

Annex XV report

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name(s): Perfluorohexane-1-sulphonic acid and its salts

EC Number(s): 206-587-1

CAS Number(s): 355-46-4

Submitted by: Swedish Chemicals Agency

Date: 2017-03-02

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ABBREVIATIONS

ADME	Adsorption, distribution, metabolism, and excretion
APFO	Ammonium perfluorooctanoate
B	Bioaccumulative
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BMF	Biomagnification factor
CLP	Classification, labelling and packaging
CMR	Carcinogenic, mutagenic and toxic for reproduction
EC	European Commission
EU	European Union
L-FABP	Liver fatty acid binding protein
P	Persistent
PBT	Persistent, bioaccumulative and toxic
PFAA	Perfluorinated alkyl acid
PFAS	Perfluoroalkyl and polyfluoroalkyl substances
PFBA	Perfluorobutanoic acid
PFBS	Perfluorobutanoic acid
PFCA	Perfluorinated carboxylic acid
PFDA	Perfluorodecanoic acid
PFDS	Perfluorodecanoicsulfonic acid
PFHpA	Perfluoroheptanoic acid
PFHxS	Perfluorohexanesulfonic acid
PFNA	Perfluorononanoic acid
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctanesulfonic acid
PFSA	Perfluorinated sulphonic acid
PFUnA	Perfluoroundecanoic acid
REACH	Registration, evaluation, authorisation and restriction of chemicals
SVHC	Substances of very high concern
TMF	Trophic magnification factor
vB	Very bioaccumulative
vP	Very persistent
vPvB	Very persistent, very bioaccumulative

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name(s): Perfluorohexane-1-sulphonic acid and its salts

EC Number(s): 206-587-1

CAS number(s): 355-46-4

- It is proposed to identify the substance(s) as very persistent and very bioaccumulative (vPvB) according to Article 57 (e) of Regulation (EC) No 1907/2006 (REACH).

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

As justified in Section 1, the abbreviation PFHxS refers to the acid Perfluorohexane-1-sulphonic acid (PFHxS) as well as to its salts, for instance ammonium and potassium salts are also covered by this abbreviation (PFHxS). PFHxS belongs to the group of perfluoroalkyl sulfonic acids (PFSA) in which perfluorooctanesulfonic acid (PFOS) is the most well-known and studied substance.

A read-across approach is taken between PFHxS and PFOS and long-chained PFCAs (see Annex I). PFHxS belongs to a group of perfluorinated substances of which several similar substances already have been assessed with respect to their POP- or PBT/vPvB-properties (see substances listed below). The substances in this group have a highly similar chemical structure with a perfluorinated carbon chain and a terminal acid group, sulphonic acid (PFSA) or carboxylic acid (PFCA) (see Annex I). The individual PFSA or PFCAs differ only in the number of CF₂-groups whereas all other fragments are the same.

The PFSA with C8-fluorinated alkyl chain; perfluorooctane sulphonic acid (PFOS), is a POP included on the UNEP POP-list of chemicals (UNEP, 2006). A substance fulfilling the POP-criteria fulfils also the vPvB-criteria of REACH ((EC, 2010a); (EC, 2010b)).

Eight entries of PFCAs have already been included into the Candidate List: the C8:s PFOA (ECHA, 2013b) and APFO (ECHA, 2013a), the C9 PFNA (ECHA, 2015) and the C10 PFDA (ECHA, 2016b) as PBT, and the C11 PFUnDA (ECHA, 2012a), the C12 PFDoDA (ECHA, 2012d), the C13 PFTrDA (ECHA, 2012c) and the C14 PFTeDA (ECHA, 2012b) as vPvB. Note that whether the vB criterion is fulfilled or not for the C9 PFNA or C10 PFDA was never assessed ((ECHA, 2016b), (ECHA, 2015)).

vPvB:

A weight-of-evidence determination according to the provisions of Annex XIII of REACH is used to identify the substance as vPvB. All available relevant information, such as the results of standard tests, monitoring and modelling, information from the application of

read-across and (Q)SAR results, was considered together in a weight-of-evidence approach.

Persistence

PFHxS has a stable perfluorinated structure and is not expected to undergo abiotic degradation under relevant environmental conditions. An available phototransformation study in water (Taniyasu, Yamashita, Yamazaki, Petrick, & Kannan, 2013), which found negligible degradation via photolysis, supports this understanding. There is no study available on biodegradation, so data from structurally similar compounds are therefore used in a read-across approach (see Annex I). A read-across with PFOS is applied for biodegradation screening test and a read-across with PFOS and PFOA is applied for the simulation tests (in water, sediment and soil).

The persistence of PFSA and PFCA can, in general, be explained by the shielding effect of the fluorine atoms, blocking e.g. nucleophilic attacks on the carbon chain. High electronegativity, low polarisability and high bond energies make highly fluorinated alkanes extremely stable organic compounds. It is not expected that the sulphonic group in PFSA alters the persistence of these chemicals. The persistence of PFOS and the eight entries of PFCA included into the Candidate List (ECHA, 2012a-d, 2013a-b, 2015b, 2016b) has already been confirmed.

Therefore, based on the knowledge of the stability of the C-F bond and the read-across approach with PFOS and PFOA, it is concluded that PFHxS 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.

Bioaccumulation

The reported BCFs and BAFs for PFHxS are below the numerical criteria 2000/5000 in REACH Annex XIII, but it is worth noting that one of the BAF values (European chub, BAF plasma) is close to the threshold of 2000 (log BAF of 3.3 equivalent to a BAF of 1995). The latter value suggests that the substance is a borderline B for some aquatic species. In addition, due to the surface active properties of the substance the appropriateness of the available BCF test and the usefulness of its result may be questioned. Further, PFHxS is expected to quickly be excreted in fish via gill permeation like the other PFSA and PFCA, due to its expected notable water solubility. PFHxS, like other PFSA and PFCA, do not follow the behaviour of traditional hydrophobic compounds with partitioning into fatty tissues, but instead bind to proteins in blood and liver. Hence, bioconcentration in gill breathing organisms and the accumulation in lipids is not the most relevant endpoint to consider for these types of substances. Field studies show that air-breathing organisms are more likely to bioaccumulate PFHxS and other PFAS compared to water breathing organisms. Therefore, the numerical bioaccumulation (B)/(vB) criteria defined for aquatic species in the REACH regulation Annex XIII (sections 1.1.2 and 1.2.2) are not suitable to assess the bioaccumulation potential of PFHxS.

REACH Annex XIII (section 3.2.2) defines information which shall be taken into account in the B assessment and can and should be used to draw conclusions in a weight-of-evidence approach. In addition to BCF-data, such data are based on Section 3.2.2(b) of Annex XIII to REACH, for example, data on the bioaccumulation potential in terrestrial species, such as elevated levels in endangered species. PFHxS was found in terrestrial species as well as in endangered species as shown in section 3 for the polar bear. The highest concentrations of PFHxS detected in wildlife have been observed in the arctic top predator polar bear (>500 µg/kg in polar bear liver). This finding and the high

concentrations of PFHxS found in humans exposed to contaminated drinking water (up to 1790 µg/L in blood serum) show that exposure to PFHxS has the potential to result in high concentrations in biota including humans. These findings indicate a bioaccumulation potential and are of high concern.

Furthermore, Annex XIII (section 3.2.2 (b)) requires to consider data from human body fluids or tissues and to take the toxicokinetic behaviour of the substance into account. Both gestational and lactational exposure in humans have been shown for PFHxS. On top of that, data from human body fluids clearly provide quantitative proof of the bioaccumulation of PFHxS: Elimination half-lives in humans range from 7-8 years and above. Data from time trend studies on human samples indicate that the bioaccumulation of PFHxS even exceeds that of PFOS.

Finally, Annex XIII (section 3.2.2 (c)) foresees that the potential for biomagnification in food chains of a substance is assessed, as part of a weight-of-evidence approach. It is not possible to draw a conclusion on trophic magnification for PFHxS due to limited reliability of the available data. However, the available field data provide biomagnification factors (BMFs) for several predator/prey relationships for PFHxS. In air breathing predators the resulting BMFs are larger than 1, especially for polar bears suggesting a potential of biomagnification that is supported by monitoring data.

The elimination half-life of PFHxS in species are similar to that of PFOS in mice, male rats, pigs, monkeys and humans. The elimination half-lives observed for PFHxS in pigs, monkeys and humans are the longest observed for any PFAS, followed by those for PFOS. The main reason why e.g. PFOA was considered to meet the B-criterion of REACH was that it was concluded to bioaccumulate in humans based e.g. on its presence in human blood of the general population, the long elimination half-life in human blood of 2-4 years and that the levels increase with age (ECHA, 2013b). This holds true also for PFHxS but it has an elimination half-life in human blood of ca 7-8 years (or longer), which is at least 2-4 times longer than the elimination half-life of PFOA.

Depending on the type of substance, the process driving the bioaccumulation will differ, from hydrophobic partitioning to species and gender specific ADME-properties. Elimination half-lives are recognised as relevant bioaccumulation metrics ((Gottardo, Hartmann, & Sokull-Kluttgen, 2014), (ECHA, 2013b)) and PFHxS has in comparison with PBT/vPvB and POP-substances among the longest human elimination half-lives reported.

The information summarised above is in high accordance with the bioaccumulation data on PFOS, the bioaccumulation potential of which corresponds to "vB" as it is included under the Stockholm Convention. A read-across to PFOS (Annex I) is performed as part of the weight-of-evidence.

Conclusion:

1. PFHxS accumulates in humans
 - a. PFHxS is present in human blood of the general population
 - b. Time trend studies indicate that the human bioaccumulation potential of PFHxS may even be larger than that of PFOS.
 - c. The human elimination half-life for PFHxS is > 7 years which is the longest of all perfluoroalkyl and polyfluoroalkyl substances (PFAS) for which data are available. It is also comparable to the longest human elimination half-lives recorded for known PBT/vPvB- and POP-substances such as some PCBs.
2. There is evidence that PFHxS preferentially bioaccumulates in air-breathing mammals, including endangered species and humans
 - a. BMFs (polar bear/seal liver) range from 20 to 373

- b. It accumulates in the air-breathing food chains at least as much as PFOS, and more than the long-chained PFCAs which have already been identified as vB on the Candidate List.
 - c. It is not possible to conclude on TMF on aquatic foodweb containing air-breathing mammals due to the limited reliability of the available data
 - d. Elevated levels of PFHxS have been measured in both humans (up to 1790 µg/L in blood serum) and wildlife (>500 µg/kg in polar bear liver) showing that exposure to PFHxS has the potential to result in high levels in biota.
3. Even if PFHxS appear to be a borderline “B” in some water breathing animals, bioaccumulation potential of PFHxS in water breathing animals is not expected to be very high since PFHxS can be quickly excreted in fish via gill permeation like the other PFSAs and PFCAs, due to its notable water solubility (2.3 g/L).
- a. BCF range from 9.6 (whole body) to 100 (liver)
 - b. Whole body BAFs range from 380 (fish, crab) to 1995 (fish)
 - c. Whole body BMFs range from 0.14 (fish, lab data) to 10 (fish, field data).
 - d. It is not possible to conclude on TMF on water breathing aquatic foodwebs due to the limited reliability of the available data

To conclude, taking all available information together in a weight-of-evidence approach, and particularly considering the very long human elimination half-life and the indication of field bioaccumulation which may be even higher than for PFOS and the long-chained PFCAs which have already been identified as vB, it is proposed that PFHxS fulfils the vB criterion of REACH Annex XIII.

Conclusion on vPvB

In conclusion, PFHxS is identified as a vPvB substance according to Art. 57(e) of REACH by comparing all relevant and available information listed in Annex XIII of REACH with the criteria set out in the same Annex, in a weight-of-evidence determination.

Registration dossiers submitted for the substance? No

PART I

Justification

1. Identity of the substance and physical and chemical properties

Perfluorohexanesulfonic acid (PFHxS) belongs to the group of perfluoroalkyl sulfonic acids (PFSA) in which perfluorooctane sulfonic acid (PFOS) is the most well-known and studied substance.

The free perfluorohexanesulfonic acid (PFHxS) stays in equilibrium with perfluorohexanesulfonate (PFHxS⁻), the conjugate base, in aqueous media in the environment and in organisms, as well as in the laboratory. The physico-chemical properties of PFHxS and PFHxS⁻ are different. Therefore, the expected environmental fate will depend on the environmental conditions, which influence the equilibrium between base and acid (pH and pKa). However, as sulphonic acids are strong acids, they will be dissociated at environmental conditions (estimated pKa:s range from -5.8 to 0.18).

It can be based on, e.g. the OECD inventory of PFAS ((OECD, 2007)), be assumed that there are several inorganic salts of PFHxS available on the global market. Two of these are found in the ECHA CLP notification database - the ammonium (PFHxS·NH₄) and potassium (PFHxS·K) salts of PFHxS. Inorganic salts of PFHxS can be assumed to be very soluble in water. Both PFHxS·NH₄ and PFHxS·K are very soluble in water and will in aqueous solutions be present as the anion PFHxS⁻ and the ammonium or the potassium cation. The dissolved anion PFHxS⁻ will in aqueous media stay in equilibrium with the corresponding acid (PFHxS).

It is not possible with available methods for direct quantification of species to get accurate distinction between PFHxS⁻ and PFHxS in samples. In the literature, the concentrations reported in environmental and human monitoring studies will always include both species (PFHxS⁻ and PFHxS).

PFHxS will in the following refer to both the acid (PFHxS) and to its conjugate base PFHxS⁻. It will only be clearly indicated which of the acid PFHxS or the conjugate base PFHxS⁻ that is meant where it is important to distinguish between both species and when species-specific information is available.

The assessment only covers the linear isomer of the substance.

For simplicity, in the discussions and conclusions in this document, PFHxS is usually referred to. Based on the reasoning above, the conclusions are, however, considered valid for PFHxS salts as well.

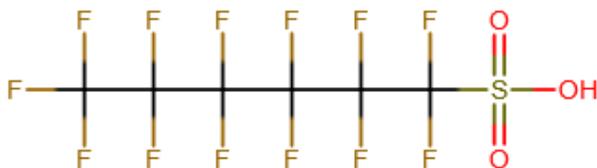
1.1 Name and other identifiers of the substance

The proposal addresses perfluorohexane-1-sulphonic acid and its salts. However, the information in **Table 1** refers specifically to the substance identity information of the perfluorohexane-1-sulphonic acid.

Table 1: Substance identity

EC number:	206-587-1
EC name:	Perfluorohexane-1-sulphonic acid
CAS number (in the EC inventory):	355-46-4
CAS name:	1-Hexanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-
IUPAC name:	1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluorohexane-1-sulfonic acid
Index number in Annex VI of the CLP Regulation	-
Molecular formula:	C ₆ HF ₁₃ O ₃ S
Molecular weight range:	400.11 g/mol
Synonyms:	Perfluorohexanesulfonic acid; 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro- Tridecafluorohexane-1-sulfonic acid; Tridecafluorohexane-1-sulfonic acid; 1-Hexanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-; 1,1,2,2,3,3,4,4,5,5,6,6,6-Tridecafluoro-1-hexanesulfonic acid; Tridecafluorohexanesulfonic acid

Structural formula:



1.2 Composition of the substance

Name: Perfluorohexanesulfonic acid (PFHxS)

Description: Mono-constituent substance

Substance type: Mono-constituent substance

Degree of purity: 80-100 %

Perfluorohexanesulfonic acid, as well as its salts are assessed in this report as mono constituent substances of high purity. The information presented for PFHxS in the following sections can be assumed to be representing pure PFHxS with no inference of impurities.

The identification as SVHC is based on the properties of the main constituent only. Therefore, in this case, other possible constituents or impurities are not relevant for the identification as SVHC.

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

A read-across approach between PFHxS, PFOS and long-chained PFCAs. Please see Annex I for the read-across justification.

Table 2. Structurally related substance(s) identity – Long Chain PFSA

Acronym	PFOS
EC number:	217-179-8
EC name:	Heptadecafluorooctane-1-sulphonic acid
SMILES:	<chem>O=S(=O)(O)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)F</chem>
CAS number (in the EC inventory):	1763-23-1
CAS name:	1-Octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-
IUPAC name:	1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluorooctane-1-sulfonic acid
Index number in Annex VI of the CLP Regulation	607-624-00-8
Molecular formula:	C ₈ HF ₁₇ O ₃ S
Molecular weight range: (g/mol)	500.13
Synonyms:	PFOS C ₈ -PFSA
Length of carbon chain	8

1.4 Physicochemical properties

Perfluorohexanesulfonic acid (PFHxS) is a strong acid which has a fully fluorinated six carbons long chain, making it both oil- and water repellent (Kissa, 2001). Not much else is known about the specific physicochemical properties of PFHxS. However, there are some characteristics which are valid for the whole group of perfluoroalkylated substances (PFAS), and therefore also PFHxS. PFAS are very resistant to chemical, thermal and biological degradation due to their strong carbon-fluorine bonds (Kissa, 2001). It is this resistance to degradation that makes many of them persistent in the environment.

Due to the scarcity of experimental values for PFHxS, estimated values are used instead. However, since PFHxS is a strong acid, which is fully dissociated in the environment, the predictions made for the neutral (non-ionised) species are uncertain. The relevance of the log K_{ow} and log D is questionable due to the surface active properties of the substance. A discussion on the reliability of the predictions is included in Annex I.

Table 4: Overview of physicochemical properties (PFHxS)

Property	Value [Unit]	Reference/source of information	Comment (e.g. measured or estimated)
Physical state at 20°C and 101.3 kPa	<i>Solid</i>	<i>(Company, 2013)</i>	<i>From MSDS for perfluorohexanesulfonic acid potassium salt</i>
Melting/freezing point (°C)	272-274	<i>(Company, 2013)</i>	<i>From MSDS for perfluorohexanesulfonic acid potassium salt</i>
Boiling point (°C)	<i>No data</i>	-	
Vapour pressure (Pa)	58.9	<i>(Wang, MacLeod, Cousins, Scheringer, & Hungerbühler, 2011)</i>	<i>Calculated from log pressure in liquid phase (log P_L) values. Estimated for neutral species.</i>
Density	<i>No data</i>	-	
Water solubility (g/L)	2.3	<i>(Z. Wang et al., 2011)</i>	<i>Estimated for neutral (non-ionised) species using COSMOtherm.</i>
Partition coefficient n-octanol/water (log value)	<i>Not applicable</i> 5.17	<i>ATSDR (2009)</i> <i>(Z. Wang et al., 2011)</i>	<i>"The log K_{ow} is not measurable since these substances are expected to form multiple layers in an octanol-water mixture."</i> <i>Estimated for neutral (non-ionised) species using COSMOtherm.</i> <i>PFHxS has surface active properties.</i>

Partitioning coefficient octanol/water (log D_{ow})	-2.75	(Danish (Q)SAR Database, 2015)	Estimated, ACD Labs/ToxSuite 2.95.1 Ionisation/LogD, at pH 1-9 PFHxS has surface active properties.
Partitioning coefficient octanol-air (log K_{OA})	7.55	(Z. Wang et al., 2011)	Estimated for neutral (non-ionised) species using COSMOtherm.
Partitioning coefficient air-water (log K_{AW})	-2.38	(Z. Wang et al., 2011)	Estimated for neutral (non-ionised) species using COSMOtherm.
Dissociation constant pK_a	-3.45 -5.8 ± 1.3	(Z. Wang et al., 2011) (Danish (Q)SAR Database, 2015)	Estimated for neutral (non-ionised) species using COSMOtherm. Estimated, ACD Labs/ToxSuite 2.95.1 Ionisation/pKa Dissociation behaviour discussed in Annex I.

Physical-chemical properties of PFOS and the C₈-C₁₄-PFCAs are provided in Table 11 in Annex 1. Note: Data on PFCAs in table 11 are from the SVHC-support document on PFNA.

2. Harmonised classification and labelling

There is no harmonised classification available for PFHxS.

3. Environmental fate properties

3.1 Degradation

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 envelope 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 the most 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.

3.1.1 Abiotic degradation

3.1.1.1 Hydrolysis

There are no available studies on hydrolysis for PFHxS.

The analogue PFOS is hydrolytically stable under environmental conditions with a half-life set to be greater than 41 years (UNEP, 2006). The related substance PFOA is also hydrolytically stable under environmental conditions with a half-life set to be greater than 92 years (ECHA, 2013b).

PFHxS is considered to be hydrolytically stable under environmental conditions based on the well-known stability of the CF-bonds of PFHxS and the read-across to PFOS and PFOA (Annex I).

3.1.1.2 Phototransformation/photolysis

3.1.1.2.1 Phototransformation in air

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

Using AOPWIN v1.92 to predict the atmospheric half-life for PFHxS results in an estimated half-life of 76.4 days (12.hr day; $1.5E6$ OH/cm³)

Using AOPWIN v1.92 to estimate the atmospheric half-life of PFOS and PFOA results in the estimated half-lives 76.4 days and 20.6 days, respectively.

PFOS, which is considered to fulfil the POP-criteria, has an expected half-life greater than two days (UNEP, 2006). PFOA has a predicted atmospheric half-life of 130 days (conclusion by analogy from short-chain perfluorinated acids) (ECHA, 2013b).

It can be based on a read-across to PFOS and PFOA (Annex I) be expected that PFHxS has an atmospheric half-life exceeding two days. The AOPWIN-predictions can add to the weight-of-evidence that PFHxS has an atmospheric half-life exceeding two days.

3.1.1.2.2 Phototransformation in water

Taniyasu and co-workers (2013) performed a field study on photolysis of several PFAS,

including PFHxS, at high altitude in Mt. Mauna (Hawaii, USA; 4200 m; September 10, 2010 - December 24, 2010) and Mt. Tateyama (Toyama, Japan; 2500 m; 20.5 h 17-18 April, 2011). The individual PFAS were dissolved in methanol and diluted in 10 mL of Milli-Q water. The final concentration of PFHxS was 2.86 µmol/L with a methanol content in the test solution < 2%. No significant photolysis was observed for PFHxS, PFETs, PFPrS, PFBS and PFBA at Mt. Mauna or Mt. Tateyama, while other PFAS showed some level of degradation. The percentage reduction in concentration, in comparison with the original concentrations for some of the PFAS at Mt. Mauna Kea/Mt. Tateyama were as follows: PFOS-29%/15%, PFDS-53%/31%, PFOA-5%/negligible, PFDA-35%/30% and PFNA-19%/26%. The long chain PFAS (PFOS, PFDS, PFNA and PFDA) degraded at higher proportions than shorter chain PFAS (<C₆) and PFCAs (<C₈). This indicates that PFHxS is negligibly degraded via photolysis.

Another study on photolysis conducted on the analogue PFOS found no evidence of direct or indirect photolysis under any of the conditions tested and the indirect photolytic half-life of PFOS at 25 °C was estimated to exceed 3.7 years (UNEP, 2006).

The related substance PFOA does not undergo direct photodegradation in natural waters and the estimated half-life for indirect photolysis (addition of Fe₂O₃) exceeds 349 days (ECHA, 2013a).

3.1.1.3 Summary on abiotic degradation

In general, PFASs and PFCAs are extremely stable. There is only one relevant abiotic degradation study available for PFHxS, the photolysis study by Taniyasu et al. (2013) which found no significant degradation of PFHxS but some degradation of the generally extremely stable PFOS and PFOA.

The data on PFOS on abiotic degradation in the atmosphere was considered to fulfil the POP-criteria of an expected half-life exceeding two days. PFOS is hydrolytically stable under environmental conditions with a half-life > 42 years and a study on photolysis found no evidence of direct or indirect photolysis under any of the conditions tested and an indirect photolytic half-life was estimated to exceed 3.7 years.

Based on the read across rationale described in Annex I, experimental data on PFHxS and PFOS and the knowledge of the high stability of the C-F bond can be used as evidence for PFHxS to conclude that it is stable under environmental conditions and abiotic degradation is expected to be as low as for the chemically similar substance PFOS.

3.1.2 Biodegradation

3.1.2.1 Biodegradation in water

3.1.2.1.1 Estimated data

According to the REACH Guidance R.11: PBT/vPvB assessment ((ECHA, 2014)) the output of the models BIOWIN 2, BIOWIN 3 and BIOWIN 6 of the software BIOWIN can be used to give a screening assessment of persistence. The following outcome indicate that a substance may be persistent: BIOWIN 2 < 0.5 and BIOWIN 3 < 2.2 (to 2.75*) or BIOWIN 6 < 0.5 and BIOWIN 3 < 2.2 (to 2.75*). (**For substances fulfilling this but BIOWIN indicates a value between 2.25 and 2.75 more degradation relevant information is generally warranted*)

BIOWIN v4.10 results in the following prediction for PFHxS:
BIOWIN 2 = 0.0000

BIOWIN 3 = 0.9340

BIOWIN 6 = 0.0000

PFHxS can, based on the above BIOWIN predictions, be said to fulfil the P-screening criteria.

The corresponding BIOWIN v4.10 predictions for the structural analogue PFOS are:

BIOWIN 2 = 0.0000

BIOWIN 3 = 0.2887

BIOWIN 6 = 0.0000

PFOS can, based on the above BIOWIN predictions, be said to fulfil the screening criteria for persistence.

Not all of the molecular fragments of the molecule are included in the training sets of the model. The confidence that may be put on BIOWIN predictions under such circumstances would not be clear in case no other information would be available for the substance as such or relevant analogues (if such are available). However, in this case the missing molecular fragment holds true not only for PFHxS but also for the close structural analogue PFOS, which is an agreed persistent substance (UNEP, 2006). The screening assessment on persistence on PFHxS, based on BIOWIN predictions, can add to the weight-of-evidence that PFHxS is persistent.

3.1.2.1.2 Screening tests

There are no experimental ready biodegradation tests available for PFHxS.

Based on the data given in Annex I, results of studies of the structurally similar substances can be used to evaluate the biodegradation of PHxS.

The analogue PFOS have been found to be not readily biodegradable (UNEP, 2006), as have PFOA (ECHA, 2013a).

In summary, based on the general stability of PFSAs and PFCAs towards degradation and the read across to PFOS (Annex I) and PFOA (Annex I), PFHxS is considered to be not readily biodegradable.

3.1.2.1.3 Simulation tests (water and sediments)

There are no experimental simulation tests (water and sediment) available for PFHxS.

The PFCA PFOA has been found to meet the criteria for being persistent and very persistent in simulation tests (ECHA, 2013a).

In summary, based on the general stability of PFSAs and PFCAs towards degradation and the read across to PFOA (Annex I), PFHxS is considered to meet the criteria for being persistent and very persistent in water and sediments.

3.1.2.2 Biodegradation in soil

There are no experimental soil degradation tests available for PFHxS.

The analogue PFOS have been found to be persistent in soil cultures (UNEP, 2006), as has

PFOA which has been found to meet the criteria for being persistent and very persistent (ECHA, 2013a).

In summary, based on the general stability of PFSAs and PFCAs towards degradation and the read across to PFOS (Annex I) and PFOA (Annex I), PFHxS is considered to meet the criteria for being persistent and very persistent in soil.

3.1.2.3 Summary and discussion on biodegradation

PFHxS fulfil the ECHA screening persistence criteria using BIOWIN predictions.

There are no available experimental biodegradation data in water or soil for PFHxS. However, results for PFOS and PFOA used in a read-across approach as described in Annex I indicate that PFHxS is not readily biodegradable.

Biodegradation of the structural analogue PFOS have been evaluated in a number of tests in several studies. Aerobic biodegradation has been tested in activated sewage sludge, sediment cultures and soil cultures. Anaerobic biodegradation has been tested in sewage sludge. PFOS did not in any of these tests show any sign of biodegradation (UNEP, 2006). The very persistence (vP) of PFOA in water, sediment and soil has also been confirmed (ECHA, 2013a).

Since the stability of PFSAs is in general based on the stability of the fluorinated carbon chain, it can also for PFHxS be concluded that no biodegradation can be expected in water, soil or sediment. Thus, it can be assumed that PFHxS is not biodegradable and is very persistent in water soil and sediment.

3.1.3 Summary and discussion of degradation

PFSAs are synthetic compounds which contain a common structural feature: a perfluorinated carbon chain combined with a sulphonic group. The chemical structure of these compounds differs only in the number of perfluorinated carbons in the carbon chain. Generally, it is known that the bond between carbon and fluorine is one of the most stable ones in organic chemistry and not subject to degradation by microorganisms occurring in the environment.

There is one abiotic degradation study on photolysis available for PFHxS (Taniyasu et al., 2013), which indicates that PFHxS is negligibly degraded via photolysis, but there is no study available on biodegradation. Data from structurally similar compounds are therefore considered in a read-across approach (see Annex I for further details).

A read-across with PFOS is applied for biodegradation screening test and a read-across with PFOS and PFOA is applied for the simulation tests (in water, sediment and soil)

A number of studies for the longer chain homologue PFOS show that this substance is extremely persistent and does not undergo abiotic or biotic degradation under environmental conditions (UNEP, 2006).

Considering the organic chemistry of PFSAs and PFCAs it seems very likely that a carbon chain being two CF₂-groups shorter is as persistent as a longer chain. It is therefore concluded that PFHxS is as resistant to degradation as has been shown for PFOS and PFOA.

In summary, considering the knowledge on the high stability of the C-F bonds and using the described read-across approach, it is concluded that PFHxS is a synthetic compound which is very resistant to abiotic and biotic degradation.

3.2 Environmental distribution

Using the described read-across approach, the environmental distribution of PFHxS is predicted to be similar to that of PFOS, with the difference that the two carbon longer alkyl chain of PFOS will result in a higher hydrophobicity of PFOS, as compared to that of PFHxS. The primary compartments for PFOS are expected to be water, sediment and soil (UNEP, 2006).

The water solubility, adsorption potential and environmental distribution express a regular pattern depending on the alkyl chain length of PFSA and PFCAs, with an increased alkyl chain length resulting in increased hydrophobic behaviour with decreased water solubility, increased sorption potential, etc. Environmental behaviour and fate of the PFSA can be assumed to be broadly similar to that of PFCAs. PFSA are persistent, mostly distributed to surface waters ((Armitage et al., 2009)), bind weakly to organic phases ((Higgins & Luthy, 2006)) compared to more hydrophobic substances.

Due to the different acidic groups of the PFSA and PFCAs, the PFSA with same perfluoroalkyl chain length as the PFCAs tend to sorb ((Higgins & Luthy, 2006)) and bioaccumulate ((Conder, Hoke, De Wolf, Russell, & Buck, 2008); (Martin, Mabury, Solomon, & Muir, 2003a)) more strongly than their corresponding PFCAs. Both PFSA and PFCAs are found in biota, with the highest concentrations detected in air-breathing organisms (see chapter 3.3 below).

3.3 Bioaccumulation

3.3.1 General remark

According to section 3.2.2 (b) and (c) of REACH Annex XIII also other information, than the numerical bioaccumulation (B) criterion based on bioconcentration factors, can be used to assess the bioaccumulation potential of a substance in a weight-of-evidence approach. This additional information, which includes measured 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, is also be considered for the assessment using a weight-of-evidence approach.

Information on the bioaccumulation potential of PFHxS in humans as well as data from analysis of human body fluids are described in section 4.1.

3.3.2 Bioaccumulation in aquatic organisms (pelagic & sediment organisms)

3.3.2.1 Bioconcentration factors (BCFs)

Bioconcentration is the process by which a chemical enters an organism and/or is adsorbed on to it as a result of exposure to the chemical in water – it often refers to a condition usually achieved under laboratory and steady state conditions. The BCF is typically measured as the ratio of the chemical concentrations in the organism and the water once a steady state has been achieved:

$$BCF = \frac{C_{Biota}}{C_{Water}}$$

or alternatively, can be determined kinetically by using the uptake rate k_1 and the depuration rate k_2 :

$$BCF = \frac{k_1}{k_2}$$

Martin and co-workers (2003a) exposed rainbow trout (*Oncorhynchus mykiss*) 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 of homologous series of perfluoroalkyl carboxylates and sulfonates, including PFHxS. To determine the bioconcentration, juvenile rainbow trout (5-10 g) were exposed to PFHxS (1.4 µg/L), PFOS (0.35 µg/L), PFOA (1.5 µg/L), PFDA (0.71 µg/L), PFUnA (0.48 µg/L), PFDoA (0.20 µg/L), or PFTeDA (0.014 µg/L) in a flow-through system. During the uptake phase, fish were taken away to determine the kinetics of uptake at seven occasions and during the depuration phase at nine occasions. To determine the tissue distribution, four immature rainbow trouts (30-48 g) were exposed in separate tanks but under the same conditions. In general, PFAS (including PFHxS) concentration was highest in blood, kidney, liver, gonads and gall bladder and lowest in adipose and muscle tissue. Steady-state was not achieved for any of the PFCAs or PFSAs. BCF was calculated by the ratio of uptake and elimination rates. The measured BCFs for PFHxS in this study range from 9.6 (carcass) to 100 (liver). The selective distribution is clearly reflected in the estimated BCFs, with substantially lower values when the BCF is based on whole-body, as compared to when it is based on liver or blood. The carcass BCFs used closely approximate the whole-body BCF, but the removal of the liver and a portion of the blood from the intact fish resulted in a minor loss of total PFAS. The resulting carcass contained between 85% (i.e. PFHxS) and 96% (i.e. PFTeDA) of total PFAS, depending on the compound. The difference between the BCFs for the two also depends on the relative weight of the blood and the liver. Based on the results of the study the authors proposed that sulfonates had larger BCFs, half-lives, and rates of uptake than corresponding carboxylate of equal perfluoroalkyl chain length, which indicates that hydrophobicity, as predicted by the critical micelle concentration, is not the only determinant of the bioaccumulation of PFAS and that the acid function also must be considered. (*Note: Critical micelle Concentration is not a direct measure of hydrophobicity*). BCFs for PFHxS, but also PFOS, PFOA, PFUnDA, PFDoDA and PFTeDA are presented in Table 5.

BCF of other PFAS

According to the UNEP POP-document for PFOS (UNEP, 2006), the BCF for fish range between 2796-3100.

According to the SVHC support document for PFOA (ECHA, 2013b) the BCFs for PFOA are below 2000.

According to the SVHC support document for PFUnDA (ECHA, 2012a) the whole body BCF for PFUnDA is above 2000 but below 5000 indicating that PFUnDA is bioaccumulative (B) but not very bioaccumulative (vB). "*Based on the BCF results there is sufficient evidence that C11-PFCA is a bioaccumulative (B) substance and likely a vB substance, but no final conclusion can be drawn on the vB properties.*" The reasons why PFUnDA nevertheless was identified as vB are included in a footnote below¹.

¹ From the support document for identification of PFUnDA as a substance of very high concern because of its vPvB properties: "*Conclusion on the bioaccumulation potential: Based on only the BCFs derived from flow-through tests, C11-PFCA clearly fulfils the B criterion but some uncertainty remains whether it fulfils the vB criterion. BCFs derived from BMFs of a fish feeding study are above 5000. Although these laboratory data indicate that the vB criterion may be fulfilled, further confirmation is sought from field data.*"

According to the SVHC support document for PFDoDA (ECHA, 2012d) all reported BCFs are above 5000 indicating a high bioaccumulation of PFDoDA.

According to the SVHC support document for PFTTrDA (ECHA, 2012c) there are no available BCF-studies for PFTTrDA. However since the structural analogues PFDoDA, which is one CF₂-group shorter, and PFTeDA, which is one CF₂-group longer, both have BCF larger than 5000 it was concluded that also PFTTrDA has a BCF larger than 5000.

According to the SVHC support document for PFTeDA (ECHA, 2012b) all reported BCFs are above 5000 indicating a high bioaccumulation potential of PFTeDA.

BCF in PFAS

Ng and Hungerbuhler (2013) derived a mechanistic bioaccumulation model in fish that considers PFAS uptake via passive diffusion at the gills, association with serum albumin in the circulatory and extracellular spaces, association with fatty acid binding proteins in the liver, and renal elimination and reabsorption facilitated by organic anion transporter proteins. Based on their results the authors suggest that renal transport may not be as important in fish as in mammals, or that active transport rates differ substantially from mammals to fish.

Bioaccumulation factors derived in field studies are clearly above the trigger of 5000 which can be considered analogous to a BCF > 5000. Furthermore, the various available field-BMFs and TMFs for this substance provide evidence that biomagnification at high level takes place in nature. It is important to note that among C11-14-PFCAs, C11-PFCA based on field-BMFs and TMFs has the highest bioaccumulation potential indicating that trophic magnification is more pronounced for C11-PFCA than for the longer chained PFCAs. C12-14-PFCAs fulfill the vB criterion. Although for a large part of available information direct comparison with the vB criterion cannot be made, this information and especially the field data provide clear evidence on that the substance behaves in a way corresponding to bioaccumulation behaviour of substances which by direct comparison of the data to the vB criterion meet the criterion. Consequently, it is concluded that C11-PFCA fulfils both the B and the vB-criteria of REACH."

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Table 5: Measured kinetic growth corrected bioconcentration factors (BCFs) of PFHxS, PFOS, PFOA, PFDoDA and PFTeDA.

Species	Tissue	Location	BCF						Reference	Reliability
			PFHxS**	PFOS**	PFOA**	PFUnDA**	PFDoDA**	PFTeDA**		
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Carcass*	Laboratory	9.6 ± 1.0	1100 ± 150	4.0 ± 0.6	2700 ± 400	18000 ± 2700	23000 ± 5300	(Martin et al., 2003a)	2
	Blood		76 ± 9.7	4300 ± 570	27 ± 9.7	11000 ± 1400	40000 ± 4500	30000 ± 4200		
	Liver		100 ± 13	5400 ± 860	8.0 ± 0.59	4900 ± 770	18000 ± 2900	30000 ± 6000		

* The carcass BCFs used closely approximate the whole-body BCF, but the removal of the liver and a portion of the blood from the intact fish resulted in a minor loss of total PFAS. The resulting carcass contained between 85% (i.e. PFHxS) and 96% (i.e. PFTeDA) of total PFAS, depending on the compound.

**Concentrations tested: PFHxS (1.4 µg/L), PFOS (0.35 µg/L), PFOA (1.5 µg/L), PFUnDA (0.48 µg/L), PFDoDA (0.20 µg/L), PFTeDA (0.014 µg/L)

3.3.2.2 Bioaccumulation factors (BAFs)

In field studies on bioaccumulation of chemicals bioaccumulation factors (BAF) are measured. The BAF is typically measured in the field as the ratio of the chemical concentrations in the organism and the surrounding medium (e.g. water in natural ecosystems). In contrast to the BCF, the uptake is not only limited to exposure via water but all routes including diet contribute to the concentration in organisms:

$$BAF = \frac{C_{Biota}}{C_{Water}}$$

where chemicals concentration in the organism (C_{biota}) is usually expressed in units of gram of chemical per kilogram of organism. The weight of the organism can be expressed on a wet weight basis or appropriately normalised, if needed, (e.g. lipid- or protein-normalised) ((Conder, Gobas, Borga, Muir, & Powell, 2012)). BCFs are measured under controlled laboratory conditions, whereas the BAF is a field measurement and therefore different from BCF. Although some authors describe BCF values in their field studies, BAFs would be more appropriate, because it cannot be excluded that the tested organisms did not take up PFHxS via the diet. BAFs are summarised in Table 6. All studies are field studies and were neither growth corrected nor normalised to a lipid content. BAFs were calculated based on wet weight.

Labadie and Chevreuril (2011) studied the partitioning behaviour of a number of perfluorinated compounds, including PFHxS, between water, sediment and the fish European chub (*Leuciscus cephalus*) in the Orge River, France. Five adult fish were collected in April 2010. The sex of each individual fish was analysed according to gonad morphology. Whole liver, gills and gonads were taken along with portions of muscle. Water and sediment samples were taken as triplicates at the same site. Large inter-individual variations, not sex-related, were observed. The concentration of PFHxS in water and sediment were 13.6 ± 1.7 ng/L and 0.10 ± 0.02 µg/kg ww, respectively. The corresponding concentrations of Σ PFASs/ Σ PFCAs in water and sediment were 36.0 ± 1.6 ng/L/ 37.0 ± 1.6 ng/L and 4.8 ± 0.5 µg/kg ww/ 3.6 ± 0.0 µg/kg ww, respectively. In the pelagic system PFOS was the dominant PFAS (24.0 ± 3.8%) followed by PFHxS (18.5 ± 1.5%). In sediment the dominant PFAS was PFOS (56.5 ± 1.5%), followed by the long-chained PFCAs (PFDoDA 20.5 ± 0.8%, PFTeDA 10.2 ± 10.3% and PFDA 3.6 ± 0.4%). PFOA was detected but could not be quantified. The calculated log BAFs for the PFAS were lowest in muscle and highest in plasma. The log BAFs for PFHxS were in increasing order 0.9 ± 0.3 (muscle), 1.5 ± 0.2 (gills), 2.1 ± 0.3 (liver), 2.4 ± 0.4 (gonads) and 3.3 ± 0.2 (plasma). Corresponding values for PFOS, PFOA, PFUnDA and PFDoDA are included in Table 6.

Naile and co-workers (2013) investigated the bioconcentration of a number of perfluorinated compounds, including PFHxS, in fish (n = 15), crab (n = 44), gastropods (n = 11), and bivalves (n = 5). However, the calculated BCFs may actually be considered as bioaccumulation factors (BAFs) instead since exposure to PFHxS via diet cannot be excluded in the study design used. Samples were collected in May 2009 from coastal and estuarine areas along the South Korean west coast. Samples of sediment (n = 12), soil (n = 13) and surface water (n = 15) were also collected at the same time. All samples within each biotic group were pooled and homogenised. BAFs were calculated based on site-specific water concentrations. The calculated log BAFs (ww) for PFHxS for fish ranged from 1.77 (gills) - 3.53 (intestine), for crabs it ranged between 2.03 ± 0.65 (legs) to 2.76 ± 0.76 (whole body), for gastropods (whole body) it was 3.28 ± 0.22 , and for bivalves (whole body) 2.61 ± 0.41 . Corresponding values for PFOS, PFOA and PFUnDA are included in Table 6 and Table 7.

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Table 6: Measured ww bioaccumulation factors (log BAFs) of PFHxS in fish. When available in the same studies BAFs for PFOS, PFOA, PFUnDA and PFDoDA are also included. Values are not growth corrected or normalised to lipid content.

Species	Tissue	Location	Log BAF					Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA		
European chub (<i>Leuciscus cephalus</i>)	Plasma	Orge River, France	3.3 ± 0.2	5.2 ± 0.1	2.1 ± 0.2	6.0 ± 0.1	6.7 ± 0.1	(Labadie & Chevreuril, 2011)*	2
	Liver		2.1 ± 0.3	4.3 ± 0.3	1.0 ± 0.1	5.0 ± 0.3	5.7 ± 0.4		
	Gills		1.5 ± 0.2	4.0 ± 0.2	Not calculated	4.9 ± 0.1	5.7 ± 0.2		
	Gonads		2.4 ± 0.4	4.0 ± 0.2	Not calculated	4.8 ± 0.1	5.5 ± 0.1		
	Muscle		0.9 ± 0.3	3.4 ± 0.2	Not calculated	4.3 ± 0.2	5.0 ± 0.1		
Fish ^b	Whole body	West coast of South Korea	2.58 ± 0.55	3.43 ± 0.69	1.05	1.92 ± 0.36	-	(Naile et al., 2013)**	2
	Liver		3.08	4.49	-	-	-		

^anc = not calculated because analyte was not detected in at least one environmental compartment

^bMean concentrations including *Hemigrapsus sanguineus*, *Sesarma pictum*, *Hemigrapsus penicillatus*, *Helice tridens*, and *Philyra pisum*.

*Concentrations in Orge River: PFHxS (13.6 ± 1.7 ng/L), PFOS (17.4 ± 2.2 ng/L), PFOA (9.4 ± 0.6 ng/L), PFUnDA (0.10 ± 0.02 ng/L), PFDoDA (0.10 ± 0.01 ng/L), PFTeDA (<0.05 ng/L)

**Concentrations (mean/median) in Yellow Sea on West coast of Korea: PFHxS (1.7/0.5 ng/L), PFOS (8.7/4 ng/L), PFOA (6.8/3.7 ng/L), PFUnDA (0.58/0.53 ng/L), PFDoDA (-)

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Table 7: Measured bioaccumulation factors (log BAFs) of PFHxS in crab, gastropod and bivalve. When available in the same studies BAFs for PFOS, PFOA and PFUnDA are also included. Values are not growth corrected or normalised to lipid content.

Species	Tissue	Location	Log BAF				Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA		
Crab ^a	Whole body	West coast of South Korea	2.58 ± 0.55	3.43 ± 0.69	1.05	1.92 ± 0.36	(Naile et al., 2013)	2
Gastropod ^b	Whole body		3.28 ± 0.22	2.33 ± 0.56	1.70 ± 0.28	1.88 ± 0.46		
Bivalve ^c	Whole body		2.61 ± 0.41	1.89 ± 0.69	1.65 ± 0.20	1.84 ± 0.16		

^a Mean concentrations including *Acanthogobius flavimanus*, *Sebastes schlegeli*, *Tridentiger obscurus*, *Hexagrammos otakii*, and *Mugil cephalus*

^b Mean concentrations including *Littorina brevicula*, *Monodonta labio*, *Umbonium thomasi*, *Glossaulax didyma*, and *Monodonta labio*

^c Mean concentrations including *Mytilus edulis*, *Mactra veneriformis*, *Nuttallia olivacea*, and *Sinonovacula constricta*

Conclusion:

The reported BCF and BAF for PFHxS are below the numerical criteria 2000/5000, but it is worth noting that one of the BAF values (European chub, BAF plasma) is close to the threshold of 2000 (log BAF of 3.3 equivalent to a BAF of 1995). The latter value suggests that the substance is a borderline B for some aquatic species. In addition, due to the surface active properties of the substance the appropriateness of the available BCF test and the usefulness of its result may be questioned. This as according to the OECD TG 305 paragraph 12: *“For surfactants it should be considered whether the aqueous bioconcentration test is feasible, given the substance properties, otherwise the dietary study is probably more appropriate. Surfactants are surface acting agents, which lower the interfacial tension between two liquids. Their amphiphilic nature (i.e. they contain both a hydrophilic and a hydrophobic part) causes them to accumulate at interfaces such as the water-air interface, the water-food interface, and glass walls, which hampers the determination of their aqueous concentration.”* The combination of log K_{OA} (7.55, estimated for neutral species using COSMOtherm) and log K_{OW} (5.17, estimated for neutral species using COSMOtherm) values also indicates that the substance may be of concern for air-breathing organisms rather than for aquatic organisms as, according to the ECHA PBT/vPvB guidance (ECHA, 2016a), *“...An efficiently absorbed, non-biotransformed neutral organic chemical with a log K_{OA} > ~5 or > 6 in combination with a log K_{OW} ≥ ~2 has the potential to biomagnify in terrestrial food chains and air-breathing marine wildlife as well as in humans”*. However, care should be applied here as 1) the log K_{OW} value is questionable for this substance as it has surface active properties, and 2) since PFHxS is a strong acid that is expected to be fully dissociated in the environment.

Thus, not meeting the B/vB criteria is not equal to a low bioaccumulation potential. BCF values below the B criteria could still lead to effects on secondary poisoning and a high exposure to humans due to fish consumptions. The numerical criteria for BCF or BAF, which are based on considerations of lipid-partitioning substances, may not be appropriate for PFHxS as it does not follow the behaviour of traditional hydrophobic compounds with partitioning into fatty tissues. Instead, it behaves similarly to what previously have been observed for other perfluorinated compounds, such as e.g. PFOS, which preferentially binds to proteins in blood and liver (L Ahrens, Siebert, and Ebinghaus (2009), (Martin et al., 2003a), Goeritz, Falk, Stahl, Schafers, and Schlechtriem (2013).

3.3.2.3 Biomagnification factors (BMFs)

Besides bioconcentration also biomagnification describes the potential of a chemical to bioaccumulate. Biomagnification factors (BMFs) can be measured in the laboratory in a fashion similar to that used in the OECD and US-EPA bioconcentration test protocols. Organisms are exposed to a chemical primarily via diet. The BMF test typically includes an uptake phase, where levels of chemicals are followed over time, ideally until the chemical concentration in the organism no longer changes with time (i.e., reaching the steady-state). If a steady-state can be reached in the experiment, the uptake phase is followed by a depuration phase where organisms are exposed to uncontaminated food. The rate of decline in chemical concentration over time measured in the depuration phase can then be used to derive the chemical uptake rate from which a hypothetical steady-state concentration can be estimated (Conder et al., 2012).

The laboratory-derived BMF is calculated using the ratio of the chemical concentrations in the test animals at steady-state and their diet:

$$BMF_{(diet)} = \frac{C_{biota}}{C_{diet}}$$

where chemical concentration in the organism (C_{biota}) and its diet (C_{diet}) are normalised, if needed, (e.g., lipid- or protein-normalised) (Conder et al., 2012).

It is from the data collected during the dietary exposure study possible to estimate tentative BCFs for comparison against the BCF criteria outlined in Annex XIII, but it needs to be remembered that these calculated BCFs may be more uncertain than the experimental BCFs due to uncertainties in the prediction of the uptake rate constant (k_1) determined from the dietary bioaccumulation study (ECHA, 2016a). These calculated BCFs should therefore only be considered as part of the body of evidence, and not used as the only values from which to draw conclusions in the PBT assessment ((ECHA, 2016a)). There are also uncertainties of the calculated BCF (from the dietary BMF) due to the surface active properties of the substance: According to paragraph 14 of the OECD TG 305 – *“It should be noted that the dietary approach yields a dietary biomagnification factor (BMF) rather than a bioconcentration factor (BCF). Approaches are available to estimate a kinetic bioconcentration factor (BCFK) from data generated in the dietary study (as discussed in Annex 8, but these approaches should be used with caution. In general, these approaches assume first order kinetics, and are only applicable to certain groups of compounds. It is unlikely that such approaches can be applied for surfactants (see paragraph 12).”*

The BMF values from field studies are based on the ratio of the concentration in the predator and the prey:

$$BMF_{(field)} = \frac{C_{predator}}{C_{prey}}$$

In case of laboratory dietary studies, it is certain based on the test design, that the diet is the sole source of exposure whereas in field studies the BMF include both diet and water exposure. It is therefore crucial to differentiate between a $BMF_{(diet)}$ and a $BMF_{(field)}$.

There are several uncertainties concerning field based BMFs similar to field based trophic magnification factors. There are factors such as species migration and seasonal variations which can influence the field measurements and hence the field-BMF. Dividing the concentration of a substance in a predator by that in a prey implies that this prey is the sole food source. However, the food sources may be diverse. Additionally, there is no standard procedure so far how to conduct such field studies, and different study designs therefore have influence. The uncertainties of field studies have been addressed and discussed by Borga et al. ((Borga et al., 2012)). As the authors actually refer to field based trophic magnification factors a summary of the discussion has been included in chapter 3.4.2.4, Trophic Magnification Factors. The report of ECETOC ((2014)) on a weight of evidence PBT/vPvB assessment has given in the chapter on bioaccumulation a review on various uncertainties in field studies.

Problems arise with increasing body size of predators because analysis is based on tissue or serum samples. This is especially true for organisms at the higher trophic levels (e.g., polar bear), while it is feasible to measure the whole-body on smaller species at lower trophic levels. Whole-body analysis is not feasible for ethical reasons, i.e. a whole whale would be needed, and due to the challenging logistics with respect to sampling and laboratory constraints. Therefore, some of the derived BMF-values are restricted to certain tissue samples rather than whole body samples. Whole body values may be estimated if the tissue mass fraction is known for the organism regarded. There may however be some uncertainties due to inter individual and geographical differences but these uncertainties cannot be quantified ((Houde et al., 2006)). BMF values based on liver samples may be overestimated. From a toxicological perspective, concentrations in individual organs, such as the liver, may be more relevant when the potential for direct organ-specific toxicity (i.e., liver toxicity) is predicted.

According to the new draft ECHA guidance there is no uniform relationship between BCF and BMF and even if a BMF from an OECD 305 dietary study bioaccumulation test is found to be <1, it cannot be considered as a good discriminator for concluding substances to be (very) bioaccumulative according to the BCF criteria of Annex XIII ((ECHA, 2016a)).

As discussed in the draft ECHA guidance ((2016a)), experimental BMF < 1 is not uncommon to observe for substances which in fact are “vB”. Only if dietary BMF>1, it should be relatively clear that the substance is vB, but in a contrary situation it does not necessarily mean that the substance is not B or not vB. Other metrics from fish feeding studies that also provide useful information are the tentative calculated BCF and the elimination rate. BMFs for PFHxS are summarised in Table 8.

3.3.2.3.1 Laboratory studies

The results from the two available experimental studies, using rainbow trout, compare reasonably well and both result in BMF<1 for PFHxS.

Martin et al. (2003b) investigated the BAFs of homologous series of perfluoroalkyl carboxylates and sulfonates, including PFHxS, in juvenile rainbow trout for 34 days in the diet, followed by a 41 day long depuration period. However, the results should rather be considered as biomagnification factors (BMFs) as the study only included uptake via the diet. The fish were fed daily with spiked food at a rate of 1.5 % food per body weight during the uptake phase. The concentration of PFHxS in the spiked food was 0.51 mg/kg. Water samples collected on day 30 of the uptake phase, before and after feeding, revealed no traces of PFAs in water indicating negligible transfer of contaminants to the water column during the feeding process and/or that the substance may have been adsorbed to the test vessels. (*An initial estimate of the amount of PFHxS in the system is 15-17 ng/L (mean initial fish mass of 2.54 g fish /initial fish loading of 2-2.2 g fish/L=1.15 L per fish; 2.54 g fish x daily feeding rate of 1.5% body weight x food-borne concentration of 0.51 µg PFHxS/g food = 0.019431 µg PFHxS/fish; 0.019431 µg PFHxS/fish / 1.15 L per fish = 0.017 µg PFHxS/L = 17 ng PFHxS/L).*) The time to reach steady state was estimated to be 30 days. Fish were collected 6 times during both the uptake and depuration phase. Carcass and liver concentrations were determined by using LC/MS/MS, and kinetic rates were calculated to determine bioaccumulation parameters. The liver BAF was not calculated, but a whole body BAF of 0.14 ± 0.021 was derived for PFHxS, 0.32 ± 0.050 for PFOS and 0.038 ± 0.0062 for PFOA. The whole body and liver elimination half-lives were determined to be 9.1 ± 1.1 and 13 ± 2.5 days for PFHxS, 13 ± 1.8 and 20 ± 5.7 days for PFOS and 3.0 ± 0.42 and 5.2 ± 0.48 days for PFOA, respectively. Corresponding values for PFOS, PFOA, PFUnDA, PFDoDA and PFTeDA are included in Table 8. The elimination half-lives obtained in this study are comparable to the elimination half-lives obtained in the accompanying aqueous exposure study (Martin et al., 2003a), indicating that elimination process is independent of the route of uptake. The calculated biomagnification factors increased with the length of the perfluorinated chain. The results indicated that sulfonates biomagnified to a greater extent than carboxylates of equivalent perfluoroalkyl chain length, indicating that hydrophobicity is not the sole determinant of the bioaccumulation potential of perfluorinated acids. It was proposed by the authors that the lack of observed biomagnification for the PFAS was due to the low natural feeding rates of the fish and that the small size of the fish led to a more rapid chemical elimination to water, relative to body size. Therefore results from this study are not robust enough for an assessment on the bioaccumulation/-magnification potential of PFHxS.

Goeritz and co-workers (2013) investigated the biomagnification potential and the substance and tissue-specific distribution of a number of PFAS, including PFHxS, in market-size Rainbow trout (*Oncorhynchus mykiss*). The fish (n = 35), with an average body weight

of 314 ± 21 g, were fed daily with food supplemented with one out of five different PFAS for 28 days, followed by a 28 day depuration phase. The animals were fed daily at a rate of 2.6 % of the average live weight and the nominal concentration of PFAS in the food was 500 $\mu\text{g}/\text{kg}$ dry weight. Analysis showed that the PFAS were distributed homogeneously in the feed pellets throughout the study. The analysis however also showed that the mean concentration of the test substances in the food differed significantly between the different PFAS, with the concentrations for PFHxS, PFOS and PFOA being 309 ± 50 $\mu\text{g}/\text{kg}$, 172 ± 13 $\mu\text{g}/\text{kg}$ and 303 ± 59 $\mu\text{g}/\text{kg}$, respectively. This result indicates that the fish were exposed to different amounts of each test substance during the accumulation period. During the study, fish were sampled eight times, 4-5 on each occasion. Perfluoroalkyl substance analysis was performed by HPLC/MS/MS with negative ionisation. Analysis of water samples taken periodically from the test basin showed that PFAS contamination of the fish surrounding water was below 15 ng/L for all test substances during the accumulation phase, excluding water as a significant uptake route. Concentrations of PFHxS and PFOS showed higher increase compared with PFOA. For the fish sampled at the end of the accumulation period ($n = 4$), the average whole-body concentrations per kg ww were 49.7 ± 21.7 $\mu\text{g}/\text{kg}$ for PFHxS, 49.0 ± 8.7 $\mu\text{g}/\text{kg}$ for PFOS and 15.4 ± 3.12 $\mu\text{g}/\text{kg}$ for PFOA, respectively. Distribution factors (DF) expressing the mean PFAS concentrations in the different tissues on day 28 in relation to the average concentration estimated for the whole body on day 28 were highest in liver (19, 9, and 8 for PFHxS, PFOS and PFOA, respectively), followed by blood (13, 5.7, and 4.9 for PFHxS, PFOA and PFOS, respectively), kidney (5.2 - 1.0 for PFOA, PFOS, and PFHxS), skin (5.2 - 1.9 for PFHxS, PFOA and PFOS), gills (1.6 - 1.2 for PFOA, PFHxS, and PFOS), and muscle (1.1 - 0.5 for PFOS, PFHxS, and PFOA). It was noted that equilibrium between uptake and elimination only was reached for PFOA and it therefore remains uncertain whether the tissue distribution for PFHxS and PFOS represent the final outcome. The perfluoroalkyl sulfonates (PFBS, PFHxS, PFOS) generally showed a higher affinity for the liver as compared to the tested perfluoroalkyl carboxylates (PFOA, PFNA). The affinity of PFAS to accumulate in the liver in this study appeared higher for the shorter chain PFAS PFHxS (DF=18.8) and PFBS (DF=15.6) as compared to longer chain homologue PFOS (DF=9.4). The calculated BMF/elimination half-life were 0.18/8.75 d, 0.42/16.1 d, and 0.04/7.12 d for PFHxS, PFOS, and PFOA, respectively. The estimated biomagnification factors were not corrected for the lipid content of the experimental animals due to the low potential of the test items to accumulate in lipids. The growth corrected depuration rate constant (k_{2g}) was estimated to be 0.058 d^{-1} .

3.3.2.3.2 Field studies

The available field studies include studies performed in southern USA with dolphins as top predators, in Barents Sea with glaucous gull as top predator and in arctic Canada and Greenland with polar bears as top predators. All of these field studies result in BMFs >1 for PFHxS, suggesting a potential of biomagnification of the substance along the food-chain. According to the ECHA PBT guidance (ECHA, 2016b) "*...indication of a biomagnification potential (BMF and/or TMF > 1) can on its own be considered as a basis to conclude that a substance meets the B or vB criteria.*"

The environmental distribution and biomagnification of several perfluoroalkyl compounds, including PFHxS, in the food web of Bottlenose dolphins (*Tursiops truncatus*) was examined by Houde and co-workers (2006). The concentrations in Bottlenose dolphins were measured at two different locations in the US, in the industrialised Charleston Harbour and in the more residential Sarasota Bay. In the Charleston Harbour area samples were collected of marine water ($n = 18$; 2004), surface sediment ($n = 17$; 2004), WWTP ($n = 4$; 2004), Striped mullet (*Mugil cephalus*; $n = 8$; 2002/2003), Pinfish (*Lagodon rhomboides*; $n = 4$; 2002/2003), Red drum (*Sciaenops ocellatus*; $n = 8$; 2002/2003), Atlantic croaker ($n = 3$; 2002/2003), Spotfish (*Leiostomus xanthurus*; $n = 10$;

2002/2003), Spotted seatrout (*Cynoscion nebulosus*; n = 11; 2002/2003), and Bottlenose dolphin (n = 24; 2004). Sampling in the Sarasota Bay area included marine water (n = 10; 2004), surface sediment (n = 8; 2004), zooplankton (n = 3; 2004), Striped mullet (n = 9; 2004), pigfish (*Orthopristis chrysoptera*; n = 10; 2004), Sheephead (*Archosargus probatocephalus*; n = 3; 2004), Pinfish (n = 10; 2004), Spotted seatrout (n = 8; 2004), and Bottlenose dolphin (n = 12; 2004). Plasma, teeth and skin were taken from dolphins from both locations and tissue samples (i.e. liver, kidney, lungs, muscle, heart, thyroid and thymus) were collected from recently deceased bottlenose dolphins in the areas (Charleston, 2003, n = 1, female, 708.4 kg. Sarasota Bay, 2002, n = 1, male, 233.5 kg). An additional 6 liver and kidney samples from stranded bottlenose dolphins were available at Sarasota Bay. The authors extrapolated tissue specific concentrations to whole body burdens based on the total body weight, the organ weights and the blood volumes. This was, according to the authors, done since the BMF is overestimated by a factor of 10-30 when serum or liver concentrations of dolphins are used. Assessing BMF through the food chain when samples are collected over a period of time introduce uncertainty. It may however be assumed that media and biota were continuously exposed to PFAS in this area throughout the years. In Charleston, the BMFs for PFHxS for four individual dolphin/prey relationships were calculated and ranged from 3.3 to 14 (PFHxS). The corresponding BMFs for PFOS and PFOA ranged from 1.2 to 2.6 and 1.8 to 13, respectively. In Sarasota Bay, the BMFs for two individual dolphin/prey relationships and two fish/zooplankton relationships were calculated. These were 1.8 and 2 for the dolphin BMFs, and 9.1 and 10 for the fish/zooplankton BMFs. The corresponding BMFs for PFOS ranged from 11 to 19. Corresponding values for PFOS, PFOA, PFUnDA, and PFDoDA are included in Table 8. No BMFs were calculated for PFOA for the Sarasota Bay. The BMFs are corrected for the step in the trophic level, e.g. if the change in trophic level between predator and prey is less or more than one trophic level. Issues of uncertainty relating to this study and the calculated BMFs are 1) the large variation in the mean concentrations, reflected in standard deviations being equal or even higher than the corresponding mean concentration, 2) the extrapolation of liver/blood concentrations to whole body concentration in dolphins, 3) PFHxS for some species were detected in less than 60% of the samples, 4) the limited sample size at each trophic level, and 5) that not all sampling were performed during one year but instead during different years (2002-2004).

The biomagnification of a number of per- and polyfluorinated alkyl substances, including PFHxS, was investigated in four selected species from the Barents Sea ice edge food web (Haukas, Berger, Hop, Gulliksen, and Gabrielsen (2007)). Samples of ice amphipod (*G. wilkitzkii*), polar cod (n = 50, size 11.5-17.0 cm), adult black guillemot (n = 18), and adult glaucous gull (n = 9) were collected in 2004. Liver samples from seabirds and polar cod were collected for analyses of contaminants, while whole amphipods were used. Due to the small size of the polar cod liver, samples from three fish of similar length (two females and one male) were pooled (n = 16) for the analyses. The amphipods (whole body) were pooled (n = 6) according to length to gain homogenised samples of at least 1 g. HPLC in combination with time-of-flight mass spectrometry was used in the analysis. Magnification factors, describing the magnitude of trophic transfer was estimating by relating ratio of stable isotopes of nitrogen ($\delta^{15}\text{N}$) to the chemical concentration. The actual measured concentrations in ice amphipod, polar cod, black guillemot, and glaucous gull are presented below in section 3.3.3. The detection frequency of PFHxS increased with increasing trophic level and were 0/6 for the ice amphipods, 9/16 for the polar cods, 17/18 for the black guillemots and 9/9 for the glaucous gull. No BMF including the ice amphipod could be calculated for PFHxS since it was not detected in the amphipods. Trophic level-corrected BMFs for Black guillemot/Polar cod, Glaucous gull/Polar cod and Glaucous gull/Black guillemot were 6.0, 7.2 and 8.5, respectively. The corresponding BMFs for PFOS were 10, 39 and 27, respectively. Since PFOA was only detected in a minority of polar cods (3/16), Black guillemot (5/16) and not detected at all in the Glaucous gull no corresponding BMFs are available for PFOA. Since pelagic polar cod and adult black guillemot only partly contributes to the diet of the Glaucous gull, the BMFs for the Glaucous gull may therefore

be over- or underestimated. It is not clear in the article if or how the concentrations used were normalised with respect to the different trophic levels. In addition, there are always uncertainties associated with food web studies, such as sample sizes, certainty of covering exclusive food chains, and migration in and out of the food chains.

Butt *et al.* (2008) measured the concentration of PFAS in ringed seals (*Phoca hispida*) from the Canadian arctic. PFHxS was only infrequently (<25%) measured above the method detection limit (MDL) of 0.78 µg/kg ww. When calculating means, for measurements where the concentrations were less than MDL the authors replaced these measurements by a random number less than half the MDL. The authors also calculated regional polar bearing seal biomagnification factors from similarly located sample collection sites using the PFAS liver concentrations. The geometric mean PFAS concentrations for polar bears were obtained from Smithwick *et al.* (2005). The calculated geometric mean for the regionally based ringed seal-polar bear BMFs for PFHxS for the regions "Southeast Beaufort Sea", "Hudson Bay", "South Baffin Island and Labrador" and "High Arctic" were 251, 373, 163, and 285, respectively, with a resulting Canadian Arctic mean of 199. The calculated geometric mean for the regionally based ringed seal-polar bear BMFs for PFOS for the regions "Southeast Beaufort Sea", "Hudson Bay", "South Baffin Island and Labrador" and "High Arctic" were 137, 163, 80, and 91, respectively, with a resulting Canadian Arctic mean of 95. The calculated geometric mean for the regionally based ringed seal-polar bear BMFs for PFOA for the regions "Southeast Beaufort Sea", "Hudson Bay", "South Baffin Island and Labrador" and "High Arctic" were 119, 125, 107, and 45, respectively, with a resulting Canadian Arctic mean of 79. Corresponding values for PFOS, PFOA, PFUnDA, PFDODA, PFTrDA and PFTeA are included in Table 8. Uncertainties related to the calculated BMFs are 1) that PFHxS only infrequently (<25%) were measured above the MDL in ringed seals, 2) sampling were performed by different authors during different years, and that 3) the fact that the very high BMFs for PFHxS are not in any way commented upon by the authors. It is not clear whether these uncertainties result in an under- or an overestimation of the calculated BMFs.

Riget *et al.* (2013) measured the concentrations of seven PFAS, including PFHxS, in livers of ringed seals from central East and West Greenland during 1982-2010 and in livers of polar bears from central East Greenland during 1984-2011. Using the measured data on liver concentrations from polar bears and ringed seals from central East Greenland to derive BMFs, from the years from which PFHxS was detected in both species, results in a median/geometric mean BMF of 20.1/16.7, which is estimated from three years (1994, 2003 and 2006). PFHxS was detected in all liver polar bear samples during these years, but only in 2/6 ringed seal samples 1994, 4/9 ringed seal samples in 2003, and 6/14 ringed seal samples during 2006. The corresponding estimated median/geometric mean BMFs (and years used in the calculations) for PFOS, PFOA and PFUnDA are 13.3/14.1 (1986, 1994, 1999, 2003, 2006, 2008, 2010), 6.8/8.7 (1999, 2006, 2008) and 7.5/6.7 (1984, 1994, 1999, 2003, 2006, 2008, 2010), respectively. PFOS and PFUnDA were detected in all polar bear and ringed seal samples during these years. PFOA was detected in all polar bear samples during 2006 (n=8) and 2008 (n=1) and in 12/16 in 1999 and in ringed samples in 2/8 in 1999, 5/14 in 2006 and 6/29 in 2008. Estimation of annual mean for those compounds with less than 80% of the values below the method detection limit (0.8 µg/kg ww for PFHxS and 1.2 µg/kg ww for PFOA) was done by Regression on Order Statistics using the library NADA of the statistical R packages. No estimation of annual mean was done in case more than 80% of the values were below the method detection limit. The lines in Figure 4 indicate that the annual changes and the concentrations in seals and polar bears follow each other rather well. Based on these estimated BMFs it appears that the bioaccumulation of PFHxS in polar bears exceeds that of PFOS, PFOA and PFUnDA. The results also indicate that the BMFs estimated by Butt *et al.* (2008) may be overestimated. It should be noted that the BMFs of PFHxS and PFOA are largely based on non-detects as regards the seal data. It is not clear whether these uncertainties result in an under- or an overestimation of the calculated BMFs.

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Table 8: Measured biomagnification factors (BMFs) of PFHxS. PFOS, PFOA, PFUnDA, PFDoDA, PFTTrDA and PFTeDA are included for comparison when measured in the described studies.

Species – tissue	Location	BMF							Reference	Reliability
		PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTTrDA	PFTeDA		
Rainbow trout (<i>Oncorhynchus mykiss</i>) – Whole body	Laboratory	0.14 ± 0.021	0.32 ± 0.05	0.038 ± 0.0062	0.28 ± 0.040	0.43 ± 0.062	-	1.0 ± 0.25	(Martin et al., 2003b)	2
		0.18	0.42	0.04	-	-	-	-	Goeritz et al. (2013)	2
Dolphin (whole, estimated)/ Striped mullet (whole)	Charleston Harbour, South Carolina, USA	4.0	2.6	13	1.9	0.2	-	-	Houde et al. (2006)	3
Dolphin (whole, estimated)/ Red drum (whole)		14	1.2	2.7	3.2	0.4	-	-		
Dolphin (whole, estimated)/ Spotfish (whole)		6.0	0.8	6.4	3.9	0.6	-	-		
Dolphin (whole, estimated)/ Seatrout		3.3	0.9	1.8	2.5	0.6	-	-		
Dolphin (whole, estimated)/ Pigfish (whole)	Sarasota Bay, Florida, USA	2.0	18	-	-	2.0	-	-		
Dolphin (whole, estimated)/ Pinfish (whole)		1.8	11	-	-	2.0	-	-		
Pigfish (whole)/ zooplankton (whole)		9.1	12	-	-	2.5	-	-		
Pinfish (whole)/ zooplankton (whole)		10	19	-	-	2.5	-	-		
Black guillemot (liver)/ Polar cod (liver)	Barents Sea	6.00	10.1	-	-	-	-	-	Haukas et al. (2007)	2
Glaucous gull (liver)/ Polar cod (liver)		7.20	38.7	-	-	-	-	-		
Glaucous gull (liver)/ Black guillemot (liver)		8.49	27.0	-	-	-	-	-		
Polar bear (liver)/	Southeast	251	137	119	21	3.5	2.7	1.4	(Butt et al.,	2

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Species – tissue	Location	BMF							Reference	Reliability
		PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTTrDA	PFTeDA		
ringed seal (liver)	Beaufort Sea								2008)	
	Hudson Bay	373	163	125	10	2.9	3.4	3.1		
	South Baffin Island and Labrador	163	80	107	8.8	3.6	2.0	8.5		
	High Arctic	285	91	45	7.1	2.3	1.6	3.0		
	<i>Canadian Arctic mean</i>	199	95	79	11	2.8	2.2	3.8		
Polar bear (liver)/ ringed seal (liver)	Greenland (central East)	20.1/ 16.7*	13.3/ 14.1*	6.8/ 8.7*	7.5/ 6.7*	-	-	-*	(Riget, Bossi, Sonne, Vorkamp, & Dietz, 2013)	2

-Not calculated since it was not detected in sufficient amount.

*Median/geometric mean

Conclusion:

All field BMFs for PFHxS are above one suggesting a biomagnification potential of the substance that is supported by monitoring data (increasing concentration levels of PFHxS among the food-chain (e.g. seals/bear)). Most BMFs, and especially the large ones (ringed seals/polar bears), are not from aquatic organisms, but instead from air-breathing organisms. Even if there are uncertainties linked to the field studies, all the field BMF values are higher than one supporting a biomagnification potential of PFHxS as part of a weight-of-evidence approach. In addition, the values for the other similar substances are from the same studies and it is therefore possible with sufficient certainty to say that PFHxS accumulates in the food chain at least as much as PFOS and more than the long-chained PFCA's which already have been identified as vPvB to the Candidate List ((ECHA, 2012a), (ECHA, 2012d), (ECHA, 2012c), (ECHA, 2012b)).

3.3.2.4. Trophic magnification factors (TMFs)

The trophic magnification factor (TMF) is a measure to evaluate biomagnification occurring in food webs. In the ECHA Guidance Document on Information Requirements, Chapter R.7.10.1.1, TMF is defined as the concentration increase in organisms with an increase of one trophic level. According to Conder et al. ((2012)), TMFs represent some of the most conclusive evidence of the biomagnification behaviour of a chemical substance in food webs. Again, a TMF greater than one indicates accumulation within the food chain.

There are several uncertainties concerning TMFs. These have been addressed and summarised by Borga et al. ((2012)). Additionally, the report of ECETOC on a weight of evidence PBT/vPvB assessment gives (in the chapter on bioaccumulation) a review on various issues concerning field studies ((ECETOC, 2014)). These include biological factors such as the differences between poikilotherms and homeotherms, sex, different energy requirements, different abilities to metabolise chemicals and slow or fast growing organisms.

Steady state between a consumer and its diet is assumed. However, as opportunistic feeders wild animals vary their diet over seasons or with life stage and point sources may influence observed TMFs. Additionally, apart from the diet there is always the possibility of a direct uptake of the substance under scrutiny and the relative importance of food versus e.g. water exposure can influence the magnitude of the TMF.

The position in the food web is quantified using relative abundances of naturally occurring stable isotopes of N ($^{15}\text{N}/^{14}\text{N}$, referred to as $\delta^{15}\text{N}$). However the relative abundance of these isotopes and thus the determination of the trophic level and TMF is influenced by the physiology of the organism and its life trait history. Rapid growth with a higher protein demand for new tissue leads to lower enrichment factors than those with slower growth rates. Insufficient food supply and fasting and starvation leads to catabolism of body proteins and an increase of ^{15}N in organisms relative to those organisms with adequate food supply.

There is no standard procedure for the conductance of TMF field studies. Hence, the conductance and sampling may vary between different studies. Disproportionate sampling of the food web or unbalanced replication of samples may significantly influence the TMF. As pointed out by Borga et al. (2012) an appropriate sample sizes is needed to achieve sufficient statistical power to evaluate TMF. The required sample sizes are affected by the design of the trophic transfer study, which improves with an advanced ecological understanding of trophic relationships.

Particular problems with averaging the TMF may occur if food webs comprise both poikilotherms and homeotherms. An investigation of an Arctic food web revealed the unequal magnification behaviour of POPs within both thermal groups ((Hop, Borga, Gabrielsen, Kleivane, & Skaare, 2002)). These results may be explained by a higher food intake, caused by a higher energy demand, and a longer life span of birds and mammals. Intrinsic differences in gastrointestinal

absorption mechanisms have also been suggested as an explanation for these differences between homeotherms and aquatic poikilotherms ((Drouillard & Norstrom, 2000)). Therefore, when the trophic magnification potential of a substance is determined via a single regression for the overall food web, the magnification in poikilotherms may be overestimated and the magnification in homeotherms, in particular apex predators, may be underestimated ((A. T. Fisk, Hobson, & Norstrom, 2001)).

Additionally, as already discussed in the BMF section, sample collection is often restricted to tissue or serum samples in large predators due to ethical reasons and due to the challenging logistics with respect to sampling and laboratory constraints.

As described above, Houde *et al.* (2006) investigated the food web of Bottlenose dolphins. In addition to sampling Bottlenose dolphins (n = 24), water (n = 18, samples analysed in duplicate) and surface sediment (n = 17, samples analysed in triplicate), as well as other biota, i.e. Atlantic croaker (n = 3), Spotted seatrout (n = 11), Pinfish (n = 4), Spotfish (n = 10), Striped mullet (n = 8), was sampled. The samples were collected between 2002 and 2004. The trophic level of each biota was determined based on stable isotope ($\delta^{15}\text{N}$) analysis. The whole body burden was calculated after the plasma and liver levels of dolphins was analysed. The extrapolation of tissue specific concentrations to whole body burdens is based on the total body weight, the organ weights and the blood volumes. For prey, whole body homogenates were analysed. The TMFs are not lipid- or protein-normalised. TMF for PFHxS was 0.2 ± 0.9 , when accounting for dolphin plasma and 0.1 ± 0.4 when accounting for whole body burdens for dolphins. Corresponding values for PFOS, PFOA, PFUnDA and PFDoDA are included in Table 9. There is a noticeable large variation in the estimated TMFs, reflected in standard errors being larger than their corresponding TMFs. In addition, the low TMFs for PFHxS also appear strange since the highest concentrations of PFHxS are reported for the highest trophic levels and also when comparing the concentrations of PFHxS at the different trophic levels with the corresponding concentrations of the other PFAS, such as PFOS and PFOA. Issues of uncertainty relating to this study and the calculated TMFs are as already mentioned above in the BMF-section. It is not possible to conclude on TMF for PFHxS due to the large uncertainties associated with the data used to estimate TMF by Houde *et al.* (2006). It should be considered that this conclusion concerns PFHxS alone from the study.

Table 9: Trophic Magnification Factors (TMFs) of PFHxS and for comparison also for PFOS, PFOA, PFUnDA and PFDODA.

Species - tissue	Location	TMF					Reference	Reliability
		PFHxS	PFOS	PFOA	PFUnDA	PFDODA		
Dolphin plasma	Charleston Harbour, South Carolina, USA	0.2 ± 0.9	4.9 ± 6.1	13 ± 22	3.0 ± 3.9	0.7 ± 0.8	Houde et al. (2006)	3
Whole body burden		0.1 ± 0.4	1.8 ± 1.2	6.3 ± 6.7	2.3 ± 2.5	0.6 ± 0.8		

Conclusion:

It is not, due to the limited reliability on the available data, possible to make a conclusion on bioaccumulation potential TMFs for PFHxS.

3.3.3 Measured levels in wildlife

As stated in the ECHA guidance on PBT assessment (ECHA, 2008), "...For a B and vB assessment all available relevant information should be taken into account." and "...because food chain transfer and secondary poisoning are basic concerns in relation to PBT and vPvB substances, an indication of a biomagnification potential can on its own right be considered to conclude that a substance meets the B or vB criteria but absence of such a biomagnification potential cannot be used to conclude that these criteria are not fulfilled."

In addition to the measurements of PFHxS in biota in relation to BCF/BAF/BMF/TMF reported above, there are also additional studies reporting concentrations of PFHxS in wildlife and humans. A non-exhaustive list of these studies is presented below and in Annex II.

PFHxS has been detected in a number of species including Arctic species such as polar cod, glaucous gull, herring gull, ringed seal, and polar bears.

The measured concentrations of PFHxS in:

- Wildlife are summarised in Figure 1. The values presented are mean values sampled per species/year/location/author(s). In case of measurements below the limit of detection (LOD), half LOD have been used. Figure 2 includes the same values as in Figure 1, apart from the values on invertebrates, fish and birds from Zhou et al. (2014), which are sampled in a region heavily polluted by perfluorinated compounds.
- Invertebrates, fish and birds are by far highest in the study by Zhou et al. (2014), with reported concentrations of PFHxS ranging from 4.1-18 µg/kg ww in invertebrates, 0.2-74 µg/kg ww in fish and 1.5-27 µg/kg ww in birds. Zhou and co-workers (2014) sampled invertebrates, fish and birds from lake Tangxun, China, which is situated in a region which is heavily polluted by perfluorinated compounds due to a lot of several small-scale fluorochemical manufacturers.
- Mammals are highest in polar bear livers (>500 µg/kg ww) (Figure 3).

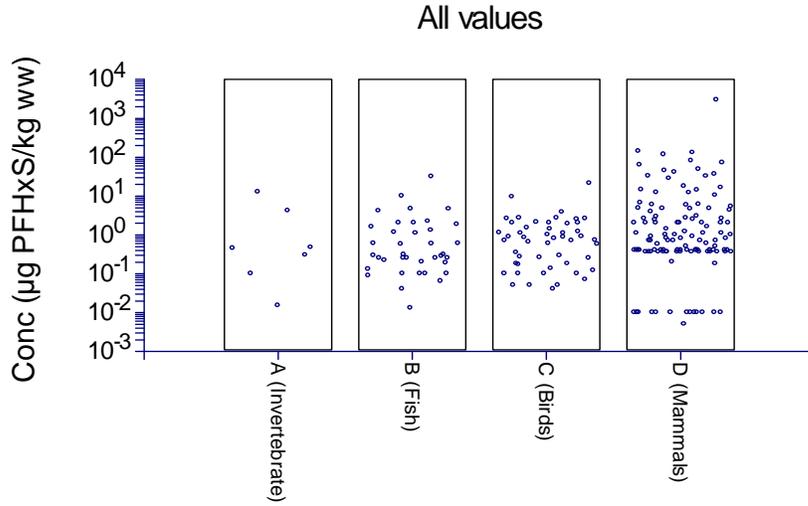


Figure 1. Measured levels of PFHxS in invertebrates, fish, birds and mammals.

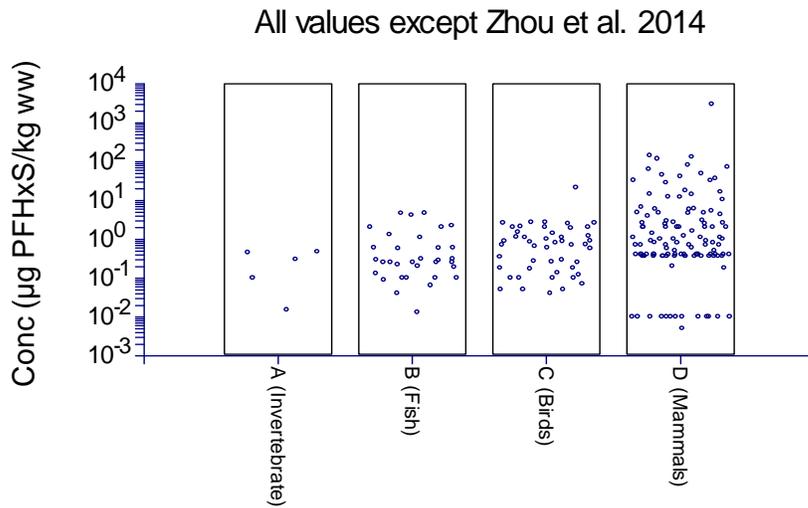


Figure 2. Measured levels of PFHxS in invertebrates, fish, birds and mammals, except for the measured values from Zhou et al. (2014). The excluded values (invertebrates, fish and birds) from Zhou et al. (2014) are sampled in a region heavily polluted by perfluorinated compounds due to a large number of small scale fluorochemical manufacturers.

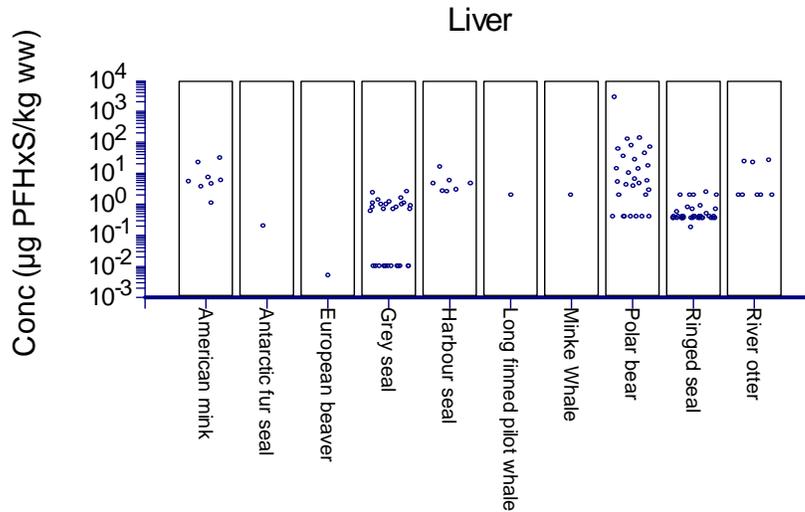


Figure 3. Measured levels of PFHxS in mammals.

In the study by Zhou et al. (2014), which includes measurements in invertebrates, fish and birds PFOS is always detected at the highest concentrations (up to more than a factor of ten higher compared to the other PFAS analysed), with PFHxS most often being the PFAS detected at the second highest levels.

With exception of the study by Zhou et al. (2014), the levels of PFHxS detected in invertebrates are roughly about the same as those of PFOS, sometimes higher, sometimes lower. In fish, birds and mammals the levels of PFOS, with only a few rare exceptions, are always higher to substantially higher than those of PFHxS.

The levels of PFHxS in invertebrates, fish, birds and mammals are sometimes higher and sometimes lower than those measured of PFOA. An observation that can be made is that the concentrations of PFHxS generally are lower than those of PFOA in seals from arctic regions, but the concentrations of PFHxS in polar bears from the same regions are generally higher, which may be an indication of biomagnification.

The concentrations of PFHxS in invertebrates are always higher than those of PFUnDA, PFDoDA and PFTeDA (when available). With the exception of the study by Zhou et al. (2014), the levels of PFHxS in fish and birds are generally lower than those of PFUnDA and PFDoDA. In mammals, the levels of PFUnDA are sometimes lower and sometimes higher than those of PFHxS, while the levels of PFDoDA are generally the same or lower than those of PFHxS. The concentrations of PFTeDA and PFTrDA are higher than PFHxS in seals but lower in polar bears.

It is however difficult to draw conclusions on similarities and/or differences in bioaccumulation between these substances based on field data as both previous and present exposure situations are unknown. Measured data are included in Table 18 in Annex II.

Kannan et al. ((2002)) measured the concentrations of four PFAS, including PFHxS, in liver samples of mink and otters from various locations in the USA. Liver samples of mink were collected in Illinois (n = 65, 1995-1996), Louisiana (n = 7, 1999), Massachusetts (n = 31,

1996), and South Carolina (n = 9, 2000). The reported concentrations of PFHxS ranged from below the limit of quantification to a maximum of 85 µg/kg ww, which was measured in Illinois. The detection of PFHxS ranged from 0% of the liver samples in Louisiana to 89% of the liver samples in South Carolina. PFOS was detected in 100% of the liver samples in all of the four examined states. The reported concentrations of PFOS ranged from 20-5140 µg/kg ww, with the highest value detected in Illinois. PFOA was not detected in any of the samples from Louisiana and South Carolina, in 8% of the liver samples from Illinois and in 58% of the samples from Massachusetts. The highest concentration of PFOA, 40 µg/kg ww, was measured in Illinois. Concentrations of PFHxS in liver samples of river otters from Oregon (n = 10, 1997-1998) and Washington state (n = 10, 1997-1998) ranged from <4 – 68 µg/kg ww and <4 – 76 µg/kg ww, respectively. The corresponding concentrations for PFOS/PFOA were 34-994/<7.5-19 µg/kg ww and 139-422/<7.5-19 µg/kg ww, respectively. PFOS was found in all liver otter samples as compared to PFHxS and PFOA which often were below the limit of quantification (which were <4 and <7.5 µg/kg ww, respectively).

Bossi *et al.* (2005) performed a preliminary screening study of four PFAS, including PFHxS, in liver samples of fish, birds and marine mammals from Greenland and the Faroe Islands. Pooled liver samples of polar bear (*Ursus maritimus*; n = 5 1999 -2001, n = 5 2000 - 2002), minke whale (*Balaenoptera acutorostrata*; n = 5 1998), ringed seal (*Phoca hispida*; East Greenland: n = 5 2002, n = 5 2002; West Greenland: n = 5 1998, n=5 1998, n = 5 2002, n = 5 2002, n = 5), black guillemot (*Cephus grille*; East Greenland: n = 5 2000, n = 5 2000; West Greenland: n = 5 2000, n = 5 2000), and shorthorn sculpin (*Myoxocephalus scorpius*; East Greenland: n = 5 2001, n = 5 2001; West Greenland: n=5 2002, n=5 2002) were obtained from Greenland and liver samples from long finned pilot whale (*Globicephala melas*; n = 11 2001, n = 16 2001, n = 3 2001) and northern fulmars (*Fulmarus glacialis*; n = 9 1998 - 1999, n = 9 1998 -1999) were obtained from the Faroe Islands. PFHxS was only detected in liver samples from polar bear with a reported concentration of <7 µg/kg ww (LOD = 4 µg/kg, LOQ = 7 µg/kg). PFOS was the predominant PFAS in the analysed biota and was found in 13/16 samples from Greenland and in all samples from the Faroe Islands. The largest concentration of PFOS was found in livers of Polar bears from east Greenland (1245-1325 µg/kg ww). The results from Greenland showed a biomagnification of PFOS along the marine food chain (polar bear>ringed seal>shorthorn sculpin). PFOA was only detected in liver samples of polar bear, <12 µg/kg ww (LOD = 7 µg/kg, LOQ = 12 µg/kg) and in 1 out of six liver samples of ringed seal at a concentration of <12 µg/kg ww (LOD = 7 µg/kg, LOQ = 12 µg/kg).

Smithwick *et al.* (2005) measured the levels of some PFAS, including PFHxS, in liver from polar bears (*Ursus maritimus*) collected in East Greenland 1999-2001. The group of bears consisted of 12 males (age 1.5-28 y) and 17 females (age 2-23 y). Arithmetic mean concentrations in liver samples for PFHxS, PFOS and PFOA were 140 ± 26 µg/kg ww, 2470 ± 246 µg/kg ww and 10 ± 2 µg/kg ww, respectively. No statistically significant effect of age or gender was identified. Corresponding values for PFUnA, PFDoA, PFTrDA and PFTeDA are included in Annex II, Table 18.

Smithwick *et al.* (2005) measured the concentration of PFAS, including PFHxS, in liver and blood of polar bears (*Ursus maritimus*) (40 males, age 0.9-28 y; 43 females, age 2 - 25 y) sampled between 1999 and 2002 from five locations in the North American Arctic and two locations in the European Arctic. The samples from Svalbard only consisted of blood collected from free-ranging bears tranquillised for research purposes. Based on a plasma to liver conversion factor from Alaskan samples a concentration in liver was estimated. PFHxS was detected in all of the polar bears from Svalbard and the variation in calculated concentrations is relatively low, however, these concentrations are very different as compared to the concentrations of PFHxS in other arctic regions. The concentrations of PFOS in the Svalbard polar bears, which was also estimated using the plasma to liver conversion factor, are however within range of the other concentrations of PFOS measured in the other arctic regions. The reasons for the unusually high PFHxS concentrations in the Svalbard polar bears are not known, but may be a consequence of local contamination, human

experimental and/or reporting errors, and/or something else. PFOS, PFHxS, and PFOA were detected at concentrations above the minimum detection limit (MDL) at all locations. The geometric mean concentrations of PFHxS in liver ranged from 35.9 µg/kg ww (range <3.3 - 263, 77.8% of samples above MDL) in the North American High Arctic to 2940 µg/kg ww (range 2260 - 4430, 100%>MDL) in Svalbard (which however is estimated from a plasma to liver conversion factor, see above). The geometric mean concentrations of PFOS in liver ranged from 729 µg/kg ww (range <435 - 1480, 100% > MDL) in the Chukchi Sea (Alaska) to 2730 µg/kg ww (range 2000 -3770, 100%> MDL) in South Hudson Bay. The geometric mean concentrations of PFOA ranged from 2.4 µg/kg ww (range <2.3-9.04, 80% > MDL) in the Chukchi Sea (Alaska) to 36 µg/kg ww (range 20 - 55.8, 100% >MDL) in South Baffin Island. The concentrations of PFOS were significantly correlated with age at four out of seven sampling locations. There was no correlation between the concentration of any PFAS and gender. Corresponding values for PFUnDA, PFDoDA, PFTrDA and PFTeDA are included in Annex II, Table 18.

Verreault *et al.* (2005) measured the concentration of a number of PFAS, including PFHxS, in plasma (n = 20) and eggs (n = 10) collected 2004 from glaucous gulls (*Larus hyperboreus*) breeding at Svalbard and Bear Island. An arithmetic mean concentration of PFHxS in eggs was not calculated since the percentage of samples above the method detection limit (MDL) for PFHS (30%) was below the limit of 60% set by the authors and therefore only a range (<0.27-1.23 µg/kg ww) was presented. The geometric mean concentration ± SE of PFHxS in plasma of glaucous gulls was 1.12 ± 0.15 (range 0.29 - 2.71, 100%>MDL). PFOS was detected in 100% of the egg and plasma samples and the geometric mean concentration ± SE in eggs and plasma were 104 ± 13.2 (range 51.7 -196) and 134 ± 16.6 (range 48.1 - 349), respectively. PFOA was not detected above the MDL in eggs (MDL = 0.7 µg/kg ww) and above the MDL in plasma in 5% of the samples (range <0.7 - 0.74). Corresponding values for PFUnDA, PFDoDA, PFTrDA and PFTeDA are included in Annex II, Table 18.

Houde *et al.* (2006) measured the concentrations of a number of PFAS, including PFHxS, in water, sediment, WWTP-effluents, zooplankton, fish and dolphins in Charleston Harbour and Sarasota Bay, USA. The authors also calculated BMFs which are presented in the BMF-section above. Sampling in the Charleston Harbour area included marine water (n = 18; 2004), surface sediment (n = 17; 2004), WWTP (n = 4; 2004), Striped mullet (*Mugil cephalus*; n = 8; 2002/2003), Pinfish (*Lagodon rhomboides*; n = 4; 2002/2003), Red drum (*Sciaenops ocellatus*; n = 8; 2002/2003), Atlantic croaker (n = 3; 2002/2003), Spottfish (*Leiostomus xanthurus*; n = 10; 2002/2003), Spotted seatrout (*Cynoscion nebulosus*; n = 11; 2002/2003), and Bottlenose dolphin (n = 24; 2004). Sampling in the Sarasota Bay area included marine water (n = 10; 2004), surface sediment (n = 8; 2004), zooplankton (n = 3; 2004), Striped mullet (n = 9; 2004), pigfish (*Orthopristis chrysoptera*; n = 10; 2004), Sheepshead (*Archosargus probatocephalus*; n = 3; 2004), Pinfish (n = 10; 2004), Spotted seatrout (n = 8; 2004), and Bottlenose dolphin (n=12; 2004). Plasma, teeth and skin were taken from dolphins from both locations and tissue samples (i.e. liver, kidney, lungs, muscle, heart, thyroid and thymus) were collected from recently deceased bottlenose dolphins in the areas (Charleston, 2003, n = 1, female, 708.4 kg. Sarasota Bay, 2002, n = 1, male, 233.5 kg). An additional 6 liver and kidney samples from stranded bottlenose dolphins were available at Sarasota Bay. The concentration of PFHxS in water was not analysed. The concentration of PFOS and PFOA in the water of Charleston Harbour/Sarasota Bay were 0.012 ± 0.015/0.0009 ± 0.0011 µg/L and 0.0095 ± 0.013/0.0036 ± 0.0092 µg/L, respectively. The concentrations of PFHxS, PFOS and PFOA in sediment in Charleston Harbour/Sarasota Bay were <0.00.9/0.3 ± 0.00.2 µg/kg ww, 0.4 ± 0.5/0.2 ± 0.2 µg/kg ww, and 0.2 ± 0.2/0.06 ± 0.02 µg/kg ww, respectively. PFHxS was not analysed in the WWTP effluents. The concentration of PFOS and PFOA in WWTP effluents in Charleston Harbour were 0.03 ± 0.013 µg/L and 0.059±0.26 µg/L, respectively. The concentrations of PFHxS, PFOS and PFOA in zooplankton from Sarasota Bay were 0.1 ± 0.07 µg/kg ww, 0.2 ± 0.07 µg/kg ww, and 0.3 ± 0.5 µg/kg ww, respectively. The concentration of PFHxS in fish sampled in Charleston Harbour/Sarasota Bay ranged from nd (Atlantic croaker, n = 3; pinfish, n =

4) – $1.1 \pm 0.5 \mu\text{g/kg ww}$ (spotted seatrout; $n = 11$; detected <60%)/nd (stripped mullet, $n = 9$; sheepshead, $n = 3$; spotted seatrout, $n = 8$) – 4.6 ± 2.3 (pinfish, $n = 10$), respectively. The concentrations of PFHxS in bottlenose dolphins from Charleston harbour ($n = 24$) and Sarasota Bay ($n = 12$) were $48 \pm 62 \mu\text{g/kg ww}$ and $115 \pm 101 \mu\text{g/kg ww}$, respectively. The concentration of PFOS in fish sampled in Charleston Harbour/Sarasota Bay ranged from $19 \pm 24 \mu\text{g/kg ww}$ (pinfish, $n = 4$) – $92 \pm 101 \mu\text{g/kg ww}$ (spotfish, $n = 10$)/ $3.1 \pm 2.5 \mu\text{g/kg ww}$ (pigfish, $n = 10$) – $4.6 \pm 2.3 \mu\text{g/kg ww}$ (pinfish, $n = 10$), respectively. The concentrations of PFOS in bottlenose dolphins from Charleston harbour ($n = 24$) and Sarasota Bay ($n = 12$) were $914 \pm 515 \mu\text{g/kg ww}$ and $340 \pm 208 \mu\text{g/kg ww}$, respectively. The concentration of PFOA in fish sampled in Charleston Harbour/Sarasota Bay ranged from $<0.5 \mu\text{g/kg ww}$ (striped mullet, $n = 8$; pinfish, $n = 4$) – $1.8 \pm 3.2 \mu\text{g/kg ww}$ (spotted seatrout, $n = 11$)/ $<0.5 \mu\text{g/kg ww}$ (all fish samples/species), respectively. The concentrations of PFOA in bottlenose dolphins from Charleston harbour ($n = 24$) and Sarasota Bay ($n = 12$) were $48 \pm 62 \mu\text{g/kg ww}$ and $115 \pm 101 \mu\text{g/kg ww}$, respectively. Corresponding values for PFUnDA, PFDoDA, PFTrDA and PFTeDA are included in Annex 2, Table 18.

Falandysz *et al.* (2007) collected blood samples from Cod (*Gadus morhua*) ($n = 18$), Velvet scoter (*Melanitta fusca*) ($n = 5$), Eider duck (*Somateria mollissima*) ($n = 16$), Long-tailed duck (*Clangula hyemalis*) ($n=10$), Razorbill (*Alca torda*) ($n=10$) and Red-throated diver (*Gavia stellata*) ($n = 7$) and liver samples from European beaver (*Castor fiber*) ($n = 10$) in Poland 2003 for analysis of PFAS. The fish and birds were sampled from the Gulf of Gdansk, Baltic Sea, in February 2003. The beavers were sampled from the River Pasleka and the Forest Inspectorate Srokowa in the northeastern part of Poland. The mean \pm SD (range) concentrations of PFHxS in whole blood of cod, velvet scoter, eider duck, long-tailed duck, red-throated diver and razorbill were 0.10 ± 0.17 (0.05-0.80) ng/L, 2.6 ± 1.2 (1.0-4.3) ng/L, 1.1 ± 0.6 (0.40-2.9) ng/L, 2.1 ± 0.5 (1.2-2.7) ng/L, 0.71 ± 0.28 (0.40 - 1.2) ng/L, and 0.27 ± 0.13 (0.12-0.50) ng/L, respectively. The concentration of PFHxS in liver samples of beaver was $<0.01 \mu\text{g/kg}$. The mean \pm SD (range) concentrations of PFOS in whole blood of cod, velvet scoter, eider duck, long-tailed duck, red-throated diver and razorbill were 17 ± 12 (6.1-52) ng/L, 8.9 ± 3.6 (4.8-14) ng/L, 22 ± 14 (12 - 38) ng/L, 22 ± 19 (6.7 - 54) ng/L, 72 ± 57 (40 - 200) ng/L, and 33 ± 6 (23 -39) ng/L, respectively. The concentration of PFOS in liver samples of beaver was 6.6 ± 11.5 (1.6 - 39) $\mu\text{g/kg}$. The mean \pm SD (range) concentrations of PFOA in whole blood of cod, velvet scoter, eider duck, long-tailed duck, red-throated diver and razorbill were 0.20 ± 0.16 (0.05 - 0.70) ng/L, 0.25 ± 0.18 (0.09 - 0.56) ng/L, 0.10 ± 0.6 (0.060 -0.10) ng/L, 0.62 ± 0.51 (0.25 - 1.8) ng/L, 0.50 ± 0.31 (0.17 - 0.85) ng/L, and 0.083 ± 0.087 (<0.05 - 0.30) ng/L, respectively. The concentration of PFOA in liver samples of beaver was 0.13 ± 0.06 (0.06 - 0.28) $\mu\text{g/kg}$.

Haukås *et al.* (2007) measured the concentration of a number of PFAS, including PFHxS, in selected species from the Barents Sea food web. The authors also calculated biomagnification factors which are presented in the BMF-section above. Samples of ice amphipod (*G. wilkitzkii*), polar cod ($n = 50$, size 11.5 - 17.0 cm), adult black guillemot ($n = 18$), and adult glaucous gull ($n = 9$) were collected in 2004. Liver samples from seabirds and polar cod were collected for analyses of contaminants, while whole amphipods were used. Due to the small size of the polar cod liver, samples from three fish of similar length (two females and one male) were pooled ($n = 16$) for the analyses. The amphipods (whole body) were pooled ($n = 6$) according to length to gain homogenised samples of at least 1 g. Mean concentrations (and proportions detected) in ice amphipod, polar cod, black guillemot, and glaucous gull for PFHxS were: not detected (<MDL: 0.03 ng/g w.w.), 0.04 ± 0.003 (9/16), 0.17 ± 0.02 (17/18), and 0.26 ± 0.006 (9/9) ng/g w.w., respectively. The corresponding concentrations (and proportions detected) for PFOS in ice amphipod, polar cod, black guillemot, and glaucous gull were: 3.85 ± 1.17 (5/6), 2.02 ± 0.13 (16/16), 13.5 ± 2.79 (17/18), and 65.8 ± 22.4 (9/9) ng/g w.w., respectively, and for PFOA only a mean concentration in ice amphipods (3.15 ± 0.34 ng/g w.w) was presented as it was only detected in a minority of the polar cod (3/16, range n.d.-1.88) and Black guillemot (5/16, range n.d. - 17.1) and not detected at all (0/9) in the Glaucous gull. PFUnDA, PFDoDA, PFTrDA and PFTeDA was not detected above the limit of detection.

Knudsen *et al.* (2007) measured the concentrations of a number of chemicals, including PFHxS, in liver samples of adult northern fulmar (*Fulmarus glacialis*, n=15) from Bear Island in the Barents Sea. PFHxS was detected in all (15/15) liver samples with a mean \pm SD of $1.0 \pm 0.3 \mu\text{g/kg ww}$ (range 0.5-1.6). PFOS was detected in 13/15 liver samples at a concentration of $3.4 \pm 2.2 \mu\text{g/kg ww}$ (range 0.8 - 8.3). There were no samples of PFOA above the detection limit in the liver samples. The authors also conducted analysis of the stable isotopes $\delta^{13}\text{C}$, which indicated that the analysed northern fulmars were highly associated to the pelagic food web, and $\delta^{15}\text{N}$, which indicated that the fulmars occupy an intermediate trophic level in the marine food web.

Bakke *et al.* (2008) report of a compilation of the results from five projects on analysis of selected contaminants of concern in various types of samples from the Barents Sea region. Measurements of PFHxS is included in the project of measuring contaminants in eggs of Brünnich's guillemot (*Uria lomvia*) sampled from 2 stations (Bear Island and Kongsfjorden) during several years (1993, 2002, 2003 and 2007) resulting in a total of five groups each consisting of five replicate eggs that were analysed individually (Bear Island 2003 and 2007; Kongsfjorden 1993, 2002 and 2007). PFHxS was detected in all samples from Bear Island at concentrations of $0.1 \pm 0.1 \mu\text{g/kg ww}$ (2003; 5/5 individual eggs) and $0.04 \pm 0.0 \mu\text{g/kg ww}$ (2007; 5/5), and in all three samples from Kongsfjorden at concentrations of $0.1 \pm 0.1 \mu\text{g/kg ww}$ (1993; 5/5), $0.1 \pm 0.0 \mu\text{g/kg ww}$ (2002; 5/5), and $0.1 \pm 0.0 \mu\text{g/kg ww}$ (2007; 4/5). PFOS was also detected in all samples from Bear Island at concentrations of $26.0 \pm 9.8 \mu\text{g/kg ww}$ (2003; 5/5 individual eggs) and $10.8 \pm 2.4 \mu\text{g/kg ww}$ (2007; 5/5), and in all three samples from Kongsfjorden at concentrations of $17.5 \pm 2.1 \mu\text{g/kg ww}$ (1993; 5/5), $10.9 \pm 1.5 \mu\text{g/kg ww}$ (2002; 5/5), and $8.5 \pm 2.0 \mu\text{g/kg ww}$ (2007; 5/5). PFOA was only detected in the sample from Bear Island from 2003 at $0.1 \pm 0.0 \mu\text{g/kg ww}$ (5/5), and in the sample from Kongsfjorden from 2002 at $0.9 \pm 0.2 \mu\text{g/kg ww}$ (5/5). Corresponding values for PFUnDA, PFDoDA, PFTrDA and PFTeDA are included in Annex II, Table 18.

Lilja *et al.* (2009) reported from a screening study performed 2008/2009 in the eastern Baltic Sea environment on the occurrence of a number of hazardous substance/substance groups, including PFAS, in water and fish liver. All water samples of PFHxS was below the LOQ (0.3 - 1.0 ng/L). PFOS and PFOA could only be detected in the Szczecin Lagoon, Poland, and their concentrations were $2.2 \mu\text{g/L}$ and $6.0 \mu\text{g/L}$, respectively. PFHxS was above the LOQ in 17 (range 0.1 - 1.1 $\mu\text{g/kg ww}$) out of a total of 23 fish liver samples. The highest concentration (1.1 $\mu\text{g/kg ww}$) was found in flounder caught in the coastal area north of Klaipeda, Lithuania. PFOS was found in all fish liver samples from all sites in the concentration range 4.3 - 61 $\mu\text{g/kg ww}$, with the highest concentration (61 $\mu\text{g/kg ww}$) found in perch caught in the Szczecin Lagoon, Poland. All measurements of PFOA in fish liver were below the LOQ (1.2 - 5.1 $\mu\text{g/kg ww}$). Corresponding values for PFUnDA are included in Annex II, Table 18. Schiavone *et al.* (2009) measured the levels of ten PFAS, including PFHxS, in eggs of Adélie penguins and Gentoo penguins and in Antarctic fur seals in South Shetland, Antarctica. The samples from the Antarctic fur seal (*Arctocephalus gazelle*) pups (≤ 2 months of age, n = 20) was collected in 2004 and consisted of muscle (n = 20) and liver (n = 17). Unhatched eggs of Adélie penguins (*Pygoscelius adeliae*, n = 13) and Gentoo penguins (*Pygoscelius papua*, n = 13) were sampled during the field season 2004/2005. PFHxS was detected in 82% of the liver samples of the fur seal pups with a mean concentration $<0.4 \mu\text{g/kg}$ (LOQ = $0.4 \mu\text{g/kg}$), but was not detected in the fur seal pups muscle samples or in the penguin eggs (LOQ = $0.1 \mu\text{g/kg}$). PFOS was detected in 100% of all the samples and the measured mean \pm SD in fur seal pup liver and muscle were $9.4 \pm 3.2 \mu\text{g/kg}$ and $1.3 \pm 0.7 \mu\text{g/kg}$, respectively, and $0.4 \pm 0.2 \mu\text{g/kg}$ and $0.3 \pm 0.1 \mu\text{g/kg}$ in eggs of Adélie and Gentoo penguins, respectively. PFOA was detected in 6% and 50% of the fur seal pup liver and muscle samples, respectively, and in 23% and 8% of the Adélie and Gentoo penguins, respectively. The reported mean concentrations of PFOA were $<0.4 \mu\text{g/kg}$ and $0.8 \pm 0.8 \mu\text{g/kg}$ in fur seal pup liver and muscle, respectively, and $<0.2 \mu\text{g/kg}$ and $<0.2 \mu\text{g/kg}$ in eggs of Adélie and Gentoo penguins, respectively. The concentrations of PFAS were significantly higher in fur seal pup liver, as compared to muscle. PFOS was the PFAS detected at the highest concentrations in the fur seal pups samples (both liver and

muscle). However, several long-chain PFCAs (PFDA, PFUnDA, PFDoDA) were detected in penguin samples at concentrations higher or no less than that of PFOS. The PFAS concentrations differed significantly ($p < 0.005$) between seals and penguins and between the two species of penguins ($p < 0.005$). The authors suggested that differences in diet and metabolism might explain the variation in concentrations observed between the different PFAS. Corresponding values for PFUnDA and PFDoDA are included in Annex II, Table 18.

Dietz *et al.* (2012) studied spatial trends of concentrations of PFAS in livers of 59 harbour seals (*Phoca vitulina*) from seven locations in Danish waters, (Wadden Sea, Limfjord, three areas in Kattegat and two areas in the western Baltic). All samples were collected during the PDV epizootic in the summer of 2002 and the sample sizes per region ranged from 5-13. PFOS was the dominating PFAS (92%) among the samples, followed by PFHxS (1.8%) with PFOA constituting 0.9% of the total amount of measured PFAS. The concentration of PFHxS was lowest in Northern Kattegat (age 1 - 9 y) with a mean concentration of $2.7 \pm 1.8 \mu\text{g/kg ww}$ ($n = 5$, range 0.9 - 5.4) and highest in the Wadden Sea (2-7 y) in the southern North Sea with a concentration of $16.3 \pm 7.9 \mu\text{g/kg ww}$ ($n = 13$, range 6.5 - 32.4). The overall PFHxS mean concentration was $7.1 \pm 6.5 \mu\text{g/kg ww}$ ($n = 59$, range 0.0 - 32.4). The concentration of PFOS was also lowest in Northern Kattegat with a mean concentration of $144.9 \pm 131.5 \mu\text{g/kg ww}$ ($n=5$, range 26.9-371.2) and highest in the Wadden Sea with a concentration of $689.1 \pm 236.2 \mu\text{g/kg ww}$ ($n = 13$, range 430 - 1284.2). The overall PFOS mean concentration was $397.5 \pm 302.8 \mu\text{g/kg ww}$ ($n=59$, range 26.9 - 1384.2). The concentration of PFOA was lowest in Southern Kattegat (1 - 7 y) with a mean concentration of $0.5 \pm 0.6 \mu\text{g/kg ww}$ ($n=10$, not all samples above the LOD. Highest measured concentration was 3.2) and highest in Limfjorden with a concentration of $3.3 \pm 1.9 \mu\text{g/kg ww}$ ($n = 11$, range <LOD-5.9). The overall PFOA mean concentration was $1.6 \pm 1.7 \mu\text{g/kg ww}$ (range: not detected - 6.1). Corresponding values for PFUnDA are included in Annex II, Table 18.

Norström and Viktor (2012) measured the levels of PFAS in water and perch samples collected during 2011 - 2012 for the RE-PATH project (Risks and Effects of the dispersion of PFASs on Aquatic, Terrestrial, and Human populations in the vicinity of International Airport). Two lakes in connection to Stockholm Arlanda Airport (Halmsjön, close to the airport; and Valloxen, background) and three lakes in connection to Göteborg Landvetter Airport (Lilla Issjön, closest to the airport; V:a Ingsjön, downstream Lilla Issjön; and Sandsjön, background) were selected for the project. PFHxS could be detected in all surface waters (range 0.45 - 2490 ng/L) which were situated in the catchment basin of the airports, but not in the reference lakes. PFHxS could be detected in all muscle samples of perch ($n = 7$) that caught in Halmsjön and the reported mean level was $0.31 \mu\text{g/kg ww}$ (range: 0.20 - 0.39). The concentrations in perch from V:a Ingsjön were lower and PFHxS could only be detected in five of the eight perch (range: < 0.03 - 0.17 $\mu\text{g/kg ww}$). The concentrations of PFOS in surface waters and fish close to the airports are substantially increased, as compared to the reference lakes. Levels of PFOS in water and perch muscle range from <2 to 7590 ng/L and 22 to 384 $\mu\text{g/kg ww}$. The concentration of PFOA in water range from <0.6 - 492 ng/L. PFOA was not detected in perch muscle. The levels of both PFHxS and PFOS decreased in water and with increasing distance from the firefighting exercise sites.

Jaspers *et al.* (2013) sampled tail feathers and soft tissues (liver, muscle, preen gland and adipose tissues) from 15 road-killed barn owl (*Tyto alba*) in the province of Antwerpen, Belgium, for analysis of PFAS. A major PFAS producing factory is located in this area and previous studies had found high levels of PFAS in biota. PFHxS could only be quantified in liver and preen oil with median concentrations of 21 $\mu\text{g/kg ww}$ ($n = 13$, 3/13 <LOD; range <6.3 - 107) and 32.1 $\mu\text{g/kg ww}$ ($n = 5$, 1/5 <LOD; range <2.1 - 59.3), respectively. PFHxS was detected in tail feathers ($n = 13$, 8/13 <LOD; range <1.9 - 8.1) and adipose tissues ($n = 7$, 6/7 <LOD; range <0.6 - 4.6). PFOS could be quantified in all tissues and the reported median concentrations were 15.8 $\mu\text{g/kg ww}$ ($n = 13$, 1/13 <LOD; range <2.2 - 55.6) in tail feathers, 135.2 $\mu\text{g/kg ww}$ ($n = 15$, 0/15 <LOD; range 11.1 - 477) in muscle, 304.5 $\mu\text{g/kg ww}$ ($n = 13$, 0/13 < LOD; range 42 - 992) in liver, 431.2 $\mu\text{g/kg ww}$ ($n=5$, 0/5 <LOD; range

78 - 1208) in preen oil, and 202.7 µg/kg ww (n = 7, 0/7 <LOD; range 51 - 609) in adipose tissue. PFOA could only be quantified in tail feathers and preen oil with median concentrations of 37.1 µg/kg ww (n = 13, 5/13 <LOD; range <14.1 - 670) and 21.5 µg/kg ww (n = 5, 2/5 <LOD; range <5.2 - 46.6), respectively. PFOA was detected in liver (n = 12, 7/12 <LOD; range <16.2 - 116) and adipose tissues (n = 7, 6/7 <LOD; range <2.3 - 22.6).

Naile *et al.* (2013) measured the concentration of a number of PFAS, including PFHxS, in water, sediment and biological samples along the Korean west coast. The authors also calculated BCFs (or rather BAFs) which are presented in the BAF-section above. Samples of sediment (n = 12), soil (n = 13) and surface water (n = 15) were collected at the same time as the biological samples. The mean/median (range; amount of samples >LOD) concentrations of PFHxS, PFOS and PFOA in water were 0.0017/0.0005 (<0.0002 - 0.0087; 12/15) µg/L, 0.0087/0.004 (0.00035 - 0.047; 15/15) µg/L and 0.0068/0.0037 (0.00054-0.031; 15/15) µg/L, respectively. PFHxS was not detected in sediment. The concentrations of PFOS and PFOA in sediments were 1.5/1 (<0.2 - 5.8; 7/12) µg/kg dw, and 1/0.69 (<0.2 - 2.4; 5/12) µg/kg dw, respectively. The biological samples consisted of bivalves (n = 5; consisting of *Mytilus edulis*, *Macra veneriformis*, *Nuttallia olivacea*, and *Sinonovacula constricta*), gastropods (n=11; consisting of *Littorina brevicula*, *Monodonta labio*, *Umbonium thomasi*, and *Glossaulax didyma*), crabs (n=44; consisting of *Hemigrapsus sanguineus*, *Sesarma pictum*, *Hemigrapsus penicillatus*, *Helice tridens tridens*, and *Philyra pisum*), and fish (n=15; consisting of *Acanthogobius flavimanus*, *Sebastes schlegeli*, *Tridentiger obscurus*, *Hexagrammos otakii*, and *Mugil cephalus*) and were collected in May 2009 from coastal and estuarine areas along the South Korean west coast. All samples within each biotic group were pooled and homogenised. The mean/median (range; amount of samples >LOD) concentrations of PFHxS in bivalves, gastropods, crabs, and fish were 0.47/0.19 (0.073 - 1.4; 5/5) µg/kg ww, 0.45/0.42 (0.16 - 1.1; 11/11) µg/kg ww, 0.30/0.15 (0.039 - 3.3; 44/44) µg/kg ww, and 0.28/0.17 (0.020 - 1.2; 15/15) µg/kg ww, respectively. The mean/median (range; amount of samples >LOD) concentrations of PFOS in bivalves, gastropods, crabs, and fish were 0.13/0.12 (0.11 - 0.17; 5/5) µg/kg ww, 0.36/0.27 (<0.046 - 0.95; 7/11) µg/kg ww, 1.1/0.83 (0.089 - 3.7; 44/44) µg/kg ww, and 13/9.3 (0.73 - 51; 15/15) µg/kg ww, respectively. The mean/median (range; amount of samples >LOD) concentrations of PFOA in bivalves, gastropods, crabs, and fish were 0.12/0.042 (<0.036 - 0.29; 3/5) µg/kg ww, 0.045/0.038 (<0.046 - 0.088; 7/11) µg/kg ww, 0.33/0.26 (<0.068 - 1.8; 40/44) µg/kg ww, and 0.062/0.021 (<0.044 - 0.23; 5/15) µg/kg ww, respectively. Corresponding values for PFUnDA and PFDoDA are included in Annex II, Table 18.

Person *et al.* (2013) measured the concentration of a number of PFAS in livers of 99 wild male mink (*Neovison vison*) from four different locations in Sweden (Baltic coast, Koster Island in Skagerrak, anthropogenic inland region, and rural inland of Northern Sweden). The sampling was performed from 2004 to 2009. The concentration of PFHxS was lowest in the rural inland of Northern Sweden with a mean concentration of 1.1 ± 1.2 µg/kg ww (n = 24, range <0.1 - 4.0) and highest in the anthropogenic inland region with a concentration of 32.1 ± 38.4 µg/kg ww (n = 25, range 0.3 - 139). The overall PFHxS mean concentration was 11.0 ± 22.8 µg/kg ww (n=99, range <0.1 - 139).

The concentration of PFOS was also lowest in the rural inland of Northern Sweden with a mean concentration of 170 ± 197 µg/kg ww (n = 24, range <0.8 - 854) and highest in the anthropogenic inland region with a concentration of 3310 ± 5850 µg/kg ww (n = 25, range 87 - 21800). The overall PFOS mean concentration was 1250 ± 3170 µg/kg ww (n = 99, range <0.8 - 21800). The concentration of PFOA was lowest in the rural inland of Northern Sweden and in the anthropogenic inland region with mean concentration of 0.7 ± 0.9 µg/kg ww (n = 11, range <0.2 - 2.8) and 0.7 ± 0.9 µg/kg ww (n = 18, range <0.2 - 3.3), respectively, and highest on the Koster Island in Skagerrack with a concentration of 3.9 ± 2.2 µg/kg ww (n = 19, range 1.0 - 9.9). The overall PFOA mean concentration was 2.0 ± 2.1 µg/kg ww (n = 99, range <0.2 - 9.9). The concentrations of PFHxS, PFOS, and PFOA detected in the minks were not influenced by age, body condition or body weight.

Corresponding values for PFUnDA, PFDODA and PFTrDA are included in Annex II, Table 18.

Zhou et al. (2014) performed a comprehensive exposure assessment of a number of PFAS, including PFHxS, in fishery employees from Tangxun Lake, China. Tangxun Lake is a shallow lake located in Hubei Province, which is one of the production bases of several small-scale fluorochemical manufacturers and users in China. Measurements of PFAS were made in blood and urine samples collected in April 2012 from fishery employees (n = 39), their family members (n = 7) and a reference group (n=9). Drinking water (n=2) and indoor dust samples (n=3) were collected from the homes of the fishery employees on two occasions in December 2011 and October 2012. Aquatic biota samples (n = 60) were collected in December 2011 and consisted of: river snail (*Viviparus*, soft tissues; 6 pooled samples, with each pool consisting of 25 individuals), shrimp (*Macrobrachium nipponese*, whole-body; 3 pooled samples, with each pool consisting of 6 individuals), silver carp (*Hypophthalmichthys molitrix*, muscle; n=6), bighead carp (*Hypophthalmichthys nobilis*, muscle; n=8), white amur bream (*Parabramis pekinesis*, muscle; n=8), grass carp (*Ctenopharyngodon idellawere*, muscle; n=8), yellow catfish (*Pelteobagrus fulvidraco*, muscle; n=8), common carp (*Cyprinus carpio*, muscle; n=8), and mallard (*Anas platyrhynchos*, muscle; n=5). The median concentrations of PFHxS range from 1.25 µg/kg ww in silver carp to 26.6 µg/kg ww in common carp. The corresponding min-max ranges for ΣPFOS were 174 µg/kg ww in river snail to 684 µg/kg ww in common carp, and for PFOA from 0.32 µg/kg ww in bighead carp to 2.14 µg/kg ww in river snail. Corresponding values for PFUnDA, PFDODA and PFTrDA are included in Annex II, Table 18.

Levels in wildlife – temporal trends

There are reports of both decrease (Swedish farmed eggs and rainbow trout from 1999-2010; Ringed seals in Greenland from 1982-2010; Polar bears on Svalbard 1998-2008), and increase followed by a level out (Swedish Peregrine Falcons from 1974-2007; Grey seals in the Baltic Sea from 1969-2008; Polar bears in East Greenland 1984-2011) of the concentrations of PFHxS in biota.

The data by Kratzer et al. (2011), and Riget et al. (2013), which both include individual data for a number of years, are presented for PFHxS and PFOS in Figure 4 below.

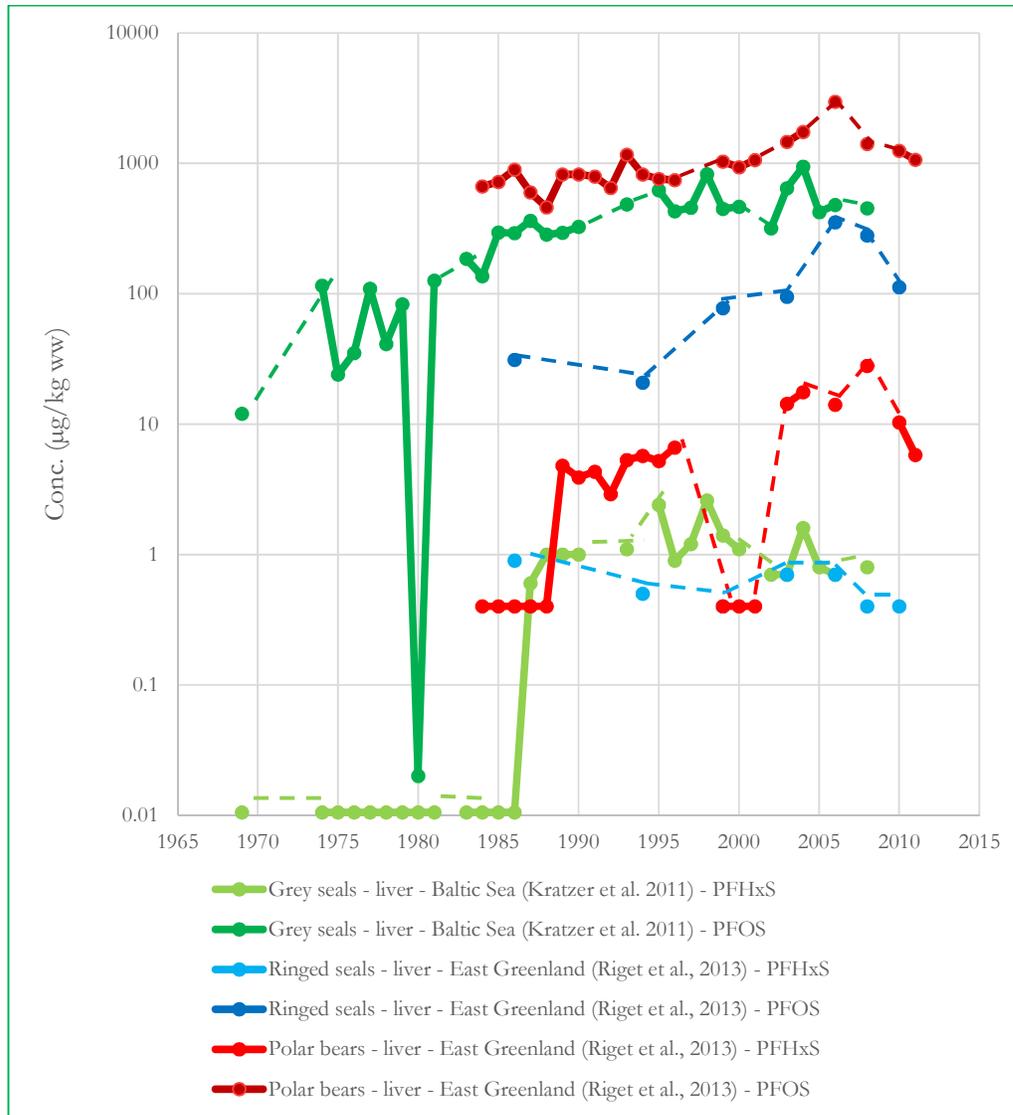


Figure 4. Concentrations of PFHxS and PFOS in seals and polar bears. Data from Kratzer et al. 2011 and Riget et al. 2013.

After an initial delay phase, with PFHxS concentrations below the limit of detection, the measured concentrations of PFHxS appear to follow the concentrations of PFOS with a relatively constant difference in concentrations, probably because PFHxS has been found as an impurity in PFOS ((Seacat et al., 2002), (Jiang, Zhang, Yang, Chu, & Zhu, 2015)). It appears that the overall concentrations are beginning to decrease after 2006/2008 and the reason for this may be a combination of the 3M phase-out of PFOS and PFHxS in the USA between 2000 and 2002 and the inclusion of PFOS on the UNEP POP-list of chemicals. It can also be seen that the concentrations in polar bears are higher than those in ringed seals from the same region which suggests a potential of biomagnification.

Butt *et al.* (2007) investigated the temporal trends of PFAS, including PFHxS, in liver samples of two populations of ringed seal (*Phoca hispida*) in the Canadian Arctic, Arviat (n=36) and Resolute Bay (n = 39). The number of individual samples available for the individual years were for Arviat: 1992 (n = 6), 1998 (n = 10), 2004 (n = 10), 2005 (n = 10) and for Resolute Bay: 1972 (n = 2), 1993 (n = 9), 2000 (n = 9), 2004 (n = 9), 2005 (n = 9). PFHxS was not detected in any of the ringed seal liver samples. The arithmetic

mean (min - max) concentrations of PFOS from Arviat from 1992-2005 were 22.7 µg/kg ww (11.7 - 41.6), 91.6 µg/kg ww (36.3-177), 35.1 µg/kg ww (20.8 - 74.1), and 19.6 µg/kg ww (8.0 - 44.1), respectively. The corresponding concentrations for Resolute Bay from 1972-2005 were 1.8 (0.58 - 3.0), 7.0 (1.6 - 14.7), 22.1 (4.4 - 49.7), 16.8 (5.9 - 27.7), and 8.1 (2.0-17.0), respectively. The arithmetic mean (min-max) concentrations of PFOA from Arviat were <0.85 µg/kg ww (nd - <0.85), 1.13 µg/kg ww, 1.67 µg/kg ww (0.98-3.61), and 0.98 µg/kg ww (0.96 - 1.01), respectively. The corresponding concentrations for Resolute Bay were 1.1 (0.97 - 1.2), 4.5 (<3.6 - 4.5), 3.9 (<3.6 - 4.1), 6.2 (<3.6 - 6.2), and <0.85, respectively. The authors proposed that the relatively short doubling times of the PFCA and PFOS disappearance half-lives support the hypothesis of atmospheric transport as the main transport mechanism of PFAS to the Arctic. Corresponding values for PFUnDA, PFDoDA, PFTrDA and PFTeDA are included in Annex II, Table 18.

Butt *et al.* (2008) examined the spatial trends of PFAS in liver samples from 11 populations of ringed seals (*Phoca hispida*) in the Canadian Arctic from 2002 to 2005. The ringed seal liver samples (n=10/site) were collected during annual hunting seasons (April-June) from 11 locations in the Canadian Arctic: Inukjuak (2002), Pangnirtung (2002), Grise Fjord (2003), Arctic Bay (2004), Gjoa Haven (2004), Pond Inlet (2004), Arviat (2005), Nain (2005), Qikiqtarjuaq (2005), Resolute Bay (2005), and Sachs Harbor (2005). PFHxS were only infrequently (<25%) measured above the method detection limit (MDL). For calculation of means, concentrations that were less than the MDL or not detected were replaced by a random number less than half the MDL. The geometric mean concentrations of PFHxS, PFOS and PFOA in livers from ringed seals ranged from <0.73 - 2.5 µg/kg ww, 6.5 - 88.8 µg/kg ww, and <0.78 - 2.0 µg/kg ww, respectively for the different locations. Corresponding values for PFUnDA, PFDoDA, PFTrDA and PFTeDA are included in Annex II, Table 18.

Bignert *et al.* ((2008), (2009), (2011)) sampled herring (n = 10 - 12/year) from six locations along the Swedish East and West coast between 2005 and 2009 as part of the monitoring activities performed within the National Swedish Contaminant Programme. The livers of herring were analysed and the highest concentration of PFHxS, 2.2 µg/kg ww, was detected in 2007 and 2008. The highest concentration of PFOS, 25.6 µg/kg ww, was measured in 2007. The highest concentrations for PFOA, 2.5 µg/kg ww, was detected in 2007/2008 and is read from a figure in Bignert *et al.* (2011).

The report by Bignert *et al.* (2013) from 2013 summarises the monitoring activities performed within the National Swedish Contaminant Programme in marine biota in which several perfluorinated compounds, including PFHxS, is included. No exact concentrations are presented in the report, only trends over several years. The concentration of PFHxS was higher in the Baltic Proper as compared to the Bothnian Bay and the Swedish west coast. The levels of PFHxS and PFOS show a similar spatial pattern, with the difference that PFOS also display increased concentrations in the northern Bothnian Bay and that the concentrations of PFOS were approximately 25 times higher. The temporal trend for PFHxS in herring liver from 2005-2011 at the six locations from the Swedish west and east coast is inconsistent, but an increasing trend is indicated at one of them (Fladen). PFOS is rather homogeneously distributed along the Swedish coast. The concentration of PFOS is about 100 - 200 times higher in guillemot eggs as compared to that in herring liver. A consistent increasing trend of PFOS in guillemot eggs has been observed throughout the whole time period, from 1968, but during the last ten years a decreasing trend is indicated. PFOA showed an increasing trend in herring livers at one of the six locations (Utlången). Corresponding values for PFUnDA and PFTrDA are included in Annex II, Table 18.

Holmström *et al.* (2010) studied the temporal trend of PFAS in Swedish peregrine falcons (*Falco peregrinus*) eggs (n = 125) collected between 1974 and 2007 within the Swedish Society for Nature Conservation monitoring program. Due to low breeding success of the peregrine falcons only few eggs were available for the first 20 years of the study period, and no eggs were available between 1987 and 1991. As a consequence of that all eggs up to 1999 were analysed individually. From year 2000 and onwards more eggs became

available and pooled samples were analysed. PFHxS and PFOS were detected in falcon eggs already from 1974, while PFOA was not detected at all above its method detection limit (MDL). However, since traces of PFOA occasionally was found in the blanks, the MDL for PFOA became elevated (mean MDL for PFOA = 2.2 µg/kg ww (range 1.4 - 2.9), as compared to the MDLs for PFHxS and PFOS which were 0.04 µg/kg ww (0.02 - 0.06) and 0.3 µg/kg ww (0.2 - 0.6), respectively). The yearly mean concentration of PFHxS and PFOS during 1974 - 2007 ranged from 0.05 µg/kg ww (1975) – 2.7 µg/kg ww (1992) and from 7 µg/kg ww (1974) – 301 µg/kg ww (1992), respectively. The arithmetic mean concentrations of PFHxS and PFOS in the ten peregrine falcon eggs collected 2006 were 0.80 µg/kg ww (range 0.52 - 1.9) and 83 µg/kg ww (range 40 - 220), respectively. Corresponding values for PFUnDA, PFDoDA, PFTTrDA and PFTeDA are included in Annex II, Table 18.

Kratzer *et al.* (2011) examined the temporal trends of PFAS in liver samples of 78 grey seals (*Halichoerus grypus*) from 1974-2008. The samples were obtained from the Environmental Specimen Bank (ESB) at the Swedish Museum of Natural History. The levels PFHxS increased significantly ($p < 0.0001$) from 1974-1997 and then decreased significantly ($p = 0.048$) from 1997-2008. PFHxS was not detected until 1987. The concentrations of PFHxS in grey seal liver samples range from not detected (1974-1986) – to a maximum of 2.6 µg/kg ww (1998, $n = 2$, 1.8 - 3.7). PFOS was detected in all individual liver samples and the predominant compound. It increased significantly from 1974-2008 ($p < 0.0001$), however the data after 1997 was very scattered and the temporal trend after 1997 was not significant. The PFOS concentrations range from 0.02 (1980, $n=1$) to a maximum of 825 µg/kg ww (1998, $n = 2$, 561 - 1213). The levels of PFOA increased significantly between 1974 and 1997 ($p < 0.0001$) and then decreased from 1997 to 2008 ($p < 0.05$). PFOA was first detected in 1977 and the reported concentrations range from not detected (1974 - 1977, 1981 - 1983) to a maximum of 11 µg/kg ww (1998, $n = 2$, 10 - 11). Corresponding values for PFUnDA, PFDoDA, PFTTrDA and PFTeDA are included in Annex II, Table 18.

Bytingsvik *et al.* (2012) measured the levels of PFASs in blood plasma from polar bear (*Ursus maritimus*) mothers and their suckling cubs-of-the-year (~4 months old) on Svalbard collected in 1998 (12 mothers, 16 cubs (4 sibling pairs)) and 2008 (9 mothers, 12 cubs (3 sibling pairs)). PFHxS was detected in all polar bear mothers. The reported mean (median) ± SEM concentration for 1998 and 2008 were 40.8 (39.0) ± 2.9 µg/kg ww and 32.6 (28.5) ± 3.4 µg/kg ww, respectively. Both PFOS and PFOA were also detected in all polar bear mothers. The corresponding concentrations for PFOS for 1998 and 2008 were 432 (455) ± 17.0 µg/kg ww and 309 (314) ± 38.2 µg/kg ww, respectively. The corresponding concentrations for PFOA for 1998 and 2008 were 6.4 (6.0) ± 0.6 µg/kg ww and 4.1 (3.7) ± 0.3 µg/kg ww, respectively. PFHxS was detected in all polar bear cubs. The reported mean (median) ± SEM concentration for 1998 and 2008 were 12.0 (10.4) ± 1.2 µg/kg ww and 12.2 (12.2) ± 0.9 µg/kg ww, respectively. Both PFOS and PFOA were also detected in all polar bear cubs. The corresponding concentrations for PFOS for 1998 and 2008 were 86.0 (83.4) ± 5.5 µg/kg ww and 65.3 (65.3) ± 0.9 µg/kg ww, respectively. The corresponding concentrations for PFOA for 1998 and 2008 were 2.1 (1.9) ± 0.3 µg/kg ww and 2.3 (2.2) ± 0.2 µg/kg ww, respectively. The concentrations of PFHxS and PFOA were not significantly different between 1998 and 2008, but the concentrations of PFOS decreased significantly between 1998 and 2008. The concentrations of PFHxS, PFOS and PFOA were higher in mothers than their cubs, and the concentration of PFHxS, PFOS and PFOA in mothers and their cubs were significantly correlated with the concentrations in their cubs. The findings confirm a maternal transfer of PFAS from polar bear mothers to their cubs. The levels found in the cubs are expected to be the result of both prenatal and postnatal transfer in addition to the influence of toxicokinetic processes in mothers and cubs during the postnatal period. Corresponding values for PFUnDA, PFDoDA, PFTTrDA and PFTeDA are included in Annex II, Table 18.

Glynn and co-workers (2012) performed a time-trend analysis of perfluorinated compounds in egg yolk, raw cow milk and farmed rainbow trout from Swedish food production from 1999 - 2010. The samples had been collected within the Swedish National Food Agency's

official food control program. A total of 36 pooled egg samples, 36 pooled milk samples and 36 individual fish muscle samples were analysed. PFHxS decreased significantly in egg yolk ($r^2 = 0.72$, $p < 0.001$) and farmed rainbow trout ($r^2 = 0.38$, $p < 0.032$) between 1999 and 2010. The median concentration in egg yolk and fish were 12 ng/kg ww (range <10 - 128) and 13 ng/kg ww (range <11 - 40), respectively. It was not possible to analyse the temporal trend of PFHxS in milk since it was only present in 4/16 samples ($n = 4$, range 1.0 - 1.1 ng/kg ww). PFOA decreased significantly in egg yolk ($r^2 = 0.80$, $p < 0.001$) and farmed rainbow trout ($r^2 = 0.63$, $p < 0.002$) between 1999 and 2010. The median concentration in egg yolk and fish were 375 ng/kg ww (range <26 - 6478) and 121 ng/kg ww (range <37 - 795), respectively. PFOS could be quantified in milk (range 3.5-7.3 ng/kg ww), but the detected concentrations were close to the minimum detection level and no trend could be identified. PFOA decreased significantly in egg yolk ($r^2 = 0.45$, $p < 0.001$) between 1999 and 2010. The median concentration in egg yolk was 21 ng/kg ww (range <14 - 225). It was only detected in one fish sample (84 ng/kg ww). It was not possible to analyse the temporal trend of PFOA in milk since it was not detected in milk. Corresponding values for PFUnDA, PFDoDA and PFTrDA are included in Annex II, Table 18.

Rigét and co-workers (2013) measured the concentrations of seven PFAS, including PFHxS, in liver of ringed seal ($n = 177$) from West Greenland and East Greenland and polar bears ($n = 148$) from East Greenland. The ringed seal samples were collected in the central East Greenland and the central West Greenland during 1982 - 2010. The polar bear samples were collected from the central East Greenland during 1984 - 2011. The age of the individual ringed seals and polar bears used for the analysis was below six years in order to minimise age influence on the time trends. The concentration of PFHxS, PFOS, and PFOA, were higher in polar bears than in ringed seals. The concentrations of PFHxS in ringed seals from West Greenland (1982 - 2010) were below LOD in 98% of the all the samples and could only be determined for the first year of the time series (mean 0.5 $\mu\text{g/kg ww}$; based on 2/10 with values above LOD). In East Greenland 79% of the samples from ringed seals were below LOD and annual means were only possible to calculate for 1986 (mean 0.9 $\mu\text{g/kg ww}$; 4/9), 1994 (mean 0.5 $\mu\text{g/kg ww}$; 2/6), and 2003 (mean 0.7 $\mu\text{g/kg ww}$; 4/9) and 2006 (mean 0.7 $\mu\text{g/kg ww}$; 6/14). PFHxS was detected in 53% of the polar bear samples. The temporal trend for PFHxS is somewhat complex as it was not detected in 1984-1988 (five years), with annual means from 2.9 to 6.6 $\mu\text{g/kg ww}$ between 1989-1996, not detected between 1999 - 2001 (three years) and from 2003 - 2011 concentrations ranging from 10.3 (2010) to 27.9 $\mu\text{g/kg ww}$ (2008). PFHxS was significantly correlated ($r = 0.43$, $p < 0.01$) with PFOS in polar bears. PFOS was by far the most dominant PFAS constituting 85% in polar bears (East Greenland), and 88% and 92% in ringed seal from East and West Greenland, respectively. It was detected in 100% of all samples of ringed seal with annual mean concentrations in ringed seals from West Greenland ranging from a minimum of 12.5 $\mu\text{g/kg ww}$ (1982) to a maximum of 397 $\mu\text{g/kg ww}$ (2006) and from East Greenland from 20.8 $\mu\text{g/kg ww}$ (1994) - 352 $\mu\text{g/kg ww}$ (2006), with the concentrations from East Greenland being significantly higher. PFOS was also detected in 100% of samples from polar bears and the concentrations ranged from 460 $\mu\text{g/kg ww}$ (1988) to 2966 $\mu\text{g/kg ww}$ (2006). The temporal trend for PFOS in polar bear and ringed seals are similar with an increase from 1984 to 2006, followed by a decrease to 2011. PFOA was not detected in 78% and 84% of the ringed seals in West and East Greenland, respectively. The concentrations of PFOA in ringed seals indicated a peak during 2006 (2.4 $\mu\text{g/kg ww}$) and 2008 (1.2 $\mu\text{g/kg ww}$) in West Greenland and during 2006 (1.6 $\mu\text{g/kg ww}$) and 2008 (2.2 $\mu\text{g/kg ww}$) in East Greenland. For polar bears 17% of the samples were below the LOD. The concentration of PFOA in polar bears ranged between LOD (1988; only one individual)/4.4 $\mu\text{g/kg ww}$ (2011; ten individuals) and 14.0 $\mu\text{g/kg ww}$ (2006). No significant correlation ($r = 0.12$, $p = 0.13$) was identified between the concentrations of PFOA and PFOS in polar bears. Corresponding values for PFUnDA are included in Annex II, Table 18.

3.3.4 Summary and discussion of bioaccumulation

The reported BCF and BAF for PFHxS are below the numerical criteria 2000/5000 in REACH Annex XIII, but it is worth noting that one of the BAF values (European chub, BAF plasma) is close to the threshold of 2000 (log BAF of 3.3 equivalent to a BAF of 1995). The latter value suggests that the substance is a borderline B for some aquatic species. In addition, due to the surface active properties of the substance the appropriateness of the available BCF test and the usefulness of its result may be questioned.

BCF for fish for the PFSA analog PFOS ranged between 2796-3100 (UNEP, 2006). It was however also noted in the UNEP (2006) document that the BCF numeric criteria may not adequately represent the bioaccumulation potential of the substance since monitoring data from top predators at various locations show highly elevated levels of PFOS and demonstrate substantial bioaccumulation and biomagnification (BMF) properties of PFOS. It was also noted that the concentration of PFOS found in livers of Arctic polar bears exceed the concentrations of all known individual organohalogenes.

BCFs for the PFCA analog PFOA are below 2000 (ECHA, 2013b), but according to the SVHC support document "*However, bioconcentration values in fish may not be the most relevant endpoint to consider, because other mechanisms of accumulation might be of relevance.*"

The numerical criterion for BCF or BAF, which are based on considerations of lipid-partitioning substances, are not appropriate for PFHxS as it does not follow the behaviour of traditional hydrophobic compounds with partitioning into fatty tissues. Instead it behaves similarly to what previously have been observed for other perfluorinated compounds which preferentially bind to proteins in blood and liver (L Ahrens et al. (2009), (Martin et al., 2003a), Goeritz et al. (2013). Ng and Hungerbuhler (2014) concluded that protein interactions are needed to explain some important features of perfluorinated alkyl acids bioaccumulation. According to the same authors (Ng and Hungerbuhler, 2014) the three key features of PFAS bioaccumulation consist of a protein component (especially to describe the accumulation in the blood compartment), elimination and reabsorption as mediated by transporter proteins and a phospholipid component (to describe the distribution into tissues where little or no specific binding occurs). Ng and Hungerbuhler (2013) suggests that renal transport may not be as important in fish as in mammals, or that active transport rates differ substantially from mammals to fish. This further illustrates that the use of fish BCF-data is less relevant when concluding on B-properties for substances such as PFHxS, where in addition the concern for bioaccumulation emanate from mammalian, not fish, data (see below).

PFHxS was found in terrestrial species as well as in endangered species as shown in section 3 for the polar bear. The highest concentrations of PFHxS detected in wildlife have been observed in the arctic top predator polar bear (>500 µg/kg in polar bear liver), which show that exposure to PFHxS has the potential to result in high concentrations in biota.

It is not possible to draw a conclusion on trophic magnification for PFHxS due to limited reliability of the available data. However, all field BMFs for PFHxS are above one suggesting a biomagnification potential of the substance that is supported by monitoring data (increasing concentration levels of PFHxS among the food-chain (e.g. seals/bear)). Most BMFs, and especially the large ones (ringed seals/polar bears), are not from aquatic organisms, but instead from air-breathing organisms. Even if there are uncertainties linked to the field studies, all the field BMF values are higher than one supporting a biomagnification potential of PFHxS as part of a weight-of-evidence approach. In addition, the values for the other similar substances are from the same studies and it is therefore possible with sufficient certainty to say that PFHxS accumulates in the food chain at least as much as PFOS and more than the long-chained PFCA's which already have been identified as vPvB to the Candidate List ((ECHA, 2012a), (ECHA, 2012d), (ECHA, 2012c), (ECHA, 2012b)).

4. Human health hazard assessment

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

The fraction of absorption in animals after oral administration range from >50% for PFHxS to >95% for PFOS, PFBA and PFOA ((ATSDR, 2015)). According to the Spanish autopsy study (Perez et al., 2013) PFHxS was found in all studied human organs/tissues: liver, kidneys, bone, brain and lungs. PFHxS is transferred to the foetus through the placenta in humans and is excreted via lactation and breast milk may therefore be an important source of exposure to breast-fed infants.

The elimination half-life of PFHxS in humans is estimated to be at least 8.5 years (arithmetic mean)/ 7.3 years (geometric mean). With the exception of rodents, PFHxS has the longest elimination half-life of all studied PFAS in pigs, monkeys and humans (**Table 10**).

The long elimination half-lives in blood might indicate that PFHxS accumulate directly in the blood or that the substance circulates between other tissues/organs and blood or both. Pharmacokinetic studies have revealed that PFASs interact with proteins such as e.g. albumin, liver fatty acid binding proteins (L-FABP) organic anion transporters and that their clearance is species-, gender- and chain length-dependent ((Andersen et al., 2008), (Ng & Hungerbuhler, 2014)).

4.1.1 Non-human information

Absorption

The fraction of absorption in animals after oral administration range from >50% for PFHxS to >95% for PFOS, PFBA and PFOA (ATSDR, 2015).

Benskin and co-workers (2009) studied the uptake, distribution and elimination of perfluorinated acids (PFAs), including PFHxS, when administered to Sprague-Dawley rats via single dose gavage. The mixture of PFAs contained a linear PFHxS isomer and two branched isomers and the PFHxS dose was estimated to be 30 µg/kg BW. The absorption for the two branched isomers, B1 and B2, were 70 and 75 % and they had a blood elimination half-life of 6.9 and 3.6 days, respectively. The blood elimination half-life for the linear isomer was 15.9 days.

Metabolism

There is no data on metabolism of PFHxS available.

The carbon-fluorine bonds are among the strongest in organic chemistry, and PFOS has been found to be metabolised (Lau et al., 2007). Based on the general stability of PFOS against metabolism and the read-across to PFOS (Annex I), PFHxS is not expected to be metabolised.

Distribution and elimination

Several animal studies in rats mice, rainbow trout, seals, whales and gulls demonstrate that PFAS accumulate preferentially in the blood and liver, while in-vitro studies have shown that they are able to strongly bind proteins such as serum albumin and liver fatty acid binding protein (L-FABP) ((Ng & Hungerbuhler, 2013), (Ng & Hungerbuhler, 2014)).

The PFHxS elimination half-lives increase from around 30 days in rodents to 141 days in monkeys and 713 days in pigs.

Benskin and co-workers (2009) studied the uptake, distribution and elimination of perfluorinated acids (PFAs), including PFHxS, when administered to Sprague-Dawley rats via single dose gavage. The mixture of PFAs contained a linear PFHxS isomer and two branched isomers and the PFHxS dose was estimated to be 30 µg/kg BW. The elimination half-life for linear PFOS and PFOA were 33.7 days and 13.4 days, respectively. For all PFAs, branched isomers generally had shorter elimination half-lives than corresponding linear isomers. The preferential elimination of branched isomers was via urine for perfluorohexanesulfonic acid, PFOS and PFOA. PFHxS concentrations were highest in the liver, lungs and heart. The calculated elimination half-life for linear PFHxS in liver was 51.8 days, three times higher than the elimination half-life in blood (15.9 days). The corresponding calculated elimination half-lives in liver for PFOS and PFOA were 51.1 days and 13.5 days, respectively.

Sundström *et al.* (2012) performed a comparative pharmacokinetic study of PFHxS in rats, mice and monkeys in order to establish pharmacokinetic parameters for PFHxS after a single administration. Three different studies were performed in rats: Dose effect on elimination; iv and oral pharmacokinetics in jugular-cannulated rats after a single dose; and a ten-week study on the elimination in serum, urine, and feces after a single iv-administration. In mice the serum uptake and urinary and fecal elimination were studied after a single oral administration of PFHxS, and in monkeys an iv pharmacokinetic study was performed.

Rats: Male and female Sprague Dawley rats (n = 4/sex/group) were administered a single oral dose (1, 10 or 100 mg K⁺PFHxS/kg bw) and monitored for 96 hours to study the effect of increasing dose on elimination. The results showed that the major excretion route was through the urine. In male rats the urinary excretion may be dose dependent since 30% of the 100 mg/kg BW dose was excreted in the urine compared to 6-8% of the 1 and 10 mg/kg BW dose. The mean daily fecal excretion was <0.5% of the administered dose at all time points. Another study investigated the pharmacokinetics in male and female rats (n = 3/sex/group) for 24 hours after oral and intravenous administration. The mean serum elimination half-lives for the iv-study were 6.83 days and 1.83 days for male and female rats, respectively. Only the female mean serum elimination half-life (0.83 d) could be estimated in the oral study. A bioavailability of 50% was estimated for female rats from the area under the curve from the oral and iv studies. However, the reliability of the bioavailability result is unclear due to the low number of test animals and the short observational period (24 h). The female C_{max} values did not differ significantly between oral and iv doses, and the T_{max} after oral dosing was estimated to be approximately 30 minutes. The later data indicates a complete bioavailability. The elimination of PFHxS in male and female rats was also studied in a 10 weeks long study. The rats (n = 8) were administered 10 mg K⁺PFHxS/kg bw via iv-injection and observed for 10 weeks and serum, fecal and urine samples were collected during the observational period. The serum elimination in males appeared to be bi-phasic with an elimination half-life of 29.1 days, while the serum elimination in females was a single-phase event with a elimination half-life of 1.64 days. Females excreted more PFHxS in their urine than males during the first week of the study. The mean daily fecal excretion never exceeded 0.5% of the administered dose and, for was the majority of measurements <0.03% of the administered dose.

Mice: Mice were given oral doses of 1 or 20 mg K⁺PFHxS/kg bw and were followed for 162 days. Mean PFHxS concentration were highest in serum followed by liver and then kidney. The mean serum elimination half-lives were rather similar between male and female mice regardless of dose, (30.50 days vs. 24.82 days at 1 mg/kg and 27.92 days vs. 26.81 days at 20 mg/kg for males and females, respectively). Less than 3% of the administered dose was recovered in the urine and faces at an given 24-h sampling period. Urinary elimination predominated.

Monkeys: Cynomolgus monkeys (n = 3/sex) were given in a single iv-administration of 10 mg K⁺PFHxS/kg bw and the serum samples were taken periodically during the 171 day study. The elimination in serum best fitted a non-compartment model and the elimination half-lives were estimated to be 141 ± 30 days and 87 ± 27 days for male and female monkeys, respectively.

Since the distribution volume at steady state in the three species studied likely were between 200 and 300 mL/kg bw, the authors proposed that PFHxS predominantly distributes in the extracellular space. They also suggest that the differences in elimination between species and gender, in rats, could be due to differences in the expression of organic anion transporters. It appears from these results that PFHxS has the shortest elimination half-life in rat, followed by mice and monkey.

Numata et al. (2014) studied the transfer of a mixture of PFAS from contaminated feed into edible tissues of 24 fattening pigs (*Sus scrofa domestica* of the German Landrace breed) during a three week feeding study. Twelve PFAS (PFASs: PFBS, PFHxS, PFHpS, PFOS, PFDS; PFCAs: PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA) were analysed (HPLC-MS/MS) in every sample. Sampling was performed on feed, tissues (blood, liver, kidney, dorsal and ventral muscles and fat tissues covering dorsal muscle tissues) and excretions (urine). The PFAS excretion via faeces were not analysed because they were presumed to be relatively small with respect to the total cumulative PFAS dose. This assumption was confirmed by mass balance since most of the PFAS dose was accounted for by tissues and urine without resorting to the faeces.

The results showed a fast equilibrium between plasma and edible tissue compartments. The plasma to meat factor was similar for PFHxS, PFHpS, PFOA, PFHpA, PFBS and PFHxA and only differs for PFOS. The unexcreted PFAS generally accumulated in plasma (up to 51%), fat and muscle tissue (collectively, meat 40-49%), liver (under 7%), and kidney (under 2%). PFOS was an exception with higher relative affinity for liver (35%) and lower for plasma (23%). The authors developed a toxicokinetic model in order to quantify absorption, distribution and excretion of the PFAS and calculated elimination half-lives. The elimination of PFASs were more slowly than that of the PFCAs. The elimination half-life for PFHxS in plasma was 713 days. The corresponding elimination half-lives for PFOS and PFOA were 634 and 236 days, respectively. The 95% variability (Student's *t* statistic) elimination half-life intervals (as measured from figure 4 in the article) – PFHxS (249-1970 d), PFOS (194-1970 d), PFHpS (113-1379 d), PFOA (46-1074 d), PFHpA (11-440 d), PFBS (13-135 d) and PFHxA (1-16 d). There were no statistically significant gender differences. The authors also calculated BMF for whole pig, meat and liver. BMF_{whole pig}, BMF_{meat} and BMF_{liver} for PFHxS were 20.1, 13.1 and 48, respectively. The corresponding figures for PFOS, PFHpS, PFOA, PFHpA, PFBS and PFHxA were 17.9/9.7/503, 12.7/8.3/81, 7.9/5.3/32.8, 2.7/1.8/7.0, 1.2/0.8/6, and 0.13/0.08/0.42, respectively.

4.1.2 Human information

4.1.2.1 Absorption

There are no studies on absorption of PFHxS in humans. However, elevated serum concentrations of perfluorochemicals, including PFHxS, have been reported for workers in fluorochemical production industry which probably reflects absorption through the respiratory tract (US HHS, 2015). In addition, based on animal studies on PFHxS, as well as on abundant findings of PFHxS in human blood, it can be assumed that PFHxS is well absorbed after oral and inhalation exposure, while absorption after dermal exposure are of lesser importance.

4.1.2.2 Levels of PFHxS in human body fluids

Exposure

Humans are primarily exposed to PFHxS via food and drinking water. PFHxS has been detected in 50% of the food groups included in the Swedish National Food Agency's food basket 2010 (with concentration between 0.001 and 0.009 ng/g fw) ((Glynn A., 2013)). Time trend studies show decreasing concentrations in eggs, more significant for PFOS, but also to some degree for PFHxS. Intake estimations demonstrate that individuals that have been drinking contaminated water (fire-fighting foams as a suspected source) are subjected to a worrying increased exposure of PFHxS. A consumption of contaminated drinking water might cause an increase by a factor of 100 of the median PFHxS intake compared to a reference group.

Exposure to humans may also occur via indoor air, mainly through dust. PFHxS has been recorded in Norwegian homes and an office ((Huber, Haug, & Schlabach, 2011)). Seven of eight analysed dust samples contained PFHxS at a median value of 1.4 ng/g whereas the dust of the indoor environment in a Norwegian office contained close to 30 ng/g. Other studies also demonstrate that PFHxS can be detected in indoor dust. Belgian homes (45 samples) and offices (10 samples) were studied in D'Hollander et al. ((D'Hollander et al., 2010)) with a reported median value of 0.1 and 0.2 ng/g respectively, a Canadian study ((Kubwabo, Stewart, Zhu, & Marro, 2005)) shows a median of 23.1 ng/g in the indoor environment and 45.5 ng/g was detected in US homes and day care centres ((Strynar & Lindstrom, 2008)). In all studies the levels of PFOS are higher compared to PFHxS.

General population

PFHxS has been detected in humans globally with the highest levels (1790 µg/L in blood serum) detected in people consuming PFHxS contaminated drinking water. Levels in plasma range from <0.05 – 80 µg/L, in serum from <1 - 1790 µg/L, in human milk <0.005 – 0.3 µg/L, in urine <0.05 – >0.454 µg/L (study median=0.454 µg/L, 95% CI 0.349-0.756 µg/L) and in stool < 0.05 – 0.318 µg/kg.

Hansen *et al.* (2001) analysed concentrations of PFAS, including PFHxS, in 65 non-industrially exposed human sera samples, purchased from biological supply companies located in the United States. The median concentrations of PFHxS, PFOS and PFOA were, 4.3 µg/L (range <LOD - 21.4; LOD ~1.5, LOQ = 5), 25.7 µg/L (LOD ~1.7, LOQ = 5; range 6.7 - 81.5), and 5.2 µg/L (LOD ~1, LOQ = 5; range <LOQ - 35.2), respectively.

The levels detected in plasma and serum are presented below in Figure 5 - Figure 7. The values in Figure 5 and Figure 6 are separated by type of exposure into background exposure, exposure at home and occupational exposure. Background exposure include those

measurements for which it has not been specifically specified that they include occupational exposure, or exposure at home at high concentrations either in food, drinking water and/or via carpet treatments. Exposure at home includes exposure via drinking water, food and carpet treatments. Figure 7 presents background concentrations of PFHxS in plasma on country basis

The serum concentrations of PFHxS in humans exposed at home may reach concentrations similar or even above those observed in occupational settings. Even though the number of measurements of PFHxS in blood varies between countries from just a few (e.g. Taiwan) to several hundred (e.g. Sweden), which make it difficult to draw any firm conclusions regarding country specific differences, it is at least clear that PFHxS may be detected in human blood globally. Measured data are included in **Table 19** in Annex II.

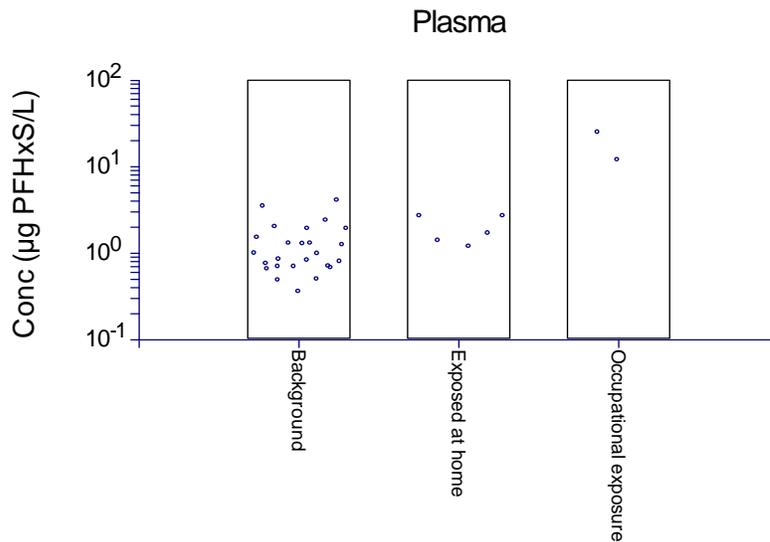


Figure 5: Concentrations of PFHxS in plasma separated by type of exposure.

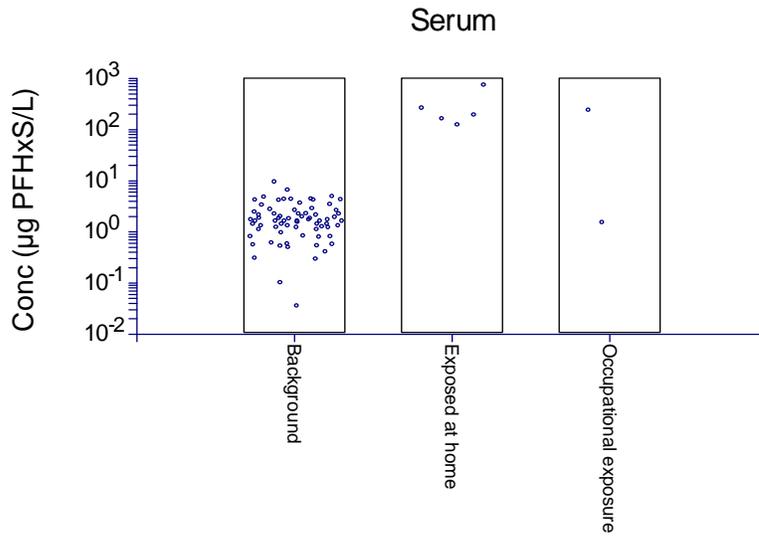


Figure 6: Concentration of PFHxS in serum separated by type of exposure.

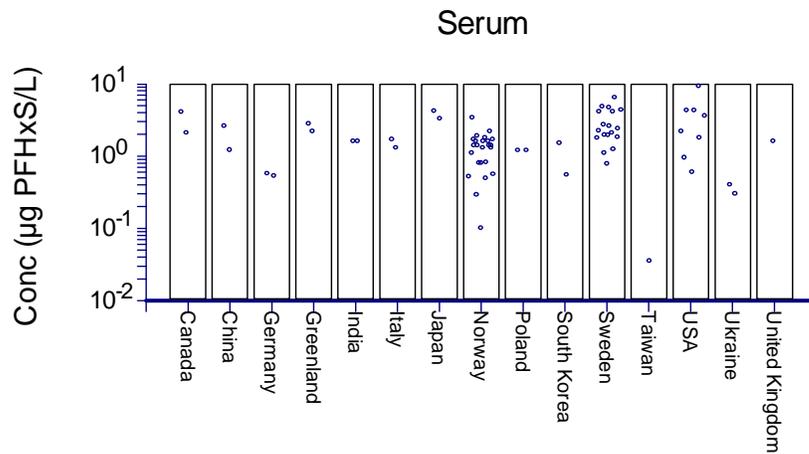


Figure 7: Background concentrations of PFHxS in plasma in countries.

Kannan and co-workers (2004) measured the concentration of PFHxS, PFOS and PFOA in 475 human blood/serum/plasma samples from Belgium (20 plasma), Brazil (29 whole blood), Colombia (56 whole blood), India (45 sera), Italy (50 sera), Japan (38 sera),

Malaysia (23 whole blood), Poland (25 whole blood), South Korea (50 whole blood) and the United States (75 sera, 30 whole blood, 70 plasma). The samples were collected from the Red Cross or local hospitals or universities from volunteer donations during 1998-2004. The authors note that the samples used in the study were only collected in cities and may therefore not necessarily be representative for the entire population in a country. Whole-blood data were converted to a serum basis by multiplying by a factor of 2. Samples with values below the LOQ were excluded in the calculation of mean and median. The median concentrations for males/females PFHxS ranged from 0.2/0.2 µg/L (Colombia) to 3.4/2.9 µg/L (South Korea). The corresponding figures for men/women for PFOS were a range from 1.3/2.5 µg/L (India) to 72/81 µg/L (USA) and for PFOA a range from <3/2.4 & <3 (men: Italy; woman: Belgium & Italy/India) to 26.8/30.9 (South Korea). In general, no relationship between age and concentration was found in serum samples.

Kärrman and co-workers (2006) used whole-blood samples from men (n = 40) in the age 19 - 46 years and their mothers (n = 26), age 46 - 75 years, to compare blood levels of 12 PFAS, including PFHxS, and POPs. The donors originated from ten counties in the southern half and one county in the northern half of Sweden. The blood samples were collected during 1997 - 2000. The average concentration of PFHxS was 1.2 times higher in plasma as compared to whole blood, with the corresponding figures for PFOS and PFOA being 1.2 and 1.4, respectively. The total median PFHxS blood level was 1.5 µg/L (range: 0.4 - 28.4), with the corresponding figures for PFOS and PFOA being 17.1 µg/L (range: 13 - 23) and 2.5 µg/L (range: 1.9 - 3.3), respectively. These measured concentrations are not considered to be representative for the entire Swedish population since the sample set is skewed in both in age and gender distribution, as well as having poor geographical distribution. However, the results show that PFAS, including PFHxS, is present in the blood of some part of the Swedish population.

Ehresman *et al.* (2007) examined the distribution of PFHxS, PFOS, PFOA and PFBS in whole blood, plasma and serum in 18 people (median age 47 years, range 29 - 79 years; 13 males and 5 females) employed at 3M Company. Sampling was performed from 2004-12 to 2005-06. Serum concentrations ranged from LOQ (5 µg/L) to 25 µg/L for PFHxS, from LOQ (5 µg/L) to 880 µg/L for PFOS and from LOQ (5 or 10 µg/L) to 7320 µg/L for PFOA. Serum to plasma ratios for PFHxS, PFOS, and PFOA were 1:1 and this ratio was independent of the level of concentration measured. Serum to plasma for whole blood ratios, regardless of the anticoagulant used approximated 2:1.

Ericson *et al.* (2007) collected whole-blood from 48 residents in Catalonia, Spain, in order to obtain information on levels of 13 PFAS, including PFHxS, in relation to gender and age (25 ± 5 and 55 ± 5 years). The reported median concentration of PFHxS was 2.92 µg/L (range: 0.65 - 19.96). The corresponding figures for PFOS and PFOA were 7.60 µg/L (range: 0.76 - 16.17) and 1.65 µg/L (range: 0.79 - 3.13), respectively. The younger age group (25 ± 5 years) had significantly higher concentrations of PFHxS as compared to the older age group (55 ± 5 years). Men had significantly higher (p < 0.05) blood levels as compared to women for PFHxS and PFOA. Corresponding values for PFUnDA and PFTeDA are included in **Table 19** in Annex II.

Kärrman *et al.* (2007) studied the relationship between levels of perfluorinated chemicals maternal serum and breast milk with matched individual milk and serum samples from 12 Swedish primiparous women collected in 2004 in Uppsala. Temporal trends of concentrations of PFAS between 1996 and 2004 were also studied using annual composite samples (25-90 women/year) of breast milk collected from Swedish women in Lund, Uppsala, Göteborg and Lycksele three weeks after delivery. The arithmetic mean/median for serum and milk concentrations sampled from 12 primiparous Swedish women in 2004 were 4.7/4.0 µg/L and 0.08/0.070 µg/L for PFHxS, 20.7/18.7 µg/L and 0.201/0.166 µg/L for PFOS and 3.8/3.8 µg/L for serum with no mean/median available for milk due to high blank level in PFOA (range: <0.209-0.492 µg/L), respectively. A significant positive association was found between levels in serum and in milk for PFHxS (r² = 0.8, p<0.05)

and PFOS ($r^2 = 0.8$, $p < 0.05$). No temporal trends could be found in the composite milk samples from 1996 and 2004 which had a total coefficient of variation of 32% and 20% for PFHxS and PFOS, respectively, which might be due to that samples were taken from different regions (Uppsala: 1996 - 2000 and 2002; Göteborg: 2001; Lund 2003; Lyckesele: 2003 - 2004). Mean/median concentrations of the composite milk samples were 0.033/0.03 $\mu\text{g/L}$ and 0.196/0.207 $\mu\text{g/L}$ for PFHxS and PFOA, respectively. PFOA was due to a relatively high blank level (0.209 $\mu\text{g/L}$) in human milk only reported in one milk sample (0.492 $\mu\text{g/L}$). Corresponding values for PFUnDA are included in **Table 19** in Annex II.

Following the contamination of drinking water 2006 in Arnsberg, Germany, Hölzer *et al.* (2008) measured the concentrations of six perfluorinated compounds, including PFHxS, in drinking water and in blood plasma of 170 children (age 5-6 years), 317 mothers (age 23-49 years), and 204 men (age 18-69 years). The cross-sectional study was performed between September and November 2006 in Arnsberg, and the two reference areas Siegen and Brilon. Male adults were recruited from Arnsberg ($n = 101$) and Brilon ($n = 103$). Mothers and children were recruited in Arnsberg (mothers = 164, children = 90) and Siegen (mothers = 153, children = 80). Age, height, body weight and sex were comparable between Arnsberg and the two reference areas Siegen and Brilon. The geometric mean concentration of PFHxS, PFOS, and PFOA in blood plasma ($\mu\text{g/L}$) of men in Arnsberg/Brilon were 2.5 / 2.2, 10.5/9.7, and 25.3/5.8, respectively. The geometric mean concentration of PFHxS, PFOS, and PFOA in blood plasma ($\mu\text{g/L}$) of children in Arnsberg/Siegen were 1.2 / 0.8, 4.9/4.6, and 22.1/4.8., respectively. The geometric mean concentration of PFHxS, PFOS, and PFOA in blood plasma ($\mu\text{g/L}$) of mothers in Arnsberg/Siegen were 1.1 / 0.6, 5.8/5.2, and 23.4/2.8., respectively. As regards drinking water, none of the six PFAS (including PFHxS, PFOS, and PFOA) were identified (LOD = 10 ng/L) in the reference areas Siegen and Brilon. PFOS was not detected in Arnsberg during the study period (September-November 2006), while the concentrations for PFOA ranged from ND – 71 ng/L (the higher concentration was measured when the newly installed waterwork charcoal filter declined in performance). The waterwork activated charcoal filter was installed in July 2006 and the concentrations of PFOS and PFOA in tap water measured in May 2006 (Skutlarek, Exner, & Farber, 2006) were 5 ng/L and 519 ng/L, respectively. The concentrations of PFHxS and PFOA were significantly increased in Arnsberg for men, children and mothers, as compared to the respective reference areas. The concentrations of PFOS were only significantly ($p < 0.05$) increased in Arnsberg for mothers, as compared to the respective reference areas. Statistically significant ($p < 0.01$) correlations existed between age and PFHxS (men in both areas, mothers in Arnsberg), PFOS (men in both areas, mothers in Siegen) and PFOA (men and mothers in both areas). Concentration of PFHxS in blood plasma was associated with consumption of drinking water ($p = 0.066$), male sex, age, and study area (all $p < 0.01$). Concentration of PFOS in blood plasma of adults was associated with age, male sex, region, and consumption of locally caught fish (all $p < 0.01$) and inversely with BMI ($p = 0.02$). Concentration of PFOA in blood plasma of adults was associated with consumption of drinking water ($p < 0.01$), locally grown fruit and vegetables ($p = 0.059$), age, male sex, region, and inversely with BMI ($p = 0.05$). As for children, the concentration in blood plasma of PFHxS were associated with region ($p < 0.01$) and male sex ($p = 0.07$) with an adjusted $R^2 = 0.16$. None of the independent variables was significantly associated with PFOS concentration in blood plasma of children. For PFOA the concentration in blood plasma were associated with consumption of drinking water and region ($p < 0.01$; adjusted $R^2 = 0.75$).

Monroy *et al.* (2008) measured the levels of several PFAS, including PFHxS, in plasma of maternal ($n = 101$) and umbilical cord ($n = 105$) blood samples in Canada. The levels (arithm. mean \pm SD) of PFHxS were 4.13 \pm 11.43 $\mu\text{g/L}$, 4.05 \pm 12.30 $\mu\text{g/L}$ and 5.05 \pm 12.92 $\mu\text{g/L}$, respectively. The corresponding levels of PFOS/PFOA were 18.31 \pm 10.95 $\mu\text{g/L}$ / 2.54 \pm 1.65 $\mu\text{g/L}$, 16.19 \pm 10.43 $\mu\text{g/L}$ / 2.24 \pm 1.61 $\mu\text{g/L}$ and 7.19 \pm 5.73 $\mu\text{g/L}$ / 1.94 \pm 1.54 $\mu\text{g/L}$, respectively.

Lin *et al.* (2009) examined 474 adolescents (aged 12 – 20 y) and 969 adults (age > 20 y) with reliable serum measures of metabolic syndrome profile from the National Health and

Nutrition Examination Survey (NHANES) 1999-2000 and 2003-2004. The concentration (arithm. mean \pm SEM) of PFHxS in blood serum of adolescents (≥ 12 - < 20 years; $n = 474$) and adults (≥ 20 years; $n = 969$) were 0.95 ± 0.10 $\mu\text{g/L}$ and 0.60 ± 0.04 $\mu\text{g/L}$. Corresponding concentrations for adolescents and adults for PFOS/PFOA were $3.11 \pm 0.05/1.51 \pm 0.05$ $\mu\text{g/L}$ and $3.19 \pm 0.04/1.48 \pm 0.04$ $\mu\text{g/L}$, respectively.

Fromme et al. (2010) measured the concentration of a number of perfluorinated compounds, including PFHxS, in maternal blood during pregnancy (at two time points; $n = 40$ and 38) and six months after delivery ($n = 47$), in cord blood ($n = 33$) and in blood of infants six ($n = 40$) and nineteen months ($n = 40$) after birth and monthly in breast milk samples during December 2007 and October 2009 in Munich, Germany. The median concentrations in maternal serum during pregnancy, at delivery and six months after delivery for PFHxS, PFOS and PFOA were $0.5/0.5/0.3$ $\mu\text{g/L}$, $3.2/3.2/2.9$ $\mu\text{g/L}$, and $2.4/1.9/1.5$ $\mu\text{g/L}$, respectively. The median concentrations in cord blood serum, in blood of infants six and nineteen months of age for PFHxS, PFOS and PFOA were $0.2/0.6/0.6$ $\mu\text{g/L}$, $1.0/3.0/1.9$ $\mu\text{g/L}$, and $1.4/6.9/4.6$ $\mu\text{g/L}$, respectively. It was possible to quantify PFHxS in 6/201 breast milk samples and the concentrations ranged from <0.02 - 0.3 $\mu\text{g/L}$. PFOS was detected in 145/201 breast milk samples with median (range) concentrations of 0.04 (<0.3 - 0.11) $\mu\text{g/L}$. PFOA was detected in 4/201 breast milk samples and the concentrations ranged from <0.15 - 0.25 $\mu\text{g/L}$.

Hamm and co-workers (2010) examined the concentrations of PFHxS, PFOS and PFOA in a cohort of 252 pregnant Canadian women who gave birth to live singletons. The arithm. mean concentrations of PFHxS, PFOS and PFOA were 2.1 $\mu\text{g/L}$, 9.0 $\mu\text{g/L}$ and 2.1 $\mu\text{g/L}$, respectively.

Hoffman and co-workers (2010) evaluated the association between exposure to PFAS and ADHD among children 12-15 years of age ($n = 571$) in the US using data from the National Health and Nutrition Examination Survey (NHANES) 1999-2000 and 2003-2004. Measured median concentrations of PFHxS, PFOS and PFOA were 2.2 $\mu\text{g/L}$, 22.6 $\mu\text{g/L}$ and 4.4 $\mu\text{g/L}$, respectively.

Jönsson *et al.* (2010) collected during 2009 and 2010 blood serum from 50 Swedish military conscripts (~ 18 years) who originated from Malmö and the surrounding area. Of out of these 100, 50 were randomly selected for analysis of a number of PFAS, including PFHxS. The medium serum concentrations of PFHxS, PFOS and PFOA were 0.78 $\mu\text{g/L}$ (range: 0.38 - 2.5 , LOD = 0.1 $\mu\text{g/L}$), 6.9 (range: 3.7 - 19 , LOD = 0.1 $\mu\text{g/L}$), and 1.9 (range: 1.2 - 3.3 , LOD = 0.1 $\mu\text{g/L}$), respectively. Corresponding values for PFUnDA are included in **Table 19** in Annex II.

Nelson and co-workers (2010) investigated the relationship between PFAS serum concentrations and lipid and weight outcomes for 860 participants (aged 12 - 80 y) from the National Health and Nutrition Examination Survey (NHANES) 2003-2004. Median concentration of PFHxS, PFOS and PFOA were 1.8 $\mu\text{g/L}$, 21.0 $\mu\text{g/L}$ and 3.9 $\mu\text{g/L}$, respectively.

Hölzer and co-workers (2011) measured the levels of a number of PFAS, including PFHxS, in fish, blood plasma of anglers ($n = 105$; 99 men, 6 women; 14 - 88 years, median 50.6 years) at Lake Möhne, Germany and in drinking water collected at the anglers home. The samples were collected in 2008. PFHxS was not detected in any fish sample. PFOA was only detected in about 20% in fish from Lake Möhne (LOD = 0.8 16 $\mu\text{g/kg}$) with a maximum concentration of 2.3 16 $\mu\text{g/kg}$ detected in eel. PFOS was detected in every fish caught in Lake Möhne ($n = 44$) with concentrations ranging from 4.5 $\mu\text{g/kg}$ (roach) to 150 $\mu\text{g/kg}$ (perch) in the fish fillets. The species differences in concentrations observed seemed to reflect feeding behaviour rather than water concentration, with piscivorous species having the highest concentrations. PFOA was only detected in 20% of the sampled fish (LOD = 0.8 $\mu\text{g/kg}$) with a maximum concentration of 2.3 $\mu\text{g/kg}$ (eel). The plasma concentration of

PFHxS in anglers ranged from 0.4 – 17 µg/L (LOD = 0.1 µg/L). The corresponding figures for PFOS and PFOA were 1.1 – 650 µg/L and 2.1 – 170 µg/L, respectively. PFHxS was not detected in any tap water. PFOS was detected in 17/39 tap water samples in the range 0.011 - 0.059 µg/L and PFOA was detected in 27/39 tap water samples in the range 0.020-0.047 µg/L. The limit of quantification for tap water used was 0.010 µg/L. The concentrations of PFHxS and PFOS in plasma of anglers were positively associated with age and the consumption of fish ($p < 0.01$). The concentration of PFOA in plasma of anglers was positively associated with age and concentration of PFOA in tap water ($p < 0.01$).

Kim and co-workers (2011) measured the concentration of PFAS in blood serum of Korean pregnant women ($n = 44$), fetal cord serum ($n = 43$) and breast milk ($n = 35$). The reported concentration of PFHxS (median, 25th-75th percentile) were 0.55 µg/L (0.46-0.85 µg/L), 0.34 µg/L (0.27-0.51 µg/L) and < 0.05 µg/L, respectively. The concentrations of PFOS and PFOA in blood serum, fetal cord serum and breast milk were 2.93 µg/L (2.08-4.36 µg/L), 1.26 µg/L (0.81-1.82 µg/L), 0.06 µg/L (0.00-0.10 µg/L) and 1.46 µg/L (1.15-1.91 µg/L), 1.15 (0.95-1.86 µg/L) and 0.05 µg/L (0.03-0.07 µg/L), respectively. Corresponding values for PFUnDA, PFTrDA, and PFTeDA are included in **Table 19** in Annex II.

Stein and Stavitz (2011) examined the cross-sectional association in children (5-18 years of age; $n = 10456$) between serum PFAS concentrations and parent or self-report of doctor-diagnosed ADHD with and without current ADHD medication in the US. Data are from the C8 Health Project, a 2005-2006 survey in a Mid-Ohio Valley community highly exposed to PFOA through contaminated drinking water. Measured levels (arithm. mean \pm SD) of PFHxS, PFOS and PFOA were 9.3 ± 13.7 µg/L, 22.9 ± 12.5 µg/L and 66.3 ± 106.1 µg/L, respectively.

Wang et al. (2011) examined the effect of pre-natal exposure to PFAS on levels of immunoglobulin E (IgE) and atopic dermatitis (AD) in 2-year old Taiwanese children ($n = 244$). Median (range) concentrations of PFHxS, PFOS and PFOA were 0.035 µg/L (0.035-0.420), 5.50 µg/L (0.11-48.36) and 1.71 µg/L (0.75-17.40), respectively.

Ji et al. (2012) measured the levels of PFAS in blood serum, total thyroxine (T4) and thyroid stimulating hormone (TSH) in a general Korean population ($n = 633$, > 12 years of age) in a mid-sized Korean city (Siheung). Measured levels (median and 25th – 75th perc) of PFHxS, PFOS and PFOA in serum were 1.51 µg/L (0.92 – 2.34 µg/L), 7.96 µg/L (5.58 – 12.10 µg/L) and 2.74 µg/L (2.04 – 3.64 µg/L), respectively. Corresponding concentrations of PFUnDA, PFDoDA, PFTrDA and PFTeDA are included in **Table 19** in Annex II,

Maisonet and co-workers (2012) analysed serum samples obtained during pregnancy from 447 British women with respect to PFHxS, PFOS, and PFOA. Sampling was performed in 1991-1992. PFHxS, PFOS and PFOA were detected in all samples with median concentrations of 1.6 µg/L (range 0.2 - 54.8 µg/L), 19.6 µg/L (range 3.8 - 112 µg/L) and 3.7 µg/L (range 1.0 - 16.4 µg/L), respectively.

Specht et al. (2012) collected and analysed serum samples from 604 fertile men (199 in Greenland (age: median 31 years, range 19 - 51), 197 in Poland (age: median 29.6 years, range 20 - 46) and 208 in Ukraine (age: median 25.1 years, range 16-45)) for the presence of four PFAS, including PFHxS. The sampling occurred between 2002 and 2004. The serum median concentrations of PFHxS in Greenland, Poland and Ukraine were 2.2 µg/L (range: 1 - 21 µg/L), 1.2 µg/L (range: 0.4 - 4 µg/L) and 0.3 µg/L (range: 0.03-3 µg/L), respectively. For PFOS, the serum median concentrations of PFHxS in Greenland, Poland and Ukraine were 44.7 µg/L (range: 12 - 161 µg/L), 18.5 µg/L (range: 8 - 40 µg/L) and 7.6 µg/L (range: 3-30 µg/L), respectively. For PFOA the serum median concentrations in Greenland, Poland and Ukraine were 4.5 µg/L (range: 2 - 14 µg/L), 4.8 µg/L (range: 2 - 16 µg/L) and 1.3 µg/L (range: 0.3 - 35 µg/L), respectively. Corresponding values for PFUnDA, PFDoDA are included in **Table 19** in Annex II.

Toft and co-workers (2012) evaluated the possible association between PFAS exposure and male semen quality in a cross country population including 588 men from Greenland (n = 196), Poland (n = 189) and Ukraine (n = 203). The median serum concentrations of PFHxS in Greenland, Poland and Ukraine were 2.2 µg/L, 1.2 µg/L and 0.3 µg/L, respectively. The corresponding median concentrations of PFOS/PFOA in Greenland, Poland and Ukraine were 44.7/4.5 µg/L, 18.5/4.8 µg/L and 7.6/1.3 µg/L, respectively.

Bjeremo and co-workers (2013) measured the levels of several PFAS, including PFHxS, in blood serum of 270 Swedish adults (age 18 - 80 years) from 21 counties in Sweden in 2010-2011 searching for correlations between levels in blood and diet/lifestyle factors nationwide in Sweden. Blood and other data were collected at four separate occasions during the study period. The results showed that the median serum concentration of PFHxS, PFOS and PFOA among the test subjects was 1.95 µg/L (p5 - p95: 0.73 - 10.29 ng/mL), 11.20 µg/L (3.89 - 25.41) and 2.25 µg/L (0.76 - 5.01), respectively. Regional differences in serum concentrations were observed, with twofold higher median concentrations of PFHxS in the Stockholm/Uppsala areas as compared to Umeå and 60 - 70% higher concentrations of median PFOS and PFOA in Lund as compared to Umeå. Test subjects with higher education had higher concentrations of PFHxS (p = 0.02) and PFOS (p = 0.004), but not of PFOA (p = 0.009). There was a significant correlation between a biomarker for fish consumption and PFOS, when including age, sex and education in the analysis. In the cluster analysis, PFHS was separated from the other PFAAs suggesting other sources of exposure and drinking water was suggested as a potential source of exposure as may explain the twofold higher median levels in the Stockholm/Uppsala areas since contamination of PFHxS has been detected in municipal drinking water from certain waterworks in these areas ((Anders Glynn, 2012), (Defoort C.)) Corresponding values for PFUnDA are included in **Table 19** in Annex II.

Brantsæter et al. (2013) investigated the plasma concentration of four PFAS, including PFHxS, in pregnant women (n = 485) in Norway. The samples were collected during 2003 and 2004 around gestation week 17. The median plasma level of PFHxS was 0.60 µg/L with an interquartile range (IQR) of 0.43 to 0.86 µg/L. The corresponding figures for PFOS and PFOA were 12.8 µg/L (IQR 10.1 - 16.6) and 2.11 µg/L (IQR 1.54 - 2.93), respectively.

Zhang et al. (2013) sampled and measured the concentrations of several PFAS, including PFHxS, in paired blood (56 serum and 30 whole blood) and urine samples from healthy volunteers (n = 86) in Shijiazhuang (capital city) and Handan (industrial city), Hebei province, China, in April to May 2010. The arithmetic/mean concentrations of PFHxS in blood and urine was 2.6/1.2 µg/L 2.4/1.1 µg/L, respectively. The corresponding concentrations of PFOS in blood and urine was 31/19 µg/L and 37/25 µg/L, respectively, and for PFOA in blood and urine 3.1/2.3 µg/L and 81/19 µg/L, respectively. Corresponding values for PFUnDA are included in **Table 19** in Annex II.

Pérez et al. (2013) analysed samples from 20 deceased persons for a number of PFAS, including PFHxS. The samples were collected during 2008 and included bone (rib), brain, kidney, liver and lung. The deceased persons had been living in Catalonia, Spain, for at least 10 years, the causes of death varied and the age ranged between 28-83 y (mean 56 y). PFHxS was most often detected in lung tissues (32% of the samples), with the highest median concentration of PFHxS in the five analysed tissues detected in kidney (median 18 µg/kg ww, range: <4.2 - 37 µg/kg ww, PFHxS was detected in 5% of the samples) and the lowest in bone (median 1.2 µg/kg ww, range: <2.4 - 13.8 µg/kg ww, PFHxS was detected in 5% of the samples). PFOS and PFOA were most often detected in liver (90%) and kidney (95%) samples, respectively. The highest median concentrations of PFOS and PFOA were found in kidney (median 55 µg/kg ww, range: <6 - 269 µg/kg ww, PFOS was detected in 45% of the samples) and bone (median 20.9 µg/kg ww, range: <3 - 234 µg/kg ww, PFOA was detected in 55% of the samples), respectively, and the lowest median concentrations of PFOS and PFOA were found in bone (median - µg/kg ww, range: <3 µg/kg ww, PFOS was detected in 0% of the samples) and brain (median - µg/kg ww, range: <4.5 µg/kg ww,

PFOA was detected in 0% of the samples), respectively. Corresponding values for PFUnDA, PFDoDA, PFTrDA and PFTeDA are included in **Table 19** in Annex II.

Jakobsson *et al.* (2014) analysed serum from 79 adults and children which had been living in a part of Källinge that were supplied with drinking water from the water plant in Brantafors that had been contaminated with PFAS due to previous use of firefighting foam at a firefighting exercise place. The median/max serum concentrations for PFHxS, PFOS and PFOA were not possible to exactly determine in the figures of the report but have been separately reported by one of the authors (B. Jönsson, 2014) and were 258/1790 µg/L, 291/1737 µg/L, and 16/92 µg/L, respectively. In the preliminary risk assessment of this population performed by Glynn (Anders Glynn, 2013) measured concentrations in the contaminated drinking water of 1.2 µg/L, 4.0 µg/L and 0.13 µg/L of PFHxS, PFOS and PFOA, respectively are presented.

Jönsson *et al.* (2014) collected during 2013 blood serum from 104 female and 97 male students from upper secondary schools in Malmö and the surrounding area, Sweden, for analysis of a number of PFAS, including PFHxS. The 5th percentile/50th percentile/95th percentile concentrations for PFHxS for females and males were 0.53/1.10/2.29 µg/L and 0.66/1.24/3.48 µg/L, respectively. The corresponding concentrations for PFOS for females and males were 1.30/3.14/5.25 µg/L and 1.76/4.12/7.53 µg/L, respectively. The corresponding concentrations for PFOA for females and males were 0.79/1.85/2.51 µg/L and 1.03/1.70/2.39 µg/L, respectively. The levels of PFHxS and PFOS were significantly higher in men as compared to females, while for PFOA the levels in females were significantly higher as compared to men. The levels of PFHxS, PFOS and PFOA in plasma of men 2013 (this study) had all decreased significantly as compared to 2010 (B. Jönsson *et al.* (2010)). Corresponding values for PFUnDA, PFDoDA, PFTrDA and PFTeDA are included in **Table 19** in Annex II.

Zhou *et al.* (2014) performed a comprehensive exposure assessment of a number of PFAS, including PFHxS, in fishery employees from Tangxun Lake, China. Tangxun Lake is a shallow lake located in Hubei Province, which is one of the production bases of several small-scale fluorochemical manufacturers and users in China. Measurements of PFAS were made in blood and urine samples collected in April 2012 from fishery employees (n = 39; male = 38, female = 1), their family members (n = 7; male = 1, female = 6) and a reference group (n = 9, male = 5, female = 4) consisting of people living in the same region but more than 30 km away from the Tangxun Lake. Generally, the fishery employees lived in the surrounding of the lake and had meals in the fishery cafeteria during working days, with the fish served in the cafeteria primarily originating from the Tangxun Lake. The family members of the fishery employees also obtained part of their fish consumption from the Tangxun Lake since the fishery employees habitually brought fish caught in the Tangxun Lake to their homes. On the date of blood and urine sampling a questionnaire for self-completion was sent to the study participants to obtain information on age, gender, height, weight, smoking and drinking habits, exposure to environmental tobacco smoke, and environmental or occupational exposure to PFAS. Drinking water (n = 2) and indoor dust samples (n = 3) were collected from the homes of the fishery employees. Drinking water and indoor dust samples were collected on two occasions in December 2011 and October 2012. Aquatic biota samples (n = 60) were collected from Tangxun Lake and are presented more in detail in the environmental monitoring section. The levels of PFHxS observed in blood serum of the fishery employees (n = 39, median 542 µg/L) were substantially higher as compared to a reference group from the same city (n = 9, median 1.22 µg/L). It was, based on comparisons of different sources of exposure, concluded that the primary source was the contaminated fish from Tangxun Lake, and that there was a positive association between serum PFAS concentrations and time of employment in the fishery. PFCAs with less than eight perfluoroalkyl carbons were primarily eliminated via urine, whereas other routes of excretion may have contributed to the elimination for long-chain PFCAs and PFSAs. The medium blood serum concentrations of PFOS and PFOA in fishery employees/reference group were 10400/18.7 µg/L and 41/2.88 µg/L, respectively. The median concentrations of PFHxS,

PFOS, and PFOA in urine samples in fishery employees/reference group were 454/42.4 ng/L, 4700/17.9 ng/L and 108/16.4 ng/L, respectively. PFSAs displayed lower renal clearance rates, as compared to PFCAs of the same perfluoroalkyl chain-length, and the lowest renal clearing rate of all PFAS was observed for PFHxS. Corresponding concentrations for PFUnDA, PFDoDA, and PFTrDA in human serum and urine are included in **Table 19** in Annex II.

Mean PFHxS, PFOS and PFOA serum concentrations reported in the general population in the USA from various studies are 1.5-3.9 µg/L, 14.7-55.8 µg/L, and 2.1-9.6 µg/L, respectively ((ATSDR, 2015)).

Levels in humans – temporal trends

The available studies indicate increasing concentrations of PFHxS in humans, even though the increase in some studies appear to start to level off. Several of these studies also report initially increasing levels of PFOS and PFOA which are followed by decreasing levels during more recent years.

The data by Haug et al. (2009), Jönsson et al. (2009), Sundström et al. (2011) and Glynn et al. (2012), which all include individual data for PFHxS and PFOS for a number of years, are presented below in Figure 8.

The concentrations of PFHxS follow the concentrations of PFOS, but at a lower level. However, the concentration gap between the two appear to decrease for both serum (Glynn et al. 2012) and milk (Sundström et al. 2011). Actually, in the study by Glynn et al. (2012) the concentration difference in blood serum between PFHxS and PFOS is almost gone at the last measurement 2010.

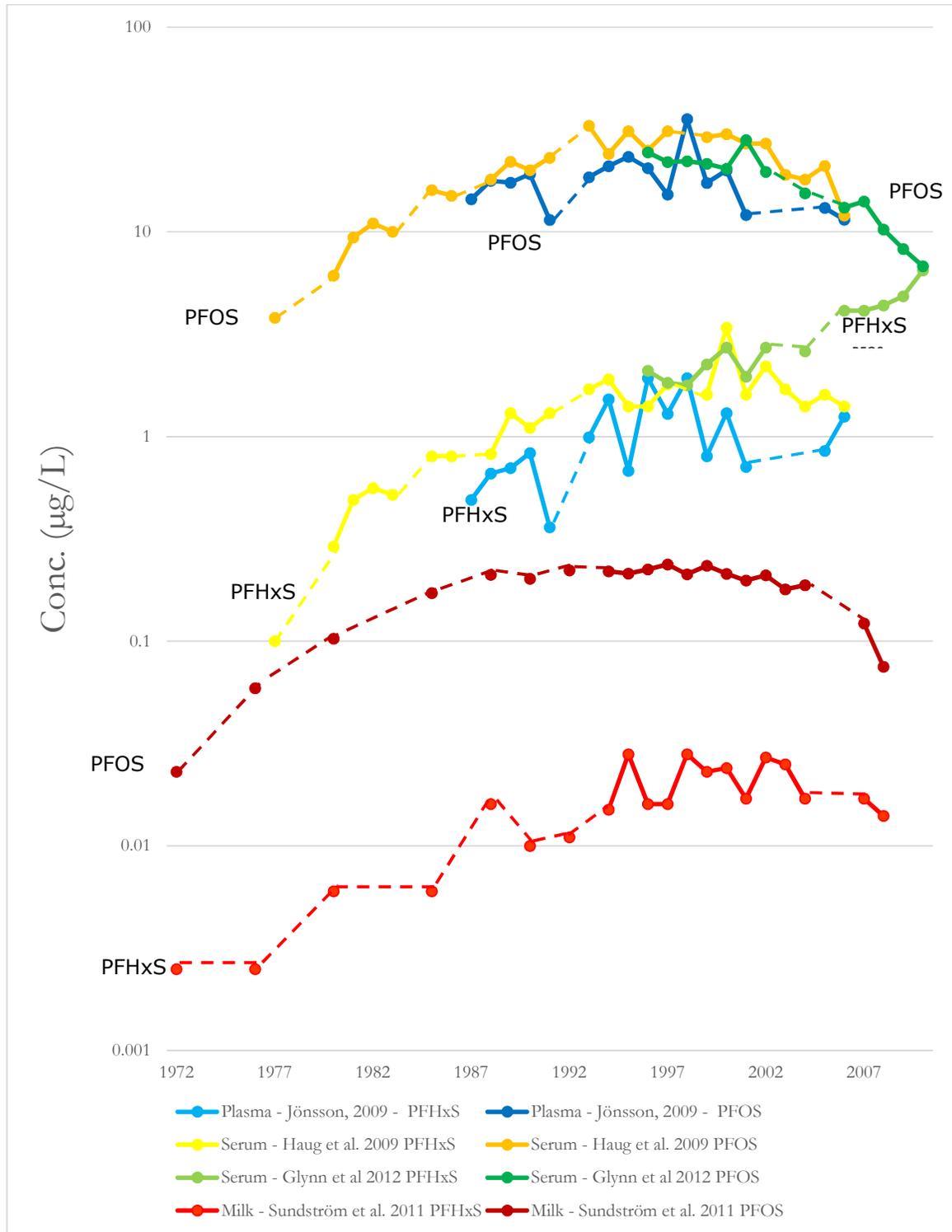


Figure 8. Concentrations of PFHxS and PFOS in human plasma, serum and milk. Data from Haug et al. 2009, Jönsson 2009, Sundström et al. 2011, and Glynn et al. 2012.

Haug and co-worker (2009) analysed 57 pooled archived human serum samples from Norway in order to assess the time trends of 19 PFAS, including PFHxS, during 1976 - 2007. Serum samples were collected from a biobank at the Norwegian Institute of Public Health. Two series of pooled serum samples were analysed in order to examine if the concentrations of the 19 PFAS from 1976 to 2007, and to evaluate the importance of age and gender in the human serum levels. PFOS (33 µg/L in 1993) was found at the highest concentrations in all samples, followed by PFOA (5.2 µg/L in 1993) and PFHxS (3.4 µg/L in 2000). Serum levels in men (age 40 - 50 years) for PFHxS increased from 1976 to the early 1990s where the levels stabilised until 2006. The concentrations for PFHxS ranged from a minimum of 0.1 µg/L in 1977 to a maximum of 3.4 µg/L (2000) and a concentration of 1.4 µg/L in 2006. The concentrations of PFOS and PFOA increased from 1976 to the early 1990s where they reached a plateau before they started to decrease around year 2000. The concentrations of PFOS and PFOA ranged from a minimum of 3.8 µg/L and 0.58 µg/L, respectively, in 1977 (both) to a maximum of 33 µg/L and 5.2 µg/L, respectively, in 1993 (both) and a concentration of 12 µg/L and 2.7 µg/L in 2006 (both), respectively. No correlation was found between concentration in serum and gender or age, but the authors also noted that the statistical power was low due to few data points used in the analysis. The concentrations of PFHxS from 1977 to 2006 were significantly correlated with the concentrations of PFOS (0.85, $p < 0.01$) and PFOA (0.89, $p < 0.01$). The concentrations of PFOS and PFOA were also significantly correlated with each other (0.95, $p < 0.01$). The authors proposed that this intercorrelation between these three PFAS in human plasma indicate a common source of exposure (such as food, dust and air) since they cannot convert directly into each other. Corresponding values for the PFUnDA, PFDoDA and PFTrDA are included in **Table 19** in Annex II.

Jönsson and co-workers (2009) analysed biobanked plasma samples from 80 healthy Swedish women (ages 36 - 56 years) from the general population for levels of a number of PFAS, including PFHxS. The samples originated from the oncology clinic in Lund, Sweden, and were collected from 1987 to 2007. The levels of PFHxS increased significantly ($p = 0.025$) with 0.017 µg/L per year during this time period. The mean level of PFHxS was 0.94 µg/L (range: 0.16 - 2.6 µg/L). The levels of PFOS decreased significantly ($p = 0.017$) with 0.27 µg/L per year during this time period. The mean level of PFOS was 17 µg/L (range: 3.6 - 37 µg/L). There was no significant change of the levels of PFOA during this time period. The mean level of PFOA was 3.2 µg/L (range: 1.1 - 7.2 µg/L).

There was a large environmental contamination of PFAS in 2006 in the area of Arnberg, Germany. Wilhelm and co-workers (2009) evaluated the levels of some PFAS, including PFHxS, in human blood before the contamination, analysing blood plasma samples from 30 young adults (19 males and 11 females; age 20-31 years) who had lived in or around Arnberg, Germany, at some point during 1977 and 2004. The blood samples were obtained from the German Environmental Specimen Bank for Human Tissues. The PFHxS plasma levels had increased steadily ($p < 0.001$) from 1977 to 2004, which was in contrast to PFOS and PFOA for which the levels remained fairly stable with a mild increasing tendency during the first 10-15 years and a decreasing tendency since about 1990-1995. The total median concentration of PFHxS for the entire time period was 1.7 µg/L (range 0.5 - 4.6 µg/L, LOD = 0.1 µg/L). The corresponding numbers for PFOS and PFOA were 18.8 µg/L (range 8.1 - 150.7 µg/L, LOD = 0.1 µg/L) and 6.1 µg/L (range 1.7 - 40.7 µg/L, LOD = 0.1 µg/L), respectively. For PFHxS males had significantly higher levels ($p < 0.05$) of PFHxS as compared to females. Using the Spearman correlation coefficients the authors found an association between PFHxS, PFOS and PFOA plasma levels (PFHxS and PFOS (0.34, $p = 0.07$), PFHxS and PFOA (0.065, $p < 0.001$) and PFOS and PFOA (0.69, $p < 0.001$), which was interpreted that it suggests similar sources for the different PFAS.

Sundström *et al.* (2011) evaluated the concentration of PFHxS, PFOS, and PFOA in Swedish pooled human milk samples from healthy mothers (age 27 - 31 years) 1972 and 2008. The milk samples were collected between the second and twelfth week after delivery by the Mother's Milk Centre (Stockholm, Sweden). A total of 20 pooled samples ($n = 15 - 116$

samples per pool) were analysed. Twenty individual (non-pooled) human milk samples were collected in 2007 and pooled to form the 2007 pool sample. These twenty samples were also analysed individually in order to evaluate sample variations. The levels of PFHxS ranged between below the limit of quantification (5 ng/L) and 28 ng/L. PFHxS, PFOS, and PFOA all displayed statistically significant increasing trends in pooled human milk samples from Stockholm from 1972 - 1980. While lower levels were observed for PFHxS, PFOS, and PFOA after 2000, the decreasing trend was only observed for PFOS ($p < 0.011$) and PFOA ($p < 0.04$), not for PFHxS ($p > 0.05$). In 2008, the concentration of PFHxS, PFOS, and PFOA in pooled human milk were 14 ng/L, 75 ng/L and 74 ng/L, respectively.

Glynn *et al.* (2012) investigated time trends of 13 perfluorinated alkyl acids, including PFHxS, in blood serum in 413 primiparous women (age 19-41 years) from Uppsala County, Sweden, sampled 3 weeks after delivery 1996-2010 with the exception of 2003 and 2005 when no sampling was performed. For each sampling year, blood samples were pooled to create three pooled serum samples. A total of 36 pooled years samples were analysed. Levels of PFHxS increased with 8.3%/year ($p < 0.001$), while the levels of PFOS and PFOA decreased with 8.4%/year ($p < 0.001$) and 3.1%/year ($p < 0.001$), respectively. The mean concentration during this period was 3.2 µg/L (range: 1.8 - 6.5). The corresponding mean concentrations for PFOS and PFOA were 17 µg/L (range: 6.8 - 28 µg/L) and 2.3 (range: 1.7 - 3.1 µg/L), respectively. The levels of PFHxS, PFOS and PFOA in the maternal serum sampled during pregnancy and the nursing period as well as in the cord blood were strongly correlated. Corresponding values for PFUnDA, PFDoDA, PFTTrDA and PFTTeDA are included in **Table 19** in Annex II.

Scott (2016) measured the concentrations of a population of 113 persons exposed via the contaminated drinking water in Kallinge, Sweden, and reported that the median concentrations of PFHxS, PFOS and PFOA in blood serum, decreased during the period June 2014 to September 2016. The decrease during that period for PFHxS, PFOS and PFOA were 33 %, 43 % and 50 %, respectively.

Professional workers

Freberg and co-workers (2010) determined the concentration of 11 perfluorinated carboxylic acids (PFCA) and eight perfluorinated sulfonic acids (PFSA), including PFHxS) in serum of 13 Norwegian professional ski waxers (mean age 40.6 years, range 28.3 - 52.9 years; average time as professional ski waxers 7 years, range 2 - 13 years). They also measured the same compounds in workroom aerosols and in the fluoro containing solid ski waxes and wax powders. Sampling was performed after season I (March 2008), at the beginning of season II (November 2008), and after season II (March 2009). The median concentrations of PFHxS at these occasions were 1.6 µg/L (range: 0.83 - 6.2 µg/L), 1.4 µg/L (range: 0.84 - 6.2 µg/L), and 1.5 µg/L (range: 0.80 - 6.4 µg/L) respectively. The corresponding levels for PFOS were 27 µg/L (11 - 91 µg/L), 24 µg/L (8.7 - 86 µg/L) and 26 µg/L (10 - 86 µg/L), respectively. The corresponding levels for PFOA were 50 µg/L (20 - 174 µg/L), 53 µg/L (15 - 173 µg/L) and 57 µg/L (20 - 162 µg/L), respectively. PFHxS and PFOS were not detected in the air samples, as compared to PFOA which was detected at median concentration of 15 g/kg dust in the respirable, thoracic and inhalable fractions. PFHxS was not detected ($< \text{LOQ}$ 0.0073 mg/kg product) in the fluorinated solid skiwax blocks or the powders. PFOS was not detected in the solid skiwax blocks and only at low concentrations (nd - 0.149 mg/kg product) in a few (3/11) of the powders. PFOA were detected in both the solid ski wax blocks (median 0.68 mg/kg product, range nd-3.8) and in the skiwax powders (median 2.7 mg/kg product, range 0.29 - 12). The concentration of PFHxS or PFOS found in the professional ski waxers resembles those found in the general Norwegian population Haug *et al.* (Haug *et al.*, 2009)), while the levels of PFOA were substantially increased. The concentration in serum was significantly positively associated with age for PFHxS, but not for PFOS and PFOA. The number of years as a ski waxer was positively correlated with serum concentration for PFOA, but not for PFHxS and PFOS. Corresponding values for PFUnDA, PFDoDA, PFTTrDA and PFTTeDA are included in Annex II.

Nilsson *et al.* (2010) performed a time trend study in 2007/2008 focusing on ski wax technicians ($n = 8$; mean age 37.6 years, range 27-51 years; mean time as wax technician 8 years, range 3 - 15 years) exposure to perfluorinated chemicals from fluorinated wax fumes. Concentrations of eight perfluorocarboxylates (PFCA) and three perfluorosulfonates (PFSA), including PFHxS, were analysed in monthly samples of whole-blood collected before the ski season, then at four FIS World Cup competitions in cross country skiing, and finally during an unexposed 5-month postseason period. The median concentration of PFHxS was 1.64 $\mu\text{g/L}$ (range 0.3 - 4.3 $\mu\text{g/L}$) and it was detected in 93% of the blood samples, which was in all except in the first four monthly samples of one of the participants. PFOS and PFOA were detected in all blood samples with median concentrations of 12.2 $\mu\text{g/L}$ (range 0.3 - 27 $\mu\text{g/L}$) and 112 $\mu\text{g/L}$ (range 4.8 - 535 $\mu\text{g/L}$), respectively. The levels of PFHxS and PFOS were considered comparable to those of the general population worldwide, while the levels of PFOA were considerably higher. Generally, levels of carboxylates PFOA, PFNA, PFDA and PFUnDA decreased with increasing carbon chain length in samples collected during the exposure period. The levels of PFOA for the three technicians with initially low levels ($<10 \mu\text{g/L}$ in pre-season blood) increased by 254, 134, and 120%, whereas the five technicians with high initial levels ($>100 \mu\text{g/L}$ in pre-season blood) were at steady state. A significant correlation ($p < 0.01$) was found between the number of years working as a ski wax technician and the levels of PFHxS ($r = 0.29$) and PFOA ($r = 0.78$). There was also a significant correlation ($p < 0.001$) between biological age and the sulfonates PFHxS ($r = 0.69$) and PFOS ($r = 0.59$). The authors noted the low statistical power due to the small study groups. The PFCAs were significantly correlated ($p < 0.001$) with each other as the PFSAs were which each other, which points to a common exposure of the PFCAs since the levels of these compounds were also significantly elevated in blood. However, the lack of correlation between sulfonates and carboxylates indicates other more important sources of the PFSAs in the blood of ski wax technicians than ski wax. Corresponding values for PFUnDA are included in **Table 19** in Annex II.

4.1.2.3 Gestational and lactational transfer

The available studies show that PFHxS is transferred to the foetus through the placenta in humans and also that it is excreted via lactation. Transfer to breast milk appears to be a significant route of elimination of PFAS during breastfeeding. Comparisons of serum concentrations of women who did or did not breastfeed their infants showed that breastfeeding significantly decreases maternal serum concentrations of PFHxS, PFOS, and PFOA ((Bjermo *et al.*, 2013), (Brantsaeter *et al.*, 2013)). The decrease was estimated to be 2-3% decrease/month of breastfeeding ((Brantsaeter *et al.*, 2013)).

Kärrman *et al.* (2007) studied the relationship between levels of perfluorinated chemicals maternal serum and breast milk with matched individual milk and serum samples from 12 Swedish primiparous women collected in 2004 in Uppsala. The authors concluded that lactation is a considerable source of PFAS exposure for infants. Corresponding values for PFUnDA are included in **Table 19** in Annex II.

Fromme *et al.* (2010) measured the concentration of a number of perfluorinated compounds, including PFHxS, in maternal blood during pregnancy (at two time points; $n = 40$ and 38) and six months after delivery ($n = 47$), in cord blood ($n = 33$) and in blood of infants six ($n = 40$) and nineteen months ($n = 40$) after birth and monthly in breast milk samples during December 2007 and October 2009 in Munich, Germany. The levels in infants increased significantly ($p < 0.001$) for PFHxS, PFOS and PFOA during the six months in between the first two samplings. A significant correlation ($p < 0.001$) for PFHxS, PFOS and PFOA was also found between maternal serum concentration at delivery and cord blood concentration.

Antignac and co-workers (2013) determined the concentration of a number of perfluoroalkylated substances, including PFHxS, in a set of 48 breast milk samples collected from French women 2007. In accordance with other similar studies PFHxS, PFOS and PFOA were detected and quantified in the majority of analysed samples (100%, 90% and 98%, respectively) and appeared as the major contributors to the total perfluoroalkylated substance exposure (25%, 38% and 37%, respectively). The reported median concentrations for PFHxS, PFOS and PFOA were 0.05 µg/L (range 0.04 - 0.07), 0.079 µg/L (range <0.05-0.33) and 0.075 µg/L (range <0.05 - 0.22), respectively.

Bjermo and co-workers (2013) measured the levels of several PFAS, including PFHxS, in blood serum of 270 Swedish adults (age 18 - 80 years) from 21 counties in Sweden in 2010-2011 searching for correlations between levels in blood and diet/lifestyle factors nationwide in Sweden. Blood and other data were collected at four separate occasions during the study period. Only PFOS had significantly higher concentrations in men as compared to women when adjusting for both energy intake and total full breastfeeding time. Correlation between serum levels and age was found for PFOS and PFOA, but not for PFHxS ($p = 0.08$). Women who had breastfed for over 12 months, had a 35 %, 32% and 46% lower adjusted mean levels of PFHxS, PFOS and PFOA, respectively, as compared to women who never breastfed full-time. Corresponding values for PFUnDA are included in **Table 19** in Annex II.

Brantsæter et al. (2013) investigated the plasma concentration of four PFAS, including PFHxS, in pregnant women ($n = 485$) in Norway. The samples were collected during 2003 and 2004 around gestation week 17. Parity was the determinant with the largest influence on plasma PFAS concentration and nulliparous women had a significantly higher PFHxS level than women who had one child or more. The plasma level was negatively correlated with time spent breastfeeding and positively correlated with time since the most recent pregnancy.

4.1.2.4 Distribution in the human body

PFAS does not tend to accumulate in fat tissue. PFOA displays the highest concentrations in liver, blood, lung and kidney (ECHA, 2013b) and other PFAS can be expected to have a similar distribution. PFHxS was found in all studied human organ/tissues in the study by Pérez et al. (2013) in which 99 samples of autopsy tissues (brain, liver, lung, bone and kidney) from 20 individuals (28-83 years) from Tarragona in Spain were analysed. PFHxS was most frequently detected in the lung (32%), but the highest median concentrations was found in the kidney 18 µg/kg wwt., followed by the lung (5.7 µg/kg wwt.)

4.1.2.5 Elimination

Elimination half-lives of PFHxS in humans have been estimated to range from 7 years up to 35 years. The human elimination half-lives of PFHxS was longer-substantially longer than those of all other PFAS examined.

Absorbed PFAS distribute from plasma to soft tissues, with the highest extravascular concentrations found in the liver. Olsen and co-workers (2003) examined the concentrations of PFHxS, PFOS and PFOSA in samples of in human donor tissues (liver and serum) from 23 deceased people. The route of exposure to PFAS was unknown. Among the 23 paired samples, the mean liver to serum ratio for PFOS was 1.3 (95% CI 0.9:1-1.7:1) and was not different in males (1.3, $n=13$) or females (1.3, $n=10$). Liver to serum ratios were not estimated for PFHxS, PFOA and PFOSA as 90% of the human liver samples had concentrations below the limit of quantification, which were <1.2 ng/ml, <3.0 ng/ml and <1.3 ng/ml, respectively.

Olsen *et al.* (2007) estimated the elimination half-life of PFHS, PFOS and PFOA in serum in 26 retired fluorochemical production workers. Since the elimination appeared linear on a semi-log plot of concentration vs. time a first-order model was used for estimation. The arithmetic/geometric mean elimination half-lives for PFHxS, PFOS and PFOA were 8.5 years (95% CI 6.4 - 10.6)/7.3 years (95% CI 5.8 - 9.2), 5.4 years (95% CI 3.9 - 6.9)/4.8 years (95% CI 4.0 - 5.8), and 3.8 years (95% CI 3.1 - 4.4)/3.5 years (95% CI 3.0 - 4.1), respectively. The authors considered that differences in species-specific pharmacokinetics, at least partly, may be due to a saturable renal resorption process.

Beesoon and co-workers (2012) studied a Canadian family of seven with unusually high levels of PFHxS in serum (range: 27.5 - 423 µg/L) and tried to identify the source(s), pathways and excretion. Urine, serum and faeces were sampled from the family members. In addition samples were taken from the carpet, dust and air in the house and a questionnaire was administered. No PFHxS was found in the stool, but was detected in the urine samples from the whole family. The urinary excretion route was considered to be the primary one. The probable source of PFHxS was identified as a Scotchgard carpet treatment formulation that had been applied 8 times during 15 years, with the route of exposure being through dust ingestion and/or inhalation. Corresponding values for PFTTrDA and PFTTeDA are included in **Table 19** in Annex II.

Zhang *et al.* (2013) collected paired blood and urine samples (n = 86) from Chinese adults and measured the concentrations of a number of perfluorinated compounds (PFAS), including PFHxS. The participants were first divided into four groups; young females (age ≤ 50 years, n = 20), older females (> 50 years, n = 19), young males (≤ 50 years, n = 32), and older males (> 50 years, n = 15). The group of young females had significantly lower levels of PFHxS than the others and therefore the three other groups were combined. The levels in urine correlated positively with the levels in blood for PFHxS, PFOS and PFOA. Perfluoroalkyl carboxylates (PFCAs) were found to be excreted more efficiently than perfluoroalkane sulfonates (PFSAs) of the same carbon chain-length. In general, shorter PFCAs were excreted more efficiently than longer ones, but in contrast for PFSAs, PFOS was excreted more efficiently than PFHxS. Among PFOS and PFOA isomers, major branched isomers were more efficiently excreted than the corresponding linear isomers. Urinary excretion was the major elimination route for short PFCAs (C≤8), but for longer PFSAs (PFOS and PFHxS) other routes of excretion likely contribute to the overall elimination). The menstrual serum clearance rate was lower than the renal clearance rate for most PFAS, but was comparable to the renal clearance estimated for PFHxS and PFOS and some longer carbon chain PFCAs and this excretion route may therefore be of importance for these compounds in young females. The estimated arithmetic (geometric) mean elimination half-lives for the young female group and the male and older female group for PFHxS, PFOS and PFOA were 7.7(7.1)/35(25) years, 6.2(5.8)/27(18) years and 2.3(1.5)/2.8(1.2) years, respectively. The authors stated that these elimination half-lives should be viewed as upper limits due to the possibility that there might be other significant elimination routes other than via the urine. Corresponding values for PFHpA, PFNA, PFDA and PFUnDA are included in **Table 19** in Annex II.

Rough estimates on human elimination half-lives of PFHxS, PFOS and PFOA on group basis in a population of 113 persons exposed via contaminated drinking water in Kallinge, Sweden, based on decreased concentrations in blood serum (Scott, 2016) were 6.8 y, 5.2 y and 4.5 y.

4.1.3 Comparison of half-lives in different species

In rat, serum elimination half-life's of PFCAs increase from a few hours for PFBA ((Chang *et al.*, 2008); (Chengelis *et al.*, 2009)) and PFHA ((Ohmori, Kudo, Katayama, & Kawashima, 2003); (Chengelis *et al.*, 2009)) to a few days for PFOA (Ohmori *et al.*, 2003) up to several tens of days for PFNA ((Ohmori *et al.*, 2003); (Tatum-Gibbs *et al.*, 2011)) and the PFDA (Ohmori *et al.*, 2003).

The same trend for PFCAs appears to exist also for mice since the serum elimination half-life increase from hours for PFBA (Chang et al., 2008) to days for the PFOA (Lou et al., 2009) and PFNA (Tatum-Gibbs et al., 2011). The increasing trend is also apparent for pigs and monkeys where the elimination half-life in pigs for PFHxA increase from 4 days (Numata et al., 2014), via 74 days in PFHpA (Numata et al., 2014) to 236 days in PFOA (Numata et al., 2014) and the elimination half-life in monkeys increase from 2-4 days in PFBA (Chang et al., 2008) to 21 d/33 days in PFOA (Butenhoff et al., 2004). The trend also exists for humans where the elimination half-life increase from 1.7 days in PFBA (Chang et al., 2008) to 3.8 years (arithm. mean)/3.5 years (geometric mean) in PFOA (Olsen et al., 2007) in occupational workers, and from one year in PFHpA, to 1.5 years in PFOA, to 1.7 years in PFNA to 4 years in PFDA and PFUnDA for young females, and from 0.8 years in PFHpA, to 1.2 years in PFOA, to 3.2 years in PFNA to 7.1 years in PFDA and 7.4 years PFUnDA for males and older females as presented in Zhang et al. (2013).

The picture with increasing elimination half-lives with increasing carbon-chain length also exists for PFSAs in rodents. In rats the elimination half-life in PFBS is reported to be 4.5 h/4 h (Olsen et al., 2009), in PFHxS 29 d/1.6 d (Sundström et al., 2012) and in PFOS 30-60 d (Chang et al., 2012). In mice the elimination half-life of PFHxS is 28-31d/25-27 d (Sundström et al., 2012) and in PFOS 43 d/36 d (Chang et al., 2012).

Increasing elimination half-lives with increasing carbon-chain length can be observed also in pigs, monkeys and humans, with the exception of PFHxS always having the longest elimination half-lives despite not having the longest carbon chain. The shortest elimination half-life in pigs was detected in PFBS with 43 d, followed by PFOS with 634 d and PFHxS, with 713 d (Numata et al., 2014). The same pattern in elimination half-life have also been observed in monkeys with PFBS having an elimination half-life of 95 h/83 h (Olsen et al., 2009), followed by PFOS, with 130 d/110 d (Chang et al., 2012) and PFHxS, with 141 d/27 d (Sundström et al., 2012). The same pattern is also observed in humans with PFBS having an elimination half-life of 25.8 h (geometric mean) (Olsen et al., 2009), followed by PFOS with 3.8 y (Olsen et al., 2007) (geometric mean) to 5.8 y/18 y (geometric mean for young females/Males and older females) (Zhang et al., 2013) and PFHxS with 7.3 y (geometric mean) (Olsen et al., 2007) to 7.1 y/25 y (geometric mean for young females/Males and older females)/ 7.7 y/35 y (arithmetic mean for young females/Males and older females) (Zhang et al., 2013).

Sundström et al. (2012) suggested that the differences in elimination between species and gender, in rats, could be due to differences in the expression of organic anion transporters.

The elimination half-lives in **Table 10** below are for illustrative reasons also presented in Figure 9, which is located directly after **Table 10**.

Table 10: Elimination half-lives (days) of PFSA and PFCAs in humans and other mammalian species.

Number of C/F-atoms	Name	Species elimination half-lives						
		Rat	Mice	Pig	Monkey	Human (Arithm. mean = AM, Geom. Mean = GM, Median = M)		
						Retired and non-retired occupational workers	Young females	Males and older females
4/7	PFBA	M: 0.38d (=9.2h), F: 0.08d (=1.8h) [a] M: 0.27d (=6.4h), F: 0.04d (=1.0h) [b]	M: 0.54d (=13h), F: 0.12d (=2.9h) [c] M: 0.67d (=16h), F: 0.13d (=3.1h) [d] M: 0.22d (=5.2h), F: 0.12d (=2.8h) [e]		M: 1.7d, F: 1.7d [f]	M: 3.0d AM, 2.7d GM [g] F: 3.6d AM, 3.4d GM [g]		
4/9	PFBS	M: 0.19d (=4.51h), F: 0.17d (=3.96h) [h]		M, F: 43 d [i]	M: 4.0d, F: 3.5d [j]	M: 27.7d AM, 25.8d GM F: 45.7 d [k]		
6/11	PFHxA	M: 0.04d (=1.0h), F: 0.02d (=0.42h) [l] M: 0.09d (=2.2h), F: 0.11d (=2.7h) [m] M: 0.11d (=2.7h), F: 0.10d (=2.4h) [n] M: 0.12d (=2.8h), F: 0.10d (=2.3h) [o] M: 0.07d (=1.7h), F: 0.02d (=0.5h) [p] M: 0.06d (=1.5h), F: 0.03d (=0.7h) [q]		M, F: 4.1d [r]	M: 0.22d (=5.3h), F: 0.10d (=2.4h) [l]			
6/13	PFHxS	M: 29.1d [s] F: 1.64d [t]	M: 31d, F: 25d [u] M: 28d, F: 27d [v]	M, F: 713d [w]	M: 141, F: 27d [x]	M, F: 3103d (=8.5y) AM, 2665d (=7.3y) GM [y]	2811d (=7.7y) AM, 2592d (=7.1y) GM, 2592d (=7.1y) M [z]	12775d (=35y) AM, 9125d (=25y) GM, 10585d (=29y) M [z]
7/13	PFHpA	M: 0.10d (=2.4h), F: 0.05d (=1.2h) [A]		M, F: 74d [B]			548d (=1.5y) AM, 365d (=1.0y) GM, 584d (=1.6y) M [z]	438d (=1.2y) AM, 299d (=0.82y) GM, 288d (=0.79y) M [z]
7/15	PFHpS			M, F: 411d [C]				
8/15	PFOA	M: 5.6d, F: 0.08d [A]	M: 22d, F: 16d [F]	M, F: 236d [G]	M: 21d, F: 33d [H]	M, F:	840d	1022d (=2.8y) AM, 438d (=1.2y) GM, 657d

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Number of C/F-atoms	Name	Species elimination half-lives						
		Rat	Mice	Pig	Monkey	Human (Arithm. mean = AM, Geom. Mean = GM, Median = M)		
						Retired and non-retired occupational workers	Young females	Males and older females
		M: 13d [D] M: 9.1d [E]			M: 20d [I] M: 21d [H]	511d (=1.4y) AM, 475d (=1.3y) GM, 475d (=1.3y) M [x]	(=2.3y) AM, 621d (=1.7y) GM, 730d (=2.0y) M [z]	(=1.8y) M [z]
8/17	PFOS	M: 38d, F: 62d [I] M: 41d, F: 71d [J] M: 8d, F: 5.6d [K]	M: 43d, F: 38d [L] M: 36d, F: 30d [M]	M, F: 634d [N]	M: 132d, F: 110d [O]	M, F: 1971d (=5.4y) AM, 1387d (=3.8y) GM [x]	2263d (=6.2y) AM 2117d (=5.8y) GM, 2190d (=6.0y) M [z]	9855d (=27y) AM 6570d (=18y) GM, 6570d (=18y) M [z]
9/17	PFNA	M: 30d, F: 2.4d [A] M: 41d [D] M: 47d, F: 2.1d [P] M: 42d [Q] M: 24d, F: 32d [R] M: 28d [S]	M: 34d, F: 26d [T] M: 228d, F: 69d [U]				913d (=2.5y) AM, 621d (=1.7y) GM, 548d (=1.5y) M [z]	1570d (=4.3y) AM, 1168d (=3.2y) GM, 1278d (=3.5y) M [z]
10/19	PFDA	M: 40d, F: 59d [A]					1643d (=4.5y) AM, 1460d (=4.0y) GM, 1533d (=4.2y) M [z]	4380d (=12y) AM, 2592d (=7.1y) GM, 3358d (=9.2y) M [z]
11/21	PFUnDA						1643d (=4.5y) AM, 1460d (=4.0y) GM, 1606d (=4.4y) M [z]	4380d (=12y) AM, 2701d (=7.4y) GM, 3358d (=9.2y) M [z]

[a] Data from Chang et al., 2008. Mean β -phase of one compartment model with first-order elimination, single oral dose of 30 mg/kg

[b] Data from Chang et al., 2008. Mean β -phase of one compartment model with first-order elimination, single IV dose of 30 mg/kg

- [c] Data from Chang et al., 2008. Mean β -phase of one compartment model with first-order elimination, single oral dose of 10 mg/kg
- [d] Data from Chang et al., 2008. Mean β -phase of one compartment model with first-order elimination, single oral dose of 30 mg/kg
- [e] Data from Chang et al., 2008. Mean β -phase of one compartment model with first-order elimination, single oral dose of 100 mg/kg
- [f] Data from Chang et al., 2008. Mean β -phase of two compartment model with first-order elimination, single IV dose of 10 mg/kg
- [g] Data from Chang et al., 2008. β -phase estimate of occupational exposure to PFBA precursors with elimination half-life calculated from two blood samples 7-11 d apart
- [h] Data from Olsen et al., 2009. Mean β -phase of two compartment model with first-order elimination, single IV dose of 30 mg/kg bw
- [i] Data from Numata et al., 2014. Mean β -phase of two compartment model with first-order elimination, 21d exposure to 132 $\mu\text{g}/\text{kg}$ dw in diet
- [j] Data from Olsen et al., 2009. Mean β -phase of three compartment model with first-order elimination, single IV dose of 10 mg/kg bw
- [k] Data from Olsen et al., 2009. Mean β -phase of one compartment model with first-order elimination, blood samples collected over a 180-day period
- [l] Data from Chengelis et al., 2009. Mean β -phase of two compartment model with first-order elimination, single IV dose of 10 mg/kg
- [m] Data from Chengelis et al., 2009. Mean β -phase of two compartment model with first-order elimination, repeated oral dose of 50 mg/kg, day 25
- [n] Data from Chengelis et al., 2009. Mean β -phase of two compartment model with first-order elimination, repeated oral dose of 150 mg/kg, day 25
- [o] Data from Chengelis et al., 2009. Mean β -phase of two compartment model with first-order elimination, repeated oral dose of 300 mg/kg, day 25
- [p] Data from Gannon et al., 2011. Mean β -phase of one compartment model with first-order elimination, single oral dose of 2 mg/kg
- [q] Data from Gannon et al., 2011. Mean β -phase of one compartment model with first-order elimination, single oral dose of 100 mg/kg
- [r] Data from Numata et al., 2014. Mean β -phase of two compartment model with first-order elimination, 21d exposure to 48 $\mu\text{g}/\text{kg}$ dw in diet
- [s] Data from Sundström et al., 2012. Mean β -phase of two compartment model with first-order elimination, single IV dose of 10 mg/kg bw
- [t] Data from Sundström et al., 2012. Mean β -phase of one compartment model with first-order elimination, single IV dose of 10 mg/kg bw
- [u] Data from Sundström et al., 2012. Mean β -phase of non compartment model with first-order elimination, single oral dose of 1 mg/kg bw
- [v] Data from Sundström et al., 2012. Mean β -phase of non compartment model with first-order elimination, single oral dose of 20 mg/kg bw
- [w] Data from Numata et al., 2014. Mean β -phase of two compartment model with first-order elimination, 21d exposure to 91.3 $\mu\text{g}/\text{kg}$ dw in diet
- [x] Data from Sundström et al., 2012. Mean β -phase of non compartment model with first-order elimination, single IV dose of 10 mg/kg bw
- [y] Data from Olsen et al., 2007. Mean β -phase of non-compartment model with first-order elimination, periodic blood samples collected over 5 years
- [z] Data from Zhang et al., 2013. β -phase estimate based on one compartment modelling of urine and blood samples. Should according to the authors be considered as upper limit estimates.
- [A] Data from Ohmori et al., 2003. Mean β -phase of two compartment model with first-order elimination, single IV dose of 48.64 mmol/kg bw
- [B] Data from Numata et al., 2014. Mean β -phase of two compartment model with first-order elimination, 21d exposure to 10.2 $\mu\text{g}/\text{kg}$ dw in diet
- [C] Data from Numata et al., 2014. Mean β -phase of two compartment model with first-order elimination, 21d exposure to 3.99 $\mu\text{g}/\text{kg}$ dw in diet
- [D] Data from Benskin et al., 2014. β -phase elimination rate, single oral dose, 0.5 mg/kg
- [E] Data from De Silva et al., 2009. β -phase elimination rate, repeated dose, 12 week exposure to 0.40 mg/kg in diet
- [F] Data from Lou et al., 2009. Mean β -phase of one compartment model with first-order elimination, single oral dose of 1 or 10 mg/kg
- [G] Data from Numata et al., 2014. Mean β -phase of two compartment model with first-order elimination, 21d exposure to 22.4 $\mu\text{g}/\text{kg}$ dw in diet
- [H] Data from Butenhoff et al., 2004. Mean β -phase of non-compartment model with first-order elimination, single IV dose of 10 mg/kg
- [I] Data from Butenhoff et al., 2004. Mean β -phase of non-compartment model with first-order elimination, repeated dose, six month oral dosing of 10 mg/kg
- [H] Data from Butenhoff et al., 2004. Mean β -phase of non-compartment model with first-order elimination, repeated dose, six month oral dosing of 20 mg/kg
- [I] Data from Chang et al., 2012. Mean β -phase of non compartment model with first-order elimination, single oral dose of 2 mg/kg bw
- [J] Data from Chang et al., 2012. Mean β -phase of non compartment model with first-order elimination, single oral dose of 15 mg/kg bw
- [K] Data from Chang et al., 2012. Mean β -phase of non compartment model with first-order elimination, single IV dose of 2 mg/kg bw
- [L] Data from Chang et al., 2012. Mean β -phase of non compartment model with first-order elimination, single oral dose of 1 mg/kg bw
- [M] Data from Chang et al., 2012. Mean β -phase of non compartment model with first-order elimination, single oral dose of 20 mg/kg bw
- [N] Data from Numata et al., 2014. Mean β -phase of two compartment model with first-order elimination, 21d exposure to 137 $\mu\text{g}/\text{kg}$ dw in diet
- [O] Data from Chang et al., 2012. Mean β -phase of non compartment model with first-order elimination, single IV dose of 2 mg/kg bw
- [P] Data from De Silva et al., 2009. β -phase elimination rate, repeated dose, 12 week exposure to 0.54 mg/kg in diet
- [Q] Data from Tatum-Gibbs et al., 2011. Mean β -phase of two compartment model with first-order elimination, single oral dose of 1 mg/kg
- [R] Data from Tatum-Gibbs et al., 2011. Mean β -phase of two compartment model with first-order elimination, single oral dose of 3 mg/kg
- [S] Data from Tatum-Gibbs et al., 2011. Mean β -phase of two compartment model with first-order elimination, single oral dose of 10 mg/kg
- [T] Data from Tatum-Gibbs et al., 2011. Mean β -phase of two compartment model with first-order elimination, single oral dose of 1 mg/kg
- [U] Data from Tatum-Gibbs et al., 2011. Mean β -phase of two compartment model with first-order elimination, single oral dose of 10 mg/kg

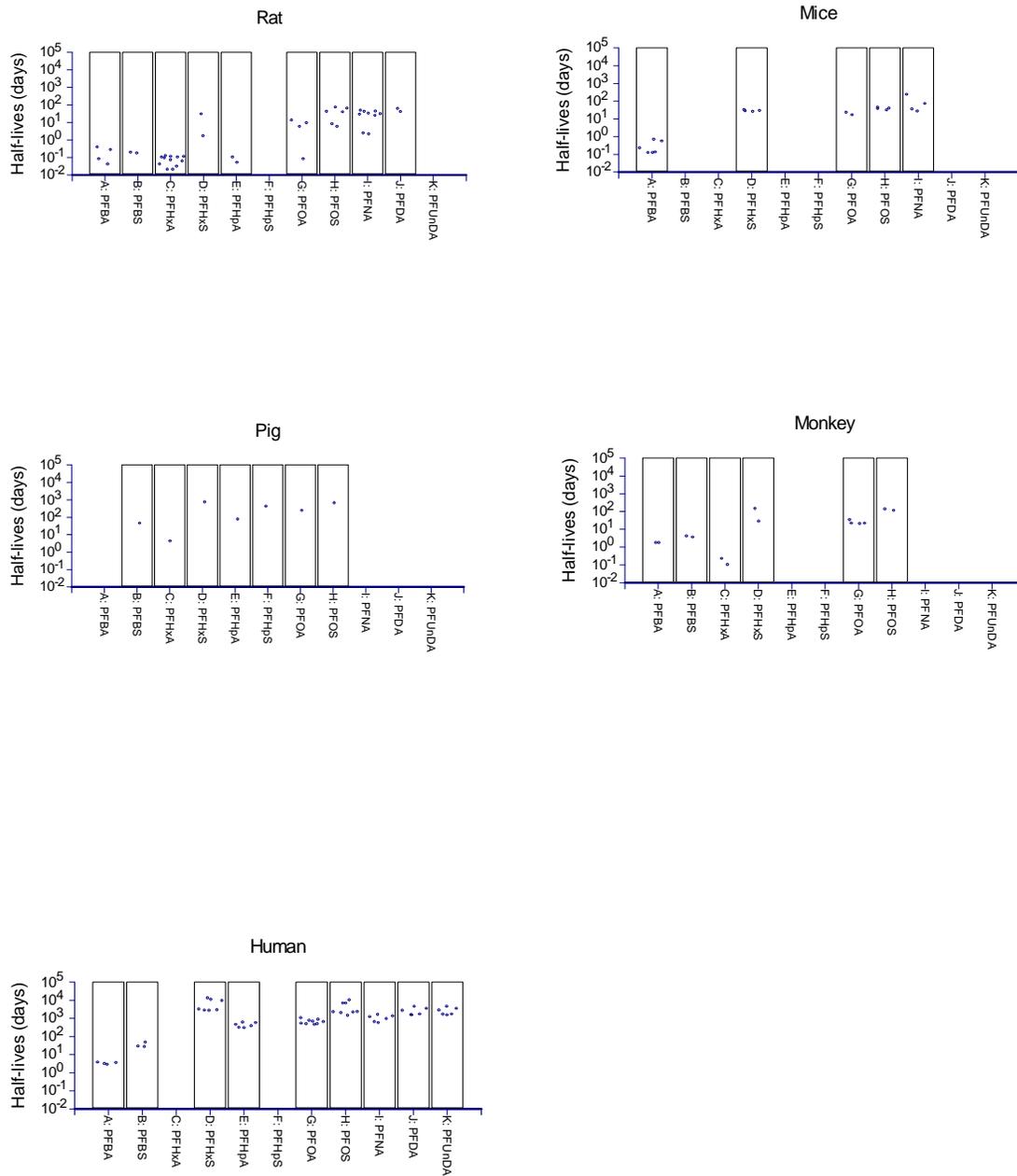


Figure 9: Elimination half-lives in days of PFBA, PFBS, PFHxA, PFHxS, PFHpA, PFHpS, PFOA, PFOS, PFNA, PFDA and PFUnDA in rat, mice, pig, monkey and human.

Rough estimates on human elimination half-lives of PFHxS, PFOS and PFOA on group basis in a population of 113 persons exposed via contaminated drinking water in Kallinge, Sweden, based on decreased concentrations in blood serum (Scott, 2016) were 6.8 y, 5.2 y and 4.5 y, respectively. These rough estimates compare relatively well with the human elimination half-

lives presented in **Table 10** and also have the same relative order, with PFHxS having the longest elimination half-life, followed by PFOS and PFOA.

4.1.4 Bioaccumulation

The data on plasma levels of PFHxS, PFOS and PFOA in humans exposed to PFAS contaminated drinking waters ((Jakobsson K., 2014), (B. Jönsson, 2014)) in Kallinge, Sweden, combined with concentrations of PFHxS, PFOS and PFOA in the corresponding contaminated drinking water (Anders Glynn, 2013), strongly indicate that the bioaccumulation potential of PFHxS in humans is at least equal to or maybe even higher than that of PFOS and PFOA. Dividing the median concentration in plasma with that in contaminated drinking water results in the ratios 215 (=258/1.2), 73 (=291/4), and 123 (=16/0.13) for PFHxS, PFOS and PFOA, respectively. However, it is due to limited number of data (concentrations in drinking water is only known prior to the closure of the water plant, although exposure to these substances has likely occurred for decades, other potential sources of exposure besides drinking water (e.g. fish), potential differences in uptake at low vs. high doses, etc.), not possible to draw conclusions beyond that PFHxS bioaccumulate to at least the same extent as PFOS and PFOA in humans. This enables at least some kind of comparative analysis of bioaccumulation of these three perfluorinated compounds in humans. Drinking water may be an important source of PFHxS exposure in humans (Gyllenhammar et al., 2012). Information on how these concentrations may have changed over time is not available but it may be assumed that the exposure of these three substances has been on-going for decades and most likely originate from the same source (i.e. firefighting foam).

It is not possible to conclude on relative human bioaccumulation of PFAS based on data from biomonitoring and the relative proportions of the various PFAS in human blood. This as the measured concentrations are the result of both previous and present exposure (direct and indirect via breakdown of precursors), which will vary between populations and countries. Figure 10 below shows the variation of relative PFAS concentration on molar basis in human blood depending on where in the world the sampling has been performed.

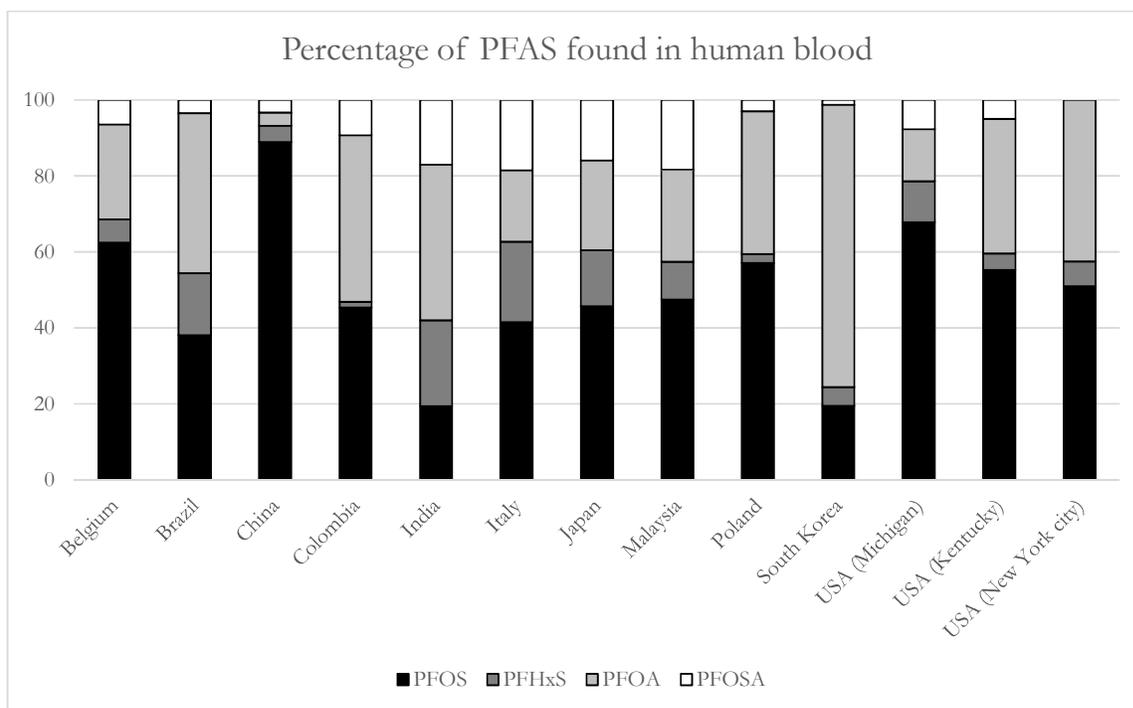


Figure 10: Percentage of PFOS, PFHxS, PFOA and PFOSA on molar basis in human blood samples from various countries. Mean values were used when constructing this figure. Half detection limit was used when the reported value was below the level of detection. Data from (Kannan et al., 2004), (Yeung et al., 2006), (Masunaga, Kannan, Doi, Nakanishi, & Giesy, 2002), (Taniyasu, Kannan, Horii, Hanari, & Yamashita, 2003).

As can be seen in Figure 10 above, profiles of the relative molar concentrations of PFAS in blood varies greatly between countries but PFOS is often (but not always!) detected at the highest relative concentrations with PFOA often being the second largest. This is probably related to a combination of factors, such as relatively large volumes of use, both direct and indirect continuous exposure (including degradation of precursors) and high substance specific potential for human bioaccumulation. It has not been possible to find information on historical and present global production and use volumes of PFHxS to compare with those of PFOS and PFOA, but they are for PFHxS expected to be substantially lower. PFHxS has been detected as an impurity in PFOS in the range of 4-10% ((Seacat et al., 2002), (Jiang et al., 2015)). However, despite substantially lower use and volumes, PFHxS may still be detected at relatively high relative proportions in human blood (see e.g. Brazil, India and Italy in Figure 10).

An important metric to evaluate, when evaluating bioaccumulation of PFAS, is the elimination half-lives in mammals (see Table 10). Some general observations from the available information that can be made are that the elimination half-lives:

- 1) of PFCAs and PFSAAs increase with increasing length of carbon chain in all species, with the exception of PFHxS and
- 2) of PFCAs are shorter than those of PFSAAs,
- 3) in pigs, monkeys and humans are longest for PFHxS among all PFCAs and PFSAAs for which there are available data. This is described in more detail below,
- 4) are shortest in rodents, especially in female rats.

The main reason why e.g. PFOA was considered to meet the B-criterion of REACH was that it was concluded to bioaccumulate in humans based e.g. on its presence in human blood of the general population, the long elimination half-life in human blood of 2-4 years and that the levels increase with age (ECHA, 2013b). This holds true also for PFHxS but it has an elimination half-life in human blood of ca 7-8 years (or longer), which is at least 2-4 times longer than the elimination half-life of PFOA. It needs to be remembered that a substance having shorter elimination half-lives in human blood compared to PFOA cannot be excluded of being bioaccumulative and fulfilling the B-criteria. This since during the B assessment of PFOA, no trigger value for elimination half-life in human blood was defined for the B criteria, and it is still missing (for both B and vB). It also needs to be remembered that even though blood is used as a proxy for the entire body, half-life in human blood is not necessarily identical with the whole body elimination half-life in humans.

A more pragmatic approach is required when concluding on bioaccumulation of substances for which the traditional numerical criteria for bioaccumulation are not appropriate. This as these substances do not follow the behaviour of traditional hydrophobic compounds with partitioning into fatty tissues, but instead bind to proteins in blood and liver. It is from monitoring data clear that PFHxS accumulate in top predators, including humans. The available studies on temporal trends in humans indicate increasing levels of PFHxS. The elimination half-life of PFHxS is the longest measured of all PFAS in humans, monkeys and pigs. The elimination kinetics of PFHxS by species are similar to that of PFOS in mice, male rats, monkeys and humans (Sundström et al., 2012). It is therefore reasonable to assume that also uptake and distribution kinetics are similar to that of PFOS. It is presently not known to what extent the elimination kinetics of the perfluoroalkylsulfonates is determined by organic anion transporter mediated processes and how these may differ between species and sex within species, but it is considered to be of importance (Sundström et al., 2012). The elimination of PFHxS in rats and the observed sex differences has been proposed to be due to differences in expression of organic anion transporters (Sundström et al., 2012). The longer elimination half-life in humans as compared to monkeys has been proposed to, at least partially, be a consequence of saturable renal tubular resorption in monkeys and a higher resorption efficiency in humans (Andersen, Clewell, Tan, Butenhoff, & Olsen, 2006). Another important factor to the long human elimination half-lives of PFHxS and PFOS that have been brought forward is enterohepatic circulation and a potential hepatic accumulation (Zhao et al., 2015). The longer human elimination half-lives can thus not only be explained by differences in body size.

It is clear, that PFHxS poses properties that indicate a very high bioaccumulation potential in humans such as high binding to blood proteins, low clearance and long elimination half-life as suggested by Tonnelier et al. (2012) to be the main factors in determining human bioaccumulation. In addition, PFHxS has the longest elimination half-life in humans of the examined PFASs and PFCAs, and that it is at least 7 years or longer. Further, the performed benchmarking (See Section 4.1.5) shows that PFHxS has an elimination half-life comparable to known bioaccumulative PBT/vPvB and POP-substances.

4.1.5 Benchmarking

Another way to evaluate the relative human bioaccumulation potential of PFHxS would be benchmarking against vB substances known to be highly accumulative in humans such as PCBs. Ritter et al (2011) calculated "intrinsic" human elimination half-lives for a number of PCB congeners using a population PK model. In their estimation of "intrinsic" elimination half-lives Ritter et al corrected their estimations by taking confounding factors such as e.g. changes in exposure and body weight in to account. The longest intrinsic elimination half-lives estimated by Ritter et al were 15.5 years for PCB-170 and 14.4 years for PCB 153. The shortest elimination half-life 2.6 years was estimated for PCB-52 (see **Table 11** below). Ritter also claims that their results gives further evidence that a maximum intrinsic elimination half-life for persistent chemicals exists and lies within the range of 10-15 years. The human elimination half-lives for PFHxS and PFOA in **Table 10** above are "apparent" elimination half-lives, i.e. they refer to

elimination half-lives that may be affected by ongoing exposure and other factors such e.g. weight changes and are therefore not directly comparable to the half-lives estimated by Ritter et al. (2011).

Data from a long term follow-up study have shown that the median concentrations of PFHxS, PFOS and PFOA in blood serum of a population of 113 persons exposed via the contaminated drinking water in Kallinge, Sweden, decreased during the period June 2014 to September 2016 ((Scott, 2016)). The decrease during that period for PFHxS, PFOS and PFOA were 33 %, 43 % and 50 %, respectively.

Wong et al. (2014) estimated the intrinsic elimination half-life in human males of PFOS to 4.7 years. This corresponds very well with the apparent elimination half-lives of 5.4 years/3.8 years (arithm. mean/geometric mean) derived from retired occupational workers (Olsen et al. 2007). It can therefore be assumed that also the apparent elimination half-life of 8.5/7.3 years (arithm. mean/geometric mean) for PFHxS derived by Olsen et al. may be in fairly good agreement with the intrinsic elimination half-life and thus be comparable with the intrinsic elimination half-lives estimated for the PCB congeners (**Table 11**).

Table 11: Human elimination half-lives, fish BCF and BMF and NHANES data on PCBs. Human intrinsic elimination half-lives (years) at background concentrations for nine PCB-congeners as estimated by Ritter et al. (2011). Fish BCF- and BMF-values shown for comparison are from Gobas et al. (1989), Lores et al. (1993), and Fisk et al. (1998). The data on increasing or decreasing concentrations of PCB in humans in the NHANES 2003-04 dataset are from Megson et al. (2013)

Congener	PCB-28	PCB-52	PCB-105	PCB-118	PCB-138	PCB-153	PCB-170	PCB-180	PCB-187
Human elimination half life (years)	5.5	2.6	5.2	9.3	10.8	14.4	15.5	11.5	10.5
Log BCF fish*		4.84, 4.9				5.0, 5.3, 5.3			
BMF fish (low, high exposure)	2.1, 1.8	2.9, 1.5	2.8, 2.3	6.0, 2.2	7.1, 2.4	16, 3.3			6.1, 2.8
Increasing/decreasing conc. with age in NHANES 2003-04 dataset	Incr.	Decr.	Incr.	Incr.	Incr.	Incr.	Incr.	Incr.	Incr.

PCB - 153 (2,2',4,4',5,5' - hexachlorobiphenyl) is the congener most often found at the highest concentrations in human plasma in "non-exposed" populations ((Weintraub & Birnbaum, 2008); (Meyer et al., 2013); (Schettgen, Alt, Esser, & Kraus, 2015)). This is explained by its resistance to metabolism manifested in its long human elimination half-life but also because it is one of the PCB-congeners with the highest concentration in food stuff like fish and meat (EFSA, 2005).

PCB-153 also has a very high log BCF in fish of 5.0 – 5.3. PCB-52 on the other hand is more rarely detected in human plasma of “non-exposed” populations and when detected it is at much lower concentrations than PCB-153 ((Weintraub & Birnbaum, 2008); (Meyer et al, 2013); (Schettgen et al., 2015)). One of the reasons is that the exposure is lower because of lower levels in food stuff than PCB-153. However, PCB-52 is also more easily metabolised with a human elimination half-life 5 times shorter than PCB-153. In a study comparing PCB-levels in plasma of residents living in PCB contaminated dwellings versus non-contaminated dwellings (Meyer et al., 2013) PCB-153 was detected in 100% of the blood samples (n=134) at concentrations ranging from 0.041 to 1.1143 µg/l (median conc. 0.346 µg/l) in the residents of non-contaminated dwellings. PCB-52 on the other hand was only detected in 12.7% of the samples (n=134) at concentration ranging from <LOQ to 0.018 µg/l (LOQ= 0.01 µg/l). The log BCF in fish for PCB-52 has been reported to be 4.8-4.9.

Both PCB-153 and-52 fulfil the vB-criterion of REACH based on their high BCF in fish. However, based on the concentrations of these congeners in human plasma in “non-exposed” populations, there seems to be a marked difference in human bioaccumulation that probably to a large extent is explained by PCB-52 being more easily metabolised than PCB-153 as indicated by the difference in human elimination half-life between these two isomers. This is illustrated by Megson et al. (2013) that performed a multivariate statistical analysis of the NHANES 2003-04 dataset on 2000 individuals in order to identify steady state and episodic congeners from background concentrations of PCB present within the US population. Some of the PCB congeners, such as PCB-52, were identified as episodic, while others, such as PCB-153, were considered steady state as they exhibited a significant increase in concentration with participants age (from 12 to 84 years). By using these results in conjunction with other reviews on PCB metabolism (Brown and Lawton 2001; Hansen 2001) in order to identify how the structure of PCBs relates to rates of biotransformation in humans the authors (Megson et al 2013) found some clear trends in the apparent rate of biotransformation and elimination of PCBs. Congeners with chlorine bonding in the 2,5 and 2,3,6 positions (and 2- in di- and tri-chlorinated congeners) are often rapidly biotransformed and so likely to be classes as episodic. PCBs with chlorine bonding in the 2,3,4, 2,4,5, 3,4,5 and 2,3,4,5 positions are often more resistant to biotransformation and are therefore likely to be classified as steady state congeners (Megson et al., 2013). An example of the former more easily biotransformed congener is PCB 52 and an example of the latter more resistant congener to biotransformation is PCB-153.

The apparent elimination half-life of PFHxS (8.5 years), which as discussed above, may fairly well be in agreement with an intrinsic elimination half-life, is not much shorter than the intrinsic elimination half-lives of some of the most bioaccumulating PCB-congeners in humans which have intrinsic human elimination half-lives in the range 9 to 15 years. It should be noted that depending on the studied human population, elimination half-lives exceeding 15 years have been estimated for PFHxS ((Zhang et al., 2013)).

Tonnelier and co-workers (2012) studied the human bioaccumulative potential of chemicals and proposed the best predictors to be metabolic clearance, plasma protein binding and renal excretion. According to their analysis the chemical with the highest potential for human bioaccumulation among these 94 chemicals was PFOS, with an estimated hBCF- of 926 (note: PFHxS was not included among the chemicals analysed). The well-known bioaccumulative compound PCB153 ended up as number 6 during this ranking with an hBCF of 44.

The performed benchmarking shows that PFHxS has an elimination half-life comparable to known bioaccumulative PBT/vPvB and POP-substances.

4.1.6 Conclusion on toxicokinetics and bioaccumulation in humans

It can be assumed that PFHxS is well absorbed after oral and inhalation exposure, and to a lesser extent after dermal exposure. PFHxS is present in human blood of the general population and elevated concentrations are seen following specific exposure to PFHxS, either environmentally (e.g. contaminated drinking water) or occupationally. PFHxS is based on read-across to PFOS (Annex I) not expected to be metabolised. The highest concentration of PFHxS are found in blood, liver, kidney and lung. Urine is the primary route of excretion. Humans have a very slow elimination compared with other species, with an elimination half-life of 7 years or above. The human elimination half-life of PFHxS is the longest of all PFAS and PFCAs for which there are available data, and comparable to the longest human elimination half-lives recorded for known PBT/vPvB and POP-substances such as PCBs. PFHxS has been shown to be transferred to the foetus through the placenta in humans and excreted via lactation. Transfer to breast milk appears to be a significant route of elimination during breastfeeding. Time trend studies indicate that the human bioaccumulation potential of PFHxS may be larger than that of PFOS.

5. Environmental hazard assessment

Not relevant for the identification of the substance as SVHC in accordance with REACH Article 57 (e), in this case.

6. Conclusions on the SVHC Properties

6.1 CMR assessment

Not relevant for the identification of the substance as SVHC in accordance with Article 57 points (e) 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 vPvB. All available relevant information (such as the results of standard tests, monitoring and modelling, information from the application of read-across and (Q)SAR results) was considered together in a weight-of-evidence approach.

6.2.1.1 Persistence

PFHxS has a stable perfluorinated structure and is not expected to undergo abiotic degradation under relevant environmental conditions. An available phototransformation study in water (Taniyasu et al., 2013), which found negligible degradation via photolysis, supports this understanding. There is no study available on biodegradation, so data from structurally similar compounds are therefore used in a read-across approach (see Annex I). A read-across with PFOS is applied for biodegradation screening test and a read-across with PFOS and PFOA is applied for the simulation tests (in water, sediment and soil).

The persistence of PFASs and PFCAs can, in general, be explained by the shielding effect of the fluorine atoms, blocking e.g. nucleophilic attacks on 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 sulphonic group in PFSA's alters the persistence of these chemicals. The persistence of PFOS (UNEP, 2006) and the eight entries of PFCAs included into the Candidate List (ECHA, 2012a-d, 2013a-b, 2015b, 2016b) has already been confirmed.

Therefore, based on the knowledge of the stability of the C-F bond and the read-across approach with PFOS and PFOA, it is concluded that PFHxS 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.

6.2.1.2 Bioaccumulation

The reported BCFs and BAFs for PFHxS are below the numerical criteria 2000/5000 in REACH Annex XIII, but it is worth noting that one of the BAF values (European chub, BAF plasma) is close to the threshold of 2000 (log BAF of 3.3 equivalent to a BAF of 1995). The latter value suggests that the substance is a borderline B for some aquatic species. In addition, due to the surface active properties of the substance the appropriateness of the available BCF test and the usefulness of its result may be questioned. Further, PFHxS is expected to quickly be excreted in fish via gill permeation like the other PFSA's and PFCAs, due to its expected notable water solubility. PFHxS, like other PFSA's and PFCAs, do not follow the behaviour of traditional hydrophobic compounds with partitioning into fatty tissues, but instead bind to proteins in blood and liver. Hence, bioconcentration in gill breathing organisms and the accumulation in lipids is not the most relevant endpoint to consider for these types of substances. Field studies show that air-breathing organisms are more likely to bioaccumulate PFHxS and other PFAS compared to water breathing organisms. Therefore, the numerical bioaccumulation (B)/(vB) criteria defined for aquatic species in the REACH regulation Annex XIII (sections 1.1.2 and 1.2.2) are not suitable to assess the bioaccumulation potential of PFHxS.

REACH Annex XIII (section 3.2.2) defines information which shall be taken into account in the B assessment and can and should be used to draw conclusions in a weight-of-evidence approach. In addition to BCF-data, such data are based on Section 3.2.2(b) of Annex XIII to REACH, for example, data on the bioaccumulation potential in terrestrial species, such as elevated levels in endangered species. PFHxS was found in terrestrial species as well as in endangered species as shown in section 3 for the polar bear. The highest concentrations of PFHxS detected in wildlife have been observed in the arctic top predator polar bear (>500 µg/kg in polar bear liver). This finding and the high concentrations of PFHxS found in humans exposed to contaminated drinking water (up to 1790 µg/L in blood serum) show that exposure to PFHxS has the potential to result in high concentrations in biota including humans. These findings indicate a bioaccumulation potential and are of high concern.

Furthermore, Annex XIII (section 3.2.2 (b)) requires to consider data from human body fluids or tissues and to take the toxicokinetic behaviour of the substance into account. Both gestational and lactational exposure in humans have been shown for PFHxS. On top of that, data from human body fluids clearly provide quantitative proof of the bioaccumulation of PFHxS: Elimination half-lives in humans range from 7-8 years and above. Data from time trend studies on human samples indicate that the bioaccumulation of PFHxS even exceeds that of PFOS.

Finally, Annex XIII (section 3.2.2 (c)) foresees that the potential for biomagnification in food chains of a substance is assessed, as part of a weight-of-evidence approach. It is not possible to draw a conclusion on trophic magnification for PFHxS due to limited reliability of the available data. However, the available field data provide biomagnification factors (BMFs) for several predator/prey relationships for PFHxS. In air breathing predators the resulting BMFs are larger than 1, especially for polar bears suggesting a potential of biomagnification that is supported by monitoring data.

The elimination half-life of PFHxS in species are similar to that of PFOS in mice, male rats, pigs, monkeys and humans. The elimination half-lives observed for PFHxS in pigs, monkeys and

humans are the longest observed for any PFAS, followed by those for PFOS. The main reason why e.g. PFOA was considered to meet the B-criterion of REACH was that it was concluded to bioaccumulate in humans based e.g. on its presence in human blood of the general population, the long elimination half-life in human blood of 2-4 years and that the levels increase with age (ECHA, 2013b). This holds true also for PFHxS but it has an elimination half-life in human blood of ca 7-8 years (or longer), which is at least 2-4 times longer than the elimination half-life of PFOA.

Depending on the type of substance, the process driving the bioaccumulation will differ, from hydrophobic partitioning to species and gender specific ADME-properties. Elimination half-lives are recognised as relevant bioaccumulation metrics ((Gottardo, Hartmann, & Sokull-Kluttgen, 2014), (ECHA, 2013b)) and PFHxS has in comparison with PBT/vPvB and POP-substances among the longest human elimination half-lives reported.

The information summarised above is in high accordance with the bioaccumulation data on PFOS, the bioaccumulation potential of which corresponds to "vB" as it is included under the Stockholm Convention. A read-across to PFOS (Annex I) is performed as part of the weight-of-evidence.

Conclusion:

1. PFHxS accumulates in humans
 - a. PFHxS is present in human blood of the general population
 - b. Time trend studies indicate that the human bioaccumulation potential of PFHxS may even be larger than that of PFOS.
 - c. The human elimination half-life for PFHxS is > 7 years which is the longest of all perfluoroalkyl and polyfluoroalkyl substances (PFAS) for which data are available. It is also comparable to the longest human elimination half-lives recorded for known PBT/vPvB- and POP-substances such as some PCBs.
2. There is evidence that PFHxS preferentially bioaccumulates in air-breathing mammals, including endangered species and humans
 - a. BMFs (polar bear/seal liver) range from 20 to 373
 - b. It accumulates in the air-breathing food chains at least as much as PFOS and more than the long-chained PFCAs which have already been identified as vB on the Candidate List.
 - c. It is not possible to conclude on TMF on aquatic foodweb containing air-breathing mammals due to the limited reliability of the available data
 - d. Elevated levels of PFHxS have been measured in both humans (up to 1790 µg/L in blood serum) and wildlife (>500 µg/kg in polar bear liver) showing that exposure to PFHxS has the potential to result in high levels in biota.
3. Even if PFHxS appear to be a borderline "B" in some water breathing animals, bioaccumulation potential of PFHxS in water breathing animals is not expected to be very high since PFHxS can be quickly excreted in fish via gill permeation like the other PFASs and PFCAs, due to its notable water solubility (2.3 g/L).
 - a. BCF range from 9.6 (whole body) to 100 (liver)
 - b. Whole body BAFs range from 380 (fish, crab) to 1995 (fish)
 - c. Whole body BMFs range from 0.14 (fish, lab data) to 10 (fish, field data).
 - d. It is not possible to conclude on TMF on water breathing aquatic foodwebs due to the limited reliability of the available data

To conclude, taking all available information together in a weight-of-evidence approach, and particularly considering the very long human elimination half-life and the indication of field bioaccumulation which may be even higher than for PFOS and the long-chained PFCAs which have already been identified as vB, it is proposed that PFHxS fulfils the vB criterion of REACH Annex XIII.

6.2.1.3 Toxicity

PFHxS has in studies on mice been shown to affect the behaviour, and levels of brain neuroproteins, after oral exposure at a critical period in brain development; similar findings have been seen for PFOS and PFOA ((Lee & Viberg, 2013), (Viberg, Lee, & Eriksson, 2013)).

In a modified OECD 422 guideline-based test, rats were treated by gavage with potassium PFHxS (control, 0.3, 1, 3, and 10 mg/kg body weight and day) 14 days prior to cohabitation, during cohabitation and until day of sacrifice (21 days of lactation). Males were treated for a minimum of 42 days. No reproductive or developmental effects were observed. There were no treatment-related effects in dams or offspring. PFHxS-induced effects noted in parental males included reductions in serum total cholesterol and prothrombin time, and, at 3 and 10 mg/kg, increased liver-to-body weight and liver-to-brain weight ratios, centrilobular hepatocellular hypertrophy, hyperplasia of thyroid follicular cells and decreased haematocrit (Butenhoff, Chang, Ehresman, & York, 2009).

Although PFHxS can induce toxic effects, it is concluded that the toxicity data available are not sufficient for classification for reprotoxicity or for specific target organ toxicity after repeated exposure in category 1 (STOT RE1).

6.2.2 Summary and overall conclusions on the PBT and vPvB properties

In conclusion, PFHxS is identified as a vPvB substance according to Art. 57(e) of REACH by comparing all relevant and available information listed in Annex XIII of REACH with the criteria set out in the same Annex, in a weight-of-evidence determination.

	Annex XIII	PFHxS	Conclusion
p/vP	<p>P</p> <p>Half-life:</p> <p>a) in marine water > 60 days, or</p> <p>b) in fresh- or estuarine water > 40 days, or</p> <p>c) in marine sediment > 180 days, or</p> <p>d) in fresh- or estuarine sediment > 120 days, or</p> <p>e) in soil > 120 days</p> <p>vP</p> <p>Half-life:</p> <p>a) in marine, fresh- or estuarine water > 60 days, or</p> <p>b) in marine, fresh- or estuarine</p>	<p>One abiotic degradation study available, which indicate that PFHxS is negligibly degraded via hydrolysis.</p> <p>Since no simulation test results (in water, sediment or soil) are available for PFHxS a read-across with PFOS and PFOA is applied.</p> <p>PFOS is extremely persistent and listed under the Stockholm Convention and the persistence (vP) of PFOA, PFNA, PFDA and C11-C14 PFCA was confirmed by the Member State Committee.</p> <p>In addition, the high stability of the C-F bond strengthens the arguments on PFHxS persistency.</p> <p>PFHxS belongs to the group of PFSA in which PFOS is the most well-known and studied substance.</p>	p/vP

	water sediment > 180 days, or c) in soil > 180 days		
B/vB	<p>(a)</p> <p>B</p> <p>BCF in aquatic species > 2000</p> <p>vB</p> <p>BCF in aquatic species > 5000</p> <p>(b) Other information on the bioaccumulation potential provided that its suitability and reliability can be reasonably demonstrated, such as:</p> <ul style="list-style-type: none"> • 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; <p>(c) Information on the ability of the substance to biomagnify in the food chain, where possible expressed by biomagnification factors or trophic magnification factors.</p>	<ul style="list-style-type: none"> • BCF range from 9.6 (whole body) to 100 (liver). • Whole body BAF values for gill breathing organisms range from 380 to 1900. • Whole body BMF values for gill breathing organisms range from 0.14 to 10 • BMFs (liver) in air breathing animals range from 20 to 373. • It is, based on available data, not possible to conclude on TMF for gill breathing organisms or air breathing animals. • PFHxS has been detected in a number of wildlife species, including Arctic species. The highest concentrations in mammals have been found in polar bear livers (>500 µg/kg ww). • PFHxS is transferred from polar bear mothers to their cubs. • PFHxS is present in blood of the general population, with the highest concentrations detected in people consuming PFHxS contaminated drinking water. • PFHxS has been shown to be transferred to the foetus through the placenta in humans and excreted via lactation. Transfer to breast milk appears to be a significant route of elimination of PFAS during breastfeeding. • PFHxS has the longest elimination half-life among studied PFAS in pigs, monkeys and humans. • The human elimination half-life is over 7 years. It is the longest human elimination half-life for all studied PFAS and comparable to the longest human elimination half-lives recorded for known PBT/vPvB- and POP-substances such as PCBs. 	B/vB
T	<p>a) NOEC < 0.01 mg/L, or</p> <p>b) meets the criteria for classification as carcinogenic (cat. 1A or 1B), germ cell mutagenic</p>	<ul style="list-style-type: none"> • Although PFHxS can induce toxic effects, it is concluded that the toxicity data available are not sufficient for classification for reprotoxicity or for specific target 	Not possible to conclude

	<p>(cat. 1A or 1B), or toxic for reproduction (cat. 1A, 1B, 2), or</p> <p>c) meets the criteria for classification as STOT RE (cat. 1 or+ 2).</p>	<p>organ toxicity after repeated exposure in category 1 (STOT RE1).</p> <ul style="list-style-type: none"> No ecotoxicity test available 	
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Part II

7. Registration and C&L notification status

7.1 Registration status

There is yet no registration dossier for PFHxS. PFHxS and potassium perfluorohexane-1-sulfonate were planned for registration on November 30th, 2010. Ammonium perfluorohexane-1-sulfonate was pre-registered with envisaged registration deadline on May 31st, 2013.

One additional pre-registrations which include perfluorohexane-1-sulfonate in the ECHA database is tridecafluorohexanesulphonic acid, compound with 2,2'-iminodiethanol (1:1) (CAS 70225-16-0; registration deadline 2013-05-31).

7.2 CLP notification status

Table 12: CLP notifications (EC No 206-587-1)

	CLP Notifications ²
Number of aggregated notifications	0
Total number of notifiers	0

8. Total tonnage of the substance

No data available since there is no registration dossier for PFHxS.

9. Information on uses of the substance

9.1 Overview of uses

The PFHxS potassium salt is marketed by at least one European company (in Italy). Furthermore, PFHxS is a known impurity in the production of PFOS. PFHxS or its related substances could also be used as a replacement for PFOS.

At present there is no available data on the production and use of PFHxS globally or in the EU. In the absence of information on use of PFHxS, the present PFOS use in EU, presented in Table 13, could give an indication that a fraction of this might be PFHxS (due to impurity).

Table 13. Best estimate of PFOS used by industry sector in the EU 2010 ((ESWI, 2011))

Industry	PFOS consumption, kg/y
Metal plating industry	6 500

² C&L Inventory database, <http://echa.europa.eu/web/quest/information-on-chemicals/cl-inventory-database> (accessed 2016-11-18)

Photographic industry	562
Semiconductor industry	9.3
Hydraulic fluids in aviation industry	730

PFASs (per- and polyfluorinated alkyl substances) in general are used due to their desirable properties in different applications, often in low concentrations. They are repellent to water, grease and dirt, temperature resistant and film-forming. PFASs are or have been used on the EU market in the following applications ((Posner, 2013), Swedish CA ((KemI, 2015b))):

- Carpets, leather and apparel, textiles and upholstery
- Paper and packaging
- Household products (such as cookware, floor polish and water repellent sprays for apparel and footwear)
- Fire-fighting foams
- Metal plating (hard metal plating and decorative plating)
- Aviation hydraulic fluids
- Electronic equipment and components
- Medical and healthcare products
- Chemically driven oil and mining production
- Construction products
- Pesticides (as active ingredients and additives)

Also, in a report from a government assignment ((KemI, 2015b)) the Swedish CA shows that PFASs can be used in less investigated areas, such as cosmetics, dental restorative materials and dirt-repellent coating for smartphones.

In Posner et al. (2013) relevant PFASs on the Nordic market are identified and the occurrence in industrial and consumer products and potential releases to humans and the environment are described. However, due to trade secrets and lack of substance identification little information is presented on which specific PFASs are used. This problem is confirmed by the Swedish CA in KEMI ((KemI, 2015b)). The information on the active ingredients in e.g. fire-fighting foams, such as fluorinated substances is often regarded as confidential. Due to significant lack of available information the Swedish CA report could not give a complete picture. The sources used in the report could only give information of uses for about half of the identified substances. This is not surprising, since many PFASs are entering the EU and Sweden through import of articles, and for those there are virtually no control. Another reason for the lack of information is that many PFASs are very effective and therefore used in low concentrations to achieve the desired effect. Within REACH there are today register requirements for the manufacturers or importers of substances from 100 tonne/year. At low volumes, which can be the case for most PFASs (such as PFHxS and PFHxS-related substances) information requirements are very low. For quantities below 100 tonne/year (1 tonne/year from June 2018) manufacturers and importers are not required to submit any information at all.

Furthermore, since most PFAS containing articles are manufactured outside EU it is not possible to get hold of sufficient information about specific PFASs (such as PFHxS and PFHxS-related substances) in imported articles.

The Danish Products Register suggests that <0.1 tonne/year of PFHxS is used in Denmark.³ There is no information about specific product categories that use PFHxS. There is no information about PFHxS in the Swedish Products Register. However, the manufacturers or importers are not obligated to report if they use PFHxS (since it is not classified).⁴ Therefore this lack of information does not mean there is no use.

³ Data from 2007.

⁴ For substances lacking harmonised classification concentrations over 5% must be reported.

9.1.1 AFFF

PFASs are used in fire-fighting foams (AFFF, AR-AFF, FFFP and AR-FFFP⁵). Fire-fighting foam is one acceptable purpose for PFOS according to the Stockholm Convention. However, since June 2011 this use is banned in the EU.⁶

AFFFs are branded mixtures used to terminate hydrocarbon fuel fires. They are often found where there are large volumes of flammable liquids and the potential for a fire exists (e.g. airports, fire departments and oil refineries). They are complex mixtures of surfactants and other components, containing many different PFASs and have been available for fire-fighting applications since the 1960s when developed by 3M Company and the US Navy ((C.A. Moody & Field, 1999)).

At the request of the Swedish CA and the Swedish Civil Contingencies Agency, Örebro University performed chemical analysis of selected fire-fighting foams on the Swedish market in 2014 ((KemI, 2015a)). The aim was to identify the presence of PFASs including precursor compounds. Both target analysis of known PFASs and non-target analysis were included to elucidate the main components and if they contain organofluorine or not. The results demonstrate that one product⁷ contained PFHxS (in low concentrations, 52 µg/kg whereas no PFOS could be detected).

9.1.2 Other uses

Studies that have investigated the PFHxS content (amongst other PFASs) in different consumer products and articles are described in short below and the results are presented in Table 14. However, it is possible that the items could contain PFHxS-related substances not analysed in the studies described below. This is a general concern, target analysis of known PFASs is likely to exclude precursors.

In 2009 SFT (The Norwegian Pollution Control Authority) and NILU (Norway) screened possible PFAS sources in Norway⁸ in household uses and industrial manufacturing ((Herzke, Olsson, & Posner, 2012)). 30 products within the following project groups were included in the study: waterproofing agents and lubricants (n=5); paints and inks (n=3); impregnated products (paper, textiles, leather and carpets, n=8); non-stick ware (n=6); electronics (n=3) and fire-fighting agents (n=5). Some of the products were labelled as containing PFASs, however in more general terms (wording such as "Teflon treated" and "fluorochemical agent"). PFHxS together with PFOS and PFBA belonged to the most discovered ionic PFASs in the 30 analysed products. Over 30% of the products contained PFHxS. Noteworthy is that PFOS, which has been restricted for several years were found in close to 50% of the tested products. None of the tested waterproofing agents contained PFHxS. PFHxS was detected in two of the analysed wet room selling paints, four non-stick products, one carpet (probably due to Teflon treatment), a pair of leather shoes and an electronic toy from Disney.

Beesoon et al. ((Beesoon et al., 2012)) demonstrated that carpets treated with Scotchguard™ had PFHxS levels of 30 µg/g dw. Today Scotchguard™ is based on C4 chemistry (e.g. PFBS). If other similar products have not replaced PFHxS, treated textiles on the market could contain high levels of PFHxS. Norin and Schulze ((2007)) investigated the PFAS content in impregnation products for textiles (weather clothing and shoes). There was limited information about content of fluorinated substances on the products or in the safety data sheets received from the distributors. 46% (6 of 13 tested products) contained PFHxS as well as PFOS.

In different studies Greenpeace has analysed perfluorinated substances in different types of

⁵ Aqueous Film-Forming Foam (AFFF), Alcohol Resistant Aqueous Film-Forming Foam (AR-AFFF), Film-Forming Fluoroprotein (FFFP), Alcohol Resistant Film-Forming Fluoroprotein (AR-FFFP)

⁶ The Stockholm Convention is implemented in the EU through the Regulation (EC) No 850/2004 on persistent organic pollutants (POPs). Fire-fighting foams that were placed on the market before 27 December 2006 could be used until 27 June 2011.

⁷ Originating from a sealed container.

⁸ Products from both Norway and Sweden were included in the study.

clothing articles. In Greenpeace ((Greenpeace, 2014b)) the presence of PFASs were analysed in 15 clothing articles for children.⁹ Among the waterproof clothes PFHxS was the predominant PFAS for two coats (with PFHxS making up 60-100% of the total PFASs) and for a pair of trousers (above 80%). 13 outdoor clothes were tested in 2012 in which PFHxS could not be detected over the detection limit ((Greenpeace, 2012)). Also, no PFHxS was detected over the detection limit neither in a study of 27 items of high fashion clothes nor in a study of 33 different football articles ((Greenpeace, 2014a) and (Greenpeace, 2014c)).

In a report from SFT ((The Norwegian Pollution Control Authority, 2006)) analysis results from different textiles are presented. PFHxS was found in close to 30% of the tested items.

Packaging materials that are in contact with food may add to the human exposure of PFHxS. In a Danish study PFHxS was detected in one popcorn bag, however at a low level ((Posner, 2013)).

A recent study from NORAP ((Nordic Risk Assessment Group, 2014)) analysed 29 different consumer products and articles such as kitchenware (baking paper, cake and cupcake pans), impregnated textiles and dental floss, but did not detect any PFHxS.

Table 14. PFHxS detected in consumer products and articles

Study	Product category	Product name	Unit	PFHxS	PFOS
Herzke et al. (2012)	Paints	Jotun wetroom filler	µg/kg	0.53	5.8
Herzke et al. (2012)	Paints	PCI Lastogum	µg/kg	0.31	4.76
Herzke et al. (2012)	Non-stick ware	Privilege pan	µg/kg	0.8	24.9
Herzke et al. (2012)	Non-stick ware	Rast camping pan	µg/kg	14.1	213
Herzke et al. (2012)	Non-stick ware	IKEA pan. 28 cm. Kavalkad	µg/kg	1.86	14.2
Herzke et al. (2012)	Non-stick ware	Eva cake form	µg/kg	11.9	415
Herzke et al. (2012)	Textiles, leather, carpets	Black shoe. leather	µg/m ²	4.81	21.2
Study	Product category	Product name	Unit	PFHxS	PFOS
Herzke et al. (2012)	Textiles, leather, carpets	Carpet brown; Element	µg/m ²	0.08	1.04
Herzke et al. (2012)	Electronics and electrics	PCB. Disney electronic toy	µg/kg	0.06	0.4
Norin and Schulze (2007)	Water proofing agents	Boston Raingard allover	ng/mL	3.5	8.6
Norin and Schulze (2007)	Water proofing agents	Kiwi select all protector	ng/mL	3.6	8.9
Norin and Schulze (2007)	Water proofing agents	Imprenex plus	ng/mL	4.2	77.1
Norin and Schulze (2007)	Water proofing agents	Springyard Waterproofofer	ng/mL	2.5	19.9
Norin and Schulze (2007)	Water proofing agents	XT	ng/mL	4.6	13.1
Norin and Schulze (2007)	Water proofing agents	Atsko Waterguard	ng/mL	0.9	4.2
The Norwegian Pollution Control Authority (2006)	Textile	Children ski pants	µg/m ²	0.04	0.02
The Norwegian Pollution Control Authority (2006)	Textile	Women all weather jacket	µg/m ²	0.38	30.1
The Norwegian Pollution Control Authority (2006)	Textile	Jacket	µg/m ²	0.02	0.24
(Greenpeace, 2014b)	Textile	Coat	µg/kg	20-300	<0.5-4.5
(Greenpeace, 2014b)	Textile	Coat	µg/kg	2.4	<1.5
(Greenpeace, 2014b)	Textile	Plastic pants	µg/kg	21-2260	<5

⁹ Consisting of seven waterproof clothing articles.

9.2 Additional information

An overview of exposure is given below. It has only been possible to relate exposure to one specific PFHxS application (use of fire-fighting foams, AFFF). However, other sources have the potential to contribute to the exposure if they contain PFHxS or PFHxS-related substances.

9.2.1 Overview of exposure

High levels of PFASs have recently been found in the groundwater in a number of municipalities in Sweden. In some cases the levels were so high that specific wells and even waterworks needed to be taken out of service. The substances that were detected at the highest levels were PFOS and PFHxS. Since the contamination in Sweden in many cases is in the vicinity of fire training sites, film-forming fire-fighting foams (AFFFs) is a suspected source, but since PFASs such as PFHxS can be used in many different applications, other sources cannot completely be excluded. It is probable that the main source of PFHxS in products such as AFFF and in the environment is due to its presence as an impurity in the PFOS production. PFOS is today regulated through the Stockholm Convention (however with exempted use areas and hence still a potential source of PFHxS). Except for AFFF there is little/no information on release and exposure from specific uses (the data available for AFFF is presented in 9.2.3). Release of PFHxS from different uses to the environment via waste water treatment plants is likely. Another potential exposure route is release from landfill that contains impregnated products. Therefore it could be appropriate that impregnated articles are incinerated at high temperatures (>1100°C according to BAT for PFOS, UNEP (2012)).

A recent screening of PFHxS and other PFASs in Swedish surface waters at 44 sites (representing 41 rivers and streams) reveals that these substances are present along the whole Swedish coastline (Ahrens et al. 2013). 13 different PFASs were detected and the highest average values found were for PFHxS and PFBS, approximately 2 ng/L for each substance¹⁰. PFOS concentrations exceeded the EQS of 0.65 ng/L (set out in the WFD) at 12 of the 44 tested sites. Four of the five tested sites with the highest PFAS levels demonstrated a similar PFAS composition (even though they were taken at sites located at completely different regions). This could indicate a common type of source. The total PFAS input from the 41 rivers to the recipient seas was estimated to around 3.2 kg/day (1 150 kg/year).

Members of the Swedish Waste Water Association, SWWA, have screened raw water or drinking water for PFASs, including PFHxS (Holmström et al. 2014). The test results were collected, evaluated and published by SWWA. PFASs were detected in 52 of 236 samples (22 %). PFASs were more abundant in water taken from surface water sources, than in ground water sources. PFOS was the most common PFAS, followed by PFOA. PFHxS, as well as other perfluorinated substances, was also detected. The water suppliers with samples that exceeded 90 ng PFAS/L, a recommended threshold set by the Swedish National Food Agency¹¹, were requested to proceed with further analysis. This study was a one time sampling campaign but results give a quick overview of the drinking water condition in Sweden when it comes to the occurrence of different PFASs.

¹⁰ This was a "one time grab sampling campaign" and the results should therefore be interpreted with caution. However, a study like this has the potential to reveal hot spots.

¹¹ The sum of 7 PFASs (PFOS, PFHxS, PFBS, PFOA, PFHpA, PFHxA, PFPeA) should not exceed 90 ng/L. which is based on TDI for PFOS.

9.2.3 Exposure from fire-fighting foams

Fire-fighting foams (AFFFs) based on PFASs have been identified as a reason for highly contaminated ground water locally in Sweden. The ones detected at particularly high levels have been PFOS and PFHxS, but also PFBS and PFOA.

Since AFFFs are (for most part) released in liquid form, this increases the possibility for the perfluorinated substances to enter the water environment (Filipovic et al., 2015). Quite a few studies have pointed out use of AFFF as a probable source of PFAS to the groundwater (Moody and Field 1999; (C. A. Moody, Hebert, Strauss, & Field, 2003); (Schultz, Barofsky, & Field, 2004); (Houtz, Higgins, Field, & Sedlak, 2013), surface water (de Solla, De Silva, & Letcher, 2012); (L. Ahrens, Norstrom, Viktor, Cousins, & Josefsson, 2015)), drinking water ((Weiss et al., 2012), and biota ((Oakes et al., 2010); (Gewurtz et al., 2014))).

One difficulty in following the exposure by environmental monitoring is that the stable degradation products of PFASs are found in the environment, not the actual produced substances originally included in the product. It is very difficult to find out which specific PFASs have converted to those which environment and humans are exposed to.

Contamination in Sweden has at this stage been identified at all big commercial airports in the three main cities (Stockholm, Malmö and Gothenburg), several military airports (Uppsala, Stockholm, Kallinge) and training sites for fire departments. These locations have been subjected to repeated exposure to PFASs in fire-fighting foams.

The concentrations in ground water of PFOS, PFHxS and PFBS vary with distance from the source and over time, probably depending on the degree of water solubility of the substances. PFOS has been found at concentrations up to 140 µg/L ground water below two military airports, but further away the ratio PFOS/PFHxS changes so that further away PFHxS may be more abundant than PFOS.

In nearby cities, using ground water as drinking water, the drinking water may get contaminated.

Starting February 2014 the Swedish National Food Agency conducted a survey of the drinking water in Sweden. The reason for the study was primarily the identified contamination of PFASs due to use of AFFFs. The aim of the survey was to make the water producers aware of the problem, initiate action at the local level to protect consumers and to gain knowledge about the extent of the problem at the national level. The results (Swedish National Food Agency 2014) indicate that just over one-third, or 3.6 million of the population, gets their drinking water from a water source that is affected by perfluorinated substances. The source of the contamination is probably AFFFs even though there are other potential sources.

In Table 15 measured concentrations in different mediums are presented. The PFHxS levels might be compared to the Environmental Quality Standard (EQS) for PFOS in surface water of 0.65 ng/L in the Water Framework Directive (WFD).

Table 15. Concentrations in the vicinity of fire training sites (EQS for PFOS is 0.65 ng/L surface water)

Sample	Medium	Unit	PFHxS	PFOS
Tullinge, Stockholm (Filipovic et al. 2014)				
Average (n=14)	Surface water	ng/L	8.5	13.4
Median (n=14)	Surface water	ng/L	8.2	7.4
Min (n=14)	Surface water	ng/L	<LOD	<LOD
Max (n=14)	Surface water	ng/L	25.1	45.1
Average (n=16)	Ground Water	ng/L	582.8	3792.8
Median (n=16)	Ground Water	ng/L	134.5	72.5
Min (n=16)	Ground Water	ng/L	<LOD	<LOD
Max (n=16)	Ground Water	ng/L	3470	42 200
Average (n=10)	Tap water wells	ng/L	2.4	0.6
Median (n=10)	Tap water wells	ng/L	<LOD	<LOD
Min (n=10)	Tap water wells	ng/L	<LOD	<LOD

Max (n=10)	Tap water wells	ng/L	22.2	1.1
Danish EPA (2014)				
B1	Ground Water	ng/L	-	15
B3	Ground Water	ng/L	14-220	17
B5	Ground Water	ng/L	34-55	37-45
B7 ¹²	Ground Water	ng/L	13-14 000	18-62 000
B9	Ground Water	ng/L	100	980
Norwegian Pollution Control Authority (2008)				
Gardermoen airport, Well BV-1	Ground Water	ng/L	2904	6762
Gardermoen airport, Well BV-2	Ground Water	ng/L	705	2394
Gardermoen airport, Well BV-3	Ground Water	ng/L	5952	40116
Gardermoen airport	Soil (Soil depth 1m, Radius from platform 31m)	kg	0.25	9.23
Mongstad	Soil (Soil depth 0.5m, Radius from platform 52m)	kg	1.46	18.12
Solberg Scandinavian AS	Soil (Soil depth 0.3m, Radius from platform 38m)	kg	0.099	0.84
Rygge	Soil (Soil depth 0.5m, Radius from platform 54m)	kg	0.06	0.63
Kallinge (11 years olds¹³), Southern Sweden (Jakobsson et al. 2014)				
Average (n=20)	Serum	ng/mL	265	349
Median (n=20)	Serum	ng/mL	269	352
Min (n=20)	Serum	ng/mL	75	102
Max (n=20)	Serum	ng/mL	480	558
Stockholm Arlanda Airport and Gothenburg Landvetter Airport (Norström et al. 2013)				
Average (n=37)	Surface water	ng/L	67.6	146
Median (n=37)	Surface water	ng/L	38.4	87
Max (n=37)	Surface water	ng/L	358	605
Min (n=37)	Surface water	ng/L	0.1	1
Average (n=44)	Perch, liver	ng/g fw	10.6	3813
Median (n=44)	Perch, liver	ng/g fw	11.5	3910
Max (n=44)	Perch, liver	ng/g fw	11.6	4260
Min (n=44)	Perch, liver	ng/g fw	8.6	3270
Average (n=3)	Perch, gills	ng/g fw	5.7	2097
Median (n=3)	Perch, gills	ng/g fw	4.6	1890
Max (n=3)	Perch, gills	ng/g fw	8.7	2880
Min (n=3)	Perch, gills	ng/g fw	3.9	1520
Average (n=3)	Perch, blood	ng/g fw	26.7	5760
Median (n=3)	Perch, blood	ng/g fw	28.1	6060
Max (n=3)	Perch, blood	ng/g fw	35.4	6370
Min (n=3)	Perch, blood	ng/g fw	16.6	4850
Average (n=3)	Perch, gonads	ng/g fw	6.3	1610
Median (n=3)	Perch, gonads	ng/g fw	3.84	1280
Max (n=3)	Perch, gonads	ng/g fw	12.24	2510
Min (n=3)	Perch, gonads	ng/g fw	2.69	1040
Average (n=16 ¹⁴)	Perch, muscle	ng/g fw	0.3	168
Median (n=16)	Perch, muscle	ng/g fw	0.1	207
Max (n=16)	Perch, muscle	ng/g fw	1.5	279
Min (n=16)	Perch, muscle	ng/g fw	0	21

10. Information on structure of the supply chain

No available data.

¹² An independent investigation conducted separately from the project. At this site remediation is taking place.

¹³ Following-up studies in Kallinge in June 2014 also included adults. The analysis results show that people who have lived in Kallinge for a long period of time demonstrate even higher serum levels of PFHxS. This suggests that the drinking water in the area has been contaminated for decades.

¹⁴ Included individuals are males and females, from 0-9 years old.

11. Additional information

11.1 Substances with similar hazard and use profiles on the Candidate List

Eight entries of long-chain PFCAs have already been included into the Candidate List (listed in Table 3). It can be assumed that PFDA can be replaced by other long-chain PFCAs as many of these substances can be found in similar mixtures/articles.

11.2 Alternatives

Potential alternatives to PFHxS are in this section first presented in general terms. Then alternatives for specific uses are listed in Table 16 (cited information from UNEP ((UNEP, 2013))).

There are three types of commercially available alternatives to PFHxS and other so called “long-chain PFASs”¹⁵ ((OECD, 2013)):

1. substances with shorter per – or polyfluorinated carbon chains;
2. non-fluorine containing substances and;
3. non-chemical techniques.

Amongst *the shorter chained PFASs* the industry has developed a various substances that might replace the use of long-chained PFASs. FluoroCouncil ((2013)) and OECD ((2013)) list the following:

- 6:2 fluorotelomer based chemicals (replaces especially their higher homologues)
- Perfluorobutane sulfonyl fluoride (PBSF)-based derivatives (replaces chemicals based on perfluorooctane sulfonyl fluoride (POSF))
- mono- and polyfluorinated-ether-functionality
- fluorinated oxetanes
- other fluorinated polymers

Non-fluorine containing substances can according to OECD (2013) and FluoroCouncil ((2013)) include:

- propylated naphthalenes or biphenyls (as water repelling agents for marine paints, coatings, rust protection systems, etc.)
- fatty alcohol polyglycol ether sulphate (as wetting and levelling agents)
- sulfosuccinates (for surface coating, varnish and paint)
- hydrocarbon surfactants (for photographic industry)
- naphthalene derivatives
- siloxanes and silicone polymers (for impregnation of textiles, carpets and leather or for surface coating, varnish and paint)
- stearamidomethyl pyridine chlorine (for impregnation of textiles, carpets and leather)

However, the industry points out that even though fluorine free substances are available for some applications they may not work as well as PFASs in all cases. For example when durable water and oil repellence or very low surface tension is needed it is, according to the industry, difficult to replace PFASs with a non-fluorine alternative.

In some situations it is possible to use *techniques based on non-chemicals methods*. For instance when it comes to leaf cutter ant control there are various physical, biological or natural control methods that have been developed. For the metal plating industry e.g. foam blankets can be used for mist suppression. The non-chemicals methods represent only a small percentage of the alternatives.

¹⁵ Perfluoroalkane sulfonic acids (PFASs), e.g. PFOS and PFHxS with perfluorinated carbons ≥ 6 are considered “long-chain PFASs”.

UNEP ((2013)) presents alternatives to PFOS and related chemicals for different applications (Table 16). Since PFHxS is similar (the only difference being the carbon chain length) it is likely that the alternatives to PFOS also can be used instead of PFHxS. In UNEP (2013) more information is available on main chemical alternatives and product trade names.

Table 16. Summary of the information on alternatives to the use of PFOS (table 4 in (UNEP, 2013))

Use	Use status	Alternatives used
Impregnation of textiles, leather and carpets	PFOS-related substances have been phased out in most OECD countries.	Other fluorinated compounds, like C ₆ -fluorotelomers and PFBS, silicone-based products, stearamidomethyl pyridine chloride, perfluorobutane sulfonate for leather. ¹⁶
Impregnation of paper and cardboard	PFOS-related substances have been phased out in most OECD countries.	Fluorotelomer-based substances and phosphates, mechanical processes meaning non-chemical alternatives include extra-dense paper that inhibits leakage of grease through the paper
Cleaning agents, waxes and polishes for cars and floors	PFOS-related substances have been phased out in most OECD countries.	Fluorotelomer-based substances, fluorinated polyethers, C ₄ -perfluorinated compounds. A shift to softer waxes that are more biodegradable or entirely biodegradable may completely eliminate the need for persistent polyfluorinated compounds. In these products, the fluorinated surfactants are replaced with non-ionic or anionic surfactants, which have good wetting properties
Surface coatings, paint and varnish	PFOS-related substances have been phased out in most OECD countries.	Telomer-based compounds, fluorinated polyethers, PFBS, propylated aromatics, silicone surfactants, sulfosuccinates, polypropylene glycol ethers
Oil production and mining	PFOS derivatives may occasionally be used as surfactants in the oil and mining industries.	PFBS, telomer-based fluorosurfactants, perfluoroalkyl-substituted amines, acids, amino acids and thioether acids
Photographic industry	A shift to digital techniques has reduced the use drastically.	Telomer-based surfactant products, hydrocarbon surfactants, silicone products, ¹⁷ C ₃ -C ₄ -fluorinated chemicals. Non-chemical alternatives to PFOS include shifting to digital photography
Electrical and electronic parts	PFOS-based chemicals are or have been used in the manufacture of digital cameras, mobile phones, printers, scanners, satellite communication, radar systems, etc.	For most of these uses, alternatives are considered as available or are being developed.
Semiconductor industry	PFOS is still used but in lower concentrations.	No substitutes with comparable effectiveness have been identified for critical uses, and doing so may take up to 5 years, according to the industry. It should be possible to use PFBS, fluorinated polyethers or telomers for non critical uses only.
Aviation hydraulic oils	PFOS-related compounds may still be used.	Other fluorinated substances and non-fluorinated phosphate compounds could be used.
Pesticides	Sulfluramid is used in Brazil for control of leaf-cutting ants from the species of <i>Atta spp.</i> and <i>Acromyrmex spp.</i> . Other fluorosurfactants may be used as inert surfactants in other pesticide products.	Although synthetic piperonyl compounds such as S-Methoprene, Pyriproxyfen, Fipronil and Chlorpyrifos are alternative active substances, sometimes used in combination. Alternative surfactants may exist. Non-chemical alternatives include use of <i>Metarrhizium anisopliae</i> , <i>Beauveria bassiana</i> and <i>Aspergillus ochraceus</i> .

¹⁶ Information provided by Argentina in 2011.

¹⁷ There are considerable datagaps of siloxane compounds used on the market for photographic applications, see reference UNEP/POPS/POPRC.8/INF/17/Rev.1.

Use	Use status	Alternatives used
Medical devices	Old video endoscopes at hospitals contain a CCD colour filter that contains a small amount of PFOS. PFOS is also used as a dispersant for contrast agents in radio-opaque catheters.	Repairing such video endoscopes requires a CCD colour filter containing PFOS. New CCD filters are PFOS-free. For radio-opaque ethylene tetrafluoroethylene, PFBS can replace PFOS.
Metal plating	PFOS-compounds are still used in hard chrome plating. Cr-III has replaced Cr-VI in decorative chrome plating.	Some non-fluorinated alternatives are marketed but they are not considered equally effective in hard chrome plating. A C ₆ -fluorotelomer is used as a substitute and may be effective. PFBS derivatives may also be used. Non-chemical alternatives include physical barriers that may also be used
Fire-fighting foams	The use of PFOS-related substances in new products has been phased out in most OECD countries. Stocks are still being used up.	C ₆ - fluorotelomers are used as substitutes in new products; fluorine-free alternatives are used for training exercises and possibly in other settings than offshore.

11.3 Existing EU legislation

Based on current knowledge there are yet no EU legislation that specifically regulates PFHxS.

11.4 Previous assessments by other authorities

Long-chain perfluorinated chemicals including PFHxS have in general been screened in the context of the more detailed assessments of the common perfluorooctyl sulfonate (PFOS) and perfluorooctanoic acid (PFOA).

In the United States - Joint Program between EPA and chemical industry (3M Company- the major manufacturer of PFHxS in the past) resulted in the phase-out of PFHxS and PFOS between 2000 and 2002.

There are no known additional assessments by other authorities on PFHxS specifically.

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Annex I - 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 considered 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 readacross 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.

A read-across approach is taken between PFHxS and PFOS and long-chained PFCAs.

Group definition and its members

It can be based on e.g. the OECD inventory of PFAS ((OECD, 2007)) be assumed that there are several inorganic salts of PFHxS available on the global market. Two of these are found in the ECHA CLP notification database - the ammonium (PFHxS·NH₄) and potassium (PFHxS·K) salts of PFHxS. Inorganic salts of PFHxS can be assumed to be very soluble in water. Both PFHxS·NH₄ and PFHxS·K are very soluble in water and will in aqueous solutions be present as the anion PFHxS⁻ and the ammonium or the potassium cation. The dissolved anion PFHxS⁻ will in aqueous media stay in equilibrium with the corresponding acid (PFHxS).

PFHxS and its salts are monoconstituent substances with various degree of purity.

Read across justification

PFHxS belongs to a group of PFAS of which several similar substances already have been assessed with respect to their POP- or PBT/vPvB-properties. The substances in this group have a highly similar chemical structure with a perfluorinated carbon chain and a terminal acid group, sulphonic acid (PFSA) or carboxylic acid (PFCA). The individual PFSAs or PFCAs differ only in the number of CF₂-groups whereas all other fragments are the same.

The sulfonic acids and sulfonates are analogous to the carboxylic acids and carboxylates with resulting similar properties. However, sulfonic acids are much stronger acids than their corresponding carboxylic acids. This primarily results from the additional oxygen atom in the sulfonic acid which provides both greater negative inductive effect to enhance ionization and additional resonance stabilization of the resulting conjugate base anion (DeRuiter, 2005); the more stable the base, the stronger its conjugate acid.

Common for both the PFSAs and PFCAs is that it can be assumed that with increasing chain length relative water solubility decreases and the sorption potential increases and that it with sufficient reliability can be assumed that the behaviour of the PFSAs and PFCAs in general follows a regular pattern.

The PFSA with C8-fluorinated alkyl chain, PFOS, is a POP included on the UNEP POP-list of chemicals (UNEP, 2006). Both PFHxS and PFOS contain a perfluorinated carbon chain and a sulfonic acid group. The two compounds differ only in the number of carbon atoms within the fluorinated carbon chain, which are six for PFHxS and eight for PFOS.

As mentioned above, the chemical structures of the PFSAs are similar to those of the PFCAs. The eight PFCAs included on the Candidate List ((ECHA, 2012a-d, 2013a-b, 2015b, 2016b)), are therefore also used for read-across.

A read-across approach is thus performed between PFHxS (and its salts) and PFOS and long-chained PFCAs.

Stability

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 envelope 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 the most stable organic compounds. These include polarizability 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.

Dissociation of C6 and C8 PFSAs and C8-14-PFCAs and their salts in aqueous media

Under environmental conditions in aqueous media the free perfluorinated sulphonic (PFSAs) and carboxylic acids (PFCAs) stay in equilibrium with their conjugate bases, the perfluorinated sulfonates or carboxylates. The fraction of each species depends on the acid dissociation constant (pKa) and the pH of the environmental compartment. Salts of PFSAs and PFCAs, which are sometimes used in laboratory experiments, will be in equilibrium with the corresponding acid in aqueous phases as well. Currently used techniques for analysis and quantification of PFSAs and PFCAs in e.g. environmental samples are not able to distinguish between both of 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 persistency, aqueous phase concentrations include both species. Experimental determination of pKa is difficult for PFSAs and PFCAs, because of the surface active properties. Calculated values should be taken with care, because for most of the models it is unclear whether PFSAs and PFCAs are within the applicability domains of the models used. For assessing the intrinsic properties of the PFSAs or PFCAs within this dossier the exact knowledge of the fraction of each species is not required, because both of the species will be available independently from the starting conditions.

However, as the sulfonic acids are stronger acids than the carboxylic acids, the PFSAs will to a larger extent be dissociated as compared to corresponding PFCAs.

Physicochemical properties and partition coefficients of C6 and C8 PFSAs and C8-14-PFCAs and some salts

The experimental determination of partition coefficients is difficult for example because of the surface active properties of the ionic PFSAs and PFCAs. The presence of ionic PFSAs and PFCAs depends on the dissociation of PFSAs and PFCAs in aqueous media. There are models available, i.e. COSMOtherm calculating partitioning coefficients of neutral PFAS. COSMOtherm is a quantum chemistry-based method that requires no specific calibration. This calibration would be difficult because of missing measured data of PFSAs and PFCAs. Therefore COSMOtherm is expected to be able to estimate properties for PFSAs and PFCAs. Studies have shown that properties estimated with COSMOtherm showed good agreement with the experimental data for a number of per- and polyfluorinated chemicals (Arp, Niederer, & Goss, 2006); (Z. Wang et al., 2011)). Again, whether neutral PFSAs and PFCAs are present in aqueous media depends on the dissociation of the acids and Z. Wang et al. (2011) states that for some PFAS, especially the strong acidic PFSAs, the neutral form will at environmentally relevant pH only represent a small fraction of all molecules and is therefore not likely to play a major role in controlling the environmental behaviour. However, it has for the PFCAs been suggested that the neutral form may be relevant in environmental transport and partitioning processes (Webster, Ellis, & Reid,

2010) and in bioaccumulation (Woodcroft et al., 2010).

There is a clear increasing trend in air-water as well as octanol-water partition coefficients with increasing chain length (I. J. Wang et al., 2011).). This can be explained by the increasing molecular volume with each additional CF₂-unit. The trend of the fate of PFASs and PFCAs with chain length is supported by information on sorption of PFASs and PFCAs on sediment. Sorption increases with increasing chain length ((Higgins & Luthy, 2006)) also under environmental conditions ((L. Ahrens et al., 2010))

Concluding remarks

To conclude, data in **Table 17** on PFHxS, PFOS and the PFCAs on the Candidate List are consistent with the hypothesis that the PFASs and PFCAs follow a regular trend which justifies that a read-across approach can be applied between PFHxS, PFASs and PFCAs.

Note: Data on PFCAs in **Table 17** below are from the SVHC-support document on PFNA.

Table 17. Basic substance information and physical chemical properties relevant to justify read across in a PBT/vPvB assessment. Note: Data on PFCAs are from the SVHC-support document on PFNA ((ECHA, 2015)).

	PFSA		PFCAs								
Abbreviation	C ₆ -PFSA	C ₈ -PFSA	C ₈ -PFCAs			C ₉ -PFCAs	C ₁₀ -PFCAs	C ₁₁ -PFCAs	C ₁₂ -PFCAs	C ₁₃ -PFCAs	C ₁₄ -PFCAs
Acronym	PFHxS	PFOS	PFOA	APFO	NaPFO	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
IUPAC Name	1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluorohexane-1-sulfonic acid	1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluorooctane-1-sulfonic acid	Octanoic acid, pentadecafluoro-	Ammonium pentadecafluorooctanoate	Pentadeca octanoic acid sodium salt	Nonanoic acid, heptadecafluoro-	Decanoic acid, nonadecafluoro-	Undecanoic acid, heneicosafuoro-	Dodecanoic acid, tricosafuoro-	Tridecanoic acid, pentacosafuoro-	Tetradecanoic acid, heptacosafuoro-
Chemical Structure	CF ₃ (CF ₂) ₅ -SO ₃ OH	CF ₃ (CF ₂) ₇ -SO ₃ OH	CF ₃ (CF ₂) ₆ -COOH	CF ₃ (CF ₂) ₆ -COO-NH ₄ ⁺	CF ₃ (CF ₂) 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	355-46-4	1763-23-1	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
Physico-chemical data											
Molecular Weight g/mol	400.11	500.13	414.07	431.1		464.08	514.08	564.0909	614.0984	664.1059	714.11
Partitioning Coefficient logK _{ow}	Not applicable (ATSDR, 2009)	Not measurable (UNEP, 2006)				2.3 – 2.48 (exp)	2.65 – 2.87 (exp)	3.19 – 3.41	logP 9.363±0.888 at 25°C (calc)	logP 10.093±0.901 at 25 °C (calc)	logP 10.823±0.914 at 25 °C (calc)
	5.17 (calc., COSMOtherm, (Z. Wang et al., 2011))	6.43 (calc., COSMOtherm, (Z. Wang et al., 2011))	5.30 (calc., COSMOtherm, (Z. Wang et al., 2011))			5.9 (calc., COSMOtherm, (Z. Wang et al., 2011))	6.5 (calc., COSMOtherm, (Z. Wang et al., 2011))	7.2 (calc., COSMOtherm, (Z. Wang et al., 2011))	7.8 (calc., COSMOtherm, (Z. Wang et al., 2011))	8.25 (calc., COSMOtherm, (Z. Wang et al., 2011))	8.90 (calc., COSMOtherm, (Z. Wang et al., 2011))
log K _{OA}	7.55 (calc., COSMOtherm, (Z. Wang et al., 2011))	8.07 (calc., COSMOtherm, (Z. Wang et al., 2011))	7.23 (calc., COSMOtherm, (Z. Wang et al., 2011))			7.50 (calc., COSMOtherm, (Z. Wang et al., 2011))	7.77 (calc., COSMOtherm, (Z. Wang et al., 2011))	8.08 (calc., COSMOtherm, (Z. Wang et al., 2011))	8.36 (calc., COSMOtherm, (Z. Wang et al., 2011))	8.63 (calc., COSMOtherm, (Z. Wang et al., 2011))	8.87 (calc., COSMOtherm, (Z. Wang et al., 2011))
log K _{AW}	-2.38 (calc., COSMOtherm, (Z. Wang et al., 2011))	-1.65 (calc., COSMOtherm, (Z. Wang et al., 2011))	-1.93 (calc., COSMOtherm, (Z. Wang et al., 2011))			-1.58 (calc., COSMOtherm, (Z. Wang et al., 2011))	-1.27 (calc., COSMOtherm, (Z. Wang et al., 2011))	-0.92 (calc., COSMOtherm, (Z. Wang et al., 2011))	-0.58 (calc., COSMOtherm, (Z. Wang et al., 2011))	-0.38 (calc., COSMOtherm, (Z. Wang et al., 2011))	0.03 (calc., COSMOtherm, (Z. Wang et al., 2011))

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Abbreviation	PFSAs		PFCAs								
	C ₆ -PFSA	C ₈ -PFSA	C ₈ -PFCA	APFO	NaPFO	C ₉ -PFCA	C ₁₀ -PFCA	C ₁₁ -PFCA	C ₁₂ -PFCA	C ₁₃ -PFCA	C ₁₄ -PFCA
Acronym	PFHxS	PFOS	PFOA			PFNA	PFDA	PFUnDA	PFDoDA	PFTTrDA	PFTeDA
Dissociation constant pKa	-3.45 (calc., COSMOtherm, (Z. Wang et al., 2011))	-3.41 (calc., COSMOtherm, (Z. Wang et al., 2011))	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., 2005)			<1.6 (Vierke et al., 2013) 0.82 (calc., COSMOtherm, Wang et al., 2011)	<1.6 (Vierke et al., 2013) 2.58 (Moroi et al., 2001)	0.52±0.10; (calculated)	0.52±0.10 (calculated)	0.52±0.10; (calculated)	0.52±0.10; (calculated)
Partition coefficients log Kd (sediment and overlapping dissolved phase)	1.8 ± 0.1 (L. Ahrens et al., 2010)	2.1 ± 0.1 (L. Ahrens et al., 2010)	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)	3.6 ± 0.1 (L. Ahrens et al., 2010)	3.8 ± 0.1 (L. Ahrens et al., 2010) 2.57 ± 0.13 ((Higgins & Luthy, 2006)) 2.5 – 3.1 ((Johnson, R.G., J.M., M.F., & R.L., 2007))	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	2.3 g/L (calc. COSMOtherm) ((Z. Wang et al., 2011))	0.52 g/L (20±0.5 °C) (UNEP, 2006) 0.68 g/L (24-25 °C) (UNEP,	9.5 g/L (25° C) 4.14 g/L (22°C)	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 concentration (Nielsen 2012)			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	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	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	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

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

	PFSAs		PFCAs									
Abbreviation	C ₆ -PFSA	C ₈ -PFSA	C ₈ -PFOA	APFO	NaPFO	C ₉ -PFCA	C ₁₀ -PFCA	C ₁₁ -PFCA	C ₁₂ -PFCA	C ₁₃ -PFCA	C ₁₄ -PFCA	
Acronym	PFHxS	PFOS	PFOA			PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA	
		2006)						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)	0.014 g/L pH 4 at 25°C 0.034 g/L pH 5 at 25°C 0.039 g/L pH 6 at 25°C 0.040 g/L pH 7 at 25°C 0.041 g/L pH 8-10 at 25°C (calculated)	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)	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)	
Vapour pressure		3.31 x 10 ⁻⁴ Pa (UNEP, 2006)	4.2 Pa (25 °C) for PFOA extrapolated from measured data 2.3Pa (20 °C) for PFOA extrapolated 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)				0.6 to 99.97 kPa (112 to 237.7°C) (calculated)	9.40E-3 Torr at 25°C(calculated)	3.59E-3 Torr at 25°C (calculated)	1.37E-3 Torr at 25 °C (calculated)	
Stability												
Phototransformation in water DT50	No photodegradation detected under relevant env. conditions	No evidence of direct or indirect photolysis under any conditions tested and an indirect photolytic half-life at 25°C	No photodegradation detected under relevant env. conditions	No photodegradation detected under relevant env. conditions		No photodegradation tested under relevant env. conditions 100 % after 12 h by use of persulfate	No photodegradation tested under relevant env. Conditions 100 % after 12 h by use of persulfate	No photodegradation tested under relevant env. Conditions 77% after 12 h by use of persulfate				

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	PFSAs		PFCAs								
Abbreviation	C ₆ -PFSA	C ₈ -PFSA	C ₈ -PFOA	APFO	NaPFO	C ₉ -PFCA	C ₁₀ -PFCA	C ₁₁ -PFCA	C ₁₂ -PFCA	C ₁₃ -PFCA	C ₁₄ -PFCA
Acronym	PFHxS	PFOS	PFOA			PFNA	PFDA	PFUnDA	PFDODA	PFTTrDA	PFTeDA
		estimated to exceed 3.7 years (UNEP, 2006)				ion (S2O8 ²⁻) in water	ion (S2O8 ²⁻) in water	ion (S2O8 ²⁻) in water			
Hydrolysis DT50		No hydrolysis (UNEP, 2006)	>97 yr			No hydrolysis tested under relevant env. conditions; 97% (absence of S ₂ O ₈ ²⁻) and 100% (by use of S ₂ O ₈ ²⁻) after 6 h in 80°C water					
Direct photolysis	No significant degradation (Taniyasu et al, 2013)	No evidence of direct or indirect photolysis under any of the conditions tested (UNEP, 2006) 15-29% reduction in conc. (Taniyasu et al, 2013)	negligible-5% reduction in conc. (Taniyasu et al, 2013)	No photodegradation		19-26% reduction in conc. (Taniyasu et al, 2013)	30-35% reduction in conc. (Taniyasu et al, 2013)				
indirect photolysis		No evidence of direct or indirect photolysis under any of the conditions tested		No photodegradation (H ₂ O ₂ ; synthetic humic water, Fe ₂ O ₃) estimated							

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	PFSAs			PFCAs								
Abbreviation	C ₆ -PFSA	C ₈ -PFSA		C ₈ -PFCA			C ₉ -PFCA	C ₁₀ -PFCA	C ₁₁ -PFCA	C ₁₂ -PFCA	C ₁₃ -PFCA	C ₁₄ -PFCA
Acronym	PFHxS	PFOS		PFOA	APFO	NaPFO	PFNA	PFDA	PFUnDA	PFDoDA	PFTTrDA	PFTeDA
		(UNEP, 2006)			half-life > 349 days (Fe ₂ O ₃)							
Ready biodegradability screening test		Not readily biodegradable (UNEP, 2006)		not readily biodegradable (OECD 301 C,F)	not readily biodegradable (OECD 301 B)		not readily biodegradable (OECD 301 F)			not readily biodegradable (OECD 301 C)		not readily biodegradable (OECD 301 C)
Simulation tests		No degradation (UNEP, 2006)		No elimination by metabolic processes, mineralization or adsorption								
Biodegradation in soil, sediment		No degradation (UNEP, 2006)		No degradation detected								

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

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA	PFTeDA			
<i>brevicula</i> , <i>Monodonta labio</i> , <i>Umbonium thomasi</i> , and <i>Glossaulax didyma</i>)												
	West coast of Korea, Yellow Sea	2009	0.45/0.42 (0.16 - 1.1) 11/11	0.36/0.27 (<0.046 - 0.95) 7/11	0.045/0.038 (<0.046 - 0.088) 7/11	0.045/0.027 (<0.046-0.13) 10/11	0.016/0.04 (<0.046-0.029) 5/11	-	-	Arithm. mean/median, (range) amount of sample >LOD n = 11	(Naile et al., 2013)	2
Ice amphipod (<i>Gammarus wilkitzkii</i>)												
-Mass sample	Svalbard, Barents Sea	2004	nd (nd) 0/6	3.85 ± 1.17 (nd - 7.41) 5/6	3.15 ± 0.34 (2.07 - 4.33) 6/6	nd	nd	-	nd	Arithm. mean ± SE, (range), number detected from a total of n = 6	(Haukas et al., 2007)	2
River snail (<i>Viviparus</i>)												
-soft tissues	Lake Tangxun, China	2011	4.14 ± 0.48, 3.99, (3.54-4.89). 6/6	176 ± 23.8, 174, (144-216). 6/6	2.43 ± 0.63, 2.14, (1.97-3.54). 6/6	0.95 ± 0.23, 0.97, (0.61-1.23). 6/6	1.47 ± 0.13, 1.47, (1.33-1.65). 6/6	0/6	-	Arithm. mean ± SD, median, (range), number detected from a total of n = 6 pooled samples. Each pooled sample consists of n = 25.	(Zhou et al., 2014)	2
Shrimp (<i>Macrobrachium nipponense</i>)												
-whole-body	Lake Tangxun, China	2011	12.6 ± 4.99, 11.2, (8.45-	218 ± 62.7, 202, (165-287).	0.34 ± 0.05, 0.37, (0.28-	3.12 ± 0.61, 3.07, (2.54-	5.82 ± 0.94, 5.29, (5.26-	1.44 ± 0.29, 1.56, (1.11-	-	Arithm. mean ± SD, median, (range),	(Zhou et al., 2014)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA	PFTeDA			
			18.1). 3/3	3/3	0.37). 3/3	3.75). 3/3	6.90). 3/3	1.64). 3/3		number detected from a total of n = 3 pooled samples. Each pooled sample consists of n = 6.		
Zooplankton												
-Mass sample	Sarasota Bay, Florida, USA	2004	0.1 ± 0.07	0.2 ± 0.2	0.3 ± 0.5	0.1 ± 0.1	0.1 ± 0.03	-	0.06 ± 0.03	n = 3 Samples from trawling using 100 µm mesh-size net	(Houde et al., 2006)	2
Fish												
Fish (<i>Acanthogobius flavimanus</i> , <i>Sebastes schlegeli</i> , <i>Tridentiger obscurus</i> , <i>Hexagrammos otakii</i> , and <i>Mugil cephalus</i>)												
	West coast of Korea, Yellow Sea	2009	0.28/0.17 (0.020 - 1.2) 15/15	13/9.3 (0.73 - 51) 15/15	0.062/0.021 (<0.044 - 0.23) 5/15	0.043/0.033 (0.014 - 0.10) 15/15	0.032/0.029 (<0.044 - 0.060) 11/15	-	-	Arithm. mean/median, (range) amount of sample >LOD n = 15	(Naile et al., 2013)	2
Atlantic croaker (<i>Micropogonias undulatus</i>)												
-homogenate	Charleston Harbour, South Carolina,	2002/2003	nd	34 ± 9	1.4 ± 1.6	5.6 ± 6.5	1.1 ± 0.9	-	nd	n = 3	(Houde et al., 2006)	2

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTTrDA	PFTeDA			
	USA											
Bighead carp (<i>Hypophthalmichthys nobilis</i>)												
-muscle	Lake Tangxun, China	2011	1.15 ± 1.25, 0.73, (0.19-3.57). 6/8	246 ± 86.6, 214, (170-413). 6/8	0.43 ± 0.35, 0.32, (0.19-1.28). 8/8	2.08 ± 0.96, 1.79, (1.18-3.77). 8/8	3.17 ± 0.94, 5.29, (5.26-6.90). 8/8	0.83 ± 0.33, 0.83, (0.60-1.06). 2/8	-	Arithm. mean ± SD, median, (range), number detected from a total of n = 8	(Zhou et al., 2014)	2
Cod (<i>Gadus morhua</i>)												
-whole blood	Baltic Sea, Gulf of Gdansk, Poland	2003	0.10 ± 0.17 (0.05 - 0.80)	17 ± 12 (6.1 -52)	0.20 ± 0.16 (0.05 - 0.70)	-	-	-	-	Arithm. mean ± SD, (range) n = 18	(Falandysz et al., 2007)	2
Common carp (<i>Cyprinus carpio</i>)												
-muscle	Lake Tangxun, China	2011	31.2 ± 18.8, 26.6, (15.5-74.0). 8/8	777 ± 222, 684, (527-1140). 6/8	1.06 ± 0.67, 0.94, (0.30-2.5). 8/8	1.48 ± 0.53, 1.37, (0.98-2.54). 8/8	1.79 ± 0.74, 1.48, (1.12-3.17). 8/8	0/8	-	Arithm. mean ± SD, median, (range), number detected from a total of n = 8	(Zhou et al., 2014)	2
Flounder												
-liver	Baltic Sea, Estonian coast	2008/2009	0.10	7.1	<1.2	0.46	-	-	-		(Lilja K., 2009)	2
	Baltic Sea, Lithuanian coast		0.40 0.59 1.1 0.26	11 15 20 6.9	<1.8 <2.1 <3.1 <1.9	1.5 1.0 <2.4 <1.2	-	-	-			
	Baltic Sea, Polish coast		0.16 0.45	6.8 48	<1.6 <3.1	<0.9 15	-	-	-			
	Baltic Sea, Swedish coast		0.25	8.9	<1.2	0.88	-	-	-			
Grass carp (<i>Ctenopharyngodon idellawere</i>)												
-muscle	Lake	2011	4.58 ±	390 ±	1.71 ±	1.92 ±	1.56 ±	0.93	-	Arithm.	(Zhou et al.,	2

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA	PFTeDA			
	Tangxun, China		2.16, 3.87, (2.94- 9.45). 8/8	60.1, 374, (312-489). 6/8	0.52, 0.94, (1.12- 2.41). 8/8	0.32, 1.87, (1.49- 2.39). 8/8	0.49, 1.41, (1.07- 2.50). 8/8	1/8		mean ± SD, median, (range), number detected from a total of n = 8	2014)	
Herring												
-liver	Swedish East and West coast	2005/2006	0.22	7.85	0.5	2.59	-	2.16	-	Pooled sample, n = 10/year Max. value	(Bignert et al., 2008)	2
	Swedish East and West coast	2007/2008	2.2	25.6	2.5	4.63	-	5.20	-	Pooled sample, n = 12/year Max. value	(Bignert et al., 2009)	2
	Swedish East and West coast	2009	1.3	18.7	2.0	3.0	-	3.3	-	Pooled sample, n = 10/year Max. value	(Bignert et al., 2011)	2
	Baltic Sea, Estonian coast	2008/2009	<0.1	7.4	<2.6	<1.5	-	-	-		(Lilja K., 2009)	2
	Baltic Sea, Latvian coast		<0.2	4.3	<3.9	<2.6	-	-	-			
	Baltic Sea, Lithuanian coast		0.24	10	<3.3	<2	-	-	-			
	Baltic Sea, Polish coast		<0.2	7.3	<4.1	<3	-	-	-			
	Baltic Sea, Swedish coast		0.39	10	<3.3	<1.5	-	-	-			
			0.25	6.5	<1.5	<0.9	-	-	-			
			0.23	6.1	<1.3	<0.8	-	-	-			
		0.30	11	<2.7	<2	-	-	-				
		0.19	5.5	<1.3	<0.7	-	-	-				
		0.57	12	<2.9	0.94	-	-	-				
Perch												
-liver	Baltic Sea, Estonian coast	2008/2009	<0.1	31	<3.1	3.6	-	-	-		(Lilja K., 2009)	2
	Baltic Sea, Latvian coast		0.18	48	<3.2	3.3	-	-	-			
	Baltic Sea, Polish coast		<0.07	11	<2.3	0.55	-	-	-			
	Baltic Sea, Polish coast		<0.2	24	<1.8	2.1	-	-	-			
	Baltic Sea, Polish coast		0.20	61	<2.4	11	-	-	-			
-muscle	Västra Ingsjön (freshwater lake),	2011-09	<0.03	22	<0.12	-	-	-	-		(Norström K., 2012)	2
			<0.03	45.2	<0.12							
			<0.03	49.6	<0.12							
			0.0548	46.4	<0.25							

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)						Remark	Reference	Reliability	
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA				PFTeDA
	Sweden		0.0496 0.0602 0.13 0.17	37.7 35.2 58.2 78.8	<0.25 <0.25 <0.25 <0.25							
	Lilla Issjön, (freshwater lake), Sweden		-	133	<0.25	-	-	-	-			
	Halmsjön, (freshwater lake), Sweden		0.355 0.305 0.321 0.287 0.196 0.295 0.388	216 240 315 384 259 166 115	<0.12 <0.12 <0.12 <0.12 <0.12 <0.12 <0.12	-	-	-	-			
Pigfish (<i>Orthopristis chrysoptera</i>)												
-homogenate	Sarasota Bay, Florida, USA	2004	4.1 ± 1.8	3.1 ± 2.5	<0.5	<0.8	<0.5	-	Nd	n = 10	(Houde et al. (2006))	2
Pinfish (<i>Lagodon rhomboides</i>)												
-homogenate	Charleston Harbour, South Carolina, USA	2002/ 2003	nd	19 ± 24	<0.5	5.1 ± 8.1	22 ± 24	-	Nd	n = 4	(Houde et al. (2006))	2
-homogenate	Sarasota Bay, Florida, USA	2004	4.6 ± 2.3	4.8 ± 4.5	<0.5	<0.8	<0.5	-	nd	n = 10	(Houde et al. (2006))	2
Polar cod (<i>Boreogadus saida</i>)												
-liver	Svalbard, Barents Sea	2004	0.04 ± 0.003 (nd - 0.07) 9/16	2.02 ± 0.13 (1.07 - 2.85) 16/16	- (nd - 1.88) 3/16	nd	nd	-	nd	Arithm. mean ± SE, (range), number detected from a total of n = 16	(Haukas et al., 2007)	2
Rainbow trout (<i>Oncorhynchus mykiss</i>)												
-muscle	Swedish	1999-	0.013	0.121	0.084	0.024 -	0.015 -	0.032 -	-	Median,	(A Glynn et	2

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Species	Location	Date	Concentration ($\mu\text{g}/\text{kg}$ ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA	PFTeDA			
	Baltic Sea coast, Swedish food production	2010	(<0.011 - 0.040)	(<0.037 - 0.795)	(only 1 >MDL)	0.074 (n = 12 > MDL)	0.088 (n = 5 > MDL)	0.051 (n = 6 > MDL)		(range), total of 36 pooled samples, 3 pooled samples/year	al., 2012)	
Red drum (<i>Sciaenops ocellatus</i>)												
-homogenate	Charleston Harbour, South Carolina, USA	2002/2003	<0.5	67 \pm 58	1.2 \pm 1.4	3.8 \pm 4.1	4.8 \pm 4	-	nd	n = 8	(Houde et al. (2006)	2
Sheephead (<i>Archosargus probatocephalus</i>)												
	Sarasota Bay, Florida, USA	2004	nd	3.4 \pm 3.6	<0.5	<0.8	16 \pm 7.9	-	nd	n = 3	(Houde et al. (2006)	2
Shorthorn sculpin (<i>Myoxocephalus scorpius</i>)												
- liver	East Greenland	2001	nd	18	nd	-	-	-	-	n = 5 (pooled) for both	(Bossi et al., 2005)	2
	West Greenland	2002	nd	nd	nd	-	-	-	-	n = 5 (pooled)		
Silver carp (<i>Ctenopharyngodon idellawere</i>)												
-muscle	Lake Tangxun, China	2011	1.59 \pm 0.91, 1.25, (0.81-3.33). 6/6	252 \pm 46.0, 248, (204-311). 6/6	0.63 \pm 0.32, 0.54, (0.33-1.19). 6/6	1.27 \pm 0.32, 1.28, (0.84-1.69). 6/6	1.66 \pm 0.29, 1.61, (1.26-2.10). 6/6	0/6	-	Arithm. mean \pm SD, median, (range), number detected from a total of n = 6	(Zhou et al., 2014)	2
Spotfish (<i>Leiostomus xanthurus</i>)												
-homogenate	Charleston	2002/	0.6 \pm 0.9	92 \pm 101	0.5 \pm 0.3	3.1 \pm 2.4	3.1 \pm 3.9	-	Nd	n = 10	(Houde et al.	2

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Species	Location	Date	Concentration ($\mu\text{g}/\text{kg}$ ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUNDA	PFDoDA	PFTrDA	PFTeDA			
	Harbour, South Carolina, USA	2003									(2006)	
Spotted seatrout												
-homogenate	Charleston Harbour, South Carolina, USA	2002/ 2003	1.1 \pm 0.5 ($<60\%$ $>LOD$)	90 \pm 51	1.8 \pm 3.2	4.8 \pm 7.2	3.1 \pm 3.4	-	nd	n = 11	(Houde et al. 2006)	2
-homogenate	Sarasota Bay, Florida, USA	2004	0.6 \pm 0.9	92 \pm 101	0.5 \pm 0.3	<0.8	3.5 \pm 4.3	-	nd	n = 8	(Houde et al. 2006)	2
White amur bream (<i>Ctenopharyng odon idellawere</i>)												
-muscle	Lake Tangxun, China	2011	1.84 \pm 0.90, 1.42, (0.83- 3.16). 7/8	363 \pm 61.4, 360, (279-452). 8/8	1.28 \pm 0.29, 1.40, (0.79- 1.55). 8/8	2.57 \pm 0.67, 2.79, (1.30- 3.39). 8/8	2.54 \pm 0.67, 2.84, (1.41- 3.14). 8/8	0.47 \pm 0.07, 0.47, (0.43- 0.52). 2/8	-	Arithm. mean \pm SD, median, (range), number detected from a total of n = 8	(Zhou et al., 2014)	2
Yellow catfish (<i>Pelteobagrus fulvidraco</i>)												
-muscle	Lake Tangxun, China	2011	9.92 \pm 2.02, 9.58, (6.19- 12.2). 8/8	374 \pm 51.6, 393, (301-460). 8/8	1.39 \pm 0.38, 1.39, (0.82- 1.97). 8/8	3.67 \pm 0.81, 3.47, (2.90- 5.50). 8/8	3.23 \pm 1.09, 2.74, (1.98- 4.69). 8/8	0.91 \pm 0.46, 0.85, (0.40- 1.64). 7/8	-	Arithm. mean \pm SD, median, (range), number detected from a total of n = 8	(Zhou et al., 2014)	2
Birds												
Adélie penguins (<i>Pygoscelius adélieae</i>)												
- eggs	Antarctica, South	2004/ 2005	nd (0/13)	0.4 \pm 0.2	<0.2 (3/13)	2.3 \pm 6.5 (11/13)	0.5 \pm 0.4 (11/13)	-	-	n = 13	(Schiaivone et al., 2009)	2

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA	PFTeDA			
- eggs	Bear Island, Barents Sea	2003 2007	0.1 ± 0.1 0.04 ± 0.0	26.0 ± 9.8 10.8 ± 2.4	0.1 ± 0.1 nd	5.4 ± 1.6 20.1 ± 5.6	1.8 ± 0.4 5.8 ± 1.3	7.2 ± 1.2 20.6 ± 4.8	0.4 ± 0.1 1.4 ± 0.3	n = 5 (pooled) for both	(Bakke T., 2008)	2
	Svalbard, Barents Sea	1993 2002 2007	0.1 ± 0.1 0.1 ± 0.0 0.1 ± 0.0	17.5 ± 2.1 10.9 ± 1.5 8.5 ± 2.0	nd (0/5) 0.9 ± 0.2 nd (0/5)	1.9 ± 0.3 6.3 ± 1.2 5.5 ± 1.4	0.6 ± 0.1 2.0 ± 0.4 1.5 ± 0.4	1.9 ± 0.7 6.1 ± 1.2 19 ± 24	<0.30	n = 5 (pooled) for all		
Chicken (<i>Gallus gallus domesticus</i>)												
-egg yolk	Swedish food production	1999-2010	0.012 (<0.010 - 0.128)	0.375 (<0.026 - 6.478)	0.021 (<0.014 - 0.225)	0.027 (<0.008 - 0.241)	0.007 (<0.006 - 0.052)	0.019 (<0.004 - 0.102)	-	Median, (range), total of 36 pooled samples, 3 pooled samples/year, 200 - 250 eggs/year	(A Glynn et al., 2012)	2
Eider duck (<i>Sommateria mollissima</i>)												
-whole blood	Baltic Sea, Gulf of Gdansk, Poland	2003	1.1 ± 0.6 (0.40 - 2.9)	22 ± 14 (12 - 38)	0.10 ± 0.06 (0.06 - 0.10)	-	-	-	-	n = 16 ng/L	(Falandysz et al., 2007)	2
Gentoo penguins (<i>Pygoscelius papua</i>)												
- eggs	Antarctica, South Shetland	2004/2005	nd (0/13) LOQ = 0.1	0.3 ± 0.1	<0.2 (1/13)	0.6 ± 0.5 (13/13)	0.3 ± 0.8 (7/13)	-	-	n = 13	(Schiavone et al., 2009)	2
Glaucous gulls (<i>Larus hyperboreus</i>)												
- eggs	Bear Island and Svalbard, Barents Sea	2004	<0.27 - 1.23 (3/10)	104 ± 13.2 (51.7 - 196)	nd (0/10)	21.4 ± 2.82 (8.74 - 38.7) 10/10	3.35 ± 0.62 (<0.78 - 7.25) 9/10	15.1 ± 3.61 (4.0 - 42.4) 10/10	<0.25	n = 10 Geometric mean ± SE	(Verreault et al., 2005)	2
- plasma			1.12 ± 0.15 (0.29 - 2.71)	134 ± 16.6 (48.1 - 349)	<0.7 - 0.74 (1/20)	74.4 ± 8.06 (32.0 - 184) 20/20	7.6 ± 1.04 (2.90 - 23.9) 20/20	11.0 ± 1.29 (3.63 - 30.2) 20/20	0.54 ± 0.14 (<0.25 - 2.77) 12/20	n = 20 Geometric mean ± SE		

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA	PFTeDA			
-liver	Svalbard, Barents Sea	2004	0.26 ± 0.06 (0.04 - 0.61) 9/9	65.8 ± 22.4 (8.49 - 225) 9/9	nd (nd) 0/9	nd	nd	-	nd	Arithm. mean ± SE, (range), number detected from a total of n = 9	(Haukas et al., 2007)	2
Long-tailed duck (<i>Clangula hyemalis</i>)												
-whole blood	Baltic Sea, Gulf of Gdansk, Poland	2003	2.1 ± 0.5 (0.0012 - 0.0027)	22 ± 19 (6.7 - 54)	0.62 ± 0.51 (0.25 - 1.8)	-	-	-	-	n = 10 ng/L	(Falandysz et al., 2007)	2
Mallard (<i>Anas platyrhynchos</i>)												
-muscle	Lake Tangxun, China	2011	9.43 ± 10.4, 4.87, (1.53-27.1). 5/5	689 ± 89.2, 671, (574-818). 5/5	0.71 ± 0.13, 0.71, (0.61-0.80). 2/5	5.66 ± 1.10, 6.06, (4.47-7.06). 5/5	12.8 ± 4.09, 13.8, (5.91-16.0). 5/5	3.70 ± 1.71, 4.48, (1.38-5.57). 5/5	-	Arithm. mean ± SD, median, (range), number detected from a total of n = 5	(Zhou et al., 2014)	2
Northern fulmar (<i>Fulmarus glacialis</i>)												
- liver	Faroe Islands	1998-1999	nd nd	29 24	nd nd	-	-	-	-	n = 9 (pooled) for both	(Bossi et al., 2005)	2
	Bear Island, Barents Sea	Not specified	1.0 ± 0.3 (0.5 - 1.6)	3.4 ± 2.2 (0.8 - 8.3) (13/15)	nd (0/15)	-	-	-	-	n = 15 Arithmetic mean ± SD	(Knudsen et al., 2007)	2
Peregrine falcon (<i>Falco peregrinus</i>)												
-eggs	Sweden	1974	0.07	7	<MDL of 2.2	<0.2	<0.2	0.13	<0.6	n = 1	(Holmstrom et al., 2010)	2
		1975	0.05	8		<0.3	<0.2	0.20	<0.4	n = 1		
		1976	0.18	14	MDL was based on blank contamination	<0.2	<0.4	0.15	<0.5	n = 1		
		1977	0.10 - 0.27	8.8 - 33		<0.4	<0.4	0.29 - 0.42	<0.7	n = 2		

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Species	Location	Date	Concentration ($\mu\text{g}/\text{kg}$ ww unless otherwise specified)						Remark	Reference	Reliability	
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA				PFTeDA
		1978	0.23 - 0.46	26 - 44		<0.4	0.15 - 0.34	0.254 - 0.50	<0.9	n = 2		
		1980	0.016 - 0.49	17 - 42		0.27 - 0.50	<0.32 - 0.47	0.37 - 0.38	0.19 - 0.37	n = 2		
		1981	0.29	22		0.33	0.30	0.29	0.49	n = 1 (2 pooled)		
		1982	2.6	41		0.41	0.37	0.59	0.47	n = 1		
		1983	0.37 - 0.83	41 - 87		0.56 - 0.74	0.60 - 0.90	0.55 - 0.76	0.28 - 0.76	n = 2		
		1985	0.88	76		0.61	1.1	0.89	0.81	n = 1		
		1992	2.7 \pm 2.2	301 \pm 204		2.1 \pm 1.2	1.9 \pm 1.1	2.6 \pm 1.1	1.5 \pm 0.17	n = 3; Arithm. mean \pm SEM		
		1993	1.5 \pm 0.87	87 \pm 29		1.7 \pm 0.65	1.2 \pm 0.49	3.9 \pm 1.94	1.8 \pm 0.70	n = 5		
		1994	0.45 - 0.85	41 - 113		1.0 \pm 1.3	1.2 - 1.3	2.5 - 3.2	1.2 - 1.3	n = 2		
		1995	0.56 - 0.58	49 - 64		1.2 - 1.2	0.70 - 1.0	1.2 - 1.7	0.60 - 0.73	n = 2		
		1996	1.1 \pm 0.20	84 \pm 16		2.1 \pm 0.41	1.4 \pm 0.64	3.5 \pm 1.45	1.8 \pm 0.95	n = 6		
		1997	0.72 \pm 0.35	87 \pm 42		1.5 \pm 0.41	1.4 \pm 0.38	3.0 \pm 0.88	1.2 \pm 0.12	n = 6		
		1998	0.89 \pm 0.06	80 \pm 13		2.5 \pm 0.62	2.1 \pm 0.26	4.4 \pm 0.87	1.9 \pm 0.30	n = 3		
		1999	2.5 \pm 1.6	138 \pm 48		3.6 \pm 2.4	2.1 \pm 0.75	5.7 \pm 2.7	1.8 \pm 0.63	n = 8		
		2000	2.7	144		12	2.9	37	2.1	n = 1 (5 pooled)		
		2001	1.9	59		2.7 - 3.7	2.6 - 3.0	7.0 - 7.3	3.1 - 3.3	n = 2 (5+5 pooled)		
		2002	0.71 - 0.97	71 - 104		2.3 - 3.7	2.3 - 3.3	7.9 - 9.3	2.5 - 2.5	n = 2 (5+6 pooled)		
		2003	0.65 -	74 - 127		3.3 - 5.7	2.3 - 4.1	7.4 - 11	2.3 - 3.2	n = 2		

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)						Remark	Reference	Reliability	
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTTrDA				PFTeDA
		2004	1.1 0.76 - 1.7	75 - 122		3.2 - 10.4	2.4 - 4.5	6.2 - 11	1.5 - 3.2	(8+7 pooled) n = 2 (5+5 pooled) n = 1 (5 pooled) n = 10		
		2005	1.4	99		3.4	3.1	7.2	2.4	n = 1 (5 pooled)		
		2006	0.80 ± 0.38	83 ± 49		4.2 ± 1.3	3.2 ± 2.3	7.3 ± 2.7	2.7 ± 1.1	n = 10		
		2007	0.70	47		2.5	1.8	3.7	1.7	n = 1 (5 pooled)		
Razorbill (<i>Alca torda</i>)												
-whole blood	Baltic Sea, Gulf of Gdansk, Poland	2003	0.27 ± 0.13 (0.12 - 0.50)	33 ± 6 (23 -39)	0.083 ± 0.087 (<0.05 - 0.30)	-	-	-	-	n = 10 ng/L	(Falandysz et al., 2007)	2
Red-throated diver (<i>Gavia stellata</i>)												
-whole blood	Baltic Sea, Gulf of Gdansk, Poland	2003	0.71 ± 0.28 (0.40 - 1.2)	72 ± 57 (40 -200)	0.50 ± 0.31 (0.17 -0.85)	-	-	-	-	n = 7 ng/L	(Falandysz et al., 2007)	2
Velvet scoter (<i>Melanitta fusca</i>)												
-whole blood	Baltic Sea, Gulf of Gdansk, Poland	2003	2.6 ± 1.2 (1.0 - 4.3)	8.9 ± 3.6 (4.8 -14)	0.25 ± 0.18 (0.09 - 0.56)	-	-	-	-	n = 5 ng/L	(Falandysz et al., 2007)	2
Mammals												
American mink (<i>Neovison vison</i>)												
-liver	Illinois, USA	1995, 1996	<7-85 (17%) 3.1 7.4 18	47-5140 (100%) 1177 1177 1177	LOQ (varied from 8-40) -24 (max) (8%) 1.5 27 20	-	-	-	-	n = 65 range (% detects) mean (LOQ as zero) mean (LOQ as detection limit)	(Kannan et al., 2002)	2

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)						Remark	Reference	Reliability	
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA				PFTeDA
										mean of detectable observations		
	Louisiana, USA	1999	<7.5 (0%) 0 7.5 0	40-320 (100%) 140 140 140	<19 (0%) 0 19 0	-	-	-	-	n = 7		
	Massachusetts, USA	1996	<4.5-12 (16%) 1.7 5.5 10	20-1100 (100%) 298 298 298	<4.5-27 (58%) 4.6 6.5 8	-	-	-	-	n = 31		
	South Carolina, USA	2000	<7.5-39 (89%) 22 23 25	650-3110 (100%) 208 208 208	<19 (0%) 0 19 0	-	-	-	-	n = 9		
-liver	Swedish Baltic coast	2004-2009	4.6 ± 4.3 (0.9 - 16.7) (24/24)	646 ± 390 (68.6 - 1460) (24/24)	2.8 ± 2.0 (<0.3 - 7.2) (11/24)	36.7 ± 17.2 (11.4 - 70.7) 19/24	6.0 ± 2.9 (1.9 - 11.9) 16/24	4.2 ± 1.6 (1.2 - 7.2) 16/24	-	Arithm. mean ± SD, (range), (fraction >LOD) n = 24	(Persson et al., 2013)	2
	Koster Island in Skagerrak		6.0 ± 3.9 (1.5 - 20.7) (26/26)	867 ± 865 (245 - 4490) (26/26)	3.9 ± 2.2 (1.0 - 9.9) (19/26)	30.9 ± 9.3 (12.0 - 48.3) 22/26	5.4 ± 1.5 (2.3 - 7.3) 13/26	2.2 ± 0.8 (1.3 - 4.1) 13/26	-	n = 26		
	Anthropogenic Swedish inland region		32.1 ± 38.4 (0.3 - 139) (25/25)	3310 ± 5850 (87 - 21800) (25/25)	0.7 ± 0.9 (<0.2 - 3.3) (18/25)	15.2 ± 12.6 (2.0 - 46.7) 19/25	5.9 ± 4.5 (1.9 - 16.2) 12/25	1.6 ± 1.6 (0.1 - 4.6) 13/25	-	n = 25		
	Rural inland of Northern Sweden		1.1 ± 1.2 (<0.1 - 4.0) (24/25)	170 ± 197 (<0.8 - 854) (24/25)	0.7 ± 0.9 (<0.2 - 2.8) (11/25)	29.0 ± 21.5 (1.8 - 79.7) 25/25	5.1 ± 4.7 (<0.3 - 16.4) 14/25	3.8 ± 3.8 (0.4 - 11.7) 15/25	-	n = 25		
Antarctic fur seal (<i>Arctocephalus gazelle</i>)												
- livers of pups (≤2)	Antarctica, South	2004/2005	<0.4 (14/17)	9.4 ± 3.2	<0.4 (1/17)	0.9 ± 0.9 (12/17)	<0.4 (1/17)	-	-	n = 17	(Schiavone et al., 2009)	2

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTTrDA	PFTeDA			
months)	Shetland		LOQ = 0.4									
- muscle of pups (≤2 months)			nd (0/20)	1.3 ± 0.7	0.8 ± 0.8 (10/20)	nd (0/20)	nd (0/20)	-	-	n = 20		
Bottlenose dolphin (<i>Tursiops truncatus</i>)												
-plasma	Charleston Harbour, South Carolina, USA	2002/ 2003	48 ± 62	914 ± 515	43 ± 24	132 ± 144	20 ± 33	-	Nd	n = 24	(Houde et al. 2006)	2
-plasma	Sarasota Bay, Florida, USA	2004	115 ± 101	340 ± 208	3.4 ± 3.5	33 ± 22	3.8 ± 2.1	-	nd	n = 12		2
Cow (<i>Bos Taurus</i>)												
-milk	Swedish food production	1999 - 2010	<MDL	(3.5-7.3) (21 samples > MDL)	<MDL	(1.4-1.8) (3 samples > MDL)	<MDL	<MDL	-	Median, (range), total of 36 pooled samples, pooled samples/ year, 10 - 25 samples/ year ng/kg fw	(A Glynn et al., 2012)	2
European beaver (<i>Castor fiber</i>)												
-liver	Poland	2003	<0.01	6.6 ± 11.5 (1.6 - 39)	0.13 ± 0.06 (0.06 - 0.28)	-	-	-	-	n = 10	(Falandysz et al., 2007)	2
Grey seal (<i>Halichoerus grypus</i>)												
- liver	Baltic Sea	1969	nd	12	nd	0.6	0.2	0.1	Nd	n = 1	(Kratzer et al., 2011)	2
		1974	nd	115 (74 - 179)	nd	1.1 (0.9 - 1.2)	0.3 (0.3 - 0.4)	0.2 (0.2 - 0.2)	Nd	n = 2		
		1975	nd	24	nd	0.3	0.1	0.1	Nd	n = 1		

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA	PFTeDA			
		1976	nd	35 (9.6 - 129)	nd	0.6 (0.4 - 0.8)	0.2 (0.1 - 0.2)	0.1 (0.1 - 0.2)	0.01 (nd-0.1)	n = 2		
		1977	nd	109 (102 - 117)	0.03 (nd - 0.2)	0.6 (0.4 - 1.0)	0.1 (0.1 - 0.2)	0.2 (0.1 - 0.2)	Nd	n = 2		
		1978	nd	41 (13 - 157)	0.01 (nd - 0.3)	0.8 (0.4 - 2.5)	0.2 (0.1 - 0.6)	0.04 (nd - 0.5)	0.004 (nd - 0.2)	n = 6		
		1979	nd	83 (13 - 157)	0.01 (nd - 0.3)	1.0 (0.4 - 2.8)	0.2 (0.1 - 0.6)	0.2 (0.1 - 0.4)	0.01 (nd - 0.1)	n = 4		
		1980	nd	0.02	nd	0.8	0.2	0.2	Nd	n = 1		
		1981	nd	126	nd	2.7	0.4	0.5	0.1	n = 1		
		1983	nd	185	nd	3.9	0.6	0.7	0.2	n = 1		
		1984	nd	136 (36 - 164)	0.06 (nd - 0.8)	2.9 (2.3 - 3.8)	0.5 (0.4 - 0.6)	0.7 (0.6 - 0.9)	0.2 (0.1 - 0.2)	n = 2		
		1985	nd	295 (245 - 355)	0.02 (nd - 0.1)	4.4	0.8	0.7	0.2 (0.2 - 0.3)	n = 2		
		1986	nd	291 (218 - 373)	0.3 (nd - 8.6)	3.8	0.6	1.0	0.03 (nd - 0.2)	n = 3		
		1987	1.0	362	0.8	9.7	1.2	1.5	0.2	n = 1		
		1988	0.6 (0.4 - 0.7)	284 (206 - 426)	0.1 (nd - 6.3)	5.6 (2.9 - 14)	0.7 (0.4 - 1.6)	1.1 (0.8 - 2.2)	0.1 (nd - 0.2)	n = 4		
		1989	1.0 (0.9 - 1.2)	293 (198 - 421)	2.1 (1.7 - 2.7)	5.8 (3.9 - 12)	0.8 (0.6 - 1.5)	1.5 (1.1 - 3.1)	0.01 (nd - 0.3)	n = 3		
		1990	1.0	326	3.3	5.8	0.7	0.6	0.1	n = 1		

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)						Remark	Reference	Reliability	
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA				PFTeDA
<i>acutorostrata</i>												
- liver	Greenland	1998	nd	29	nd	-	-	-	-	n = 5 (pooled)	(Bossi et al., 2005)	2
Polar bear (<i>Ursus Maritimus</i>)												
- liver	East Greenland	1999-2001 2000-2002	<7 <7 LOD = 4 LOQ = 7	1245 1325	<12 <12 LOD = 7 LOQ = 12	-	-	-	-	n = 5 (pooled) n = 5 (pooled)	(Bossi et al., 2005)	2
	East Greenland	1999-2001	140 ± 26	2470 ± 246	10 ± 2	114 ± 7	8 ± 0.6	20 ± 2	3 ± 0.4	n = 29	(M. Smithwick et al., 2005)	2
	Chukchi Sea, Alaska	1999-2002	129 (35.2 - 325)	729 (435 - 1480)	2.40 (<2.3 - 9.04)	26.7 (14.6 - 70)	1.44 (<0.6 - 26.0)	1.54 (<0.6 - 9.55)	1.21 (0.63 - 3.07)	Geometric mean (min-max)	(M. Smithwick et al., 2005)	
	Northwest Territories, Canada		44.8 (<3.2 - 261)	1320 (982 - 2160)	16.3 (10.2 - 33.3)	101 (77.9 - 146)	3.09 (0.75 - 5.71)	3.87 (<0.6 - 8.34)	<0.6 (<0.6 - 1.86)	Total number = 83		
	High Arctic, Canada		35.9 (<3.2 - 263)	1170 (263 - 2410)	18.6 (8.64 - 31.8)	34.5 (6.39 - 81.8)	1.77 (<0.6 - 3.15)	1.62 (<0.6 - 3.15)	<0.6 (<0.6 - 1.08)	The concentrations from Svalbard represent measured blood plasma converted to liver concentrations via a plasma to liver conversion factor		
	South Baffin Island, Canada		71.4 (<3.2 - 417)	1390 (977 - 2100)	36 (20 - 55.8)	45.2 (17.4 - 162)	2.82 (<0.6 - 11.4)	3.32 (0.75 - 25.3)	2.37 (<0.6 - 17.53)			
	South Hudson bay, Canada		62.3 (<3.2 - 321)	2730 (2000 - 3770)	24.9 (18.6 - 31.2)	114 (108 - 120)	4.99 (3.47 - 6.59)	10.6 (7.37 - 14.6)	1.05 (<0.6 - 2.94)			
	East Greenland		80.2 (4.39 - 544)	2140 (911 - 6340)	9 (<2.3 - 57.1)	104 (39.8 - 179)	7.86 (3.7 - 16.6)	18.6 (7.87 - 46.9)	3.27 (<0.6 - 16.19)			
	Svalbard, Barents Sea		2940 (2260 - 4430)	1290 (756 - 1990)	20.6 (11.9 - 37.5)	112 (82.6 - 161)	14.8 (10.3 - 19.8)	22.4 (17.2 - 35)	<0.6			
	East Greenland	1984	<MDL (0/3)	665 ± 273	6.1 ± 2.9	17.1 ± 3.2	-	-	-	n = 3	(Riget et al., 2013)	2
		1985	<MDL (0/2)	718 ± 87.7	5.6 ± 0.9	29.7 ± 6.1				n = 2		
		1986	<MDL (0/2)	893 ± 91.9	7.7 ± 0.4	37.3 ± 0.1				n = 2		
		1987	<MDL (1/5)	599 ± 126	5.7 ± 2.0	28.0 ± 8.7				n = 5		

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Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)						Remark	Reference	Reliability	
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTTrDA				PFTeDA
		1988	<MDL (0/1)	460	<MDL (0/1)	14.8				n = 1		
		1989	4.8 ± 2.3 (2/4)	821 ± 217	9.4 ± 2.3 (2/4)	23.3 ± 4.7				n = 4		
		1990	3.9 ± 2.0 (7/18)	822 ± 240	7.1 ± 3.1 (15/18)	28.2 ± 9.2				n = 18		
		1991	4.3 ± 0.9	791 ± 141	5.8 ± 1.3	28.5 ± 6.2				n = 5		
		1992	2.9 ± 1.9 (3/4)	648 ± 178	5.6 ± 1.4	29.1 ± 5.0				n = 4		
		1993	5.3 ± 1.8 (5/8)	1165 ± 958	8.8 ± 3.7 (6/8)	41.5 ± 27.8				n = 8		
		1994	5.7 ± 0.3	819 ± 227	8.0 ± 1.1	31.0 ± 4.5				n = 4		
		1995	5.2 ± 2.3	759 ± 247	10.6 ± 4.2	36.1 ± 17.5				n = 5		
		1996	6.6 ± 5.6 (1/5)	742 ± 493	7.8 ± 6.5 (3/5)	30.0 ± 18.1				n = 5		
		1999	<MDL (3/16)	1028 ± 539	6.8 ± 4.9 (12/16)	58.6 ± 54.4				n = 16		
		2000	<MDL (4/22)	932 ± 627	6.9 ± 3.0 (15/22)	44.6 ± 26.6				n = 22		
		2001	<MDL (0/12)	1060 ± 588	8.8 ± 10.0 (8/12)	44.2 ± 28.2				n = 12		
		2003	14.3 ± 3.5	1461 ± 435	13.2 ± 5.0	77.6 ± 23.6				n = 5		
		2004	17.6 ± 4.8	1738 ± 861	8.2 ± 2.4	80.1 ± 22.2				n = 4		
		2006	14.1 ± 5.3	2966 ± 736	14.0 ± 2.5	101 ± 37				n = 8		
		2008	27.9	1405	9.0	111				n = 1		
		2010	10.3 ±	1248 ±	12.3 ± 3.2	60.7 ±				n = 4		

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Species	Location	Date	Concentration ($\mu\text{g}/\text{kg}$ ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA	PFTeDA			
		2011	1.2 5.8 \pm 3.8	523 1061 \pm 274	4.8 \pm 2.7	11.6 71.8 \pm 36.9				n = 10		
-plasma	Svalbard, Barents Sea	1998	40.8 \pm 2.9	431.9 \pm 17.0	6.4 \pm 0.6	18.1 \pm 1.0	1.8 \pm 0.2	3.5 \pm 0.3	0.5 \pm 0.5	Mothers, n = 12	(Bytingsvik et al., 2012)	2
			12.0 \pm 1.2	86.0 \pm 5.5	2.1 \pm 0.3	4.2 \pm 0.3	0.6 \pm 0.1	1.0 \pm 0.1	Nd	Cubs, n = 12		
		2008	32.6 \pm 3.4	309 \pm 38.2	4.1 \pm 0.3	28.3 \pm 4.3	3.3 \pm 0.5	5.8 \pm 0.9	0.6 \pm 0.6	Mothers, n=9		
			12.2 \pm 0.9	65.3 \pm 7.4	2.3 \pm 0.2	8.4 \pm 1.0	1.3 \pm 0.4	2.5 \pm 0.3	nd	Cubs, n = 9 Arihm. mean \pm SEM		
Ringed seal (Phoca hispida)												
- liver	East Greenland	2002	nd nd	67 52	nd nd	-	-	-	-	n = 5 (pooled) for both	(Bossi et al., 2005)	2
	West Greenland	1998	nd nd	27 27	nd nd	-	-	-	-	n = 5 (pooled) for all		
		2000	nd	13	nd							
		2002	nd nd	<10 10	nd <12							
	Canadian Arctic, Aviat	1972	nd	22.7 (11.7 - 41.6)	<0.85 (nd - <0.85)	5.5 (2.4 - 12.1)	1.4 (0.5 - 3.6)	2.0 (0.6 - 0.4)	0.3 (0.06 - 1.05)	n = 6	(Butt et al., 2007)	2
		1993	nd	91.6 (36.3 - 177)	1.13	15.6 (8.2 - 31.5)	2.8 (1.8 - 3.7)	4.0 (2.5 - 8.1)	0.49 (0.28 - 1.02)	n = 10		
		2000	nd	35.1 (20.8 - 74.1)	1.67 (0.98 - 3.61)	17.6 (12.4 - 36.0)	2.9 (2.1 - 5.8)	4.5 (3.4 - 6.5)	0.51 (0.35- 0.79)	n = 10		
		2005	nd	19.6 (8.0 - 44.1)	0.98 (0.96 - 1.01)	12.0 (5.9 - 22.4)	1.9 (1.2 - 3.1)	3.3 (2.1 - 4.9)	0.37 (0.26- 0.49)	n = 10		
	Canadian	1972	nd	1.8	1.1	0.34	0.55	0.11	0.04	n = 2		

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)							Remark	Reference	Reliability
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA	PFTeDA			
	Arctic, Resolute Bay	1993	nd	(0.58 - 3.0) 7.0 (1.6 - 14.7)	(0.97 - 1.2) 4.5 (<3.6 - 4.5)	(0.20 - 0.48) 2.8 (0.8 - 4.0)	(0.17 - 0.98) 0.47 (0.10 - 0.85)	(nd - 0.11) 0.54 (0.23 - 0.78)	(0.01 - 0.06) 0.16 (0.08 - 0.29)	n = 9		
		2000	nd	22.1 (4.4 - 49.7)	3.9 (<3.6 - 4.1)	6.4 (2.8 - 13.4)	1.2 (0.47 - 2.4)	2.1 (0.76 - 5.5)	0.39 (0.14 - 0.76)	n = 9		
		2004	nd	16.8 (5.9 - 27.7)	6.2 (<3.6 - 6.2)	11.0 (7.0 - 13.6)	1.4 (1.1 - 1.8)	2.0 (1.2 - 2.6)	0.27 (0.09 - 0.51)	n = 9		
		2005	nd	8.1 (2.0 - 17.0)	<0.85	7.5 (2.8 - 14.8)	0.96 (0.40 - 2.0)	n/a	0.21 (0.06 - 0.46)	n = 9		
	East Greenland	1986	0.9 ± 0.5 (4/9)	31 ± 16.7	<MDL (0/9)	3.5 ± 1.8	-	-	-	n = 9	(Riget et al., 2013)	2
		1994	0.5 ± 0.3 (2/6)	20.8 ± 6.4	<MDL (0/6)	2.8 ± 1.3				n = 6		
		1999	<MDL (1/8)	77.4 ± 34.0	1.0 ± 0.5 (2/8)	7.8 ± 2.9				n = 8		
		2003	0.7 ± 0.2 (4/9)	94.8 ± 25.4	<MDL (0/9)	8.9 ± 1.3				n = 9		
		2006	0.7 ± 0.1 (6/14)	352 ± 175	0.6 ± 0.5 (5/14)	12.1 ± 7.0				n = 14		
		2008	<MDL (0/20)	280 ± 122	2.2 ± 0.6 (6/20)	16.8 ± 4.9				n = 20		
		2010	<MDL (0/16)	112 ± 37.2	<MDL (0/16)	19.9 ± 5.5				n = 16		
	West Greenland	1982	0.4 ± 0.5 (2/10)	12.5 ± 5.7	<MDL (1/10)	1.3 ± 0.8 (9/10)	-	-	-	n = 10		
		1994	<MDL (0/8)	29.8 ± 19.4	<MDL (0/8)	2.0 ± 1.0				n = 8		
		1999	<MDL (0/10)	31.3 ± 24.4	<MDL (0/10)	3.6 ± 0.8				n = 10		

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)						Remark	Reference	Reliability	
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA				PFTeDA
		2003	<MDL (0/10)	27.9 ± 11.2	<MDL (0/10)	3.6 ± 1.3				n = 10		
		2006	<MDL (0/19)	397 ± 159	2.4 ± 1.5 (12/19)	8.6 ± 2.6				n = 19		
		2008	<MDL (0/19)	262 ± 139	1.2 ± 0.9 (8/19)	11.0 ± 6.7				n = 19		
		2010	<MDL (0/19)	16.3 ± 10.0	<MDL (0/19)	8.5 ± 2.9				n = 19		
	Inukjuak, Canadian Arctic	2002	2.5 (2.0 - 3.0)	88.8 (40.1 - 189)	1.5 (nd - 3.7)	26.2 (13.0 - 71.6)	4.9 (2.6 - 8.1)	5.3 (2.4 - 9.3)	0.65 (0.30 - 1.4)	Geometric mean, (range) n = 10	(Butt et al., 2008)	2
	Pangnirtun g, Canadian Arctic	2002	0.18 (nd - 0.80)	10.7 (3.5 - 26.6)	1.2 (<0.78 - 2.9)	2.2 (1.0 - 5.6)	0.32 (0.54 - 0.94)	0.93 (0.48 - 2.1)	0.23 (0.16 - 0.38)	n = 10		
	Grise Fjord, Canadian Arctic	2003	<0.73	37.4 (13.2 - 96.9)	2.0 (0.93 - 13.9)	7.5 (3.8 - 15.3)	1.9 (0.80 - 4.1)	1.9 (0.89 - 4.5)	0.13 (0.19 - 0.81)	n = 10		
	Arctic Bay, Canadian Arctic	2004	<0.73	10.4 (5.1 - 18.4)	0.22 (<0.78 - 2.4)	4.2 (1.8 - 9.6)	0.71 (<0.42 - 1.5)	0.93 (0.48 - 1.7)	0.13 (<0.10 - 0.31)	n = 10		
	Gjoa Haven, Canadian Arctic	2004	<0.73	61.2 (12.8 - 189)	1.1 (<0.78 - 3.5)	13.4 (4.3 - 35.3)	2.0 (0.68 - 4.0)	2.3 (0.94 - 4.2)	0.25 (0.13 - 0.52)	n = 10		
	Pond Inlet, Canadian Arctic	2004	<0.73	11.1 (5.8 - 20.4)	0.22 (nd - 1.6)	2.7 (1.7 - 6.9)	0.40 (<0.42 - 1.1)	0.76 (0.45 - 1.5)	0.11 (<0.10 - 0.2)	n = 10		
	Arviat, Canadian Arctic	2005	nd	16.8 (7.6 - 43.7)	<0.78	10.9 (5.8 - 22.3)	1.7 (1.1 - 3.0)	3.1 (2.1 - 4.9)	0.33 (0.23 - 0.46)	n = 10		
	Nain, Canadian Arctic	2005	0.81 (<0.73 - 2.0)	21.9 (9.7 - 48.4)	0.19 (<0.78 - 1.2)	6.7 (3.4 - 13.6)	1.1 (0.45 - 1.9)	2.3 (1.2 - 4.0)	0.32 (0.14 - 0.59)	n = 10		
	Qikiqtarjua q, Canadian Arctic	2005	0.57 (<0.73 - 1.7)	22.1 (15.0 - 44.4)	<0.78	9.0 (5.3 - 12.2)	1.4 (0.73 - 2.4)	2.2 (1.3 - 3.4)	2.2 (1.3 - 3.4)	n = 10		
	Resolute Bay, Canadian Arctic	2005	<0.73	6.5 (1.7 - 16.6)	<0.78	6.6 (2.8 - 14.7)	0.61 (0.55 - 1.9)	0.68 (0.22 - 1.4)	0.11 (0.10 - 0.43)	n = 10		
	Sachs Harbor,	2005	<0.73	9.6 (0.89 -	<0.78	4.9 (1.5 -	0.88 (0.87 -	1.4 (0.37 -	0.21 (0.10 -	n = 10		

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Species	Location	Date	Concentration (µg/kg ww unless otherwise specified)						Remark	Reference	Reliability	
			PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTrDA				PFTeDA
	Canadian Arctic			31.3)		14.6)	2.2)	3.1)	0.39)			
River otter (Lutra Canadensis)												
-liver	Oregon, USA	1997-1998				-	-	-	-	Mean (range)	(Kannan et al., 2002)	2
	Nehalem River		<4	82.8	<7.5					n = 1		
	Willamette River		(<4-68)	579 (97-994)	(<7.5-19)					n = 7		
	Yaquina River		<4	39 (34-45)	(<7.5-9.9)					n = 2		
	Washington, USA	1997-1998				-	-	-	-	Mean (range)		
	Bremerton		<4	288	<7.5					n = 1		
	Egdon		<4	297 (173-422)	<7.5					n = 2		
	Fort Ward		(<4-76)	156 (139-189)	(<7.5-19)					n = 3		
	Silverdale		(<4-52)	199 (151-248)	(<7.5-11)					n = 2		
	Soleduck River		<4	<4	<7.5					n = 2		

Table 19. Concentrations in humans of PFHxS, and when available in the same study also PFOS, PFOA, PFUnDA, PFDoDA, PFTTrDA and PFTeDA.

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		PFHxS	PFOS	PFOA	PFUnDA	PFDoDA	PFTTrDA	PFTeDA			
Blood plasma											
Belgium	1998, 2000	<1/<1 (<1) 0%	11.1/10.4 (4.9 - 19) 100%	4.1 (<1 - 7.6) 75%	-	-	-	-	Female: n = 4	(Kannan et al., 2004)	2
		1.3/1.2 (<1 - 1.4) 50%	16.8/17.6 (4.5 - 27) 100%	5.0/4.3 (1.1 - 13) 100%					Male: n = 16 Arithm. mean/median, (range) % positive		
USA	2002	4.1/2.9 (0.2 - 23) 100%	42.8/42 (16 - 83) 100%	27.5/25.2 (14 - 56) 100%	-	-	-	-	n = 70 New York City		
Sweden	2004	2.4, 3.0, 4.0, 2.3, 1.4	17.3, 18.9, 34.1, 17.3, 14.8	2.6, 2.1, 4.5, 5.1, 2.2	-	-	-	-	Female 36 years, Male 27 years, M41, F29, F24	(Karrman et al., 2006)	2
USA	2004-2005	EDTA	EDTA	EDTA	-	-	-	-	Employees at 3M;	(Ehresman et	2

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Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		- 2.1)	153/153	(0.7 - 9.2)							
		151/15 3	6.3 ± 2.8/5.8	153/153					Arnsberg;		
		1.2 ± 0.6/1.1	(1.7 - 16.7)	26.7 ± 13.8/23					n = 164		
		(<LOD - 5.7)	164/164	(5.4 - 99.7)							
		162/16 4		164/164					Men		
			12.4 ± 11.5/9.7						Brilon (ref);		
		2.4 ± 1.0/2.2	(1.7 - 92.5)	6.4 ± 2.8/5.8					n = 103		
		(0.7- 5.4)	103/103	(1.1 - 15.3)							
		103/10 3	11.8 ± 6.1/10.5	103/103					Arnsberg;		
			(2.7 - 36.2)						n = 101		
		2.7 ± 1.1/2.5	101/101								
				28.5±12.9							
		(0.7 - 8.7)		(6.1-77.5)					Arithm. mean ± SD/ geometric mean, (range) no.>LOD		
		101/10 1		101/101							
Sweden	1987	0.49/0. 30	14.43/13.1	2.46/2.60	-	-	-	-	n=3	(B. A. G. Jönsson et al., 2009)	2
		(0.28 - 0.90)	(8.28 - 21.81)	(1.75 - 3.02)							

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)						Remarks	Reference	Reliability
	1988	0.66/0.65	17.75/21.3	3.70/3.72				n = 8		
		(0.41 - 0.89)	(8.55 - 25.83)	(1.23 - 6.85)						
	1989		17.37/16.7					n = 9		
		0.70/0.64	(11.12 - 25.0)	2.68/2.63						
	1990	(0.49 - 1.51)	19.12/16.7	(1.54 - 4.20)				n = 4		
			(10.69 - 32.3)	2.31/1.78						
	1991	0.83/0.81	11.42	(1.56 - 4.12)				n = 1		
		(0.44 - 1.26)								
	1993		18.46							
				1.70				n = 1		
	1994	0.36	20.91/20.9							
			(20.19 - 21.6)	4.90				n = 2		
		0.99								
	1995	1.52/1.52	23.24/22.1	3.89/3.89						
		(1.13 - 1.90)	(15.69 - 33.0)	(3.73 - 4.05)				n = 4		
	1996		20.46/19.5	5.03/4.64						
		0.68/0.	(11.07 -	(3.65 -				n = 8		

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)						Remarks	Reference	Reliability
		68	36.7)	7.18)						
	1997	(0.52 - 0.82)	15.22/17.4	3.92/3.81				n = 3		
	1998	1.93/1.93	(10.02 - 18.2)	(2.32 - 6.33)				n = 1		
	1999	(0.52 - 1.70)	35.50	3.70/2.97				n = 2		
	2000	1.29/0.88	17.34/17.3	(2.81 - 5.32)				n = 8		
	2001	(0.73 - 2.26)	18.98/16.7	5.51				n = 1		
	2006	1.93	(10.24 - 27.6)	2.50/2.50				n = 15		
	2007	0.80/0.80	12.08	(1.88 - 3.11)				n = 10		
		(0.49 - 1.11)	13.08/10.4	3.27 - 3.32				All n = 80 were females		
			(3.65 - 27.5)	(1.40 - 5.08)						
		1.300/1.29	11.46/10.2	2.22						
		(0.65 - 2.64)	(4.07 - 20.0)	2.69/2.51						
		0.71		(1.19 -						

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		0.85/0.89 (0.16 - 1.54)		4.65)					Arithm. mean/median, (range),		
		1.25/0.93 (0.33 - 2.35)		3.08/2.93 (1.29 - 5.24)							
Germany	1997-20004	1.7 (0.5 - 4.6)	18.8 (8.1 - 150.7)	6.1 (1.7 - 40.7)	-	-	-	-	Median, (range) n = 30	(Wilhelm et al., 2009)	2
Germany	2006	2.7 (0.4 - 17)	25 (1.1 - 650)	10 (2.1 - 170)	-	-	-	-	Median (range) n = 105 (99 M and 6 F, age 14-88 y)	(Holzer et al., 2011)	2
Norway	2003-2004	0.76/0.60 (0.43 - 0.86) Two samples <LOQ (0.05)	13.7/12.8 (10.1 - 16.6)	2.35/2.11 (1.54 - 2.93)	-	-	-	-	n = 487 mothers, blood sample taken at w. 17 of gestation. Mean/median, (IQR)	(Brantsaeter et al., 2013)	

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Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
Blood serum											
USA	2000	4.3 (<LOD - 21.4) (LOD ~1.5, LOQ = 5)	25.7 (6.7 - 81.5) (LOD ~1.7, LOQ = 5)	5.2 (<LOQ - 35.2) (LOD ~1, LOQ = 5)	-	-	-	-	Median (range) n = 65 Non-industrially exposed	(Hansen et al., 2001)	2
India	2000	1.6/1.6 (<1 - 1.8) 36%	2.3/2.5 (<1 - 3) 55%	<3/<3 (<3) 0%	-	-	-	-	Arithm. mean/median, (range) % positive Female: n = 11 Male: n = 34	(Kannan et al., 2004)	2
Italy	2001	1.3/1.3 (<1 - 1.4) 37.5%	4.4/3.5 (<1 - 8) 87.5%	<3/<3 (<3) 0%	-	-	-	-	Female: n = 8 Male: n = 42		
		1.7/1.7 (<1 - 2.1)	4.3/4.2 (<1 - 10.3)	<3/<3 (<3) 0%							

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Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		33%	90.5%								
Japan	2002	3.3/3.3 (<2.6 - 4.7) 23%	20.1/18.3 (6.3 - 40.3) 100%	12.3/12.3 (<6.8 - 12.3) 8%	-	-	-	-	Female: n = 13 Male: n = 25		
		4.2/3.7 (<2.6 - 4.7) 27%	14.1/12.4 (4.1 - 38) 100%	<6.8/<6.8 (<6.8) 0%							
USA	2000	3.6/2.8 (<1.3 - 13.2) 85%	32.5/28.9 (<1.3 - 91.7) 91%	4.7/4.4 (<3 - 7.3) 46%	-	-	-	-	Female: n = 46 Male: n = 29		
		4.3/3.3 (<1.3 - 13.6) 76%	32.9/26.2 (<1.3 - 124) 93%	5.7/4.4 (<3 - 14.7) 45%							
Sweden	2004	4.7 ± 2.9 4.0 (1.8 - 11.8) 12/12	20.7 ± 10.5 18.7 (8.2 - 48.0) 12/12	3.8 ± 1.0 3.8 (2.4 - 5.3) 12/12	0.40 ± 0.35 0.28 (0.20 - 1.5) 12/12	-	-	-	Mean ± SD, Median, (range), Number >LOD n = 12 primiparous women	(Karrman et al., 2007)	2

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Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
USA	1998-2004	290/19 3 (16 - 1295)	799/626 (145 - 3490)	691/408 (72 - 5100)	-	-	-	-	Retirees from the 3M company n = 26 <i>Initial conc.</i> Arithm. mean/ median (range) <i>Final conc.</i> Arithm. mean/ median (range)	(Olsen et al., 2007)	2
		182/11 7 (10 - 791)	403/295 (37 - 1740)	262/148 (17 - 2435)							
Canada	2004-01 – 2005-06	4.13 ± 11.43 (1.44 – 3.06) (46.5%) 4.05 ± 12.30 (1.33 – 2.66) (45.5%	18.31 ± 10.95 (10.8 – 22.9) (100%) 16.19 ± 10.43 (9.19 – 20.22) (100%)	2.54 ± 1.65 (10.8 – 22.9) n = 101 (100%) 2.24 ± 1.61 (1.33 – 2.64)	-	-	-	-	Maternal serum at 24- 28 weeks n = 101 Maternal serum at delivery n = 101 Umbilical cord blood n = 105	(Monroy et al., 2008)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
)		(100%)					Mean ± SD		
		5.05 ±12.92	7.19 ± 5.73	1.94 ±1.54					(range)		
		(1.4 – 2.77)	(3.92 – 9.11)	(1.09 – 2.37)					(% of detection)		
		(20%)	(100%)	(100%)							
Sweden	1977	0.10	3.8	0.58	<0.050	<0.050	0.067	-	Pooled samples from Males 40-50 y	(Haug et al., 2009)	2
	1980	0.29	6.1	1.3	0.069	0.056	<0.050				
	1981	0.49	9.4	1.4	0.097	<0.050	0.073				
	1982	0.56	11	1.4	0.13	0.055	0.088				
	1983	0.52	10	1.5	0.28	<0.050	0.090				
	1985	0.80	16	2.2	0.27	<0.050	0.13				
	1986	0.80	15	2.6	0.61	0.062	0.18				
	1988	0.82	18	2.7	0.19	0.051	0.085				
	1989	1.3	22	3.1	0.31	<0.050	0.088				
	1990	1.1	20	3.3	0.29	<0.050	0.11				
	1991	1.3	23	3.4	0.17	0.054	0.072				
	1993	1.7	33	5.2	0.27	0.051	0.11				
	1994	1.9	24	4.1	0.22	<0.050	0.092				
	1995	1.4	31	4.4	0.21	<0.050	0.13				
	1996	1.4	25	4.0	0.20	<0.050	0.10				
	1997	1.8	31	4.2	0.21	<0.050	0.15				

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Location	Date	Concentration (µg/L)						Remarks	Reference	Reliability	
	1999	1.6	29	4.0	0.17	0.070	0.13				
	2000	3.4	30	4.5	0.24	0.084	0.12				
	2001	1.6	27	4.9	0.24	0.054	0.16				
	2002	2.2	27	3.9	0.30	0.21	0.053				
	2003	1.7	19	3.8	0.23	0.23	<0.050				
	2004	1.4	18	3.4	0.18	0.063	0.11				
	2005	1.6	21	3.5	0.25	0.065	0.20				
	2006	1.4	12	2.7	0.14	<0.050	0.071				
USA	1999-2000, 2003-2004	0.95 ± 0.10 0.60 ± 0.04	3.11 ± 0.05 3.19 ± 0.04	1.51 ± 0.05 1.48 ± 0.04	-	-	-	-	Adolescents (≥12 - <20 years; n = 474) Adults (≥ 20 years; n = 969) Arithm. mean ± SEM	(Lin et al., 2009)	2
Norway	2008/2009	1.6 (0.83 - 6.2) 1.4 (0.84 - 6.2) 1.5 (0.80 -	27 (11 - 91) 24 (8.7 - 86) 26 (10 - 86)	50 (20 - 174) 53 (15 - 73) 57 (20 - 162)	0.96 (0.32 - 3.4) 0.88 (0.16 - 3.5) 0.88 (0.21 -	2.0 (0.51 - 9.1) 1.2 (0.32 - 7.3) 1.3 (0.46 -	0.26 (0.11 - 1.0) 0.17 (0.009 - 0.65) 0.21 (0.06 -	1.2 (0.26 - 4.4) 0.40 (0.03 - 2.10) 0.36 (0.11 - 2.9)	Median, (range) Ski wax technicians World Cup in skiing n = 13 A: After season I (March) B: Before	(Freberg et al., 2010)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)						Remarks	Reference	Reliability	
		6.4)			3.3)	8.3)	0.76)		season II (November) C: After season II (March)		
Germany	2007-2009	0.6/0.5	3.5/3.2	2.6/2.4	-	-	-	-	Arithm. mean/media n	(Fromme et al., 2010)	2
		(1.3)	(6.8)	(5.5)					(95 th perc.)		
		43/44	44/44	44/44					n>LOQ		
		0.6/0.5	3.5/3.2	2.3/1.9					<i>Mother</i>		
		(1.5)	(6.1)	(5.2)					Pregnancy		
		37/38	38/38	38/38					At delivery		
		0.4/0.3	3.2/2.9	1.7/1.5					6 months after delivery		
		(0.9)	(6.3)	(3.9)					----- ---		
		45/47	47/47	47/47					<i>Fetus/infant</i>		
		----- -----	-	-----					Cord blood		
		0.3/0.2	1.1/1.0	1.7/1.4					6 months after birth		
		(0.9)	(2.2)	(3.7)					19 months after birth		
		24/33	33/33	33/33							
		0.7/0.6	3.3/3.0	8.0/6.9							
				(19.5)							

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		(1.6) 39/40	(8.1) 40/40	40/40 5.1/4.6							
		0.7/0.6 (1.2) 24/24	2.2/1.9 (4.6) 24/24	(11.4) 24/24							
Canada	2005-12 – 2006-06	2.1 (<0.25 – 43) 233/ 252	9.0 (<0.25 – 35) 251/ 252	2.1 (<0.25 – 18) 227/ 252	-	-	-	-	Pregnant women, week 15-16 Arithm. mean (range) Detected/ total	(Hamm et al., 2010)	2
USA	1999-2000, 2003-2004	2.2 (<0.1/ <0.3 – 64.1)	22.6 (2.1 – 87.2)	4.4 (0.4 – 21.7)	-	-	-	-	Children age 12-1 years n = 571 Median (range)	(Hoffman et al., 2010)	2
USA	2003-2004	1.8 (0.2 – 27.1)	21.0 (1.4 – 392)	3.9 (0.1 – 37.3)	-	-	-	-	Age 20 – 80 years of age n = 860 Median (range)	(Nelson et al., 2010)	2
Korea	2008-08 –	0.55	2.93	1.46	0.60	< 0.27	0.24	<0.27	Median (25 th perc – 75 th)	(Kim et al.,	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		(0.46 – 0.85)	(2.08 – 4.36)	(1.15 – 1.91)	(0.50 – 0.99)		(0.17 – 0.31)				
	2009-03								perc.) Pregnant women n = 44 Fetal cord n = 43	(2011)	
USA	2005-2006	9.3 ± 13.7	22.9 ± 12.5	66.3 ± 106.1	-	-	-	-	Arithm. mean ± SD n = 10546 Children age 5-18 y	(Stein & Savitz, 2011)	2
Taiwan	2004	0.035 (0.035 – 0.420)	5.50 (0.11 – 48.36)	1.71 (0.75 – 17.40)	-	-	-	-	Cord blood Median (range) n = 244	(I. J. Wang et al., 2011)	2
Sweden	1996	1.61/ 2.44/ 2.24	22.7/ 27.3/ 23.3	2.18/ 2.92/ 2.69	0.189/ 0.212/ 0.163	<0.1/ <0.1/ <0.1	<0.15/ <0.15/ <0.15	<0.25/ <0.25/ <0.25	n = 19, 3 pools	(A. et al., 2012)	2
	1997	2.30/ 1.55/ 1.63	24.8/ 20.3/ 20.7	3.07/ 2.26/ 2.54	0.228/ 0.154/ 0.261	<0.1/ <0.1/ <0.1	<0.15/ <0.15/ <0.15	<0.25/ <0.25/ <0.25	n = 62, 3 pools		
	1998	1.16/ 1.99/ 2.19	20.2/ 23.1/ 23.0	2.22/ 2.66/ 2.35	0.168/ 0.223/ 0.202	<0.1/ <0.1/ <0.1	<0.15/ <0.15/ <0.15	<0.25/ <0.25/ <0.25	n = 74, 3 pools		
	1999	2.00/ 2.95/ 1.80	20.0/ 21.5/ 23.0	2.38/ 3.11/ 2.49	0.153/ 0.262/ 0.144	<0.1/ <0.1 <0.1	<0.15/ <0.15/ <0.15	<0.25/ <0.25/ <0.25	n = 17, 3 pools		
	2000	2.40/	18.7/ 22.0	2.65/ 2.50	0.198/	<0.1/ <0.1 <0.1/	<0.15/ <0.15/ <0.15	<0.25/ <0.25/ <0.25/ <0.25/ <0.25/	n = 20, 2 pools n = 9, 1 pool		

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
	2001	3.03	28.1	3.05	0.201/ 0.32	<0.1/ <0.1 <0.1/ <0.1	<0.15 <0.15/	<0.25 <0.25/ <0.25/ <0.25	n = 31, 3 pools		
	2002	1.96	17.0/ 18.7/ 23.2	2.17/2.59/ 2.98	0.228/ 0.272/ 0.274	<0.1/ <0.1/ <0.1	<0.15/ <0.15/ <0.15	<0.25/ <0.25/ <0.25	n = 32, 3 pools		
	2004	2.25/ 3.04/ 2.87	16.0/ 16.6/ 13.6	2.12/ 2.12/ 2.15	0.303/ 0.299/ 0.180	<0.1/ <0.1/ <0.1	<0.15/ <0.15/ <0.15	<0.25/ <0.25/ <0.25	n = 30, 3 pools		
	2006	2.16/ 3.82/ 1.85	16.5/ 12.2/ 10.7	2.11/ 1.89/ 1.70	0.240/ 0.175/ 0.241	<0.1/ <0.1/ <0.1	<0.15/ <0.15/ <0.15	<0.25/ <0.25/ <0.25	n = 29, 3 pools		
	2007	3.87/ 5.26/ 3.24	15.1/ 18.3/ 8.80	2.41/ 2.42/ 1.36	0.245/ 0.225/ 0.185	<0.1/ <0.1/ <0.1	<0.15/ <0.15/ <0.15	<0.25/ <0.25/ <0.25	n = 30, 3 pools		
	2008	4.48/ 4.68/ 3.20	7.14/ 8.68/ 8.89	1.54/ 2.40/ 1.80	0.208/ 0.254/ 0.262		<0.15/ <0.15/ <0.15		n = 30, 3 pools		
	2009	5.05/ 3.92/ 4.12	7.61/ 5.11/ 7.62	1.96/ 1.71/ 1.39	0.281/ 0.247/ 0.285		<0.15/ <0.15/ <0.15				
	2010	4.00/ 4.58/ 5.95			0.311/ 0.232/ 0.188		<0.15/ <0.15/ <0.15				
Korea	2008	1.51 (0.92 – 2.34)	7.96 (5.58 – 12.10)	2.74 (2.04 – 3.64)	1.75 (1.11 – 4.58)	0.92 (0.21 – 1.13)	0.39 (0.27 – 0.57)	<0.05	n = 633 Median, (25 th – 75 th percentiles)	(Ji et al., 2012)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
Sweden	2009-2010	0.78 (0.38 - 2.5)	6.9 (3.7 - 19)	1.9 (1.2 - 3.3)	<0.1 (<0.1 - 0.83)	-	-	-	Median, (range) Male: n = 50	(B. Jönsson et al., 2010)	2
Canada	2008	45.2, 27.5, 77.1, 32.3, 215, 423, 222	15.2, 17.7, 19.9, 16.4, 78.4, 108, 72.3	3.68, 2.55, 4.96, 2.40, 9.02, 9.23, 6.84	-	-	<0.05, <0.05, <0.05, <0.05, <0.05, <0.05, <0.05	<0.05, <0.05, <0.05, <0.05, <0.05, <0.05, <0.05	Family members; M-52, F-48, M-23, M.21, F-18, M-17, M-15	(Beesoon et al., 2012)	2
United Kingdom	1991-1992	1.6 (0.2 - 54.8) ----- ----- ----- 1.5 (0.7 - 3.6) 1.6 (0.2 - 54.1) 1.9 (0.7 - 17.5) 1.4 (0.9 - 4.4) 1.6 (0.5 -	19.6 (3.8 - 112) ----- ----- 16.9 (11.1 - 42.9) 20.1 (3.8 - 112) 20.9 (11.3 - 47.6) 19.2 (9.4 - 74.2) 17.3 (8.5 - 94.5) -----	3.7 (1.0 - 16.4) ----- ----- 3.5 (1.2 - 8.3) 3.8 (1.0 - 15.7) 3.7 (1.9 - 6.5) 3.6 (2.1 - 11.1) 3.5 (1.3 - 16.4) -----	-	-	-	-	Median, (range) N = 447 Maternal conc. ----- <i>Overall</i> ----- <i>Maternal pregnancy BMI</i> Underweight Normal Overweight Obese Missing ----- <i>Maternal age at delivery</i>	(Maisonet et al., 2012)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)						Remarks	Reference	Reliability
		54.8)	-	-----				Missing		
		1.4	21.5	-				-----		
		(0.3 - 2.8)	(6.5 - 94.5)	4.4						
		-----	18.2	(1.5 - 16.4)				<i>Smoking during pregnancy</i>		
		-----		3.1				Yes		
		1.8	(3.8 - 74.2)	(1.0 - 13.8)				No		
		(0.4 - 54.8)	-----	-----				Missing		
		1.5	17.2	-				-----		
		(0.2 - 49.8)	(7.6 - 39.6)	3.4						
		-----	20.9	(1.2 - 7.5)				<i>Low birth weight</i>		
		-----		3.9				Yes		
		1.6	(4.3 - 112)	(1.0 - 16.4)				No		
		(0.2 - 9.5)	18.0	3.2				Missing		
		1.7	(3.8 - 74.2)	(1.1 - 11.1)				-----		
		(0.3 - 54.8)	-----	-----				<i>Preterm delivery</i>		
		1.4	21.8	-				Yes		
		(0.4 - 24.9)	(4.3-112)	4.1				No		
		-----	19.6	(1.0 - 11.1)				Missing		
		-----	(3.8-94.5)	3.7				-----		
		1.7	-----	(1.1 - 16.4)				<i>Breast-feeding in firs 4 weeks</i>		
		(0.3 -	-	-----				Yes		
		23.9	-----	-----						

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		54.8)									
Greenland	2002-2004	2.8/2.2 (1 - 21) 100% >LOD	51.9/44.7 (12 - 161) 100% >LOD	4.8/4.5 (2 - 14) 100% >LOD	1.7/ 1.3 (0.2 - 13) 94.4% >LOD	0.2/ 0.1 (0.04 - 2) 80.6% >LOD	-	-	Mean/median, (range) n = 199 men	(Specht et al., 2012)	2
Poland		1.2/1.2 (0.4 - 4) 100% >LOD	18.6/18.5 (8 - 40) 100% >LOD	5.1/4.8 (2 - 16) 100% >LOD	0.3/ 0.3 (0.2 - 0.7) 11.6% >LOD	0.1/ 0.1 (0.04 - 0.2) 8.4% >LOD	-	-	n = 197 men		
Ukraine		0.4/0.3 (0.03-3) 99.5% >LOD	8.1/7.6 (3-30) 100% >LOD	1.8/1.3 (0.3-35) 92.1% >LOD	0.3/ 0.2 (0.1 - 1) 51.2% >LOD	0.3/ 0.3 (0.02 - 0.5) 12.3% >LOD	0.1/ 0.1 (0.04 - 0.1) 3% >LOD	-	n = 208 men		
Greenland	2011	2.2	44.7	4.5	-	-	-	-	Median n = 196	(Toft et al., 2012)	2
Poland		1.2	18.5	4.8					Median n = 189		
Ukraine		0.3	7.6	1.3					Median n = 203		
Sweden	2010-2011	1.95 (0.73 - 10.29)	11.20 (3.89 - 25.41)	2.25 (0.76 - 5.01)	0.33 (0.11 - 0.86)	-	-	-	Median, (p5 - p95) n = 270	(Bjerme et al., 2013)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
									Adults (18 - 80 years)		
China	2010	2.6/1.2 (<LOD - 16) 84/86	31/19 (1.4 - 180) 86/86	3.1/2.3 (0.26 - 29) 86/86	0.21/ 0.18 (<LOD - 0.82) 84/86	-	-	-	Arithm. mean/median, (range) No. >LOD n = 86	(Zhang et al., 2013)	2
Sweden	2013	258/1790 478/866	291/1737 500/881	16/92 26/47	-	-	-	-	n = 79 Median/max 75 th /95 th percentile	(Jakobsson K., 2014) (B. Jönsson, 2014)	2
Sweden	2013	0.53 0.79 1.10 1.61 2.29 0.66 0.98 1.24 1.80 3.48	1.30 2.11 3.14 3.86 5.25 1.76 2.89 4.12 5.11 7.53	0.79 1.24 1.85 2.51 3.59 1.03 1.38 1.700 1.95 2.39	0.05 0.10 0.14 0.20 0.29 <0.04 0.08 0.13 0.17 0.31	<0.03 <0.03 <0.03 <0.03 0.06 <0.03 <0.03 <0.03 <0.03 0.06	<0.01 0.01 0.03 0.04 0.07 <0.01 <0.01 0.02 0.03 0.05	<0.01 <0.01 <0.01 0.01 0.02 <0.01 <0.01 <0.01 <0.01 0.02	5 th percentile 25 th perc. 50 th perc. 75 th perc. 95 th perc. Female: n = 104 Male: n = 97	(Jönsson B., 2014)	2
China	2012	1.21±0.63	19.8 ± 10.7	3.53 ± 2.09	0.72 ± 0.34	0/9	-	-	Reference group (n=9)	(Zhou et al., 2014)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		1.22	18.7	2.88	0.68						
		9/9	9/9	9/9	9/9						
		726 ± 578	11400 ± 6760	43.5 ± 27.3	18.2 ± 8.87	3.87 ± 4.20			Fishery employee (n=39)		
		542	10400	41.0	17.3	2.60					
		39/39	39/39	39/39	39/39	39/39					
						1.17 ± 0.95			Fishery family (n=7)		
		189 ± 106	3150 ± 754	12.5 ± 4.01	6.11 ± 2.61	1.02			Mean ± SD		
		150	3540	11.7	6.72	7/7			Median		
		7/7	7/7	7/7	7/7				Number detected		
USA		1.5-3.9	14.7-55.8	2.1-9.6	-	-	-	-	Mean values in the general population resulting from various studies	(ATSDR, 2015)	2
Blood – whole											

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
Brazil	2003	5.4/2.2 (<0.6 - 15.3) 52.9%	10.7/8.4 (4.3 - 35) 1005	<20/<20 (<20) 0%	-	-	-		Whole-blood data were converted to a serum basis by multiplying by a factor of 2.	(Kannan et al., 2004)	2
		1.0/0.8 (0.6 - 1.9) 100%	13.5/12.7 (6.8 - 24) 100%	20/<20 (<20) 0%					Mean/median, (range) % positive Female: n = 17 Male: n = 10		
Colombia	2003	0.2/0.2 (<0.4) 0%	8.0/7.3 (4.6 - 13) 100%	6.1/5.6 (3.7 - 9.2) 100%	-	-	-	-	Female: n = 25		
		0.2/0.2 (<0.4 - 0.9) 10%	8.5/8.1 (6.2 - 14) 100%	6.2/5.9 (3.9 - 12.2) 100%					Male: n = 31		
Malaysia	2004	2.4/2.3 (1.2 - 4.2) 100%	11.7/12.7 (7.6 - 17) 100%	<10/<10 (<10) 0%	-	-	-	-	Female: n = 7		
		1.8/1.4	13.2/13.1 (6.2 -	<10/<10					Male: n = 16		

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		(1.2 - 6.8)	18.8)	(<10)							
		100%	100%	0%							
Poland	2003	1.3/1.2	33.3/33.8	21.9/23.2	-	-	-	-	Female: n = 15		
		(0.5 - 2.6)	(16 - 60)	(9.7 - 34)					Male: n = 10		
		100%	100%	100%							
		1.3/1.2	55.4/40.9	20.5/18.4							
		(<0.4 - 1.8)	(21 - 116)	(11 - 40)							
		90%	100%	100%							
South Korea	2003	3.8/2.9	15.1/11.3	88.1/30.9	-	-	-	-	Female: n = 25		
		(0.9 - 20)	(3.0 - 61.3)	(<15 - 256)					Male: n = 25		
		100%	100%	19%							
		4.1/3.4	27.1/27.1	35.5/26.8							
		(1.3 - 9.6)	(6.6 - 92)	(<15 - 71.4)							
		100%	100%	25%							
USA	2002	4.2/1.1	66/81	23/20	-	-	-	-	Female: n = 11		
		(<1 - 32)	(11 - 130)	(15 - 39)					Male: n = 19		
		55%	100%	100%							

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		4.0/2.2 (<1 - 20) 95%	73.2/72.0 (19 - 164) 100%	41.6/38.1 (11 - 88) 100%							
Sweden	2004	1.7 (0.4 - 28.4) 40/40 1.2 (0.4 - 2.5) 26/26	17.7 (1.7 - 37) 40/40 16.9 (4.6 - 32.8) 26/26	2.7 (LOD(0.5) -12.4) 40/40 2.1 (0.8 - 4.1) 26/26	0.2 (<0.1 - 0.6) 0.1 (<0.1 - 0.7) Total 42/66	-	-	-	Median, (range), number detected n = 40 (men; age 19-46 years) n = 26 (their mothers; age 46-75 years)	(Karrman et al., 2006)	2
		2.2, 2.6, 2.9, 2.0, 1.2	14.2, 15.2, 27.8, 15.0, 11.3	2.0, 1.7, 3.8, 3.9, 1.2	-	-	-	-	Female 36y, Male 27y, M41, F29, F24		
USA	2004- 2005	<i>EDTA</i> 19 ± 12 16 (5 - 32) <i>Heparin</i> 19 ± 12 15 (5 - 36)	<i>EDTA</i> 69 ± 104 46 (8-449) <i>Heparin</i> 68 ± 105 47 (7 - 450)	<i>EDTA</i> 535 ± 1050 106 (8-3730) <i>Heparin</i> 535 ± 1035 110	-	-	-	-	Employees at 3M; production, corporate, research Arithm. mean ± SD, median, (range) PFHxS: n = 7 PFOS: n =	(Ehresman et al., 2007)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
				(9 - 3670)					17 PFOA: n = 12		
Spain	2006	3.56 ± 2.97 2.92 (0.65 - 20.0)	7.64 ± 3.54 7.60 (0.76 - 16.2)	1.80 ± 0.66 1.65 (0.79 - 3.13)	0.34 ± 0.19 0.20 (nd - 0.84)	-	-	<0.44	n = 48 Arithm. mean ± SD, median, (range)	(Ericson et al., 2007)	2
Sweden	2007/2008	<0.30 <0.30 <0.30 1.9 1.6 - 2.1 3.3 - 4.3 1.4 0.78 - 1.5 0.96 - 3.3 1.70 1.7 - 1.9 1.6 - 2.0	0.28 00.30 - 0.39 0.34 - 0.36 24 23 - 26 21 - 25 14.9 12 - 14 12 - 17 13 11 - 13 10 - 11	4.8 6.3 - 17 17 - 20 8.50 10 - 20 19 - 23 151 146 - 150 134 - 153 127 114 - 131 101 - 122	0.11 0.14 - 0.39 0.30 - 0.46 0.18 0.36 - 0.55 0.31 - 0.47 0.79 1.0 - 2.2 1.1 - 2.5 1.0 0.73 - 1.2	-	-	-	Ski wax technicians World Cup in skiing n = 8 A: pre-season (Sep) B: during World Cup season (Dec-Mar) C: post season (Apr-Aug) = No sample was provided	(Nilsson et al., 2010)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		(0.031 - 0.1722) 12/12	0.470 12/12	(<0.209 - 0.492) 1 ^a /12					>LOD n = 12 primiparous women ^a Eleven additional samples were >LOD(0.01) but the blank level (0.209) was >50% of the detected concentratio ns.		
Sweden									^a Levels were >LOD(0.01) but the blank level (0.209) was >50% of the detected concentratio ns.		
Uppsala	1996	0.037	0.209	<0.209 ^a	-	-	-	-			
Uppsala	1997	0.030	0.207	<0.209 ^a							
Uppsala	1998	0.040	0.219	<0.209 ^a							
Uppsala	1999	0.044	0.213	<0.209 ^a							
Uppsala	2000	0.028	0.191	<0.209 ^a							
Göteborg	2001	0.028	0.258	<0.209 ^a							
Uppsala	2002	0.051	0.194	<0.209 ^a							
Lund	2003	0.025	0.153	<0.209							
Lycksele	2003-2004	0.016	0.123	<0.209							
Germany	2007-2009	- (<0.02	0.04 (<0.3 -	- (<0.15 -	-	-	-	-	Median, (range),	(Fromme et al., 2010)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		- 0.3)	0.11)	0.25)							
		6/201	145/201	4/201					No. >LOQ n = 201		
Sweden	1972	<0.005	0.023	0.019	-	-	-	-	n = 75	(Sundström et al., 2011)	2
	1976	<0.005	0.059	0.041					n = 78		
	1980	0.006	0.103	0.060					n = 116		
	1984/1985	0.006	0.172	0.078					n = 102		
	1988	0.016	0.211	0.148					n = 20		
	1990	0.010	0.202	0.106					n = 20		
	1992	0.011	0.222	0.111					n = 20		
	1994	0.015	0.219	0.106					n = 20		
	1995	0.028	0.214	0.139					n = 20		
	1996	0.016	0.224	0.111					n = 20		
	1997	0.016	0.237	0.138					n = 20		
	1998	0.028	0.212	0.128					n = 20		
	1999	0.023	0.234	0.120					n = 20		
	2000	0.024	0.213	0.124					n = 20		
	2001	0.017	0.198	0.098					n = 20		
	2002	0.027	0.210	0.118					n = 20		
	2003	0.025	0.179	0.098					n = 15		
	2004	0.017	0.188	0.100					n = 20		
	2007	0.017	0.122	0.086					n = 20		
	2008	0.014	0.075	0.074					n = 18		

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
France	2007	0.049/ 0.050 (0.040 - 0.066) 48/48	0.092/0.07 9 (<0.05 - 0.330) 43/48	0.082/0.07 5 (<0.05 - 0.224) 47/48	-	-	-	-	Arithm. mean/media n, (range), Number >LOD n = 48,	(Antignac et al., 2013)	2
Urine											
Canada	2008	<0.05, <0.05, 0.052, 0.054, 0.324, 0.318, 0.248	0.175, <0.05, <0.05, <0.05, 0.390, 0.074, <0.05	<0.05, <0.05, <0.05, <0.05, <0.05, <0.05, <0.05	-	-	<0.05, <0.05, <0.05, <0.05, <0.05, <0.05, <0.05	<0.05, <0.05, <0.05, <0.05, <0.05, <0.05, <0.05	Family members; M-52, F-48, M-23, M.21, F-18, M-17, M-15	(Beeson et al., 2012)	2
China	2010	0.0024 /0.001 1 (<LOD -0.035) 84/86	0.037/0.02 5 (0.002 - 0.184) 86/86	0.122/0.02 3 (0.0035 - 1.869) 86/86	0.00042/ 0.00030 (<LOD - 0.0024) 84/86	-	-	-	Arithm. mean/media n, (range) No. >LOD n = 86	(Zhang et al., 2013)	2
China	2012	0.042 ± 0.004 0.042 2/9 0.55 ± 0.57	0.016 ± 0.007 0.018 5/9 8.0 ± 9.0 4.7	0.019 ± 0.01 0.016 5/9 0.13 ± 0.095	-	-	-	-	Reference group (n=9) Fishery employee (n=39)	(Zhou et al., 2014)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability	
		0.45	39/39	0.11						Fishery family (n=7)		
		33/39		39/39								
			2.5 ± 1.5							Mean ± SD		
		0.065 ± 0.068	2.4	0.038 ± 0.022						Median		
			7/7	0.043						Number detected		
		0.055										
		4/7		7/7								
Stool (µg/kg)												
Canada	2008	<2.50, <2.50, <2.50, <2.50, <2.50, <2.50, <2.50	<2.50, <2.50, <2.50, <2.50, <2.50, <2.50, <2.50	<2.50, <2.50, <2.50, <2.50, <2.50, <2.50, <2.50	<2.50, <2.50, <2.50, <2.50, <2.50, <2.50, <2.50	<2.50, <2.50, <2.50, <2.50, <2.50, <2.50, <2.50	<2.50, <2.50, <2.50, <2.50, <2.50, <2.50, <2.50	<2.50, <2.50, <2.50, 4.80, <2.50, 7.80, 9.10	<2.50, <2.50, <2.50, <2.50, <2.50, 3.20, <2.50	Family members; M-52, F-48, M-23, M.21, F-18, M-17, M-15	(Beesoon et al., 2012)	2
Other human tissues (µg/kg)												
Spain	2008									Arithm.mean /median (range) (% detected)	(Perez et al., 2013)	2

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		1.8/1.2	-/-	60.2/20.9	-/-	16.6/5.1	15.8/0.3	-/-	Bone (rib)		
		(<2.4-13.8)	(<3)	(<3-234)	(<0.3)	(<0.98-169)	(<0.6-311)	(<0.001)			
		(5%)	(0%)	(55%)	(0%)	(70%)	(5%)	(0%)			
		3.2/2.3	4.9/1.9	-/-	-/-	13.2/1.5	9.9/1.4	24.8/1.4	Brain		
		(<4.5-14.4)	(<3-20.6)	(<2.4)	(<18)	(<1.3-102)	(<2.9-167)	(<3-336)			
		(5%)	(10%)	(0%)	(0%)	(25%)	(10%)	(30%)			
		20.8/18	75.6/55	2.0/1.5	7.1/1.5	14.7/4.5	-/-	6.2/30.8	Kidney		
		(<4.2-37)	(<6-269)	(<3-11.9)	(<3-55.4)	(<2.3-91.4)	(<6)	(<0.002-?)			
		(5%)	(45%)	(95%)	(10%)	(15%)	(0%)	(25%)			
		4.6/1.8	102/41.9	13.6/4.0	-/-	2.4/1.5	2.1/<0.001	-/-	Liver		
		(<3-20.6)	(<3-405)	(<3-98.9)	(<0.003)	(<1.45-20.2)	(<0.001-32)	(<0.001)			
		(10%)	(90%)	(45%)	(0%)	(5%)	(10%)	(0%)			
		8.1/5.7	29.1/28.4	29.2/12.1	2.8/1.4	20.7/<4.8	139/6.9	9.8/1.5	Lung		
		(<3.3-47.6)	(<3-61.8)	(<6-87.9)	(<2.7-20.4)	(<4.8-253)	(<3-1582)	(<2.9-82.8)			
			(89%)	(42%)	(11%)	(11%)	(42%)	(16%)	Autopsy samples, age 28-83y (mean 56 y). Varying cause of		

ANNEX XV – IDENTIFICATION OF PFHxS AS SVHC

Location	Date	Concentration (µg/L)							Remarks	Reference	Reliability
		(32%)							death.		