ski seasons (during which no significant exposure is assumed to occur), suggesting that these substances accumulate over the years.

In a subsequent study (Nilsson *et al*., 2013; Reliability 2) blood was sampled from eleven ski waxers (including the eight ski waxers sampled in Nilsson *et al*. (2010a)) in the years 2009-2011 (January to March and one individual in May). This study analysed in blood PFCAs, but also FTOHs and intermediates of FTOHs, as Nilsson *et al*. (2010b) showed that ski waxers are exposed to very high concentrations of 6:2, 8:2 and 10:2 FTOHs in air during their profession. Formation of PFCAs from these intermediates could have influenced the concentrations of PFCAs outside the ski season. However, this formation seems limited. Firstly, because the intermediate concentrations in blood were relatively low compared to the concentrations of PFHpA, PFOA and PFNA. Secondly, PFHxA, which is also formed in significant amounts from FTOHs, was rarely detected outside the ski seasons and if so, in low concentrations only.

No elimination half-lives were reported in the original studies (Nilsson *et al*., 2010a; 2013). However, for six of the eleven ski waxers (technicians 1-4, 6 and 8), concentrations in at least two consecutive blood samples in between ski seasons were available from which half-lives could be estimated. Since no exact dates were given for the sampling dates, it was assumed that the sampling occurred around the same date each month. If blood concentrations were below the LOD, 0.5*LOD was used. If multiple consecutive concentrations were below the LOD, only the first value was taken into account. A time series was only taken into account if at the first time point the data were above the LOD. For the calculation of the half-lives, a linear regression of the natural logarithms of the blood concentrations was performed. For PFHpA, almost all data used were above the LOQ, with three exemptions of which two for technicians 2 and one for technician 5. The blood concentrations for the last three months of the period in between ski seasons were below the LOD for technician 2.

For technicians 6 and 8 half-lives could be calculated for PFHxA, PFHpA and PFOA, showing that (as expected) the half-lives of PFHpA (107 and 124 days, respectively) are in between PFHxA

(36 and 17 days, respectively) and PFOA (575 and 691 days, respectively). For technicians 1, 3 and 4 half-lives could only be estimated for PFHpA (87, 62 and 66 days, respectively) and for PFOA (120, 608 and 581 days, respectively), but not for PFHxA. Interestingly, only for technician 2 could no half-life be derived for PFOA (no decline), and was the half-life for PFHxA (33 days) higher than for PFHpA (10 days). The pattern observed for technician 2 deviates thus from the patterns observed for the other technicians. The geometric mean half-life for PFHpA is 60 days when technician 2 is included. Excluding technician 2 yields an average half-life of 89 days, a geometric mean of 86 days and a median value of 87 days. It is worth nothing that the data by Nilsson *et al.* (2013) were recalculated by Russell *et al.* (2015). While there might have been differences in the approach (data points considered, model assumptions) the presented half-lives for PFHpA are nevertheless in the same range as presented above: i.e. the geometric mean half-life calculated by Russell *et al.* (2015) is 70 days when technician 2 is included, and 74 days when excluded. Russell also observed a deviating pattern for technician 2 (half-life of PFHxA > PFHpA) compared to the other technicians.

Finally, there is a remarkable difference between PFHpA and the short-chain C_4-C_6 PFCAs. The latter group were hardly detected outside the ski season, while PFHpA is similar to the long-chain PFCAs detected in almost all samples. The blood concentrations at the first sampling point after the ski season (April or May) contained on average 6.4 ng PFHpA/mL with a range of 1.7 to 12.4 ng/mL. There seems to be a rather strong correlation between the initial concentration and the estimated half-life.

Table 9. PFHpA blood serum half-lives deduced from data on blood concentration in the period between two ski seasons (April-August).

PFAS	Half-life [d]	N	Half-life [d]	N	r^2	Half-life [d]	N	r^2
	Technician 1		**Technician 2**			**Technician 3**		
PFBA	17	2	n.d.			n.d.		
PFPeA	n.d.		n.d.			n.d.		
PFHxA	n.d.		33	3	0.76	n.d.		
PFHpA	**87**	**2**	**10**	**3**	**0.92**	**62**	**4**	**0.96**
PFOA	120	2	No decline*	5	0.39	608	4	0.90
PFNA	41	2	No decline	5	0.03	287	4	0.66
PFDA	29	2	No decline	5	0.39	305	4	0.16
PFUnDA	50	2	No decline	5	0.03	312	4	0.11
PFDoDA	86	2	215	5	0.71	434	4	0.72
PFTrDA	25	2	No decline	5	0.15	No decline	4	0.44
PFTeDA	51	2	85	5	0.55	No decline	4	0.62
PFHxDA	28	2	134	5	0.05	No decline	4	0.58
PFOcDA	46	2	No decline	5	0.40	No decline	4	0.40
	Technician 6		**Technician 4**			**Technician 8**		
PFBA	n.d.		n.d.			n.d.		
PFPeA	n.d.		n.d.			n.d.		
PFHxA	36	2	n.d.			17	3	1.00
PFHpA	**107**	**2**	**66**	**5**	**0.94**	**124**	**4**	**0.96**
PFOA	575	2	581	5	0.59	691	4	0.60
PFNA	174	2	9033	5	0.01	606	4	0.24
PFDA	No decline	2	461	5	0.78	164	4	0.60
PFUnDA	No decline	2	19745	5	0.00	242	4	0.04
PFDoDA	534	2	291	5	0.56	148	4	0.88
PFTrDA	No decline	2	285	5	0.43	No decline	4	0.15
PFTeDA	No decline	2	109	5	0.93	851	4	0.78
PFHxDA	No decline	2	No decline	5	0.41	n.d.		
PFOcDA	No decline	2	No decline	5	0.60	n.d.		

* No decline indicates that linear regression (or two consecutive time points) showed an increase instead of decrease of concentrations. When the substance was not detected at the first time point this is indicated by n.d. The number of months with a sampling point is indicated by N. If N>2, the r_2 indicates the regression coefficient.

Third study: General population

Zhang *et al.* (2013b) examined paired blood and urine samples (56 serum and 30 whole blood) taken from adult individuals from the Hebei province in China. The participants were 47 females, whose age ranged from 21 to 85 years and 39 males with age ranging between 22 and 88 years. Urine and serum with added internal standards were loaded on conditioned solid phase cartridges, washed with 0.1 M formic acid and a mixture of methanol and 0.1 M formic acid, and eluted with eluted with 1% ammonium hydroxide in methanol. The eluate was evaporated to dryness, dissolved in a water/methanol mixture and analysed by HPLC-MS/MS. To whole blood with internal standards 0.5 M tetrabutylammonium hydrogensulfate and 0.25 M sodium carbonate buffer were added and mixed. To this mixture MTBE was added and shaken for 20 min. Phases were separated by centrifugation and the MTBE was removed. This procedure was repeated two times, before the joint MTBE fraction was evaporated to dryness, dissolved in a water/methanol mixture and analysed by HPLC-MS/MS. Recovery experiments were performed with calf serum, blood and artificial urine. The following PFASs were analysed: C_7-C_{11} PFCAs, PFHxS and PFOS, PFOSA, and individual isomers of PFOA and PFOS. Blood concentrations were converted to serum concentrations by accounting for an average haematocrit content of whole blood. From the ratio of the measured concentrations in serum and urine the renal clearance (CL) was estimated (mL serum/d/kg body weight). The calculation of the renal clearance was done by assuming daily urine volume of 1.2 and 1.4 L

(or 0.9 and 1.1 g creatine) and body weights of 55 and 65 kg for females and males, respectively. These values result in almost similar ratio of L urine per kg body weight per day for males and females. This ratio was multiplied by the concentration ratio in urine and blood to obtain the renal clearance. This renal clearance was recalculated to a half-life by means of the volume of distribution (V), which characterises the volume of serum that contains the same amount of a chemical as 1 kg body weight. The excretion rate (/d) is the renal clearance divided by the volume of distribution and thus the human-toxicological half-life is represented by the following formula:

$$\text{Half-life} = \ln(2)*V/CL$$

The assumed volumes of distribution were 170 and 230 mL serum per kg body weight for PFCAs and PFSAs, respectively. It should be noted that this calculation of the half-life could be an overestimation of the real half-life, because it does not account for other routes of elimination than urinary excretion. The authors made the assumption that urinary excretion is the primary elimination route based on literature data for PFOA and PFOS in rats and PFOA in monkeys, while fecal elimination in rats became increasingly more important for PFCAs longer than PFOA. In the study with pigs by Numata et al. (2014) presented in section 4.1.1 the same assumption was made. However, especially for longer-chain PFASs, such as PFHxS, PFOS, PFDA and PFUnDA, fecal excretion becomes more important. Indeed, for these PFASs average half-lives based solely on urinary excretion of 35, 27, 12, and 12 years were found, respectively, for the group of all males and older (>50 y) females. A notable difference was observed with young (<50 y) females, for which the calculated average half-lives were 7.7, 6.2, 4.5 and 4.5 years, for the four PFASs respectively. The difference is partly due to the fact that for young females, loss due to menstrual clearance was taken into account in the calculation of the half-live as well (0.029 mL/d/kg). Contrary, for ΣPFOA the half-lives for both groups were almost similar with 2.1 years for young females and 2.6 years for males and older females. These values are comparable with human half-lives for PFOA derived elsewhere. These findings show that for PFCAs with chain lengths up to PFOA, urinary excretion is indeed the primary excretion route.

The average renal clearance of PFHpA was 0.61 mL/d/kg for the groups of both young females and the combined group of males and older females. For younger females (N=12), the geometric mean was 0.27 mL/d/kg and the median value 0.12 mL/d/kg with a 95% confidence interval of 0.022 to 1.2 mL/d/kg. This led to an average half-life of 1.5 ± 0.3 year with a range of 0.11 to 3.3 year, a geometric mean of 1.0 year and a median value of 1.6 year. For the combined group of males and older females (N=31), the geometric mean of the renal clearance rate was 0.39 mL/d/kg and the median value 0.41 ml/d/kg with a 95% confidence interval of 0.38 to 0.83 mL/d/kg. This led to an average half-life of 1.2 ± 0.2 year with a range of 0.12 to 5.1 year, a geometric mean of 0.82 year and a median value of 0.79 year. It should be noted that from the reported clearance rates, the geometric mean and the median values for the half-lives can rather precisely be recalculated, while this is not the case for the mean values.

Because it can be assumed that urinary excretion is the major route of excretion, the reported half-lives are good estimates of the overall half-lives. Also, the choice of the volume of distribution is of influence on the final outcome of the half-lives. However, these values appear to be rather constant over different PFASs, reducing the uncertainty of the assumption. Nevertheless, for long-chain PFASs the volume of distribution might get higher, as demonstrated for PFDA in rats. The assumed value of 170 mL serum/kg body weight should be considered a relatively low value, allocating a significant part of the whole body burden of PFCAs in the serum and thus a small extrapolation from serum to whole body concentrations. Overall, the derived half-lives for PFHpA should be considered reliable estimates. The minimum value in the total of 43 people for which both urine and serum concentration could be determined is 40 days. However, geometric and median values were much higher with values around 300 days and higher. The highest value was 5.1 years, and it can be concluded that the variability between individuals is considerable. The minimum, median, mean and maximum concentrations of PFHpA in serum were <0.030, 0.058, 0.085 and 0.37 ng/mL. These values are considerably lower than the concentrations in serum of the ski waxing technicians.

Fourth Study: Airport employees

Xu *et al.* (2020) examined employees from an airport in Arvidsjaur in northern Sweden that were exposed to high concentrations of PFASs in drinking water at the airport due to firefighting trainings. Shortly after the exposure to contaminated drinking water stopped, 9 employees were sampled once (eight males, one female, average age 33 years, ranging from 22 to 61 years). In addition to that, 17 employees were involved in this first blood sampling as well as in repeated blood and urine sampling (four times at monthly intervals) (eleven males, six female, average age 50 years, ranging from 24 to 62 years). Next to that, a reference group containing 58 people was involved without being exposed to elevated PFASs levels (21 males, 37 female, average age 34 years, ranging from 22 to 49 years). Both blood and urine were sampled and blood was centrifuged for 10 minutes. Serum and urine were stored at -80 and -20 °C, respectively. Serum was mixed with water, methanol and internal standards in 50% acetonitrile and acetonitrile, for urine the same procedure was followed without the additional acetonitrile. The samples were shaken and centrifuged afterwards. Analysis was performed by LC-MS/MS. Calf serum and human urine were used for the calibration series. The analysed PFASs were PFHxA, PFHpA, PFOA, PFBS, PFPeS, PFHxS, PFHpS and PFOS (individual isomers).

Especially the concentrations of PFPeS and PFHxS were highly elevated in the serum of the employees in comparison with the reference group, with serum concentrations being hundreds of times higher. However, for PFOA and PFOS this difference was less than a factor of 10. The concentrations in the drinking water were measured as well. Initial serum concentrations obtained shortly after contaminated drinking water intake stopped (within two weeks), were higher than the concentrations in drinking water for all PFASs, but especially the concentrations of PFHxS, PFOS and PFOA were highly elevated in serum compared to drinking water. For PFHpA the concentration ratio of serum to drinking water was 4.74. Of the studied compounds, the concentration ratio of urine to serum was highest for PFHpA with a median of 0.086 for the 17 individuals and a range from 0.018 to 0.32. It should be noted that this ratio is higher than from the study from China by Zhang *et al.* (2013b), where this ratio is on average 0.028 and median values of 0.008 and 0.019 for young females and the rest, respectively (calculated from the data for renal clearance). This indicates a rather high renal clearance in this study from Sweden. The half-lives of PFASs were estimated from the 5 monthly serum concentrations. This was done by fitting the data for all individuals with one generic slope (excretion rate) and by fitting the data for each of the 17 individuals separately. With the model with an overall excretion rate for all individuals, no significant decline was observed for PFHxA, leading to a half-life of 1.63 year. Although the authors suggest that this could be due to the fact that PFHxA should be better analysed in blood instead of in serum, this could be the result as well of ongoing contribution from other sources, leading to a more or less constant serum concentration instead of a decline. The half-life for PFHpA was 0.17 year, i.e., 62 days, while for PFOA, PFHxS and linear PFOS, half-lives were estimated of 1.77, 2.86 and 2.91 year, respectively. For these substances, the decline in serum concentrations was significant. For the 17 individual employees, the half-lives for PFHpA varied from 32 to 281 days, with an average half-life of 90 days, a geometric mean of 74 days and a median value of 65 days. Although paired urine and serum concentrations were determined in the study for the 17 individual employees, these values were not further used to calculate a half-life, despite the fact that the study of Zhang *et al.* (2013b) is cited in a comparison of half-lives. If from the reported ratios of urine and serum concentrations the half-lives are calculated in exact the same manner as is done in Zhang *et al.* (2013b), a half-life of 63 days is obtained for PFHpA with a range of 17 to 302 days. This value is thus very similar as the one determined from the decay in serum concentrations, although for the other PFASs with longer half-lives than PFHpA, the values determined from the urine/serum ratios are significantly higher than the values determined from the regression of serum concentrations in time. Serum concentrations of PFHpA ranged from 0.17 to 0.53 ng/mL, which is higher than in the general population in the Hebei province in China, but considerably lower than the values in the blood or serum from the ski waxers. In these employees from the airport, only for PFHpA there was a positive correlation between the excretion rate and the serum concentration.

Fifth study: General population exposed to contaminated drinking water

One third of the population of Ronneby in Sweden has been exposed to PFASs by contaminated drinking water due to firefighting foam from a nearby airport. 114 people from this group (ranging from 4 to 84 years old, 53% female) participated in a study in which blood was sampled during ten rounds over 4 years (Li *et al.*, 2022a). A reference group of 64 people ranging from 20 to 50 years from a nearby municipality was included too. Blood was collected in blood collection tubes, centrifuged and serum stored at -80 °C. Analysis was performed by LC-MS/MS, equal to Xu et al. (2020). For PFHpA only limited data are reported. The initial serum concentrations of PFHpA from blood sampled half a year after the consumption of contaminated drinking water stopped was 0.085 ng/mL (geometric mean) and 0.095 ng/nL (median value) with a range of <0.05 to 2.4 ng/mL (n=114). In the reference group (n=68) all values were <0.1 ng/mL. At the tenth round 4.4 years after the exposure via contaminated drinking water was stopped, the geometric mean and median concentration were <0.05 ng/mL, while the maximum concentration was 0.11 ng/mL. If the maximum concentration of PFHpA at the end of the study is taken into account, the estimated half-life is 320 days for this individual if the highest concentration at the start of the study also belongs to this individual, otherwise the estimated half-life would be longer. From the other data no conclusion can be drawn with regard to the half-life of PFHpA as the data are below the detection limit. Further, it is also not clear to what extent exposure from other sources during the duration of the study could have influenced the results. For PFHxA for example, only a limited decline in concentrations was observed during the study. However, this is likely not the result of a very long half-life, but rather of a continued exposure during the study, although for both PFHxA and PFHpA concentrations at the beginning of the study were higher in the exposed group than in the reference group. Half-live without correction for background exposure was 2.99 years for PFOA and with correction for background exposure it was 2.47 years. Information from this study is limited, but it confirms the observation that for individuals the half-life of PFHpA can be as long as 320 days.

4.1.3 Conclusion on toxicokinetics

The half-life of PFHpA in air-breathing organisms and humans, has been determined in several studies, using blood/serum concentrations in time and serum: urine concentrations ratios. These studies show that there is considerable variation of the half-lives of PFHpA in blood/serum between individuals and between different populations. This is also true for studies that used the same methodology and it can be concluded that this variability is thus not dependent on the experimental setup or calculation of the half-life. The half-lives determined for individuals vary from 10 days to 3.3 years. Average half-lives from all studies are at least 76 days (see Figure 3).

As presented in section 4.1.1, in different air-breathing organisms variable results are seen. The half-life for both male and female rats is less than 1 day. This does not indicate a potential for accumulation. For pigs, a much longer half-life was observed. The variability between individual pigs was large. The lowest values were around 10 days, but the highest values in the order of 500 days. The geometric mean half-life is 74 days, a value that will cause biomagnification from food. A biomagnification factor of 2.7 was indeed calculated in this study. Such long (average) half-lives are an indication of the potential of a substance to biomagnify in air-breathing organisms. When biomagnification occurs, the substance should be considered very bioaccumulative. Therefore, PFHpA should be concluded as very bioaccumulative in at least some air-breathing species such as the pig.

As presented in section 4.1.2, several studies are available that are relevant for the half-life of PFHpA in the human body. The half-lives determined for individuals vary from 10 days to 3.3 years. The average half-lives from all studies are at least 76 days (see Figure 3). A value of 70 days was derived to indicate biomagnification in humans, assuming that humans eat 0.01 kg food per kg body weight per day (i.e. 700 g food for a person weighing 70 kg). This value was in principle developed for lipophilic substances under the assumption that food and human

body have equal lipid contents (Goss et al. 2013). In this case the assumption on the lipid contents of food and human body has a direct effect on the derived critical half-life. However, lipophilic partitioning is not relevant for PFAS such as PFHpA. For this type of chemicals concentrations are not normalised to lipid content. The critical half-life associated with biomagnification is solely determined by the food intake rate. The (non-normalised) concentration in the human body becomes higher than that in food if the elimination rate is lower than the uptake rate by food. It is important to realise that the critical half-life in humans of 70 days, has been derived by assuming that the food intake is 0.01 kg food per kg body weight per day (i.e. 700 g food for a person weighing 70 kg) (Goss et al, 2013). It is however likely that the typical food consumption exceeds this daily intake. The most recent Dutch national food consumption survey (www.wateetnederland.nl) shows that an average food intake of 700 g food per day is only applicable to girls from 1 to 18 years. All other groups (boys from 1 to 18, adult women and men) have a higher average daily intake. The average daily intake over the whole population is about 1 kg. This value does not include drinks, otherwise the daily intake would be a factor three higher. Taking the average daily food intake of 1 kg per day for an average person of 70 kg into account, a critical half-life of about 50 days is obtained, which is substantially lower than the proposed critical half-life value of 70 days. This value is an average value. Some people will consume more than this average, and a value of 1.6 kg food per day for a person of 70 kg would lead to a critical half-life of as low as 30 days. In Figure 3, the half-lives in humans are shown per study, with dotted lines at 30 and 70 days (i.e. 50 days in the middle of the two lines). Although there is considerable variation between individuals and between study groups, average half-lives exceed the upper range of guiding values of 70 for all studies, and thus, the half-lives observed for PFHpA are high enough to reach higher concentration of PFHpA in the human body than in the food consumed. Further supporting high bioaccumulation potential of PFHpA and its salts in humans is the observed build up over the years in humans. Therefore, it can be concluded that PFHpA is very bioaccumulative in humans.

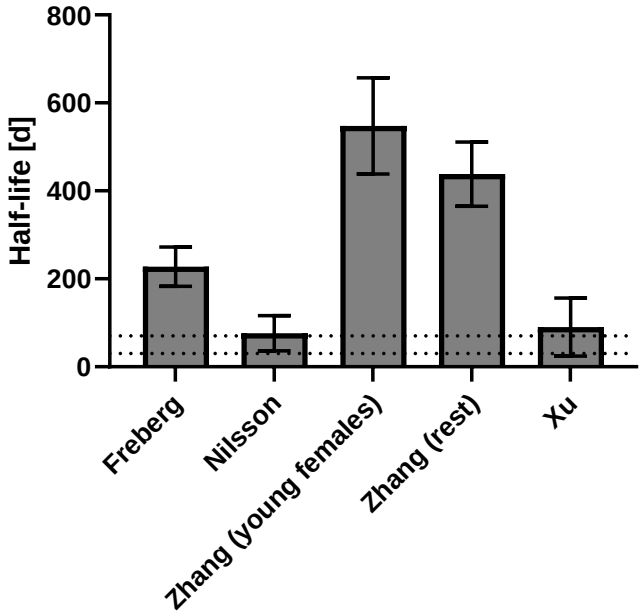

Figure 3. PFHpA half-lives in humans*

*The half-lives are arithmetic means ± standard deviation

Overall, PFHpA is very bioaccumulative in humans and at least in some other air-breathing mammalian species. PFHpA is considered very bioaccumulative, based on a weight of evidence.

This is in line with the close structural analogue PFOA that is one perfluorinated carbon in chain length longer than PFHpA. Although PFOA was not proposed and identified as a vPvB substance

under REACH in 2013, the Persistent Organic Pollutants Review Committee (POPRC) concluded at its twelfth meeting in September 2016 that PFOA is persistent, bioaccumulative and toxic to animals including humans (UNEP/POPS/POPRC.12/11/Add.2). Under the POP regulation the B criterion for aquatic organisms is defined as 5000 L/kg, which equals the vB criterion under REACH. The POPRC thus concluded that the half-life in humans is of similar concern as the vB criterion for aquatic organisms.

5. Environmental hazard assessment

PFHpA and its salts have not been registered under REACH, and limited information on environmental toxicity of PFHpA is available in the public domain.

5.1 Aquatic compartment (including sediment)

5.1.1 Fish

There are no studies available that investigated the short- or long-term toxicity of PFHpA to fish.

5.1.2 Aquatic invertebrates

5.1.2.1 Short-term toxicity to aquatic invertebrates

Boudreau (2002; reliability 2) investigated the acute toxicity of PFHpA to two daphnia species according to ASTM guideline E 729-96. Daphnids (neonates < 24 h old) were exposed for 48 hours to PFHpA. The nominal test concentrations were 62.5, 125, 250, 500 and 1000 mg/L. It was indicated that the maximum concentration did not exceed the critical micelle concentration. Control was included. Treatment consisted of three or four replicates (not clear from description). Medium was well water diluted with deionised water to achieve a range of 200 to 225 mg/L of $CaCO_3$. Test vessels were polypropylene disposable containers each containing 10 dapnids in 150 mL medium. Temperature was held constant at 21 ± 1° C with a 16:8 h light:dark photoperiod. There was no feeding during testing. Actual test concentrations were not determined. Endpoints were lethality and immobility. No significant effects were observed. For both *Daphnia magna* and *Daphnia pulicaria* the 48h-EC_{50} were reported as >1000 mg/L. These values are based on nominal values that exceed the estimated water solubility of PFHpA of 3.65 mg/L (see Table 4), however, the solubility of the sodium salt of PFHpA is 1936 mg/L, which would indicate that the highest dose is close to the water solubility of the dissociated species (Perfluoroheptanoate, PFHp). An exact value can thus not be derived, but the data do show that the acute toxicity of PFHpA to daphnids is low (exceeding or close to the water solubility).

Hoke *et al.* (2012) (reliability 4) compared publicly available toxicity data of C_{4-10}-PFCAs and reported for PFHpA a 48-h LC5O in daphnids of >100 mg/L referencing thereby Boudreau (2002) with no details provided.

5.1.3 Algae and aquatic plants

There are two studies that investigated the toxicity of PFHpA to algae.

Latała *et al.* (2009; reliability 2) investigated the toxicity of C_{6-9}-PFCAs to three representative marine algae in the Baltic Sea according to modified ISO guidelines 10253:1995 and 8692:1993. Main modifications were the selected test strains, the medium used and the applied

photoperiod (16:8 h light:dark photoperiod). Medium was f/2 medium. Salinity was similar to that in the southern Baltic Sea. pH was maintained at 7.6–7.8. The nominal test concentrations were not detailed, except that they were in the range of 0.000005 to 50 mM. From the available figures in the publication, it appears that for PFHpA 8-10 concentrations were tested per species. Controls were included. Each treatment was tested in triplicate. Tests were conducted in 25 cm^3 glass conical flasks containing 9.5 cm^3 aliquots of algal suspension made by mixing a known number of cells in the log growth phase with sterile medium, and 0.5 cm^3 of PFHpA solution. The initial cell number was constant and was measured as the optical density. After 72 h incubation in culture chambers, the number of cells was determined by measuring optical density spectrophotometrically. For PFHpA, 72h-EC_{50} values of 5.21 ± 0.26 mM, 2.40 ± 0.12 mM, and 1.42 ± 0.07 mM were reported for the green alga *Chlorella vulgaris*, the diatom *Skeletonema marinoi* and the blue-green alga *Geitlerinema amphibium*, respectively. Expressing them in mg/L yields 72h-EC_{50} values of 1896 ± 95, 874 ± 44 and 517 ± 25 mg/L, respectively. EC_{10} or NOECs have not been reported. These reported effect concentrations likely underestimate the toxicity, as they are based on nominal values that exceed the estimated water solubility of PFHpA of 3.65 mg/L (see Table 4), however, the solubility of the sodium salt of PFHpA is 1936 mg/L, which would indicate that the highest dose is close to the water solubility of the dissociated species (Perfluoroheptanoate, PFHp). The data do show a clear dose response relationship for PFHpA in all three algal species (as is also the case for the other PFCAs). The 72h-EC_{50} values for PFHxA, PFHpA and PFOA amount to 12.84, 5.21 and 2.36 mM for *C. vulgaris*; 4.72, 2.40 and 0.89 mM for *S. marinoi*, and 3.18, 1.42 and 0.60 mM for *G. amphibium*, respectively. These data show that the algal toxicity of PFCAs increases with each additional CH_2-group to the alkyl chain and that the algal toxicity of PFHpA is between PFHxA and PFOA.

Boudreau (2002; reliability 2) investigated the toxicity of PFHpA to the green algae *Selenastrum capricornutum* and *Chlorella vulgaris* according to ASTM guideline E 1218-97a, and the *Lemna gibba* according to ASTM guideline E 1415-91. The nominal test concentrations were 62.5, 125, 250, 500 and 1000 mg/L for all tests. It was indicated that the maximum concentration did not exceed the critical micelle concentration. Controls were included. Treatment consisted of three or four replicates (not clear from description). For the algal test, duration was 96 hours. Medium was Bristol's algal growing medium. Test were conducted in 60 x 15 mm polyethylene disposable petri dishes containing 20 mL medium that were manually shaken twice a day. Initial cell density was 1.5 x 10^4 cells/mL. Incubation was at 23 ± 1° C with continuous illumination. Endpoints were cell density and chlorophyll(a) content. For the lemna test, duration was 7 days. Medium was Hunter's growing medium. Test were conducted in 60 x 15 mm polyethylene disposable petri dishes containing 10 mL medium. Incubation was at 25 ± 1° C with continuous illumination. Endpoints were mean frond number and biomass, measured as wet weight. The qualitative physical appearance (chlorosis, necrosis, and relative root length) of all plants was recorded. It was reported that PFHpA exhibited significant effects on the growth of both algal species at the highest test concentration, but this was insufficient to calculate a EC50 from the data. The *S. capricornutum* and *C. vulgaris* 96h-EC_{50} values were reported as >1000 mg/L. No significant effects were observed for *L. gibba*, and the 96h-EC_{50} was reported as >1000 mg/L. No NOEC of EC_{10} values were reported. Based on the above, 96h-NOECs could be determined as 500 mg/L for the algal species, and ≥1000 mg/L for *L. gibba*, respectively. These values are based on nominal values that exceed the estimated water solubility of PFHpA of 3.65 mg/L (see **Table 4**), however, the solubility of the sodium salt of PFHpA is 1936 mg/L, which would indicate that the highest dose is close to the water solubility of the dissociated species (Perfluoroheptanoate, PFHp). Exact values can thus not be derived, but the data do show that the toxicity of PFHpA to algae and aquatic plants is low.

5.2 Other effects

5.2.1 Reprotoxicity

PFHpA has a harmonised classification as Repro 1B (see section 4). PFHpA has been shown to cause reprotoxic effects in mice and it can be expected that mammalian populations in the environment can be affected similarly.

5.2.2 Endocrine Disruption

In the study according to OECD TG 422 (requested during first SEv Draft Decision), exposure of F0 males to 10 and 50 mg/kg bw/day PFHpA induced significant lower mean total T4 values (Anonymous, 2017). A decrease of T4 was already observed at the lowest dose of 0.5 mg/kg bw/day (5.42, 4.67, 3.71**, 2.95** µg/dL at 0, 0.5, 10 and 50 mg/kg bw/day respectively) (measurement performed at week 15). The decrease can be considered dose-dependent. A gender comparison is not available, as T4 was not measured in F0 females. T4 measurements in pups were done at PND 21 (while the OECD TG 422 test guideline states that the measurement has to be done at PND 13 and if relevant also at PND 4). In F1 males and females (PND 21), there were no significant changes in T4. Differences in T4 concentration cannot be excluded between PND 4 and PND 21, especially if the dam has a reduced T4 concentration. F1 males and females were directly exposed to the substance, following weaning, from PND 22 to PND 42. The serum samples of the F0 females and the F1 culled pups PND 4 were not analysed.

Based on the data of the OECD TG 422 study, potential interference of PFHpA with the thyroid hormones *in vivo* is still a concern. This concern is not taken into account in the ELoC assessment.

5.3 Summary and discussion of the environmental hazard assessment

PFHpA has been shown to cause reprotoxic effects in mice and it can be expected that mammalian populations in the environment can be affected similarly.

The limited available aquatic toxicity data on PFHpA suggest low acute toxicity to algae, aquatic plants and aquatic invertebrates. There is no data on PFHpA toxicity in fish. For the structurally similar compound PFOA, more data on acute and chronic aquatic toxicity data are available. These data show low toxicity of PFOA. Considering that PFOA is one fluorinated carbon longer, and thus expected to be slightly more toxic than PFHpA, it can be concluded that toxicity of PFHpA to aquatic organisms is expected to be low.

6. Conclusions on the SVHC Properties

6.1 CMR assessment

PFHpA is covered by index number 607-761-00-3 of Regulation (EC) No 1272/2008. Pursuant to Commission Delegated Regulation (EU) 2022/692 of 16 February 2022, PFHpA will be classified in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child') and Specific target organ toxicity — repeated exposure category 1, STOT RE 1 (H372 (liver))[6].

[6] Commission Delegated Regulation (EU) 2022/692 of 16 February 2022 amending, for the purposes of its adaptation

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification in the hazard class:

toxic for reproduction category 1A or 1B in accordance with Article 57 (c) of REACH.

6.2 PBT and vPvB assessment

6.2.1 Assessment of PBT/vPvB properties

A weight-of-evidence determination according to the provisions of Annex XIII of REACH is used to identify the substance as PBT/vPvB. All available information (such as the results of standard tests, monitoring and modelling data, information from the application of the category and analogue approach (grouping, read-across) and (Q)SAR results) was considered together in a weight-of-evidence approach.

6.2.1.1 Persistence

PFHpA is, based on its stable structure, not expected to undergo abiotic degradation under relevant environmental conditions.

In general, the persistence of PFHpA can be explained by the shielding effect of the fluorine atoms, blocking *e.g.,* nucleophilic attacks to the carbon chain. High electronegativity, low polarisability and high bond energies make highly fluorinated alkanes the most stable organic compounds. It is not expected that the carboxylic group in perfluorinated carboxylic acids (PFCAs) alters the persistence of these chemicals. The persistence of seven long-chain PFCAs (PFOA/APFO (C_8-PFCA), PFNA (C_9-PFCA), PFDA (C_{10}-PFCA), and C_{11}-C_{14} PFCAs) (P and vP) has already been confirmed by the Member State Committee prior to their inclusion into the Candidate list (European Chemicals Agency, 2012a-d, 2013a-b, 2015b, 2019). In RAC's opinion on the PFHxA (C_6-PFCA) restriction proposal it was concluded that PFHxA is considered to exceed by far the trigger of being very persistent defined in REACH Annex XIII (RAC, 2021).

Annex XIII, point 3.2.1.(d) of the REACH Regulation requires that any relevant information for the assessment of the persistence of the substance be considered. Therefore, based on the weight of evidence, knowledge of the stability of the C-F bond and the read-across approach with PFHxA, PFOA, PFNA, PFDA and C_{11}-C_{14} PFCAs it is concluded that PFHpA is expected to undergo no or extremely limited degradation in the environment and thus fulfils the P- and vP-criteria in accordance with the criteria and provisions set out in Annex XIII of REACH.

6.2.1.2 Bioaccumulation

Based on a direct comparison with the bioaccumulation criteria for aquatic organisms, PFHpA is not bioaccumulative. However, bioaccumulation in aquatic species may not be the most relevant endpoint to consider because other mechanisms of accumulation might be more relevant. The expected high water solubility of PFHpA may enable fish and mussels to quickly excrete PFHpA via gill permeation, facilitated by the high water throughput whereas air-breathing homeotherms are unable to efficiently eliminate PFHpA to avoid accumulation.

In air-breathing organisms results appear to differ between species. In rats, the elimination half-life for both males and females is less than 1 day. In pigs much longer half-life have been reported with the observed geometric mean half-life being 74 days. This half-life corresponds to a biomagnification factor of 2.7, indicating that the substance has the potential to biomagnify

to technical and scientific progress, Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the 18th ATP to CLP). Pursuant to the second paragraph of Article 2 of this Regulation, this new harmonised classification applies from 23 November 2023. However, pursuant to the third paragraph of that provision substances and mixtures may already be classified, labelled and packaged in accordance with this classification.

in air-breathing organisms. Therefore, PFHpA should be considered as very bioaccumulative (vB) in at least some air-breathing species such as the pig.

Several studies in humans point to high half-lives with an average of at least 76 days. These half-lives exceed the range of guiding values for biomagnificating substances in humans that are considered to be in the range of 30 to at most 70 days. Therefore, PFHpA should be considered as very bioaccumulative in humans.

Overall, PFHpA is very bioaccumulative in humans and in at least some other air-breathing mammalian species. Overall, taking all available information together in a weight-of-evidence approach, the data from pigs and humans is given a high weight and indicates that PFHpA bioaccumulates. Annex XIII, point 3.2.2.(b) of the REACH Regulation requires that data from the toxicokinetic behaviour of the substance be considered. Therefore, it is concluded that the vB criterion of REACH Annex XIII is fulfilled.

6.2.1.3 Toxicity

PFHpA is covered by index number 607-761-00-3 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3 (the list of harmonised classification and labelling of hazardous substances) and it is classified in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child') and STOT RE 1 (H373) (liver).

As a consequence, the toxicity criterion of REACH Annex XIII is fulfilled.

An overview of the properties leading to the PBT and vPvB concern is given in Table 10.

Table 10. Overview of information relevant for the PBT / vPvB assessment

	Annex XIII	PFHpA	Conclusion
P/vP	A substance fulfils the persistence criterion (P) if the degradation half-life: (a) in marine water > 60 days, or (b) in fresh or estuarine water > 40 days, or (c) in marine sediment > 180 days, or (d) in fresh or estuarine water sediment > 120 days, (e) in soil > 120 days. A substance fulfils the "very persistent" criterion (vP) if the degradation half-life: (a) in marine, fresh or estuarine water > 60 days, or (b) in marine, fresh or estuarine water sediment > 180 days, or (c) in soil > 180 days	No screening, nor simulation tests available => read-across to PFOA and other PFCAs: All studies for PFCAs demonstrate the extremely high persistence of the compounds. No environmental half-life could be determined during duration of the studies => Persistence (vP) of PFOA, PFNA, PFDA, and C_{11-14} was confirmed by Member State Committee and PFHxA by the Risk Assessment Committee. Furthermore, the high stability of the C-F bond strengthens the arguments on PFHpA persistence.	P and vP
B/vB	Assessment of B or vB properties can be based on: (a) results from a bioconcentration or bioaccumulation study in aquatic species: ▪ A substance fulfils the bioaccumulation criterion (B) when the bioconcentration factor in aquatic species is higher than 2000. ▪ A substance fulfils the "very bioaccumulative" criterion (vB) when the bioconcentration factor	BCF, BAF and TMF values obtained for PFHpA in the aquatic environment show that PFHpA is not bioaccumulative in aquatic species. In air-breathing organisms the results differ between species. PFHpA is not bioaccumulative in rats with half-lives in male and female rats of less than 1 day. In pigs, the geometric mean half-life is 74 days and a	B and vB

	in aquatic species is higher than 5000. (b) other information on the bioaccumulation potential provided that its suitability and reliability can be reasonably demonstrated, such as: Results from a bioaccumulation study in terrestrial species; Data from scientific analysis of human body fluids or tissues, such as blood, milk, or fat; Detection of elevated levels in biota, in particular in endangered species or in vulnerable populations, compared to levels in their surrounding environment; Results from a chronic toxicity study on animals; Assessment of the toxicokinetic behaviour of the substance; (c) Information on the ability of the substance to biomagnify in the food chain, where possible expressed by biomagnification factors or trophic magnification factors.	biomagnification factor of 2.7 was calculated. PFHpA is considered very bioaccumulative in pigs. Several studies in humans point to high half-lives with an average of at least 76 days. These half-lives exceed the range of guiding values for biomagnificating substances in humans that are considered to be in the range of 30 to at most 70 days. Therefore, PFHpA should be considered as very bioaccumulative in humans. Overall, PFHpA is very bioaccumulative in humans and at least in some air-breathing mammalian species.	
T	A substance fulfils the toxicity criterion (T) in any of the following situations: (a) NOEC/EC_{10} < 0.01 mg/L, or (b) Classified as carcinogenic (cat. 1A or 1B), germ cell mutagenic (cat 1A or 1B), or toxic for reproduction (cat. 1A, 1B or 2), or (c) Classified as STOT RE cat. 1 or 2	PFHpA is classified as Repr. 1 B and STOT RE 1 and thus fulfils the T criterion.	T

6.2.2 Summary and overall conclusions on the PBT and vPvB properties

A weight-of-evidence determination according to the provisions of Annex XIII of REACH has been used to identify the substances as PBT and vPvB. Available relevant information, such as the results of standard tests, monitoring and modelling, information from the application of the category and analogue approach (grouping, read-across) and (Q)SAR results, was considered together in a weight-of-evidence approach.

Persistence

In general, the persistence of PFHpA and its salts can be explained by the shielding effect of the fluorine atoms, blocking *e.g.,* nucleophilic attacks to the carbon chain. High electronegativity, low polarisability and high bond energies make highly fluorinated alkanes one of the most stable organic compounds. It is not expected that the carboxylic group in perfluorinated carboxylic acids (PFCAs) or their salts alters the persistence of the perfluorinated carbon chain.

The persistence (P and vP) of seven long-chain PFCAs (PFOA/APFO (C_8-PFCA), PFNA (C_9-PFCA), PFDA (C_{10}-PFCA), and C_{11}-C_{14} PFCAs) and a short-chain PFCA (HFPO-DA (C_6-PFCA where two chains of three carbon atoms are joined by an ether bond)) has already been confirmed by the Member State Committee prior to their inclusion into the Candidate List. In the RAC opinion on the PFHxA (C_6-PFCA) restriction proposal it was concluded that PFHxA exceeds by far the trigger of being very persistent and clearly exceeds the threshold values for being "very persistent" (vP) as defined in REACH Annex XIII.

Considering the stability of the C-F bond and the read-across approach with PFHxA, HFPO-DA, PFOA, PFNA, PFDA and C_{11}-C_{14} PFCAs, it can be concluded that PFHpA and its salts will undergo, no or extremely limited, degradation in the environment.

Monitoring data support the above conclusion. The detection and/or quantification of PFHpA in remote areas such as the Arctic (in air, snow, fresh- and marine water (including sediments) and soil) and the Antarctic (snow), in locations far away from point sources, point towards persistence of PFHpA.

Based on a weight-of-evidence approach, it is concluded that PFHpA and its salts are very persistent. Annex XIII, point 3.2.1.(d) of the REACH Regulation requires that any relevant information for the assessment of the persistence of the substance be considered. Therefore, it is concluded that PFHpA and its salts fulfil the P- and vP- criteria in accordance with the criteria and provisions set out in Annex XIII of REACH.

Bioaccumulation

Based on a direct comparison with the bioaccumulation criteria for aquatic organisms, PFHpA and its salts do not seem to be bioaccumulative in water-breathing organisms.
In air-breathing organisms results appear to differ between species. In rats, the elimination half-life for both males and females is less than 1 day. In pigs, however, much longer elimination half-lives have been reported with the highest values being in the order of 500 days. There was considerable variation between individual pigs though, resulting in a geometric mean elimination half-life of 74 days. The latter value corresponds to a biomagnification factor of 2.7, showing that PFHpA and its salts have the potential to biomagnify in pigs. Therefore, PFHpA and its salts should be considered very bioaccumulative (vB) in at least some air-breathing species such as the pig. The elimination half-life of PFHpA of 74 days fits well between values derived for PFOA (236 days) and PFHxA (4.1 days). that are the closest structural analogues differing only by one perfluorinated carbon in chain length.

Several studies in humans point to high elimination half-lives with the highest value being 3.3 years. As seen for other mammalian species, there is considerable variation between individuals, resulting in an average elimination half-life in humans that is at least 76 days. This value exceeds the range of guiding values for biomagnification of substances in humans that are considered to be in the range of 30 to at most 70 days and thus, the half-lives observed for PFHpA are high enough to reach higher concentration of PFHpA in the human body than in the food consumed. Further supporting high bioaccumulation potential of PFHpA and its salts in humans is the observed build up over the years in humans. Therefore, PFHpA and its salts are considered very bioaccumulative in humans.

This is in line with the close structural analogue PFOA that is one perfluorinated carbon in chain length longer than PFHpA. Although PFOA was not proposed and identified as a vPvB substance under REACH in 2013, the Persistent Organic Pollutants Review Committee (POPRC) concluded at its twelfth meeting in September 2016 that PFOA is persistent, bioaccumulative and toxic to animals including humans (UNEP/POPS/POPRC.12/11/Add.2). Under the POP regulation the B criterion for aquatic organisms is defined as 5000 L/kg, which equals the vB criterion under REACH. The POPRC thus concluded that the half-life in humans is of similar concern as the vB criterion for aquatic organisms.

Overall, taking all available information together in a weight-of-evidence approach, thereby giving the data from pigs and humans a high weight, a high bioaccumulation potential of PFHpA and its salts in humans and at least some other air-breathing mammalian species has been identified. Annex XIII, point 3.2.2.(b) of the REACH Regulation requires that data from the toxicokinetic behaviour of the substance be considered. Therefore, it is concluded that the vB criterion of REACH Annex XIII is fulfilled.

Toxicity

PFHpA is covered by index number 607-761-00-3 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3 (the list of harmonised classification and labelling of hazardous substances) and it is classified in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child') and STOT RE 1 (H373) (liver)[7]. Therefore, the toxicity criterion of REACH Annex XIII is fulfilled. It is therefore concluded that PFHpA and its salts meet the toxicity criterion (T) in accordance with Annex XIII, points 1.1.3 (b) and (c), of the REACH Regulation.

Conclusion on the P, B and T properties
In conclusion, PFHpA and its salts meet the criteria for PBT and vPvB substances according to Article 57 (d) and (e) of the REACH Regulation.

6.3 Assessment under Article 57(f)

An assessment is made in order to conclude whether PFHpA, should be regarded as "substances for which there is scientific evidence of probable serious effects to human health and the environment which give rise to an equivalent level of concern to those of other substances listed in Article 57 points (a) to (e) of the REACH Regulation".

The assessment follows a case-by-case approach and is based on available information in a weight of evidence evaluation. Perfluoroheptanoic acid (PFHpA) and its salts will all exist in water under environmental conditions and in the human body in the (dissociated) form of perfluoroheptanoate. The assessment therefore applies to both PFHpA and its salts.

6.3.1 Summary of the data on the substance properties and other evidence

6.3.1.1 Persistency – Abiotic and Biotic Degradation

As mentioned in section 6.2.1.1. PFHpA and its salts are expected to undergo no or extremely limited degradation in the environment and thus fulfils the P- and vP- criteria in accordance with the criteria and provisions set out in Annex XIII of REACH.

6.3.1.2 Mobility

Due to its low to very low adsorption potential (log K_{OC} 1.63-1.7), high water solubility (salts and dissociated form of PFHpA >1000 mg/L) and low tendency to volatise from water to air (Henry's Law constant of 6.38 $Pa \cdot m^3/mol$ for the ammonium salt), PFHpA predominantly resides in the aquatic compartment. These properties make PFHpA very mobile in the aquatic environment. Once PFHpA has entered the aquatic environment, e.g., surface waters, there are limited fate processes that would prevent it from being distributed to groundwater and to the marine environment. Monitoring data show that PFHpA has been detected in surface waters, tap water, bottled drinking water and groundwater which supports the conclusion that PFHpA and its salts are mobile in water. A recent global survey of drinking water detected PFHpA in 42% of bottled water and in 90% of tap water (Kaboré *et al.*, 2018). In a survey of 164 individual ground-water samples from 23 European countries, PFHpA was present in 30% of the samples (Loos et al, 2010).

6.3.1.3 Removal from the environment and drinking water

Since PFHpA and its salts have a preference for the aqueous phase in the environment, the

[7] Commission Delegated Regulation (EU) 2022/692 of 16 February 2022 amending, for the purposes of its adaptation to technical and scientific progress, Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the 18th ATP to CLP). Pursuant to the second paragraph of Article 2 of this Regulation, this new harmonised classification applies from 23 November 2023. However, pursuant to the third paragraph of that provision substances and mixtures may already be classified, labelled and packaged in accordance with this classification.

most important compartment for removal of PFHpA and its salts is water. The same properties that make PFHpA and its salts mobile in the environment are also the reason why their removal is challenging. Due to the high aqueous solubility and the low sorption potential, PFHpA and its salts will only bind to a low extent to adsorption materials and will rather remain in the water phase during the purification process.

PFHpA is not readily removed with conventional surface water treatment processes (coagulation, flocculation, sedimentation, filtration, disinfection with free chlorine), nor by several advanced water treatment processes, including raw and settled water ozonation, biofiltration, and disinfection with medium-pressure ultraviolet (UV) lamps (Hopkins *et al.*, 2018)). PFHpA is not effectively removed by granular activated carbon (GAC) or powdered activated carbon (PAC) filters (Eschauzier *et al.*, 2012; Rahman *et al.*, 2014; Zaggia *et al.*, 2016).

The presence of PFHpA precursors may complicate the water treatment process even further as the precursors may behave differently through the purification steps and may break down to PFHpA and its salts either during or after purification, or even as a consequence of the processes (biological and non-biological) used for treatment.

The methods available today to remove PFHpA from drinking water and lower the human exposure are expensive and not commonplace. The Swedish National Food Agency has recommended limits for drinking water based on the presence of 11 PFASs (PFBS, PFHxS, PFOS, 6:2 FTSA, PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA and PFDA)[8]. If the sum of these 11 PFASs occurs at concentrations greater than 0.09 µg/l, the Agency recommends that measures are taken as soon as possible to reduce the pollution. That PFHpA is specified as one of the 11 PFASs covered by the limit value, demonstrates that there is specific concern associated with this particular compound.

6.3.1.4 Long-range transport

Modelling and monitoring data indicate that the combination of extreme persistence and mobility lead to a high potential for long-range transport in the environment, which takes place via the atmosphere and oceanic currents. This may also apply to PFHpA-precursors to varying degrees. Occurrence of PFHpA in remote regions such as Arctic, Antarctic and at high altitude in remote areas of the European Alps has been confirmed by measurements in snow. PFHpA is detected in practically all compartments of the Arctic. Thus, vulnerable remote ecosystems are currently exposed to PFHpA.

6.3.1.5 Bioaccumulation and bioavailability

As indicated in section 6.2.1.2, PFHpA is very bioaccumulative in humans and in at least some other air-breathing mammalian species. Overall, taking all available information together in a weight-of-evidence approach, it is concluded that the vB criterion of REACH Annex XIII is fulfilled.

6.3.1.6 Enrichment in plants

Field irrigation with contaminated surface or ground waters and the use of contaminated sewage sludge as a soil conditioner are sources of PFASs to crops. Studies have demonstrated the uptake of PFHpA in crops including lettuce, tomato, carrots, corn, radish and soybeans (Blaine *et al.* (2013); Liu *et al.* (2022)). From the plants PFASs can transfer to humans and

[8] https://www.livsmedelsverket.se/en/business-legislation-and-control/legislation-food-business/drinking-water-production-and-control/t#Recommendation_-_the_risk_management_of_PFAS_in_drinking_water

wildlife through the food chain. Due to the uptake observed in crops, consumption of these by humans and wildlife will contribute to the total exposure to PFHpA and its salts.

6.3.1.7 Effects on human health

As mentioned in section 6.2.1.3, PFHpA is classified in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child') and STOT RE 1 (H373) (liver) and therefore, the toxicity criterion of REACH Annex XIII is fulfilled.

6.3.1.8 Environmental toxicity and secondary poisoning

The direct toxicity of PFHpA to aquatic and terrestrial species, such as algae, daphnids, fish, earthworms and plants, is assumed to be low and was not considered as the highest concern in the context of the present equivalent level of concern assessment. However, concern for secondary poisoning may be significant, as mammals show more toxic effects of PFHpA than lower organisms – the classification of PFHpA as Repro cat. 1B is based on clear reproductive effects in mice. Relatively stringent safety levels may result from the fact that a particular food item such as terrestrial plants and fish are often the sole energy source for a specific mammalian or avian species, leading to a relatively high PFHpA intake. Furthermore, the very high persistence and ubiquitous presence of PFHpA in surface waters and uptake in edible crops leads to a continuous, life-long exposure of environmental organisms. Hence, PFHpA exposure may be of concern to wildlife and secondary poisoning is therefore considered as a relevant endpoint for the equivalent level of concern assessment (see also section 5).

6.3.2 Concerns arising from the substance properties

6.3.2.1. Concern for an irreversible and increasing presence in the environment

The available information on physicochemical properties, persistence and environmental presence of PFHpA gives rise to concern that once the substance enters the environment, its presence will be irreversible. This concern is supported by the monitoring data on PFHpA, detecting this substance in -remote areas without any apparent emission source. The information provided in Section 3.1 and summarised in section 6.3.1.1 shows that the degradation potential of PFHpA in all environmental compartments can be concluded to be very low or negligible. Based on the available experimental and QSAR information on PFHpA, it is concluded that PFHpA meets the P and vP-criteria of REACH Annex XIII by far (see also section 6.2.2). This finding is also supported by read-across of available information on structurally related substances, and implies that PFHpA will remain in the environment for very long times, much longer than many other substances that are identified as exhibiting P or vP properties. This means that PFHpA may remain in the environment for such long times that it becomes increasingly difficult to predict possible effects from life-long exposures.

The concern is that as long as PFHpA releases to the environment continue, its presence may continue to increase and consequently, slowly increasing environmental concentrations may be unavoidable.

Monitoring data from all over the world show that PFHpA is very frequently detected in ground water, surface waters, drinking water (both tap and bottled) in or well above the ng/L ranges.
6.3.2.2. Decontamination of PFHpA from the environment and from drinking water

PFHpA predominantly resides in the aquatic compartment due to its low adsorption potential, high water solubility and low to moderate tendency to volatise from water to air. These properties make PFHpA (very) mobile in the aquatic environment and very difficult to remove from (contaminated) aqueous sites e.g., for drinking water remediation or groundwater clean-up. The usually applied techniques in wastewater treatment plants are not capable of removing PFHpA from the environment. Also for water treatment plants different studies show that even though different techniques are applied they do not effectively remove PFHpA from the water.

But also studies investigating more advanced treatment techniques show a lack of removal of PFHpA. Once PFHpA has entered the aquatic environment, e.g., surface waters, there are limited fate processes that would prevent it from being distributed to groundwater and to the marine environment.

6.3.2.3. Toxicity

PFHpA is classified for human health toxicity concerns as Repro 1b and STOT RE 1 (liver). The direct toxicity of PFHpA to aquatic and terrestrial species, such as algae, daphnids, fish, earthworms and plants, is assumed to be low and is not considered the highest concern in the context of the present equivalent level of concern assessment. However, concern for secondary poisoning may be significant, as mammals show more toxic effects of PFHpA than lower organisms – the classification of PFHpA as Repro cat. 1B is based on clear reproductive effects in mice.

6.3.2.4. Societal concern

Article 7.3 of the Water Framework Directive (2000/60/EC) stipulates that "Member States shall ensure the necessary protection for the bodies of water identified with the aim of avoiding deterioration in their quality of water to reduce the level of purification treatment required in the production of drinking water." Due to its mobility and persistence, PFHpA is found in groundwater, tap water and bottled water. Decontamination can only be achieved at high societal costs. Furthermore, PFHpA is classified as Repro 1b and STOT RE 1 (liver) and humans will be exposed via consumption and use of drinking water. Consequently, there is societal concern for the presence of PFHpA in drinking water that requires immediate action.

6.3.2.5. Continuous presence in water results in continuous exposure of humans and environment

Water is used for drinking and cooking each day and it is the basis of all food over the whole life of humans. That is why PFHpA presence in drinking water is of high concern.

In regard to the extreme persistence of PFHpA and its presence in the environment for decades the results of the toxicity studies may be of limited value as they do not regard cross generational effects. Additionally PFASs are continuously introduced into environment and are ubiquitously present in complex mixtures, including other highly similar PFAS substances, which is not covered by a single substance test. PFHpA has been measured in different species of wildlife, including polar bears. Polar bears are listed on the IUCN red list of threatened species. Monitoring data indicate that birds and mammals are of concern for uptake via fish/plants contaminated with PFHpA.

6.3.2.6. Concern for yet unknown effects and inability to derive a safe concentration in the environment

The high persistency and the lack of natural removal processes as well as the long elimination half-lives in some air-breathing mammal species raise the concern of yet unknown effects on the environment that were not observed in the standard toxicity tests (if they are available) or may only develop after life-long exposure. Indeed, the concern for effects that may emerge only after lifetime exposure is part of the concern for PBT/vPvB substances. ECHA Guidance R11, page 11 states "vPvB substances are characterised by a particular high persistence in combination with a high tendency to bioaccumulate, which may, based on experience from the past with such substances, lead to toxic effects and have an impact in a manner which is difficult to predict and prove by testing, regardless of whether there are specific effects already known or not." PFHpA meets the criteria as a PBT and vPvB substance.

Due to its high persistence, it will remain in the environment for a long time and due to its high water solubility and low adsorption potential, it will remain in the water compartment and will

be available for uptake by wildlife or humans. Furthermore, environmental concentrations will inevitably increase with continued release. However, there are currently no test systems available that are capable of detecting effects which may appear in long-living wildlife after lifelong (i.e. potentially decades of) exposure. Due to persistency of the substance, intergenerational effects may be possible. Drinking water protection requires protection of the water sources. For these reasons a safe concentration cannot be derived and a quantitative risk assessment cannot be performed.

6.3.2.7 Possibility for co-exposure with other -exposure with other PFECAs and PFASs

As is described in Section 4.9.1.4, monitoring data indicate that often more than one PFAS can be identified in environmental samples suggesting that PFASs are likely to co-occur as contamination in soil, groundwater or drinking water. Zeilmaker *et al.* (2018) derived so-called Relative Potency Factors (RPFs) for several perfluorocarboxylic acids (PFCAs), perfluorosulphonic acids (PFSAs) and PFHpA, to allow for risk assessment of combined toxicity to a mixture of PFASs based on the principle of dose-addition. This concept is developed assuming that these PFASs act in a similar manner, with the same mechanism/mode of action, resulting in dose-responses with the same shape but with different potencies for each of the individual substances. In principle, the RPF method scales the dose of each substance, according to its potency. Based on available subacute and subchronic oral toxicity studies in rodents, relative potency factors (RPFs) were derived for 20 individual PFASs, including PFHpA. From this work is derived that the potency of e.g. PFOA > PFTeDA ≥ PFHpA > PFHxA > PFHxDA > PFBS. Hence, based on the proposed RPFs for 20 PFASs in Zeilmaker *et al.* (2018), the combined effect on the liver can be estimated. Rushing et al. (2017) suggests that a similar exercise could be conducted for immune effects of PFCAs.
To conclude, PFHpA is contributing to the overall combined (additive) toxicity of the group of PFASs.

6.3.2.8 Overview of all concerns

The elements which are used for assessing the level of concern and description of how PFHpA compares to those elements are listed in Table 11.

Table 11. Overview of the qualitative components relevant for assessing the level of concern

Irreversibility of the exposure of wildlife and man via environment	PFHpA has high potential to cause irreversible exposures. The degradation potential of PFHpA in all environmental compartments can be concluded to be very low or negligible. Its high persistency implies that PFHpA will remain in the environment for much longer than most other substances that are identified as exhibiting P or vP properties. PFHpA by far exceeds the criteria for P and vP as laid down in Annex XIII of 1907/2006. Exposures are not expected to decrease upon cessation of releases because of the high persistence of the substance. In addition, the high potential to cause long-term exposures causes a difficulty to quantify exposures with sufficient certainty
Potential for rapid and wide geographic scale contamination	Due to the global water cycle and the fact that the aqueous compartments are all well connected, the high persistency and the high mobility of PFHpA lead to long distance transport processes in the environment. PFHpA has already been found at a diversity of locations in surface water, sea water, ground water and drinking water despite a limited number of known releasing sites.
Potential to continuous increase of exposures	PFHpA has a very high potential to cause an increasing pollution stock due to the combination of high persistence and difficulty of using end-of-pipe emission reduction measures (as a result of low adsorption potential, negligible degradation potential and the water solubility). Furthermore, as a mobile substance, there are no local or intermittent sinks for the pollution stock and therefore the substance has high potential to cause continuous increase of exposure of wildlife. Additionally, due to the inefficiency of decontamination and remediation

	techniques for this substance, it has a high potential to cause continuously increasing exposure of humans via environment. It is very difficult to remove PFHpA from water. Adsorption of PFHpA to soil, sediment and organic matter is very poor. Available techniques suggest that remediation of PFHpA containing water comes with high costs for society and the generation of serious amounts of waste from the water purification process. Removing PFHpA from the water compartment of the environment is considered impossible in practice due to the high mobility of the substance and the presence of diffuse emission sources as suggested by monitoring data
Potential for causing serious effects although those would not be observed in standard tests (including secondary poisoning)	Because PFHpA stays in the water phase, the whole released mass of the substance will be continuously bioavailable to organisms that live in water, organisms that drink water, plants that extract water from soil, animals that drink water and eat plants or water living organisms and humans who will be exposed e.g. through food and via drinking water. This in combination with the high potential to cause continuously increasing pollution stock (see above) trigger high potential for increased internal exposures and thereby a high likelihood of reaching levels which would cause effects and -in progress of time- serious effects even for endpoints where the substance would show a low or moderate intrinsic toxicity based on standard tests, or no effects at all. This mechanism also applies to secondary poisoning. Wildlife feeding on plants and fish which accumulate PFHpA may be susceptible to reaching effect levels.
Potential for causing serious effects on human health (known and unknown), and the environment (including the potential for irreversible effects)	PFHpA is classified for human health toxicity concerns as Repro 1b and STOT RE 1 (liver). The direct toxicity of PFHpA to aquatic and terrestrial species, such as algae, daphnids, fish, earthworms and plants, is assumed to be low and is not considered the highest concern in the context of the present equivalent level of concern assessment. However, concern for secondary poisoning may be significant, as mammals show more toxic effects of PFHpA than lower organisms – the classification of PFHpA as Repro cat. 1B is based on clear reproductive effects in mice.
Delay of effects	The highly mobile character of PFHpA together with its high persistence cause exposures that may occur with a delay, as measured from the moment of emission especially since PFHpA is a transformation product of commercially relevant PFAS precursors. It can be argued for PFHpA it is equally difficult to manage or prevent effects when exposure could occur with a delay, as it is difficult to manage or prevent effects that could occur after a short-time exposure.
Potential to cause combined effects (co-exposure)	PFHpA is expected to contribute to cumulative exposure with several other PFASs. Co-exposure may eventually occur and may last for a very long time as the natural degradation processes for these substances are slow or negligible.
Uncertainties in deriving safe concentration limits	The irreversibility and high potential for increasing exposures increases the potential of PFHpA to cause yet unknown health effects. This uncertainty is of concern for both human health and the environment. With time, effects may be discovered that may lead to more stringent safety levels for PFHpA. The derivation of safe exposure levels may therefore be possible in principle but is considered not to be of sufficient reliability
Uncertainties in quantifying exposures with sufficient certainty	Due to its high persistency and long-range transport potential a quantification of future exposures of PFHpA encompasses high uncertainties. There are no such exposure tools available which would with acceptable reliability predict exposures which would occur after decades of pile up and distribution of the substance. Also development of such estimation tools would take an unreasonable long time considering that the exposures are irreversible
Potential to impair humans and the environment at large	PFHpA has a very high potential to impair humans and the environment at large due to the combination of high potential of PFHpA to wide geographic scale contamination (as described above) and the high potential for causing serious effects although those would not be observed in standard tests (as described above). There are no natural barriers or environmental sinks that may reduce

	exposure, neither is it feasible to establish man-made barriers. Therefore the concern is that the mobility of PFHpA, in combination with its high persistence and possible adverse effects may eventually give rise to an uncontrollable and unpredictable risk for human health.
Inter-generational effects	PFHpA shows negligible or very slow degradation under environmentally relevant conditions and hence will remain in the environment for long periods of time, possibly stretching across generations. As such, effects of current emissions may be observed or only become apparent in next generations.
Societal concern	Art. 7.3 of the Water Framework Directive (2000/60/EC) stipulates that "Member States shall ensure the necessary protection for the bodies of water identified with the aim of avoiding deterioration in their quality of water to reduce the level of purification treatment required in the production of drinking water." The European drinking water association EurEau (2021) and several drinking water companies have indicated that they already detect pFAS including PFHpA in some of their drinking water sources and that the decontamination can only be achieved against high societal costs if at all. This shows the societal concern for the possible presence of PFHpA in drinking water that requires immediate action. Because of the high persistency and mobility, as well as transformation processes from PFHpA precursors, exposure will occur far away from the point of release. Effects may therefore come with a delay and will be difficult to manage in a timely manner.

6.3.3 Equivalent Level of Concern (ELoC) Assessment

The level of concern is considered very high due to the combination of the following concern elements:

- the high potential for irreversible exposure due to very high persistence and, in the case of human exposures via environment, the difficulty to decontaminate the drinking water,
- the high potential for increasing contamination and increasing, high bioavailability and difficulty to remove the substances after release,
- the high potential for rapid and wide geographic scale contamination,
- the high potential for causing serious effects,
- potential for inter-generational effects,
- high societal concerns.

6.3.4 Conclusion on the hazard properties and ELoC assessment

PFHpA is identified as substances of very high concern in accordance with Article 57(f) of Regulation (EC) 1907/2006 (REACH) because there is scientific evidence of probable serious effects to the environment and human health which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e) of Article 57 of REACH.

Intrinsic properties of PFHpA and its salts

Persistency
PFHpA and its salts is expected to undergo extremely limited degradation in the environment and thus fulfils the P- and vP- criteria in accordance with the criteria and provisions set out in Annex XIII of REACH.

Mobility
Due to its low to very low adsorption potential (log K_{oc} 1.63-1.7), high water solubility (salts

and dissociated form of PFHpA >1000 mg/L) and low tendency to volatise from water to air (Henry's Law constant of 6.38 $Pa \cdot m^3/mol$ for the ammonium salt). PFHpA predominantly resides in the aquatic compartment. These properties make PFHpA very mobile in the aquatic environment. Once PFHpA has entered the aquatic environment, e.g., surface waters, there are limited fate processes that would prevent it from being distributed to groundwater and to the marine environment. Monitoring data show that PFHpA or its salts has been detected in tap water, bottled drinking water and groundwater which supports the conclusion that PFHpA and its salts are mobile in water.

Removal from the environment and drinking water
Since PFHpA and its salts have a preference for the aqueous phase in the environment, the most important compartment for removal of PFHpA and its salts is water. The same properties that make PFHpA and its salts mobile in the environment are also the reason why their removal is challenging. Due to the high aqueous solubility and the low sorption potential, PFHpA and its salts will only bind to a low extent to adsorption materials and will rather remain in the water phase during the purification process.

PFHpA is not readily removed with conventional or advanced surface water treatment processes. The methods available today to remove PFHpA from drinking water and lower the human exposure are expensive and not commonplace. The presence of PFHpA precursors may complicate water treatment processes even further as the precursors may behave differently through the purification steps and may break down to PFHpA and its salts either during or after purification.

Long-range transport
Modelling and monitoring data indicate that the combination of extreme persistence and mobility lead to a high potential for long-range transport in the environment, which takes place via the atmosphere and oceanic currents. This may also apply to PFHpA-precursor substances to varying degrees. Occurrence of PFHpA in remote regions such as Arctic, Antarctic and high altitude remote areas in the European Alps has been confirmed by measurements in snow. PFHpA is detected in practically all compartments of the polar regions. Thus, vulnerable remote ecosystems are currently exposed to PFHpA.

Bioaccumulation and bioavailability
PFHpA is very bioaccumulative in humans and in at least some other air-breathing mammalian species. Overall, taking all available information together in a weight- of- evidence approach, it is concluded that the vB criterion of REACH Annex XIII is fulfilled.

Enrichment in plants
Studies have demonstrated the uptake of PFHpA in crops including lettuce, tomato, carrots, corn, radish and soybeans. From the plants PFASs can transfer to humans and wildlife through the food chain. Due to the uptake observed in crops, consumption of these by humans and wildlife will lead to inevitable exposure to PFHpA and its salts.

Toxicity
PFHpA is classified in the hazard class toxic for reproduction category 1B (H360D: 'May damage the unborn child') and STOT RE 1 (H373) (liver) and therefore, the toxicity criterion of REACH Annex XIII is fulfilled.

Environmental toxicity and secondary poisoning
The direct toxicity of PFHpA to aquatic and terrestrial species, such as algae, daphnids, fish, earthworms and plants, is assumed to be low and was not considered as the highest concern in the context of the present equivalent level of concern assessment. However, concern for secondary poisoning may be significant, as mammals show more toxic effects of PFHpA than organisms from lower trophic levels. Relatively stringent safety levels may result from the fact that a particular food item such as terrestrial plants and fish are often the sole energy source for a specific mammalian species, leading to a relatively high PFHpA intake. Hence, PFHpA

exposure may be of concern to wildlife. Secondary poisoning is therefore considered a relevant endpoint for the equivalent level of concern assessment.

Concerns arising from the substance properties

Several concerns are caused by these intrinsic properties of PFHpA and its salts. Overall, they have a very high potential to cause effects in wildlife and in humans exposed via environment, due to their persistence, mobility, potential for long-range transport, and toxicity. The very high persistence together with low adsorption potential and high mobility imply a very high potential for increasing pollution stock in the environment and for irreversible and increasing exposure of both wildlife and humans exposed via the environment. Also, their low adsorption potential and high water solubility imply that PFHpA and its salts are highly bioavailable for uptake via water. Together, these elements of concern lead to a very high potential for irreversible effects once effect levels have been reached, as well as an increasing seriousness of effects while exposures keep increasing.

Its properties make PFHpA (very) mobile in the aquatic environment and very difficult to remove from (contaminated) aqueous sites e.g., for drinking water remediation or groundwater clean-up. The usually applied techniques in wastewater treatment plants are not capable of removing PFHpA from the environment. Also for water treatment plants different studies show that even though different techniques are applied they do not effectively remove PFHpA from the water. But also studies investigating more advanced treatment techniques show a lack of removal of PFHpA. Once PFHpA has entered the aquatic environment, e.g., surface waters, there are limited fate processes that would prevent it from being distributed to groundwater and to the marine environment.

Due to its mobility and persistence, PFHpA is found in surface waters, groundwater, tap water and bottled water. Decontamination can only be achieved at high societal costs. Furthermore, PFHpA is classified as Repro 1b and STOT RE 1 (liver) and humans will be exposed via consumption and use of drinking water. Water is used for drinking and cooking each day and it is the basis of all food over the whole life of humans. That is why its presence in drinking water is of high concern. Consequently, there is societal concern for the presence of PFHpA in drinking water that requires immediate action.

Due to the extreme persistence of PFHpA and its very long presence in the environment, results of toxicity studies may be of limited value as they do not regard cross generational effects. Additionally PFASs are continuously introduced into aquatic ecosystems and are ubiquitously present in complex mixtures which is not covered by a single substance test. PFHpA has been measured in different species of wildlife, including polar bears which are listed on the IUCN red list of threatened species. Monitoring data indicates that birds and mammals show a concern for uptake via fish/plants contaminated with PFHpA. For these reasons also a safe concentration cannot be derived and a quantitative risk assessment cannot be performed.

Monitoring data indicate that often more than one PFAS can be identified in environmental samples suggesting that PFASs are likely to co-occur as contamination in soil, groundwater or drinking water. Literature indicates that different PFAS have similar, additive, effects, increasing the concern for serious effects in the environment.

Equivalent level of concern

The level of concern is considered very high due to the combination of the following concern elements:

- high potential for irreversible exposure due to very high persistence and, in the case of human exposures via environment, the difficulty to decontaminate the drinking water,
- high potential for increasing contamination and increasing fully bioavailable exposures, and the intrinsic properties cause difficulties to remove the substance after release,
- high potential for rapid and wide geographic scale contamination,

- high potential for causing serious effects (PFHpA fulfills the criteria for classification as Reprotoxic cat.1B and STOT-RE),
- potential to cause combined effects with other PFAS
- potential for inter-generational effects,
- high societal concerns.

The irreversibility of exposure to PFHpA due to its persistence adds to the concern. Furthermore, it may be difficult in practice to control exposure due to the high mobility of PFHpA (and its salts) and the fact that exposure may take place at a different location than where releases occurred and at a different moment in time. Furthermore, the high persistence and high mobility of PFHpA (and its salts) lead to a concern for co-exposure with other contaminants with similar health effects. Co-exposure may eventually occur and may last for a very long time, because natural degradation processes for these substances are slow or negligible. This is brought into the weight-of-evidence as supportive information.

Limitations of the available remediation techniques raise a concern that the removal of PFHpA and its salts from drinking water as well as waste water and, may only be possible with high societal costs. Remediation of environmental pollution may be practically impossible due to PFHpA's (and its salts) high solubility in water, its low adsorption potential and its high mobility. Remediation is also difficult because PFHpA (and its salts) will quickly diffuse from contaminated sites.

Therefore, the substances are identified as substances of equivalent level of concern having probable serious effects to the environment and human health to those of other substances listed in points (a) to (e) of Article 57 of Regulation (EC) No 1907/2006 (REACH) according to Article 57(f) of REACH Regulation.

Conclusion

In conclusion, perfluoroheptanoic acid and its salts meet the criteria for Reproductive toxicity according to Article 57(c) and PBT and vPvB substances according to Articles 57(d) and (e). The combined intrinsic properties which demonstrate scientific evidence of probable serious effects to human health and the environment and which give rise to an equivalent level of concern according to Article 57(f) are the following: very high persistence, high mobility in water, potential for being transported in the water phase over long distances, difficulty of remediation and water purification. The observed probable serious effects for human health and the environment are reproductive toxicity. However, the combination of substance properties may also lead to yet unknown environmental effects that are not detectable in standard toxicity tests and that may only emerge after life-long exposure. Together, these elements lead to a very high potential for irreversible effects.

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Annex I - Additional information on the read across approach

In general, the read-across approach can be applied for substances of which physicochemical and/or toxicological and/or ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity. Those substances may be regarded as a group or a category of substances, as indicated in Annex XI Section 1.5 of REACH. According to ECHA`s practical guide 6 "How to report read-across and categories" similarities may be due to a common functional group, common precursor or breakdown products, constant pattern in changing potency or common constituents or chemical class.

Category definition and its members

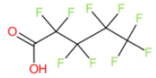
Category Hypothesis

The substances in the category are perfluorinated carboxylic acids (PFCAs) with C_4-C_{14} carbon chain lengths and HFPO-DA. The compounds in the category differ only in the number of carbon atoms in the fluorinated carbon chain, except for HFPO-DA that contains an ether bond in the perfluoro chain. The ether bond a perfluorinated carbon atom at each bond has a very high inertness to chemical and more importantly to biological transformations, comparable to the -CF_2- group itself. The ether bond does not change the steric conformation of the (perfluoro)carbon-chain as compared to PFCAs. The length of the C-O bond in the ether group is not very different from the length of the C-C bond in an (perfluoro)alkyl chain. Also, the angle of the C-O-C bond (~120 degrees) is close to the C-C-C bond in an alkyl chain of 109 degrees. The backbone of HFPO-DA consists of a perfluoropropylene group, ether bond and a perfluoro acetic acid group, and will therefore have approximately the same length as linear PFHxA and in structure resemble the branched form of PFHpA (2m-PFHpA). Considering the above, HFPO-DA and C_4- to C_{14}-PFCAs belong to the same chemical class and contain not only a common functional group but are highly similar according to their chemical structure as well as to their physico-chemical properties and toxicokinetics/environmental fate. The substances are thus expected to behave in a predictable manner and the category approach can therefore be used for read-across in a weight-of-evidence approach in the assessment of persistency and mobility.

Category members

In Table A.1 the chemical structures of HFPO-DA and C_4 to C_{14}-PFCAs are displayed. All contain a carboxylic acids group and a perfluorinated carbon chain. The compounds differ only in the number of carbon atoms within the fluorinated carbon chain. The exception being HFPO-DA that contains an ether bond.

Table A.1: CAS Numbers and structures of HFPO-DA and C_4- to C_{14}-PFCAs

EC name (abbreviation)	Structural Formula	EC number	CAS number
Heptafluorobutanoic acid (C_4-PFCA; PFBA)		206-786-3	375-22-4
Nonafluoropentanoic acid (C_5-PFCA; PFPeA)		220-300-7	2706-90-3
2,3,3,3-tetrafluoro-2-(heptafluoropropoxy) propionic acid, its salts and its acyl halides (HFPO-DA)		236-236-8	13252-13-6
Undecafluorohexanoic acid (C_6-PFCA; PFHxA)		206-196-6	307-24-4
Tridecafluoroheptanoic acid (C_7-PFCA; PFHpA)		206-798-9	375-85-9

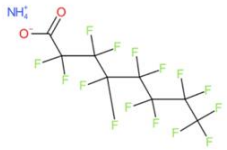
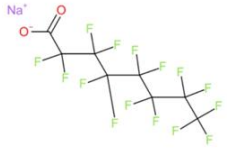
Ammonium pentadecafluorooctanoate (C_8-PFCA; APFO)		223-320-4	3825-26-1
Sodium pentadecafluorooctanoate (C_8-PFCA; NaPFO)		206-404-5	335-95-5
Pentadecafluorooctanoic acid (C_8-PFCA, PFOA)		206-397-9	335-67-1
Heptadecafluorononanoic acid (C_9-PFCA; PFNA)		206-801-3	375-95-1
Nonadecafluorodecanoic acid (C_{10}-PFCA,PFDA)		206-400-3	335-76-2

Table A.1 (continued): CAS Numbers and structures of HFPO-DA and C_4- to C_{14}-PFCAs

EC name (abbreviation)	Structural Formula	EC number	CAS number
Henicosafluoroundecanoic acid (C_{11}-PFCA; PFUnDA)		218-165-4	2058-94-8
Tricosafluorododecanoic acid (C_{12}-PFCA; PFDoDA)		206-203-2	307-55-1
Pentacosafluorotridecanoic acid (C_{13}-PFCA; PFTrDA)		276-745-2	72629-94-8
Heptacosafluorotetradecanoic acid (C_{14}-PFCA; PFTeDA)		206-803-4	376-06-7

Purity / Impurities

The PFCAs (including their salts) are monoconstituent substances with various degree of purity.

Category justification

The C_4- to C_{14}-PFCAs are similar in their functional groups (trifluoromethyl-, difluoromethylene- and carboxylic acid-), differing only in the carbon chain length (nr. of difluoromethylene groups, -CF_2-). HFPO-DA additionally has an ether bond, but as explained above HFPO-DA has approximately the same length as linear PFHxA and in structure and inertness to chemical biological transformation resembles the branched form of PFHpA. Therefore, there is a clear trend in chemical and physicochemical properties of all category members. Comparing the experimental and estimated data, it is clear that the behaviour of the PFCAs follows a regular pattern (Tables A.2).
The properties of one PFCA will be relatively similar to the PFCA with one more or one less difluoromethylene (-CF_2-) group.

Dissociation of PFCAs in aqueous media

Under environmental conditions in aqueous media the free perfluorinated carboxylic acids (PFCAs) are in equilibrium with their conjugate bases, the perfluorinated carboxylates. The fraction of each species depends on the acid dissociation constant (pKa) and the pH of the environmental compartment. Salts of PFCAs, which are sometimes used in laboratory experiments, will thus be in equilibrium with the corresponding acid in aqueous phases. Currently used techniques for analysis and quantification of PFCAs in environmental samples are not able to distinguish between the species. Therefore, reported concentrations always include the acids as well as the bases. If reported concentrations are used for the determination of bioaccumulation factors or for experiments determining the persistence, aqueous phase concentrations include both species. Experimental determination of pKa is difficult for PFCAs because of the surface active properties. Calculated pKa values are uncertain since it is unclear, for most of the models, whether PFCAs are within their applicability domain. For assessing the intrinsic properties of the PFCA within this dossier the exact knowledge of the fraction of each species is not required, because both species will be available independently from the starting conditions.

Physicochemical properties and partition coefficients of HFPO-DA, C_4-C_{14} PFCAs and some salts

The experimental determination of partition coefficients is difficult because of the surface-active properties of the ionic PFCAs. The presence of ionic PFCAs depends on the dissociation of PFCAs in aqueous media. Nevertheless, there are models available, e.g., COSMOtherm, calculating partitioning coefficients of neutral PFCAs. COSMOtherm is a quantum chemistry-based method that requires no specific calibration. This calibration would be difficult because of missing measured data of PFCAs. Therefore, COSMOtherm is expected to be able to estimate properties for PFASs. Studies have shown that properties estimated with COSMOtherm show good agreement with the experimental data for a number of per- and polyfluorinated chemicals, e.g., PFOA (Arp et al. 2006; Wang et al.2011)). Again, whether neutral PFCAs are present in aqueous media depends in the dissociation of the acids. Air-water as well as octanol-water partition coefficients are of course different for PFCAs with 8 to 10 carbon atoms but they show a clear increasing, trend with chain length (see Table A.2 below, (Wang et al. 2011)). This can be explained

by the increasing molecular volume with each additional CF_2-unit. The trend of the fate of PFCAs with chain length is supported by information on sorption of PFCAs on sediment. Sorption increases with increasing chain length (Higgins and Luthy, 2006) also under environmental conditions (Ahrens et al. 2010) (Table A.2).

Concluding remarks

To conclude, all data in Table A.2 are consistent with the hypothesis that the HFPO-DA and the C_4- to C_{14}-PFCAs behaviour follow a regular trend across the category which can be used in a weight-of-evidence approach in the PBT assessment.

Table A.2: Basic substance information and physical chemical properties relevant to justify read across in the PBT assessment

Abbreviation	C4-PFCA	C5-PFCA	HFPO-DA	C6-PFCA	C7-PFCA	C8-PFCA			C9-PFCA	C10-PFCA	C11-PFCA	C12-PFCA	C13-PFCA	C14-PFCA
Acronym	PFBA	PFPeA	HFPO-DA	PFHxA	PFHpA	PFOA	APFO	NaPFO	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
IUPAC Name	Butanoic acid, heptafluoro-	Pentanoic acid, nonafluoro-	2,3,3,3-Tetrafluoro-2-(heptafluoropropoxy)propanoic acid	Hexanoic acid, undecafluoro-	Heptanoic acid, tridecafluoro-	Octanoic acid, pentadecafluoro-	Ammonium pentadec a-fluoro-octanoate	Pentadeca octanoic acid sodium salt	Nonanoic acid, heptadeca - fluoro-	Decanoic acid, nonadeca - fluoro-	Undecanoic acid, heneicosa - fluoro-	Dodecanoic acid, tricosafluo ro-	Tridecanoic acid, pentacosa - fluoro-	Tetradecanoic acid, heptacosa - fluoro-
Chemical Structure	$CF_3(CF_2)_2$-COOH	$CF_3(CF_2)_3$-COOH	$CF_3(CF_2)_2O$ $CF(CF_3)COOH$	$CF_3(CF_2)_4$-COOH	$CF_3(CF_2)_5$-COOH	$CF_3(CF_2)_6$-COOH	CF3(CF2)6 - COO- NH4+	CF3(CF2)6-COO-Na+	$CF_3(CF_2)_7$-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 No	375-22-4	2706-90-3	13252–13–6	307-24-4	375-85-9	335-67-1	3825-26-1	335-95-5	375-95-1	335-76-2	2058-94-8	307-55-1	72629-94-8	376-06-7
Molecular Weight g/mol	214.04	264.05	330.06	314.05	364.06	414.07	431.1	436.05	464.08	514.08	564.0909	614.0984	664.1059	714.11
Partitioning Coefficient logKow	2.82 (calc., COSMOtherm , (Wang et al., 2011)) 3.39± 0.60 (calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02)	3.43 (calc., COSMOtherm , (Wang et al., 2011))	3.36 (Calc., EpiSuite v 4.11)	4.06 (calc., COSMOtherm , (Wang et al., 2011)) 4.13 (exp. value, MSDS LabNetwork)	4.67 (calc., COSMOtherm , (Wang et al., 2011)) 4.15 (calc., KOWWin v1.68, USEPA, 2002-2012).	5.30 (calc., COSMOtherm , (Wang et al., 2011))			5.9 (calc., COSMOtherm, (Wang et al., 2011)) 7.27 (Predicted using US EPA EPI-Suite (KOWWIN v1.67))	6.5 (calc., COSMOtherm, (Wang et al., 2011)) 7.667 (exp. value, MSDS LabNetwork)	7.2 (calc., COSMOtherm, (Wang et al., 2011)) 8.548 (exp. value, MSDS LabNetwork)	7.8 (calc., COSMOtherm, (Wang et al., 2011)) 9.429 (exp. value, MSDS LabNetwork)	8.25 (calc., COSMOtherm, (Wang et al., 2011))	8.90 (calc., COSMOtherm, (Wang et al., 2011)) 11.191 (exp. value, MSDS LabNetwork)
log K_{OA}	6.04 (calc., COSMOtherm, (Wang et al., 2011)) 4.45 (Calc., EpiSuite v 4.11)	6.33 (calc., COSMOtherm, (Wang et al., 2011)) 4.40 (Calc., EpiSuite v 4.11)	5.44 (Calc., EpiSuite v 4.11)	6.04 (calc., COSMOtherm, (Wang et al., 2011)) 4.35 (Calc., EpiSuite v 4.11)	6.92 (calc., COSMOtherm, (Wang et al., 2011)) 4.30 (Calc., EpiSuite v 4.11)	7.23 (calc., COSMOtherm, (Wang et al., 2011))			7.50 (calc., COSMOtherm, (Wang et al., 2011))	7.77 (calc., COSMOtherm, (Wang et al., 2011))	8.08 (calc., COSMOtherm, (Wang et al., 2011))	8.36 (calc., COSMOther m, (Wang et al., 2011))	8.63 (calc., COSMOther m, (Wang et al., 2011))	8.87 (calc., COSMOther m, (Wang et al., 2011))
log K_{AW}	-3.23 (calc., COSMOtherm , (Wang et al., 2011)) -2.31 (Calc., EpiSuite v 4.11)	-2.90 (calc., COSMOtherm , (Wang et al., 2011)) -1.59 (Calc., EpiSuite v 4.11)	-2.08 (Calc., EpiSuite v 4.11)	-2.58 (calc., COSMOtherm , (Wang et al., 2011)) -0.87 (Calc., EpiSuite v 4.11)	-2.25 (calc., COSMOtherm , (Wang et al., 2011)) -0.15 (Calc., EpiSuite v 4.11)	-1.93 (calc., COSMOtherm, (Wang et al., 2011))			-1.58 (calc., COSMOtherm, (Wang et al., 2011))	-1.27 (calc., COSMOtherm, (Wang et al., 2011))	-0.92 (calc., COSMOtherm, (Wang et al., 2011))	-0.58 (calc., COSMOtherm, (Wang et al., 2011))	-0.38 (calc., COSMOther m, (Wang et al., 2011))	0.03 (calc., COSMOtherm, (Wang et al., 2011))
Dissociation constant pKa	-1.07 (MarvinSketch v16.10.24)	0.32–0.42 (exp. value, potentiometric titration of aq. sol.; Cabala, 2017) 0.34 (MarvinSketch v16.10.24)	-0.77 (MarvinSketch v16.10.24)	-0.16 (Zhao et al., 2014) -0.78 (MarvinSketch v16.10.24)	-2.24 (MarvinSketch v16.10.24)	0.5 (Vierke et al., 2013) 2.5 (Ylinen et al., 1990) 2.8 in 50% aqueous ethanol (Brace, 1962) 1.3 (López-Fontán et al.,			<1.6 (Vierke et al., 2013) 0.82 (calc., COSMOther m, Wang et al., 2011) 2.58 (exp. value, measurement of the PFCAs solubility	<1.6 (Vierke et al., 2013) 2.58 (Moroi et al., 2001) 2.61 (exp. value, measurement of the PFCAs solubility change with pH; Cabala,	<1.6 (Vierke et al., 2013) 3.13 (exp. value, measurement of the PFCAs solubility change with pH; Cabala, 2017)			

Abbreviation	C4-PFCA	C5-PFCA	HFPO-DA	C6-PFCA	C7-PFCA	C8-PFCA			C9-PFCA	C10-PFCA	C11-PFCA	C12-PFCA	C13-PFCA	C14-PFCA
Acronym	**PFBA**	**PFPeA**	**HFPO-DA**	**PFHxA**	**PFHpA**	**PFOA**	**APFO**	**NaPFO**	**PFNA**	**PFDA**	**PFUnDA**	**PFDoDA**	**PFTrDA**	**PFTeDA**
						2005)			change with pH; Cabala, 2017)	2017)				
Partition coefficients log Kd (sediment and overlapping dissolved phase)				1.4 – 3.1 (Li et al., 2011)		0.04 (Ahrens et al., 2010)*			0.6 (Ahrens et al., 2010) *	1.8 (Ahrens et al., 2010) *	3.0 (Ahrens et al., 2010) *			
Log Koc (sediment organic carbon-normalized distribution coefficient)	1.81 (Calc., EpiSuite v 4.11, fragment method), 1.34 (Calc., EpiSuite v 4.11, based on log Kow)	2.46 (Calc., EpiSuite v 4.11, fragment method), 1.71 (Calc., EpiSuite v 4.11, based on log Kow)	2.48 (Calc., EpiSuite v 4.11, fragment method), 1.92 (Calc., EpiSuite v 4.11, based on log Kow)	1.63 – 2.35 (Sepulvado et al., 2011) 3.12 (Calc., EpiSuite v 4.11, fragment method), 2.08 (Calc., EpiSuite v 4.11, based on log Kow)	3.77 (Calc., EpiSuite v 4.11, fragment MCI method), 2.45 (Calc., EpiSuite v 4.11, based on log Kow)	2.06 (Higgins and Luthy, 2006) 1.09 (Ahrens et al., 2010) *			2.39 (Higgins and Luthy, 2006), 2.4 (Ahrens et al., 2010) *	2.76 (Higgins and Luthy, 2006), 3.6 (Ahrens et al., 2010) *	3.3 (Higgins and Luthy, 2006) , 4.8 (Ahrens et al., 2010) *			
Water solubility	316 mg/L (Calc., EpiSuite v 4.11, fragment method), 1373 mg/L (Calc., EpiSuite v 4.11, based on log Kow) 563 g/L (calc. COSMOtherm, Wang et al., 2011)	17 mg/L (Calc., EpiSuite v 4.11, fragment method), 197 mg/L (Calc., EpiSuite v 4.11, based on log Kow), 113 g/L (calc. COSMOtherm, Wang et al., 2011	17 mg/L (Calc., EpiSuite v 4.11, fragment method), 27 mg/L (Calc., EpiSuite v 4.11, based on log Kow)	15.7 g/L (25 °C) (Zhang et al., 2014) 0.85 mg/L (Calc., EpiSuite v 4.11, fragment method), 27 mg/L (Calc., EpiSuite v 4.11, based on log Kow), 22 g/L (calc. COSMOtherm, Wang et al., 2011	0.042 mg/L (Calc., EpiSuite v 4.11, fragment method), 3.6 mg/L (Calc., EpiSuite v 4.11, based on log Kow), 4.2 g/L (calc. COSMOtherm, Wang et al., 2011	9.5 g/L (25° C), (Kauck and Diesslin, 1951) 4.14 g/L (22°C), (Prokop et al., 1989) 0.77 g/L (calc. COSMOtherm, Wang et al., 2011	0.033 mol/L, 14.2 g/L at 2.5 °C (Nielsen 2012)	0.036 mol/L at 8.0 °C at critical micelle concentrati on (Nielsen 2012)	131 mg/L (calc. COSMOtherm, Wang et al., 2011	25 mg/L (calc. COSMOtherm, Wang et al., 2011	1.2E-4 g/L; pH 1 at 25°C 9.0E-4 g/L; pH 2 at 25°C 8.5E-3 g/L; pH 3 at 25°C 0.056 g/L; pH 4 at 25°C; 0.14 g/L; pH 5 at 25°C 0.16 g/L; pH 6-10 at 25°C (calculated), 4 mg/L (calc. COSMOtherm, Wang et al., 2011	2.9E-5 g/L pH 1 at 25°C 2.2E-4 g/L pH 2 at 25°C 2.0E-3 g/L pH 3 at 25°C 0.014 g/L pH 4 at 25°C; 0.034 g/L pH 5 at 25°C g/L pH 6 at 25°C g/L pH 7 at 25°C g/L pH 8-10 at 25°C (calculated), 0.7 mg/L (calc. COSMOtherm, Wang et al., 2011	7.3E-6 g/L; pH 1 at 25 °C 5.5E-5 g/L; pH 2 at 25 °C 5.1E-4 g/L; pH 3 at 25 °C 3.5E-3 g/L; pH 4 at 25 °C; 8.6E-3 g/L; pH 5 at 25 °C 0.0100 g/L; pH 6-10 at 25 °C (calculated), 0.1 mg/L (calc. COSMOtherm, Wang et al., 2011	1.9E-6 g/L; pH 1 at 25°C 1.4E-5 g/L; pH 2 at 25°C 1.3E-4 g/L; pH 3 at 25°C 9.3E-4 g/L; pH 4 at 25°C; 2.2E-3 g/L; pH 5 at 25°C 2.6E-3 g/L; pH 6-10 at 25°C (calculated), 0.02 mg/L (calc. COSMOtherm, Wang et al., 2011
Vapour pressure	2000 Pa (Calc., EpiSuite v 4.11); 3890 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011)	688 Pa (Calc., EpiSuite v 4.11); 1349 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011)	92 Pa (Calc., EpiSuite v 4.11)	263 Pa (Calc., EpiSuite v 4.11); 457 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011)	149 Pa (Calc., EpiSuite v 4.11); 158 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011) 17.7 Pa (US EPA Chemistry Dashboard	4.2 Pa (25 °C) for PFOA extrapolate d from measured data 2.3Pa (20 °C) for PFOA extrapolate d from measured data 128 Pa (59.3 °C) for PFOA measured	0.0081 Pa at 20 °C, calculated from measured data <0.1 hPa at 20 °C 0.012 Pa at 25 °C 0.0028 Pa at 25 °C (Nielsen 2012)		18 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011)	6.6 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011)	0.6 to 99.97 kPa (112 to 237.7°C) (calculated); 2.2 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011)	9.40E-3 Torr at 25°C(calcul ated); 0.7 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011)	3.59E-3 Torr at 25°C (calculated); 0.3 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011)	1.37E-3 Torr at 25 °C (calculated); 0.1 Pa (calc. from log pressure in liquid phase, COSMOtherm, Wang et al., 2011
Boiling point	123 °C	145 °C	187 °C	165 °C	185 °C	204 °C			218 °C (Yaws,	218 °C	238.4 °C	249 °C (SRC	260.7 °C	270 °C (Source

Abbreviation		C4-PFCA	C5-PFCA	HFPO-DA	C6-PFCA	C7-PFCA	C8-PFCA			C9-PFCA	C10-PFCA	C11-PFCA	C12-PFCA	C13-PFCA	C14-PFCA
Acronym		**PFBA**	**PFPeA**	**HFPO-DA**	**PFHxA**	**PFHpA**	**PFOA**	**APFO**	**NaPFO**	**PFNA**	**PFDA**	**PFUnDA**	**PFDoDA**	**PFTrDA**	**PFTeDA**
		(Calc., EpiSuite v 4.11); 120.0 °C (Cabala, 2017)	(Calc., EpiSuite v 4.11);	(Calc., EpiSuite v 4.11)	(Calc., EpiSuite v 4.11); 157 °C (Savu, 2010)	(Calc., EpiSuite v 4.11); 175 °C (Siegemund 2000)	(Calc., EpiSuite v 4.11); 189.0 °C (Cabala, 2017)			2008)	measured (Kauck and Diesslin, 1951)	(Kaiser et al., 2005) (calculated)	PhysProp Database)	(Calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02 (©1994-2012 ACD/Labs))	BIG –BIG)
Henrys Law constant		1.19E-004 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)	6.26E-004 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)	2.05E-004 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)	3.29E-003 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	1.73E-002 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10))	9.08E-002 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)			4.77E-001 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)	2.51E-000 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)	1.32E+001 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)	6.93E+001 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)	3.64E+002 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)	1.94E+008 atm-m3/mole at 25°C (Predicted using US EPA EPI-Suite (Bond Method, HENRYWIN v3.10)

*pH of the water samples analysed 7.1-8.3 Temp.: 15.3 – 17.7 °

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Annex II - OECD LRTP Tool calculation outcomes

OECD Pov & LRTP Screening Tool

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Overall Persistence POV (days)	Transport Potential CTD (km)	Transport Potential Transfer Efficiency (%)
128	26165	1.03E+02

	POV (days)	CTD in air (km)	CTD in water (km)	Surface Transfer Efficiency (%)
Emission to air	128	26165		1.03E+02
Emission to water	101		127	1.26E+01
Emission to soil	127			8.14E+01

Partition Coefficients:
LogKow = 0.33
LogKaw = -2.2

Half Lives (hours):
Air: 3120
Water: 1440
Soil: 4320

Bulk Compartment Properties	Volume (m3)	Depth (m)	Area (m2)	Density (kg/m3)	Z (mol/Pa.m3)	Equilibrium	Emission to air	Emission to water	Emission to soil
(1) Air	3.06E+18	6000	5.10E+14	1.185	4.03E-04	34.77%	60.31%	26.43%	54.54%
(2) Water	3.62E+16	100	3.62E+14	1000	6.39E-02	65.22%	39.68%	73.56%	41.83%
(3) Soil	1.48E+13	0.1	1.48E+14	1500	2.04E-02	0.01%	0.02%	0.01%	3.62%

Sub-compartment Properties	Volume (m3)	Vol Fraction	Fraction OC	Density (kg/m3)	Z (mol/Pa.m3)	Comp. Partitioning
(1,1) Air	3.06E+18	1	0	1.185	4.03E-04	100.00%
(3,1) Aerosols	6.12E+07	2E-11	0	2400	5.74E-02	0.00%
(2,2) Water	3.62E+16	0.9999995	0	1000	6.39E-02	100.00%
(3,2) Suspended sediment	1.81E+10	0.0000005	0.1	2400	1.15E-02	0.00%
(1,3) Soil air	2.96E+12	0.2	0	1.185	4.03E-04	0.40%
(2,3) Pore water	4.44E+12	0.3	0	1000	6.39E-02	93.98%
(3,3) Soil solids	7.40E+12	0.5	0.02	2400	2.30E-03	5.63%

Degrading Reactions	D (mol/Pa.h)	*k (h-1)*	*t1/2 (h)*	Eair Rate (mol/h)	water Rate (mol/h	Esoil Rate (mol/h)
(1,5) Air	2.74E+11	2.22E-04	3.12E+03	40.37	14.10	35.84
(2,5) Water	1.11E+12	4.81E-04	1.44E+03	57.55	85.02	59.57
(3,5) Soil	4.84E+07	1.60E-04	4.32E+03	0.01	0.00	1.72
Physical Removal						
(1,4,1) Air-Stratosphere	1.32E+10	1.07E-05	6.50E+04	1.94	0.68	1.72
(2,4,1) Water particle sinking	9.01E+04	3.89E-11	1.78E+10	0.00	0.00	0.00
(2,4,2) Water deep mixing	2.64E+09	1.14E-06	6.08E+05	0.14	0.20	0.14
(3,4,1) Soil convective sinking	7.71E+03	2.55E-08	2.71E+07	0.00	0.00	0.00
(3,4,2) Soil water leaching	2.84E+07	9.40E-05	7.38E+03	0.00	0.00	1.01
Mass balance check				100 : OK	100 : OK	100 : OK
Inter-compartment Exchange						
(1,2) Total air-water	6.02E+11	4.87E-04	1.42E+03	88.58	30.94	78.65
(1,3) Total air-soil	3.30E+09	2.67E-06	2.59E+05	0.49	0.17	0.43
(2,1) Total water-air	6.00E+11	2.59E-04	2.68E+03	30.96	45.74	32.04
(3,1) Total soil-air	2.38E+09	7.89E-03	8.78E+01	0.41	0.14	84.61
(3,2) Total soil-water	3.69E+08	1.22E-03	5.67E+02	0.06	0.02	13.10
(1,2,1) Air-water diffusion	6.00E+11	4.86E-04	1.43E+03	88.25	30.82	78.36
(1,2,2) Air-water dry deposition	4.49E+03	3.64E-12	1.91E+11	0.00	0.00	0.00
(1,2,3) Air-water rain dissolution	2.25E+09	1.82E-06	3.81E+05	0.33	0.12	0.29
(1,2,4) Air-water wet deposition	8.07E+03	6.53E-12	1.06E+11	0.00	0.00	0.00
(1,3,1) Air-soil diffusion	2.38E+09	1.93E-06	3.59E+05	0.35	0.12	0.31
(1,3,2) Air-soil dry deposition	1.83E+03	1.49E-12	4.67E+11	0.00	0.00	0.00
(1,3,3) Air-soil rain dissolution	9.17E+08	7.43E-07	9.33E+05	0.14	0.05	0.12
(1,3,4) Air-soil wet deposition	3.29E+03	2.67E-12	2.60E+11	0.00	0.00	0.00
(2,1,1) Water-air diffusion	6.00E+11	2.59E-04	2.68E+03	30.96	45.74	32.04
(3,1,1) Soil-air diffusion	2.38E+09	7.89E-03	8.78E+01	0.41	0.14	84.61
(3,2,1) Soil-water water runoff	3.69E+08	1.22E-03	5.67E+02	0.06	0.02	13.10
(3,2,2) Soil-water solids runoff	7.81E+03	2.59E-08	2.68E+07	0.00	0.00	0.00