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): Nonadecafluorodecanoic acid (PFDA) [1] and its sodium [2] and ammonium [3] salts

EC Number(s): 206-400-3 [1], Not applicable [2], 221-470-5 [3]

CAS Number(s): 335-76-2 [1], 3830-45-3 [2], 3108-42-7 [3]

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ABBREVIATIONS

APFO	Ammonium perfluorooctanoate
B	Bioaccumulative
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BMF	Biomagnification factor
BSAF	Biota-sediment accumulation factor
CL_{renal}	Renal clearance
CL_{total}	Total clearance
CLP	Classification, labelling and packaging
CMR	Carcinogenic, mutagenic and toxic for reproduction
EC	European Commission
EU	European Union
i.a.	inter alia
i.p.	Intraperitoneal
i.v.	Intravenous
L-FABP	Liver fatty acid binding protein
P	Persistent
PBT	Persistent, bioaccumulative and toxic
PFAA	Perfluorinated alkyl acid
PFAS	Perfluorinated alkyl substances
PFBA	Perfluorobutanoic acid
PFBS	Perfluorobutane sulfonate
PFC	Fluorocarbons, perfluorocarbons
PFCA	Perfluorinated carboxylic acid
PFDA	Perfluorodecanoic acid
PFDoDA	Tricosafluorododecanoic acid
PFD-S	Sodium perfluorodecanoate
PFD-A	Ammonium perfluorodecanoate
PFHpA	Perfluoroheptanoic acid
PFHxS	Perfluorohexane sulfonate
PFNA	Perfluorononanoic acid
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctane sulfonate
PFSA	Perfluorinated sulfonic acid
PFTeDA	Heptacosafluorotetradecanoic acid
PFTrDA	Pentacosafluorotridecanoic acid
PFUnDA	Perfluoroundecanoic acid
RAC	Risk assessment committee
REACH	Registration, evaluation, authorisation and restriction of chemicals
SVHC	Substances of very high concern
ThOD	Theoretical oxygen demand
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): Nonadecafluorodecanoic acid (PFDA) [1] and its sodium [2] and ammonium [3] salts

EC Number(s): 206-400-3 [1], Not applicable [2], 221-470-5 [3]

CAS number(s): 335-76-2 [1], 3830-45-3 [2], 3108-42-7 [3]

- The substances are proposed to be identified as a substance meeting the criteria of Article 57 (c) of Regulation (EC) No 1907/2006 (REACH)[1] owing to the adopted opinion (European Chemicals Agency, 2015a) by the Committee for Risk Assessment (RAC) which has agreed that the substance and its sodium and ammonium salts meet the criteria for classification as toxic for reproduction category 1B according to Regulation (EC) No 1272/2008 (CLP)[2]. It is foreseen that this proposal for harmonised classification and labelling will be voted on by the REACH Committee in September 2016 for inclusion in the 10th ATP to CLP.
- It is proposed to identify the substance(s) as persistent, bioaccumulative and toxic (PBT) according to Article 57 (d) of Regulation (EC) No 1907/2006 (REACH).

Summary of how the substance meets the criteria set out in Article 57 (c) and 57 (d) of REACH.

As justified in Section 1, the abbreviation PFDA refers to the acid (PFDA) as well as to its ammonium (PFD-A) and sodium (PFD-S) salts where these are not specified.

PFDA belongs to the chemical group of long-chain perfluorinated carboxylic acids (PFCAs). The substances in this group have a highly similar chemical structure: a perfluorinated carbon chain and a carboxylic acid group. They differ only in the number of CF_2-groups whereas all other fragments are the same within the group. As a result of comparing the experimental and estimated data of other PFCAs with experimental and estimated data on PFDA, it can be concluded that with increasing chain length water solubility decreases and the sorption potential increases (see Annex I). It can be stated with sufficient reliability that the behaviour of the PFCAs follows a regular pattern.

Seven entries of long-chain PFCAs have already been included into the Candidate List:

[1] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC.

[2] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

Table 1: PFCAs on the Candidate List

EC number	CAS number	Substance name	Length of the carbon chain	Details on SVHC-identification	Reference
223-320-4	3825-26-1	Ammonium pentadecafluorooctanoate (APFO)	8	Toxic for reproduction (Article 57 c); PBT (Article 57 d)	European Chemicals Agency (2013a)
206-397-9	335-67-1	Pentadecafluorooctanoic acid (PFOA)	8	Toxic for reproduction (Article 57 c); PBT (Article 57 d)	European Chemicals Agency (2013b)
206-801-3	375-95-1 [1] 21049-39-8 [2] 4149-60-4 [3]	Perfluorononanoic acid (PFNA) [1] and its sodium [2] and ammonium salts [3]	9	Toxic for reproduction (Article 57 c); PBT (Article 57 d)	European Chemicals Agency (2015b)
218-165-4	2058-94-8	Henicosafluoroundecanoic acid (PFUnDA)	11	vPvB (Article 57 e)	European Chemicals Agency (2012a)
206-203-2	307-55-1	Tricosafluorododecanoic acid (PFDoDA)	12	vPvB (Article 57 e)	European Chemicals Agency (2012b)
276-745-2	72629-94-8	Pentacosafluorotridecanoic acid (PFTrDA)	13	vPvB (Article 57 e)	European Chemicals Agency (2012c)
206-803-4	376-06-7	Heptacosafluorotetradecanoic acid (PFTeDA)	14	vPvB (Article 57 e)	European Chemicals Agency (2012d)

Toxicity for reproduction, category 1B:

In its opinion of 4 December 2015 on the proposal for harmonised classification and labelling at EU level of *Nonadecafluorodecanoic acid (PFDA) and its ammonium (PFD-A) and sodium (PFD-S) salts* (European Chemicals Agency, 2015a), ECHA´s Risk Assessment Committee (RAC) concluded that the evidence is sufficiently convincing to classify PFDA for developmental effects as Repr. 1B, H360Df ("May damage the unborn child. Suspected of damaging fertility") in accordance with the CLP criteria (Regulation (EC) No 1272/2008). It is foreseen that this proposal for harmonised classification and labelling will be voted on by the REACH Committee in September 2016 for inclusion in the 10th ATP to CLP.

Therefore, PFDA and its sodium and ammonium salts meet the criteria of Article 57 (c) of the REACH regulation.

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

Persistence

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

In general, the persistence of PFDA can be explained by the shielding effect of the fluorine atoms, blocking *e.g.* nucleophilic attacks to the carbon chain. High electronegativity, low polarizability and high bond energies make highly fluorinated alkanes the most stable organic compounds. It is not expected that the carboxylic group in PFCAs alters this persistence of these chemicals. The persistence of six PFCAs (PFOA/APFO, PFNA and C_{11}-C_{14} PFCAs) (P and vP) was already confirmed by the Member State Committee (see Table 1) (European Chemicals Agency, 2012a-d, 2013a-b, 2015b).

Therefore, based on the knowledge of the stability of the C-F bond and the read-across approach with PFOA, PFNA and C_{11}-C_{14} PFCAs it is concluded that PFDA is not degraded 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

Due to its expected notable water solubility, PFDA is, like the other PFCAs expected to be quickly excreted in fish via gill permeation. Hence, bioconcentration in gill-breathing organisms is not the most relevant endpoint to consider, as reflected by the differences between bioaccumulation data for gill- and air-breathing organisms. Field studies show that air-breathing organisms are more likely to bioaccumulate PFDA and other PFCAs compared to gill-breathing organisms. Based on the BCF values for PFDA it cannot be excluded that PFDA is bioaccumulative in fish: BCF values range from 450 to 2700 for carcass, liver and blood. Conclusions on bioaccumulation should be based on whole body values and carcass is seen as a good approximation for whole body. Based on the BCF of carcass PFDA does not bioaccumulate in fish. However, as shown in this report, PFDA does not accumulate in lipid but rather binds to protein and membrane phospholipids, therefore the carcass or whole-body BCF values are less relevant. Based on the BCF value in the blood of rainbow trout (2700±350), PFDA can be considered bioaccumulative.

Annex XIII (section 3.2.2) defines information which shall be taken into account in the assessment and can be used to draw conclusions on the assessment even when the numerical criterion is not applicable. Such data are, for example, data on the bioaccumulation potential in terrestrial species, such as elevated levels in endangered species. PFDA was found in terrestrial species as well as in endangered species as shown for the polar bear and the beluga whale. These findings indicate a bioaccumulation potential.

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 assessed into account. For PFDA, gestational and lactational exposure in humans has been shown, which is of special concern as the foetus and newborn babies are highly vulnerable to exposure by xenobiotic substances. On top of that, data from human body fluids clearly provide quantitative proof of the bioaccumulation of PFDA; elimination half-lives in humans are ≥ 4 years. In addition, recent studies, taking into account relevant

confounding factors, show that PFDA blood concentrations in humans increase with increasing age.

Finally, Annex XIII (section 3.2.2 (c)) foresees that the potential for biomagnification in food chains of a substance is assessed. The available field data provide evidence that bioaccumulation and trophic magnification do occur in certain food webs in the environment. For PFDA, field studies provide trophic magnification factors (TMFs) or biomagnification factors (BMFs) in aquatic and terrestrial food chains. When air breathing organisms are the top predators in these food chains, biomagnification could be demonstrated by calculation of TMFs and BMFs to be > 1 in several food chains, for example for wolves, dolphins and beluga whales.

The data summarised above is in high accordance with the bioaccumulation data on the other PFCAs. Altogether these show a regular pattern of bioaccumulation which depends on the chain-length of the perfluorinated alkyl chain (see Annex I for read-across as part of the weight-of evidence approach).

Conclusion:

1. PFDA accumulates in humans.
   a. PFDA is present in human blood of the general population. PFDA has also been detected in human brain, lungs and kidney.
   b. Elimination half-lives are ≥ 4 years, which is longer than for PFNA and PFOA (see Table 14).
   c. PFDA levels increase with age after adjusting for relevant confounding factors.

2. There is evidence that PFDA preferentially bioaccumulates in air-breathing mammals, including endangered species and humans.
   a. BMFs range from 2.4 to 8.8 based on estimated whole body values in marine food web.
   b. TMFs range from 2.2 to 12.1 referring to either whole body measurements or estimated whole body values in marine wood web.

3. For part of the aquatic food chains investigated, PFDA accumulates in water-breathing animals.
   a. BCFs range from 450 (carcass) to 2700 (in blood).
   b. whole body BAFs range from 714 to 7943.
   c. whole body BMFs range from 0.21 to 4.4.
   d. whole body TMFs range from 0.39 to 3.67 in aquatic piscivorous food webs.

4. The bioaccumulation data on PFDA in environmental species, in laboratory mammals and in humans are consistent with the data on other long-chain perfluorinated carboxylic acids. Recent mechanistic bioconcentration models explain the substantial bioaccumulation of PFCAs by taking into account the observed pattern of animal tissue distribution, the relationship between chain length and bioaccumulation and the species and gender-specific variation in elimination half-life.

To conclude, taken all available information together in a weight-of-evidence approach, the elimination half-lives from humans and other mammals show that PFDA bioaccumulates. The available field data also indicate that bioaccumulation and trophic magnification occur in certain food webs in the environment. The data on PFDA are in line with the expected regular pattern of fate properties of the already assessed PFOA/APFO, PFNA and C_{11}-C_{14} PFCAs. Therefore, it is considered that the B criterion of REACH Annex XIII is fulfilled. Whether the vB criterion is fulfilled has not been assessed.

Toxicity

There is evidence based on the RAC opinion on PFDA and its sodium and ammonium salts that these substances meet the criteria for classification as toxic for reproduction in accordance with Article 57 (c) of the REACH Regulation. It is foreseen that this proposal for harmonised classification and labelling will be voted on by the REACH Committee in September 2016 for inclusion in the 10th ATP to CLP.

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

Conclusion on PBT

In conclusion, PFDA and its sodium and ammonium salts meet the criteria for a PBT substance according to Article 57 (d) of the REACH Regulation.

Registration dossiers submitted for the substance: No

PART I

Justification

1. Identity of the substance and physical and chemical properties

The free nonadecafluorodecanoic acid (PFDA) stays in equilibrium with nonadecafluorodecanoate (PFD), the conjugate base, in aqueous media in the environment and in organisms, as well as in the laboratory. The physico-chemical properties of PFDA and PFD are different. Therefore, the expected environmental fate will depend on the environmental conditions, which influence the equilibrium between base and acid (pH and pKa).

The sodium (PFD-S) and ammonium (PFD-A) salts are very soluble in water. In aqueous solution at neutral pH they will be present as the anion (PFD) and the sodium or the ammonium cation. The dissolved anion (PFD) will stay in equilibrium with the corresponding acid (PFDA) in aqueous media.

It is not possible with currently available analytical methods to distinguish between PFD and PFDA in samples. In the literature, the concentrations reported in environmental and human monitoring studies will always include both species (PFDA and PFD).

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

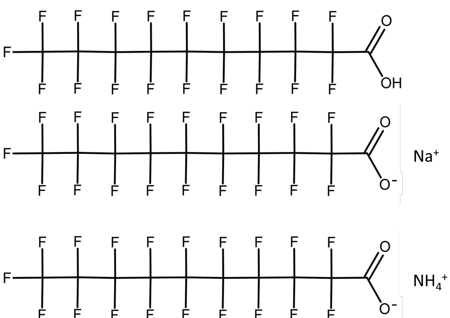
For simplicity, in the discussions and conclusions in this document, PFDA is usually referred to. Based on the reasoning above, the conclusions are, however, considered valid for PFD-S and PFD-A as well.

1.1. Name and other identifiers of the substance

Table 2: Substance identity

EC number:	206-400-3 [1], Not applicable [2], 221-470-5 [3]
EC name:	Nonadecafluorodecanoic acid [1] Not applicable [2] Ammonium nonadecafluorodecanoate [3]
CAS number (in the EC inventory):	335-76-2 [1], 3830-45-3 [2], 3108-42-7 [3]
CAS name:	Decanoic acid, 2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-nonadecafluoro- [1] Decanoic acid, 2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-nonadecafluoro-, sodium salt (1:1) [2] Decanoic acid, 2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-nonadecafluoro-, ammonium salt (1:1) [3]
IUPAC name:	Nonadecafluorodecanoic acid [1] Sodium nonadecafluorodecanoate [2] Ammonium nonadecafluorodecanoate [3]
Index number in Annex VI of the CLP Regulation	It is foreseen that the harmonised classification and labelling proposal will be voted on by the REACH Committee in September 2016. (607-720-00-X, 10th ATP)
Molecular formula:	$C_{10}HF_{19}O_2$ [1] $C_{10}F_{19}NaO_2$ [2] $C_{10}H_4F_{19}NO_2$ [3]
Molecular weight range:	514.08 g/mol [1] 536.06 g/mol [2] 531.11 g/mol [3]
Synonyms:	PFDA C_{10}-PFCA Perfluorodecanoic acid

Structural formula:



1.2. Composition of the substance

Name: Nonadecafluorodecanoic acid (PFDA)

Description: Mono-constituent substance

Degree of purity: Minimum concentration level: 80%

Nonadecafluorodecanoic acid, as well as its sodium and ammonium salts, are mono-constituent substances. 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)

The following substances belong to the same substance category of long-chain perfluorinated carboxylic acids (PFCAs). Please see Annex I for the read across justification.

Table 3: Long-chain PFCAs

EC number	CAS number	Substance name	Length of the carbon chain
223-320-4	3825-26-1	Ammonium pentadecafluorooctanoate (APFO)	8
206-397-9	335-67-1	Pentadecafluorooctanoic acid (PFOA)	8
206-801-3	375-95-1	Perfluorononanoic acid (PFNA)	9
218-165-4	2058-94-8	Henicosafluoroundecanoic acid (PFUnDA)	11
206-203-2	307-55-1	Tricosafluorododecanoic acid (PFDoDA)	12
276-745-2	72629-94-8	Pentacosafluorotridecanoic acid (PFTrDA)	13
206-803-4	376-06-7	Heptacosafluorotetradecanoic acid (PFTeDA)	14

1.4. Physicochemical properties

Table 4: Overview of physicochemical properties (PFDA)

Property	Value	Reference/source of information	Comment (e.g. measured or estimated)
Physical state at 20°C and 101.3 kPa	The substance is a solid		
Melting/freezing point	87.4-88.2 °C	Hare *et al.* 1954	Measured
Boiling point	218 °C 203.4 °C 219.4 °C	Kauck and Diesslin 1951 Kaiser *et al.* 2005 Kaiser *et al.* 2005	Measured Estimated Estimated
Vapour pressure	3.1 to 99.97 kPa (129.6 to 218.9 °C)	Kaiser *et al.* 2005	Calculated
Density	No data		
Water solubility	5.14 g/L at 25 °C	Kauck and Diesslin 1951	Measured
Partition coefficient n-octanol/water (log value)	6.5 (temp. not specified)	Wang *et al.* 2011	Estimated using COSMOtherm. PFDA has surface active properties.
Dissociation constant (pKa)	<1.6 2.58	Vierke *et al.* 2013 Moroi *et al.* 2001	Estimated values. Dissociation behaviour is discussed in Annex I.

Physicochemical properties of the other C_8- to C_{14}-PFCAs are provided in Table A.2 in Annex I.

2. Harmonised classification and labelling

The RAC has adopted an opinion at RAC-35 that nonadecafluorodecanoic acid (PFDA) and its ammonium (PFD-A) and sodium (PFD-S) salts meet the following criteria for classification and labelling (European Chemicals Agency, 2015a) as indicated in Table 5.

It is foreseen that the harmonised classification and labelling proposal will be voted on by the REACH Committee in September 2016.

Table 5: The RAC opinion on classification and labelling in accordance with Regulation No 1272/2008 (CLP)

Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s)	Hazard statement code(s)	Suppl. Hazard statement code(s)		
607-720-00-X (10th ATP)	Nonadecafluorodecanoic acid [1], ammonium nonadecafluorodecanoate [2], sodium nonadecafluorodecanoate [3]	206-400-3 [1]; 221-470-5 [2]; - [3]	335-76-2 [1]; 3108-42-7 [2]; 3830-45-3 [3]	Carc. 2 Repr. 1B Lact.	H351 H360Df H362	GHS08 Dgr	H351 H360Df H362	-	-	-

H360Df: May damage the unborn child. Suspected of damaging fertility.

3. Environmental fate properties

3.1. Degradation

3.1.1. Abiotic degradation

3.1.1.1. Hydrolysis

There are no studies on the hydrolysis of PFDA available. Based on the data given in Annex I, results of studies of structurally similar substances of the same chemical group could be used to evaluate the hydrolysis of PFDA.

The analogue PFOA (C_8-PFCA) is hydrolytically stable under environmental conditions with a hydrolytic half-life greater than 97 years (European Chemicals Agency, 2013b).

Hence, based on read across to PFOA (Annex I), PFDA is considered to be hydrolytically stable under environment conditions.

3.1.1.2. Phototransformation/photolysis

3.1.1.2.1. Phototransformation in air

There are no studies on phototransformation in air for PFDA available. However, the atmospheric lifetime of PFOA has been predicted to be 130 days (conclusion by analogy from short-chain perfluorinated acids) (European Chemicals Agency, 2013b).

3.1.1.2.2. Phototransformation in water

The photochemical decomposition of long-chain PFCAs in water by use of persulfate ion ($S_2O_8^{2-}$) in an aqueous/liquid CO_2 biphasic system was examined by Hori *et al.* (2005) (Reliability = 2). The decompositions after 12 hours in the biphasic system were 100% for PFDA. The reaction product was mainly F^- (73.4 %, of (moles of F- formed)/(moles of fluorine content in PFDA)) and the minor reaction products were shorter chain PFCAs ($C_nF_{2n+1}COOH$; n=1-6). Since the conditions in this studies are not relevant for an aqueous environment (wave length used for irradiation <300 nm), the studies were not described in detail.

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

3.1.1.3. Summary on abiotic degradation

In general, the perfluorinated carboxylic acids are extremely stable. As there are no degradation studies under relevant environmental conditions available for PFDA, data from similar substances need to be considered and discussed. Based on the data given in Annex I, results of studies of structurally similar substances of the same chemical group are used to evaluate the abiotic degradation of PFDA.

The data on PFOA indicate that abiotic degradation in the atmosphere is expected to be slow (atmospheric lifetime = 130 days; conclusion by analogy from short-chain perfluorinated acids). Under relevant environmental conditions PFOA is hydrolytically stable (estimated half-life > 97 years) and does not undergo direct photodegradation in natural waters. The estimated half-life for indirect photolysis (Fe_2O_3) is greater than 349 days.

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

3.1.2. Biodegradation

3.1.2.1. Biodegradation in water

3.1.2.1.1. Estimated data

For PFDA a half-life in water of 4722 days and a half-life in soil of 9444 days was estimated (Lambert *et al.* 2011). Nevertheless, these estimations can be assumed to be low because 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.

3.1.2.1.2. Screening tests

There are no studies available for the PFDA. Based on the data given in Annex I, results of studies of a structurally similar substance (PFOA) of the same chemical group could be used to evaluate the biodegradation of PFDA.

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

In a further test the ready biodegradability (OECD 301 C) of PFOA and its ammonium salt was investigated (using 100 mg/L test substance and 30 mg/L activated sludge). Only 5% and 7% degradation was observed by BOD for PFOA and its ammonium salt, respectively (National Institute of Technology and Evaluation, 2007) (Reliability 2).

In summary, based on the read across to PFOA (Annex I) PFDA is considered to be not readily biodegradable.

3.1.2.1.3. Simulation tests (water and sediments)

For PFDA no experimental degradation test is available.

3.1.2.2. Biodegradation in soil

For PFDA no experimental degradation test is available.

3.1.2.3. Summary and discussion on biodegradation

Screening studies for PFDA are not available. However, results from screening studies of PFOA and PFNA used in a read-across approach as described in Annex I indicate that PFDA is not readily biodegradable.

Results from non-standard degradation studies (aerobic/anaerobic biodegradation simulation test described in European Chemicals Agency, 2013b) of the chemically similar substance PFOA, used in a read-across approach as described in Annex I, indicate that PFDA is not biodegradable. The results on PFOA provide good evidence that no biodegradation in water, soil and sediment occurs. Since the stability of PFCAs is in general based on the stability of the fluorinated carbon chain it can be concluded that also for PFDA no biodegradation in water, soil and sediment can be expected. Thus, it can be assumed that PFDA is not biodegradable.

3.1.3. Summary and discussion of degradation

For PFDA there is no degradation study under environmental conditions available. Therefore, data from a chemically similar substance are considered in a read-across approach (see Annex I for further details). Generally, it is known that the bond between carbon and fluorine is one of the most stable ones in organic chemistry and not subject to degradation by microorganisms occurring in the environment.

A number of studies for the shorter chain homologue PFOA show that this substance is extremely persistent and does not undergo abiotic or biotic degradation at all under environmental conditions. The persistence of PFOA was already confirmed by the Member State Committee that identified the substance as SVHC i.a. based on its PBT properties (European Chemicals Agency, 2013b).

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

The stability of organic fluorine compounds has been described in detail by Siegemund *et al.* (2000). When all valences of a carbon chain are satisfied by fluorine, the zig-zag-shaped carbon skeleton is twisted out of its plane in the form of a helix. This situation allows the electronegative fluorine substituents to 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.

Based on their molecular properties, it is thus clear that researchers could not measure degradation of PFOA or its salts. Considering the organic chemistry of this substance group it seems very likely that a carbon chain being two CF_2-groups longer is as persistent as a shorter chain. We therefore conclude that PFDA is as resistant to degradation as has been shown for PFOA.

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

3.2. Environmental distribution

Based on information in the Table entitled “Basic substance information and physical chemical properties relevant to justify read across in the PBT assessment” in the support documents for PFCAs, the distribution of PFCAs is influenced by the pH of the environment (please see the references listed in Table 1 above). The water solubility, the adsorption potential and hence the distribution in the environment express a regular pattern depending on the alkyl chain length of the PFCA.

3.3. Bioaccumulation

3.3.1. General remarks

According to section 3.2.2 (b) and (c) of Annex XIII of REACH not only the numerical bioaccumulation (B) criterion based on bioconcentration factors can be used to assess the bioaccumulation potential of a substance but also other information can be used in a weight of evidence approach. This additional information which includes elevated levels in

biota, information on the ability of the substance to biomagnify in the food chain, data from analysis of human body fluids or tissues and assessment of toxicokinetic behaviour of the substance should also be considered for the assessment using a weight-of-evidence approach.

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

3.3.2. Bioaccumulation in aquatic organisms (pelagic and sediment organisms)

3.3.2.1. Bioconcentration factor BCF

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 be determined kinetically by using the uptake rate k_1 and the depuration rate k_2:

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

There is one study available which determined the BCFs for PFDA. In this study, rainbow trout (*Oncorhynchus mykiss)* were exposed in a flow-through system for 12 days followed by a depuration time of 33 days in fresh water to determine tissue distribution and bioconcentration (Martin *et al.* 2003a). For determination of bioconcentration, juvenile fish (5-10g) were exposed simultaneously to PFCAs of varying chain length. No adverse effects were observable based on fish mortality, growth and liver somatic index. The exposure concentration of each PFCA was analytically checked. PFCA concentrations were stable throughout the uptake phase. For PFDA the measured concentration was 0.71 µg/L with a relative standard deviation of 24%. There was an initial decrease between 0.25 h and 24 h which is considered to be caused by the rapid uptake of the PFCAs. At 7 occasions during the uptake period and 9 occasions during the depuration phase, three fish from the exposure tank and one fish from the control were removed to determine the kinetics of uptake and depuration. The BCFs (carcass, blood and liver) were determined on the basis of the uptake and depuration kinetics and results are given in Table 6. All tissue concentrations were corrected for growth dilution. Additionally, for the tissue distribution study, four immature trout (30 – 48 g) were exposed in separate tanks but under the same uptake conditions. The BCFs reported from laboratory experiments are summarised in Table 6.

The tissue distribution study showed that, unlike lipophilic organic compounds, PFCAs did not preferentially accumulate in adipose tissue. Hence a lipid-normalisation of the BCFs would not be reasonable. PFCA concentrations were highest in blood, kidney, liver and gall bladder and low in the gonads, adipose and muscle tissue. Within the blood, the plasma contained between 94 – 99 % of PFCA, with only a minor fraction detectable in the cellular fraction. Recovery from hearts and spleen was low (<10%). Based on high

blood, liver and gall bladder concentrations and slow depuration the authors assume that PFCA enter the enterohepatic recirculation in fish. That means the compounds are continuously transferred between the different organs (Martin *et al.* 2003a).

Table 6: Measured growth corrected bioconcentration factors (BCF) of PFDA

Location	Species (tissue)	BCF	Reliability	Reference
Laboratory	*Oncorhynchus mykiss* Rainbow trout (carcass)	450 ± 62	2	Martin *et al.* 2003a
Laboratory	Rainbow trout (blood)	2700 ± 350		
Laboratory	Rainbow trout (liver)	1100 ± 180		

Conclusion:
Unlike lipophilic organic compounds, PFCAs do not preferentially accumulate in adipose tissue but in the liver and blood rich tissues. Based on the BCF for blood, PFDA may be regarded as bioaccumulative. Although conclusions on bioaccumulation should normally be based on whole body values for lipid-accumulating substances, for this case the BCF for blood and liver are considered most relevant as PFCAs preferentially bind to protein and membrane phospholipids rather than lipid. Based on the BCF for carcass representing the whole-body, it cannot be concluded that PFDA is bioaccumulative. However, bioconcentration values in fish may not be the most relevant endpoint to consider because other mechanisms of accumulation might be more relevant.

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:

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

The 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 *et al.* 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 since it cannot be excluded that the tested organisms did not take up the relevant chemicals via the diet.

BAFs for PFDA are summarised in Table 7. Loi *et al.* (2011) investigated a subtropical pelagic food web in a nature reserve including phytoplankton (n=1), zooplankton (n=2), gastropod (n=3), worm (n=2-3), shrimp (n=2-3), fish (n=2-6), and water bird (n=3). Samples were collected between 2008 and 2010. Surface water (n=12) and sediment samples (n=6) were collected concurrently with the biota samples. Liver samples from water birds were all collected in 2003. A BAF of 765 was derived for PFDA in phytoplankton.

Labadie and Chevreuil (2011) investigated the partitioning of various PFCAs in the Orge River, an urban tributary of the Seine River. Bioaccumulation and tissue distribution were studied in European chub (*Leuciscus cephalus*), a common cyprinid in European

freshwater and a benthopelagic fish. 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. In agreement with the findings made by Martin *et al.* (2003a), tissue distribution shows that PFDA is especially accumulated in blood and liver. The results of this study are summarised in Table 7. All values are above 5000, although this trigger value relates to whole body BCFs. This study thus suggests that PFDA is very bioaccumulative.

In a study conducted by Furdui *et al.* (2007), individual whole body homogenates of 4 year old lake trout (*Salvelinus namaycush*) sampled and collected in 2001 from Lake Superior (n= 10), Lake Michigan (n = 10), Lake Huron (n = 10), Lake Erie (n = 6) and Lake Ontario (n = 10) were analysed for PFCAs. The samples from all five lakes showed similar concentrations of PFCAs. Whole body BAFs were calculated by dividing the average concentration of PFASs in lake trout by the average concentration in water from each lake.

Furthermore, BAFs were calculated from water and biota concentrations reported in the studies of Loi *et al.* (2011) and Houde *et al.* (2006) (see Table 7). The study of Houde is described in detail in section 3.3.2.4. Variations in calculated BAFs originate from variations in measured concentrations in fish.

All studies are field studies and were neither growth corrected nor normalised to a lipid content. BAFs were calculated based on wet weight.

Table 7: Examples of measured bioaccumulation factors (BAF) of PFDA

Location	Species (tissue)	BAF	Reliability	Reference
Mai Po Marshes Nature Reserve	phytoplankton	765	2	Loi *et al.* 2011
all of the Great Lakes	*Salvelinus namaycush* Lake trout / water concentration from each Great Lake (whole)	7943	2	Furdui *et al.* 2007
Orge river	*Leuciscus cephalus* European chub (plasma)	158489	2	Labadie and Chevreuil, 2011
	European chub (liver)	15848		
	European chub (gills)	12589		
	European chub (gonads)	7943		
	European chub (muscle)	2511		
South Carolina,	*Mugil cephalus* Striped mullet	2143	2	Houde *et al.* 2006

Charleston	(whole)			
	Lagodon rhomboides Pinfish (whole)	714		
	Sciaenops ocellatus Red drum (whole)	2619		
	Micropogonias undulatus Atlantic croaker (whole)	2476		
	Leiostomus xanthurus Spotfish (whole)	2286		
	Cynoscion nebulosus Spotted seatrout (whole)	2619		
Mai Po Marshes Nature Reserve	*Mugil cephalus* Grey mullet (whole)	1473	2	Loi *et al.* 2011
	Oreochromis mossambicus Mozambique tilpia (whole)	2122		
	Channa asiatica Small snakehead (whole)	5368		
	Elops saurus Ladyfish (whole)	1421		
	Ambassis miops Flag-tailed glass perchlet (whole)	1035		

Conclusion: BAFs vary for PFDA. Some BAF values indicate that there is no bioaccumulation whereas other values indicate that PFDA is very bioaccumulative. The majority of data does however indicate that PFDA is bioaccumulative.

3.3.2.3. Biota-sediment accumulation factors (BSAFs)

For evaluating the bioaccumulation potential of chemicals also biota-sediment accumulation factors (BSAFs) can be used. BSAFs are field-based measurements for the chemical concentration in the organism and the sediments calculated according to the following equation:

$$BSAF = \frac{C_{Biota}}{C_{Sediment}}$$

where C_{Biota} is the chemical concentration in the organism at steady-state, and $C_{Sediment}$ is the sediment chemical concentration at steady-state (Conder *et al.* 2012).

For assessing the bioaccumulation from fresh water sediments (n=3), a study using oligochaete blackworm (*Lumbriculus variegatus)* was commenced (Higgins *et al.* 2007). This benthic-dwelling worm species is a deposit feeder and serves as an entry point for sediment-bound contaminants into food webs. During the screening one uncontaminated field sediment, laboratory-spiked with PFDA, and two contaminated field sediments were applied, respectively. After attaining steady state (56 days) in all cases the calculated BSAFs ranged from 0.06 to 1.02. The data were also lipid–normalised. Lipid-normalization was based on lipid analysis in one worm for each jar. However, lipid-normalization is not straight forward in the case of PFDA as this substance is ‚proteinophilic' (Kelly *et al.* 2009). These results indicate an uptake of PFDA during worm´s sediment ingestion.

Table 8: Biota-sediment accumulation factors (BSAF) analysed with blackworm (*Lumbriculus variegatus*)

Location	Sediment	BSAF		Reliability	Reference
		Lipid normalised	non lipid-normalised	2	
Downstream from two WWTP, California	Sediment 1 (CA1 (56 days	77 ± 11	0.06 ± 0.4		Higgins *et al.* 2007
	Sediment 2 (CA2 (56 days	107 ± 16	0.59 ± 0.08		
Laboratory	estimated steady-state values	35 ± 15	1.02 ± 0.23		

<u>Conclusion:</u> One study is available providing BSAFs for PFDA. The results of this study indicate a higher concentration in the benthic-dwelling worm than in the surrounding environment if data are lipid-normalised. However, this approach is not straight-forward because PFDA does not enrich in lipids. Non-lipid normalised BSAF do not show an increased concentration in the worms. However, the data should be used with caution. BSAF are influenced by sorption characteristics. These are usually assessed by the K_{OC} which is calculated on the basis of the K_{ow}. However, as discussed this metric is not appropriate for PFDA.

3.3.2.4. 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 cannot 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:

$$BMF = \frac{C_{biota}}{C_{diet}}$$

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

BMF values based on 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 this is not necessarily the case. 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 (see below) with regard to food webs. There are biological, ecological factors which can influence the outcome of a 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 may therefore have an influence. The uncertainties of field studies have been addressed and discussed by Borgå *et al.* (2012). As the authors actually refer to field based trophic magnification factors a summary of the discussion has been included in chapter 3.3.2.5. Trophic magnification factors. The report of ECETOC on a weight of evidence PBT/vPvB assessment has, in the chapter on bioaccumulation, given a review on various issues concerning field studies (ECETOC, 2014).

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 sampled. 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. As shown by Kudo *et al.* (2000) PFCAs cause hepatomegaly in rodents which is an indicator for hepatotoxicity. This study investigated PFCAs with 7–10 carbon chain lengths. Upham *et al.* (1998) showed in their study that PFOA and PFDA can inhibit gap junctional intercellular communication in a dose-dependent manner. This mode-of-action has been

linked to the tumour-promoting properties of many carcinogens and might explain hepatocarcinogenic effects of PFASs.

At present, no internationally accepted trigger value for BMF exists. The question whether only enrichment of a substance in predator is proof of biomagnification or whether transfer from prey to predator already may be sufficient is still up for discussion. In a scientific context a BMF or TMF above 1 suggest biomagnification (Conder *et al.* 2012). However, also a BMF or TMF below 1 may be of concern as this indicates that a substance is taken up into the organism and the uptake may cause an adverse effect. A high accumulation in representatives at lower trophic levels directly causing adverse effects may cause reduced prey supply. In case of a reduced supply chain, this may rather affect predators than the trophic magnification of pollutants. Thus no observable trophic magnification or an observed trophic dilution as single fact do not necessarily imply that there is no potential risk (Ehrlich *et al.* 2011). Experiences with revision or development of test guidelines show that even substances known to be bioaccumulative may show BMF < 1 in laboratory test systems (Inoue *et al.* 2012). However, keeping this in mind, a BMF ≥ 1 will be used here as indicator for field data for the sake of decision making.

Laboratory derived BMF values and field-based BMFs for PFDA are discussed below and summarised in Table 9. None of the studies were lipid- or protein-normalised.

Martin *et al.* (2003b) exposed juvenile rainbow trout (*Oncorhynchus mykiss*) for 34 days to PFCAs in the diet, followed by a 41 day depuration period. Although the authors describe their results as BAF the results of this study should rather be assigned as BMFs according to the above mentioned definition as uptake only derived from the diet. During the uptake period, animals were daily fed with spiked food at a rate of 1.5 % food per body weight. Spiked food concentrations were 0.39 mg/kg for PFDA. Water samples collected before and after feeding revealed no traces of PFCAs in water. At 6 occasions during uptake period and during depuration period, fish were removed to determine the kinetics of uptake and depuration. The authors estimated the steady state to be reached after 10 days. Carcass and liver concentrations were determined by using liquid chromatography-tandem mass spectrometry, and kinetic rates were calculated to determine bioaccumulation parameters (assimilation efficiency = 110±8.0%, depuration half-live = $70 \pm 9.4 \times 10^{-3}$ 1/d, half-live = 9.9±1.3 d). Assimilation efficiencies were ranged between 59-130 %, depuration half-live between $20\text{-}230 \times 10^{-3}$ 1/d for C_8-C_{14} PFCAs). Bioaccumulation (carcass) increased with increasing chain length but was not larger than one: 0.23 ± 0.035 for PFDA (see also Table 9).

The results of the study by Martin *et al.* suggests that a dietary exposure will not result in biomagnification in juvenile trout. However, for substances which are already known to have bioaccumulative properties BMFs do not indicate bioaccumulation (BMFs < 1 for $C_{11,12}$-PFCAs and perfluorooctanoic sulfonic acid -PFOS). A published comparison of BCFs and BMFs investigated 9 substances in a laboratory fish feeding study with carp (Inoue *et al.* 2012). Five substances showed BCFs larger than 5000 but only two of these substances were likely to biomagnify. Hence, for laboratory based dietary studies on fish showing BMFs below 1 it cannot be concluded that the substance is not bioaccumulative. Martin *et al.* assume that the lack of observed biomagnification was likely due to the small size of fish used in the study, resulting in more rapid chemical elimination to water, relative to body size and that their natural feeding rate is too low. This more rapid chemical elimination would reduce the BMF more than what would be observed for larger species or size classes (Martin *et al.* 2003b). Therefore results from this study are not secure enough for an assessment on the bioaccumulation potential of PFDA. Furthermore, gill breathing organisms are investigated which might not be the most relevant endpoints to be considered as explained above.

Besides the laboratory studies discussed above, BMFs have also been estimated from field studies. Transfer of PFDA was elucidated in Lake Ontario (Martin *et al.* 2004)

including one 4-membered pelagic food chain. Whole body samples were collected. The sampled organisms included a top predator fish, lake trout (*Salvelinus namaycush*), three forage fish species including rainbow smelt (*Osmerus mordax*), slimy sculpin (*Cottus cognatus*), and alewife (*Alosa pseudoharengus*), and two invertebrates Diporeia (*Diporeia hoyi*) and Mysis (*Mysis relicta*), which were considered as primary prey. Trout were sampled in 2001. Seven samples were selected every three years (*i.e.* 7 individual fish samples per year). Forage fish species, including sculpin, smelt, and alewife, and invertebrate samples were collected on October 9th 2002 at an offshore site near Niagara-on-the-Lake, Lake Ontario. Due to the inherent uncertainties correlated with constitution of diet four individual combinations of rainbow trout and its prey were considered. In all examples BMF for PFDA ranged between 0.21 and 4.4 (Table 9). A striking finding of this study was the high content of PFDA in both macro invertebrates occupying the lowest trophic level. Concentrations in Diporeia were as high as 32 ng/g and the mechanism leading to this exceptional accumulation still needs to be revealed. As a consequence, sculpin as Diporeia´s consecutive predator still shows significant levels of PFDA (29 ng/g). Given that Diporeia is a benthic invertebrate species, and sculpin feed mainly in the benthic environment, this contamination may be considered a benthic contamination source.

Tomy *et al.* (2009) investigated beluga whale (*Delphinapterus leucas*), ringed seal (*Phoca hispida*), arctic cod (*Boreogadus saida*), fish pelagic amphipod (*Themisto libellula*) and arctic copepod (*Calanus hyperboreus*) of the Western Canadian Arctic. The animals selected were from the sample archived repository at Fisheries and Oceans, Canada. Blubber and liver of beluga (n = 10, all males,) from Hendrickson Island and ringed seal (n = 10, all males) from Holman Island were collected in 2007 and 2004, respectively. Fish species collected in 2004 and 2005 included the marine pelagic Arctic cod (n = 10) from the Amundsen Gulf, the marine coastal Pacific herring (n = 10) from the Mackenzie Shelf and the anadromous Arctic Cisco (n = 9) from the Mackenzie estuary. The marine pelagic amphipod (pooled samples, n = 2) and the marine arctic copepod (pooled samples, n = 5) were collected in 2004 from the eastern Beaufort Sea and Amundsen Gulf region. The authors state that differences in sampling years may influence the interpretation of the food web transfer. Again some of the derived BMF-values are restricted to the liver and the resulting BMFs may be overestimates. The BMF-values reported range from 0.1 for Arctic cod (liver)/ marine pelagic amphipod (whole body) and 87 for Beluga whale (liver)/ Pacific herring (liver). Uncertainties coming from the fact of samples from different year are expected to be minimal, because of minimal concentration changes in remote regions. Except for the arctic cod and either amphipod or copepod relationships BMFs >1 suggest bioaccumulation of PFDA. BMFs >1 are based on organ specific concentrations and might therefore be overestimated. Anyhow, it is not possible to quantify this overestimation and due to target organ toxicity accumulation of PFDA in liver is of special concern.

Houde *et al.* (2006) investigated the biomagnification of PFDA in the food web of bottlenose dolphins (*Tursiops truncatus*). In the course of the study PFDA concentrations in bottlenose dolphins were examined at two different habitats, whereby BMFs and TMFs were calculated for only one of these habitats (Charleston Harbor and its tributaries (*i.e.* the Cooper, Ashley, and Wando rivers) and the Stono River estuary, South Carolina) because for the other habitat concentrations in fish were below the detection limit. Marine water (n=18), surface sediment (n=17), Atlantic croaker (*Micropogonias undulates*) (n=3), pinfish (*Lagodon rhomboids*) (n=4), red drum (*Sciaenops ocellatus*) (n=8), spotfish (*Leiostomus xanthurus*) (n=10), spotted seatrout (*Cynoscion nebulosus*) (n=11), striped mullet (*Mugil cephalus*) (n=8), and bottlenose dolphin samples (n=24) were collected around the Charleston Harbor area. Dolphin plasma, skin, and teeth were collected from both locations and additionally, dolphin tissue samples (*i.e.*, liver, kidney, muscle, lungs, heart, thyroid, and thymus) were collected from a recently deceased bottlenose dolphin (Charleston, (n = 1, female, 708.4 kg). The authors claim that utilization of serum or liver concentrations of dolphins will overestimate the BMF by a factor of 10-30. Therefore they extrapolated tissue specific concentrations to whole body

burdens based on the total body weight, the organ weights and the blood volumes. Samples were collected between 2002 and 2004, thus entailing some uncertainty when assessing BMF through the food chain. It may be assumed that media and biota were continuously exposed to PFDA in this area throughout the years. BMFs ranging from 2.4 to 8.8 for individual dolphin/prey relationships were stated using recalculated PFDA whole body burdens for dolphin. Wastewater treatment plant discharges in the Charleston area may have resulted in non–steady state concentrations in the food web. Even if these results come with uncertainties (samples from different years, whole body estimation and non-steady state concentrations resulting from wastewater treatment plant discharges) they clearly indicate bioaccumulation of PFDA.

Butt *et al.* (2008) conducted a study in the Canadian Arctic. Ringed seal (*Phoca Hispida*) liver samples (n=10 per site) were provided by local hunters from 11 different locations in the Canadian Arctic. Sample collection years for ringed seal populations varied from 2002 to 2005. However, for this remote region concentration variation in different years are expected to be minimal. The age of the animals was determined via tooth aging and for a few samples the age was estimated using length-age correlations. Stable isotope analysis was done with ^{15}N to ^{14}N and ^{13}C to ^{12}C. Based on liver samples from polar bears obtained from Smithwick *et al.* (2006) and ringed seal data measured in this study BMFs were calculated. The polar bear sample sites were associated with ringed seal populations. In four different regions these factors ranged from 17 to 43 with a mean of 23 clearly indicating biomagnification even if the factors might be overestimated due to tissue specific concentrations.

Table 9: Biomagnification factors (BMF) for PFDA

Location	Species (tissue)	BMF	Reliability	Reference
Laboratory	*Oncorhynchus mykiss* Juvenile rainbow trout (carcass)	0.23	2	Martin *et al.* 2003b
Lake Ontario	*Salvelinus namaycush* Lake trout (whole)/ *Alosa pseudoharengus* Alewife (whole)	4.4	2	Martin et al., 2004
	Lake trout (whole)/ *Osmerus mordax* Smelt (whole)	1.0		
	Lake trout (whole)/ *Cottus cognatus* Sculpin (whole)	0.21		
	Lake trout (whole)/ prey (weighted)	2.7		
US, South Carolina	*Cynoscion nebulosus* Seatrout (whole)/ *Lagodon rhomboides* Pinfish (whole)	3.7	2	Houde *et al.* 2006
	Tursiops truncatus Dolphin (whole, estimated)/ *Mugil cephalus* Striped mullet (whole)	2.9		
	Dolphin (whole, estimated)/ Pinfish (whole)	8.8		
	Dolphin (whole, estimated)/ *Sciaenops ocellatus*	2.4		

	Red drum (whole)			
	Dolphin (whole, estimated)/ *Micropogonias undulatus* Atlantic croaker (whole)	2.5		
	Dolphin (whole, estimated)/ *Leiostomus xanthurus* Spotfish (whole)	2.8		
	Dolphin (whole, estimated)/ Seatrout (whole)	2.4		
Canadian Arctic	*Ursus maritimus* Polar bear (liver)/ *Phoca Hispida* Ringed seal (liver)	17-43	2	Butt *et al.* 2008
Western Canadian Arctic	Ringed seal (liver)/ *Boreogadus saida* Arctic cod (liver)	2.5	2	Tomy *et al.* 2009
	Delphinapterus leucas Beluga whale (liver)/ Arctic cod (liver)	55		
	Beluga whale (liver)/ *Clupea pallasi* Pacific herring (liver)	87		
	Beluga whale (liver)/ *Coregonus autumnalis* Arctic cisco (liver)	44		
	Arctic cod (liver)/ *Calanus hyperboreus* Marine arctic copepod (whole)	0.4		
	Arctic cod (liver)/ Marine pelagic amphipod (whole)	0.1		

Conclusion: The biomagnification potential of PFDA was investigated in several field studies. Gill breathing organisms like fish as predators either show biomagnification of PFDA or not. The expected[3] high water solubility of PFDA may enable fish and mussels to quickly excrete this substance via gill permeation, facilitated by the high water throughput (Kelly *et al.* 2004; Kelly *et al.* 2009; Martin *et al.* 2003a; Martin *et al.* 2003b). However, air-breathing homeotherms are unable to efficiently eliminate PFDA to water via body surfaces such as gills. The study of an Arctic marine food web conducted by Kelly *et al.* (2009) showed these differences between piscivorous and marine mammalian food webs. This study is discussed in Section 3.3.2.5 below. For predator prey relationships including seals, beluga whales, dolphins and polar bears, studies provide data showing bioaccumulation (BMFs 2.4-87). These data support the conclusion that PFDA is bioaccumulative. Overall these findings provide further indication that different accumulation mechanisms are going on for gill and air breathing organisms and that gill breathing organisms are not the most relevant organisms to be considered, whereas for air breathing organisms bioaccumulation occurs. These different accumulation mechanisms may be due to the partitioning to protein-rich compartments

[3] Based on the data of the analogue PFOA, see Annex I.

which may lead to different toxicokinetics as Kelly *et al.* (2009) postulated.

3.3.2.5. 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 Borgå *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 ($^{15}N/^{14}N$, referred to as $\delta^{15}N$). 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 Borgå *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 *et al.* 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 and 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 (Fisk *et al.* 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.

TMFs derived for PFDA are summarised in Table 10. With the exception of the study conducted by Kelly *et al.* (2009) none of the studies were protein-normalised. None of the studies were lipid normalised.

Martin *et al.* (2004) examined PFDA contents in the food web from Lake Ontario (Canada). Adult lake trout (top predator) were collected at various locations in Lake Ontario in 2001. Samples of prey fish (sculpins, smelts and alewives) and macroinvertebrates (*Mysis sp., Diporeia sp.*) were collected at one location in October 2002. Lake trout samples analysed represented individual whole fish homogenates. The other species were processed as composites of whole individuals. The authors note that *Diporeia sp*. is a benthic invertebrate species, and sculpins feed mainly in the benthic environment. Benthic contamination may therefore be the source of contamination of this food web. As for PFDA, there is no significant association with trophic level for Diporeia/slimy sculpin in the food web of Lake Ontario but the content in predators is higher than in prey species for Mysis/alewife/rainbow smelt/lake trout, thus indicating trophic biomagnification of PFDA.

Houde *et al.* (2006) investigated the food web of bottlenose dolphins. The authors sampled different biota, *i.e.* Atlantic croaker (n=3), pinfish (n=4), spotfish (n=10), spotted seatrout (n=11), striped mullet (n=8) and samples from livecaptured bottlenose dolphins (n=24), as well as water (n=18, samples analysed in duplicate) and surface sediment (n=17, samples analysed in triplicate). Sample collection was conducted between 2002 and 2004. Based on stable isotope (^{15}N) analysis the trophic level of each biota sample was determined. PFDA was additionally analysed in plasma, liver, lung, kidney, heart, thymus, thyroid and muscle of two freshly dead dolphins and afterwards a whole body burden was calculated. 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 for PFDA. TMFs indicate bioaccumulation of PFDA when dolphin plasma concentrations were taken into account as well as when whole body burdens for dolphins were considered (Table 10). Wastewater treatment plant discharges in the Charleston area may have resulted in non–steady state concentrations of perfluorinated compounds in the food web.

Kelly *et al.* (2009) measured PFDA in the Canadian Arctic marine food web. Concentrations in sediment (n=9) and in different organisms (lichens, macroalgae (n=6), bivalves, fish (n=3-6)) and tissues and organs (stomach contents, liver, muscle, blubber and/or milk) of common eider ducks (n=5), seaducks (n=4), and marine mammals beluga whales and ringed seals were used to calculate TMFs (Table 10). Sample collection was conducted between 1999 and 2003 along the eastern Hudson Bay coastline in close proximity to the Inuit village Umiujaq. PFDA was measured in different tissues/fluids of the beluga whale including blood (n=18), muscle (n=18), liver (n=22), milk (n=6) and also in foetuses (n=2). The authors showed that PFDA especially accumulates in protein rich compartments such as blood and liver and that the TMFs of perfluorinated compounds such as PFDA correlate with the partitioning behaviour between protein and water and protein and air. Wet weight PFCA concentrations were expressed on a protein weight basis (ng/g protein wt) using total protein content (P_{TOTAL}) values of biological tissues/fluids of fish, birds and mammals. P_{TOTAL} values of 2% for macroalgae, 25% for muscle, 25% for bird and mammalian liver tissue (25%), 7% for beluga blood and 11% for beluga milk were used. A pharmacokinetic model for beluga whales was used (Hickie *et al.* 1999) to estimate the whole body burden. The basis for the model development were PCBs. Because PFCAs are primarily retained in protein-rich compartments (blood and liver), organism- and compartment-specific protein turnover rates may influence the toxicokinetics of these compounds. Comparisons of different food webs show that the TMF is below one in the case of piscivorous food webs if air breathing organisms are excluded but becomes larger than one if air breathing organisms are taken into account. TMFs for the food web of the beluga whale are >1, indicating bioaccumulation, when they are normalised to protein contents as well as without that normalization.

Xu *et al.* (2014) investigated the bioaccumulation of perfluorinated compounds in a food web in Taihu Lake in China. As the study by Martin *et al.* (2004) this is a study for fresh water food web. As stated by Loi *et al.* (2011) bioaccumulation patterns depend on salinity. Taihu Lake, is the second largest lake in China and serves as a drinking water supply, irrigation water, aquaculture farm as well as recreational attractions. From the late 1980s, water and soil pollution from industry, agriculture, and urban wastes has been increasing significantly in the Taihu Lake region. Surface water (n=30), surficial sediment (n=30), phytoplankton (mainly include *Chlorophyta, Bacillariophyta* and *Cyanophyta*), zooplankton (mainly include *Copepoda, Cladocera*, and *Rotifers*), two zoobenthos species (*Bellamya sp.* (snail) (n=9) and *Corbiculidae* (bivalve) (n=8)), white shrimp (*Exopalaemon modestus Heller*) (n=18), fish samples of nine different species, *i.e. Hypophthalmichthys molitrix* (n=10), *Protosalanx hyalocranius* (n=6), *Hemiculter leucisculus* (n=7), *Aristichthys nobilis* (n=4), *Hyporhamphus intermedius* (n=6), *Pelteobagrus fulvidraco* (n=4), *Erythroculter ilishaefor* (n=8), *Cyprinus carpio* (n=7), *Coilia ectenes* (n=22), and two egret bird species (Egrets and Night Herons) as prey animals were collected from Taihu Lake in May 2010. In order to investigate the diet relationship in this food web stable isotope ratios ($\delta^{13}C$ and $\delta^{15}N$) were determined. Following groups were formed: zooplankton and zoobenthos (Bellamya sp. and Corbiculidae) (11-12‰), herbivorous fish (14-16‰), omnivorous fish (17-18‰), and carnivorous fish and egrets (19-21‰). Among the 12 analysed PFCAs (C_8-C_{12}) were detected in all biological samples. In water, PFCAs with six to nine carbons were regularly detected. The long-chain PFCAs (C_{11}, C_{12}) were only detectable in sediments. PFDA concentrations were ranged in the different biological samples as follows: 0.07 (phytoplankton), 0.055 (zooplankton), 0.15 (zoobenthos), 1.83 (white shrimp), 1.41-6.17 (fish), 10.29 (egrets) ng/g wet weight. PFCAs with nine to twelve carbons were significantly biomagnified, with a TMF value of 3.7 for PFDA (Table 10).

Table 10: Trophic Magnification Factors (TMF) of PFDA

Location	Species (tissue)	TMF	Reliability	Reference
Lake Ontario	Diporeia/slimy sculpin (all whole)	No significant association with trophic level	2	Martin *et al.* 2004
	Mysis/alewife/rainbow smelt/lake trout (all whole)	3.67		
US, South Carolina	Dolphin plasma croaker, pinfish, spotfish, spotted seatrout (fish all whole)	3.4 ± 5.1	2	Houde *et al.* 2006
	Whole dolphin body burden	2.2 ± 2.4		
Hudson Bay (north-eastern Canada	**Marine mammalian food web:** Sediment/ macroalgae (whole)/ bivalves(whole)/ fish(muscle)/eider duck (liver)/seaduck (liver)/ ringed seal (liver) beluga whale (estimated whole body)	5.68-12.1 3.31-6.99 (protein corrected)	2	Kelly *et al.* 2009
	Piscivorous food web: Sediment/ macroalgae (whole)/ bivalves (whole)/ fish (muscle)	0.39-0.99 (protein corrected)		
Taihu Lake/ China	zooplankton and zoobenthos, herbivorous fish, omnivorous fish, and carnivorous fish and egrets	3.7	2	Xu *et al.* 2014

Conclusion: A number of field studies are available which analysed the trophic magnification potential of PFDA. In the same manner as BMFs also TMFs are lower if gill breathing organisms are top predators of the investigated food chain (TMF 0.39 – 3.67). If air breathing animals are top predators in the food chains all studies indicate trophic magnification of PFDA (3.4 – 12.1).

3.3.3. Bioaccumulation in terrestrial organisms (soil dwelling organisms, vertebrates)

3.3.3.1. Bioaccumulation in soil dwelling organisms

There are two studies available which investigated the bioaccumulation of PFASs in earthworms. In the first study (Zhao *et al.* 2013), earthworms were exposed to artificially contaminated soils with ten PFASs with different chain length. A soil without detectable PFASs was collected and spiked with one mL of a mixed solution of 10 PFASs. The soil concentration of each PFAS was 100, 200, and 500 ng/g, respectively. The soil was then incubated in dark for 4 days at room temperature. Mature earthworms (*Eisenia fetida*) were exposed for up to 30 days. Samples were taken at day 2, 4, 6, 8, 12, 16, 20, 24, 28 and 30. All the 10 PFASs were detected in the earthworms already after an exposure for 2 d, indicating that they can be taken up by earthworms from soil quickly. The estimated time to steady state was 27.7 days. An important finding is that the uptake increased with increasing chain length. The bioaccumulation was calculated as a biota to soil accumulation factor (BSAF) which was normalised for the organic carbon content in

the soil. The BSAF values ranged from 0.078-0.117 for PFDA. The BSAF Values for PFOA were 0.131 and ranged between 0.213-3.408 for PFNA, PFUnA and PFDoA.

In the second study (Rich *et al.* 2015), bioaccumulation was investigated exposing *Eisenia fetida* to contaminated soil. As stated by the authors, spiked soil as used in the study by Zhao *et al.* (2013) may not reflect typical field conditions. Therefore, in the study by Rich *et al.* contaminated soil was collected instead; one soil that had received long-term field application of municipal biosolids, an industrial impacted soil and two soils from a former firefighting training area either adjacent to the source zone or 180 m from the source zone. Five adult earthworms per container were exposed for 28 days to achieve steady state values. For the determination of kinetic values, additional sets of triplicate containers were prepared for sampling on day 1, 3, 5, 7, 9, 12, 16 and 21. Biota to soil accumulation factors not normalised to the carbon content in the soil (BAFs) as well as BSAFs normalised to the different carbon contents were reported (Table 11). The BSAF values ranged from 0.034-0.038 for PFNA and 0.019-0.02 for PFOA and ranged between 0.033-0.105 for the longer chained PFDA, PFUnA and PFDoA.

Table 11: Bioaccumulation in soil of PFDA

Location	**species**		**BSAF**[g_{oc}/g_{ww}] **/BAF**[$g_{dw,soil}/g_{dw,worm}$]	**Reliability**	**Reference**
Laboratory	*Eisenia fetida* Earthworm	BSAF	0.117±0.017 (100 ng/g) kinetic 0.104±0.006 (200ng/g) kinetic 0.078±0.023 (500ng/g) kinetic	2	Zhao *et al.* 2013
Laboratory field soils	*Eisenia fetida* Earthworm	BAF	5.27±1.79 (estimated steady state) 5.17±1.08 (measured)	2	Rich *et al.* 2015
		BSAF	0.049±0.019 (estimated steady state) 0.048±0.010 (measured)		

<u>Conclusion:</u>
According to the REACH PBT guidance it is not possible to give any threshold values for BAF and BSAF in soil as there are not enough scientific data available at the present time. A case-by-case assessment based on expert judgement of the reliability and relevance of the available information is required in order to be able to give BAF and BSAF values an appropriate weight in the B/vB assessment. It can, however, be concluded that the BSAF values for PFDA are in the same order of magnitude as the longer chained PFCAs and PFOA which have been identified as PBT and /or vPvB.

3.3.3.2. Bioaccumulation in vertebrates

Müller *et al.* (2011) conducted a terrestrial food web study consisting of lichen and plants, caribou (*Rangifer tarandus groenlandicus*), and wolves (*Canis lupus*) from two remote northern areas in Canada. This food web is considered as a relatively well documented example and in particular caribous have been studied intensively due to their economic and social importance for indigenous people in the Canadian Arctic. Furthermore, the food web is relatively simple as caribous feed mostly on lichen (in summer the diet also consists of willow, sedges and grasses) and wolves living near barren-ground caribou herds almost exclusively feed on them. Liver, muscle, and kidney samples (n=7 for the Porcupine herd food web and n=10 for the Bathurst food web) from two caribou herds were collected; from the Porcupine herd in northern Yukon Territory and the Bathurst herd in the Northwest Territories (NWT)/western Nunavut. Wolf (n=6 for the Porcupine herd food web and n=10 for the Bathurst food web), lichen, and plant

samples were collected in the same region as the caribou. Plant samples included cottongrass, aquatic sedge, willow, moss, and mushrooms. Liver and muscle samples were collected from the sampled wolves. Lichen, moss and mushrooms were collected as a whole grass and willow without roots. Plant samples are from the same season (summer 2008 in Porcupine and summer 2009 in Bathurst) whereas wolf and caribou samples are from different years (2007 and 2010 in Porcupine and 2008 and 2007 in Bathurst). As variations in concentrations in remote regions are expected to be low the influence of sample from different years is expected to be low as well. Whole body concentrations were calculated for each individual caribou and wolf based on the concentration in the specific tissue and the mass fraction of this tissue. If one tissue has not been measured in this study, the concentration was estimated based on data in the literature, *i.e.* concentration in blood and lungs were assumed to be half of that of liver and the carcass was assumed to have half the concentration found in muscle tissue. Bones were excluded from the whole body calculation because per- and polyfluorinated chemicals are assumed to not enrich in this media and bones are not part of the diet of wolves. As the authors state, it is very complex and laborious to obtain all information needed to calculate whole body concentrations for larger animals. Concentrations or body composition need to be estimated. If not all information is available, uncertainties are introduced. For caribou, PFDA concentrations in liver were 1.9±0.1 and 3.2±0.2 ng/g wet weight for the Porcupine and Bathurst herds, respectively. For wolves, PFDA concentrations in liver were 2.0 ± 0.2 and 3.2±0.2 ng/g wet weight for the Porcupine and Bathurst herds, respectively. Mean PFCA concentrations were higher in the Bathurst samples. The authors assume that this might be due to differences in distance from source regions in North America. PFCA concentrations in muscle and kidney were 10 to 20 times lower. For caribou, PFDA concentrations in muscle were 0.033±0.007 and 0.075±0.009 ng/g wet weight for the Porcupine and Bathurst herds, respectively. For wolves, PFDA concentrations in muscle were 0.11± 0.02 and 0.21±0.03 ng/g wet weight for the Porcupine and Bathurst herds, respectively. The study illustrates a considerable carry over between plants and caribou. Caribou is a major human food source in numerous arctic communities. This food-chain may also be considered comparable to the pasture-cow food-chain in temperate regions. The results of the study, BMFs as well as TMFs, are shown in Table 12 and Table 13. Due to the large difference between lichen and caribou compared to usually assumed trophic enrichment, the TMF values must be treated with caution. Tissue concentrations and whole body concentrations were used for calculations. Tissue based BMFs differ considerably. Therefore, it is concluded that BMFs based on whole body concentrations are more appropriate. Overall, although there are uncertainties in this study the results clearly indicate bioaccumulation of PFDA within this food chain.

In order to understand how PFCAs are accumulated and transferred through agricultural food chains the bioaccumulation of PFCAs in dairy cows receiving naturally contaminated feed and drinking water was investigated by conducting a mass balance of PFCAs for a herd of dairy cows (*Bos Taurus*) in a barn on a typical Swedish dairy farm (Vestergren *et al.* 2013). The farm was selected to represent a background contaminated agricultural area with no known point sources of PFCAs in the proximity. Silage, barley, and feed supplements were collected monthly from November 2010 to April 2011 (n=6) from the daily feed portion just before being distributed to the animals. The average individual intake of silage (38.5 kg per day), barley (8.8 kg per day), and supplements (8.6 kg per day) was derived from the total annual consumption on the farm divided by the average number of cows present in the barn. Drinking water was sampled from the farm water supply. The cow's drinking water intake was estimated to be 50 L/day. Milk samples were collected from a milk tank, where milk from the entire farm is stored after milking. Muscle, liver, and whole blood samples were obtained from five individual cows from the slaughterhouse on two different occasions (April and June 2011). Tissue-specific BMFs were calculated for liver, blood, and muscle. BMFs were highly tissue and homologue specific. The highest concentrations of PFCAs in cow tissues were observed in liver samples and similar to those observed in caribou from the Canadian Arctic (Müller *et al.* 2011). Consumption of silage was identified as the dominant intake pathway for all

PFCAs (75-81%). Drinking water intake was negligible for the total intake. The results suggest that long-chain PFCAs have a relatively high potential for transfer to milk and beef from the diet of dairy cows. Tissue specific BMFs are >1 for blood and liver and near 1 for muscle.

Table 12: BMFs for PFDA in a terrestrial food chain

Location	Species (tissue)	BMF	Reliability	Reference
Porcupine in northern Yukon Territory and Bathurst in the Northwest Territories of Canada	*Rangifer tarandus groenlandicus* Caribou (muscle)/ lichen	1.3 ± 0.6(Porcupine) 1.1± 0.7(Bathurst)	2	Müller *et al.* 2011
	Caribou (liver)/ lichen	75± 25(Porcupine) 33± 19(Bathurst)		
	Canis lupus Wolf (muscle)/ Caribou (muscle)	3.3± 0.8(Porcupine) 2.8 ± 0.6(Bathurst)		
	Wolf (liver)/ Caribou (liver)	1.0± 0.1(Porcupine) 1.4 ± 0.1(Bathurst)		
	Caribou (whole)/ lichen	6.1± 2.2(Porcupine) 2.9± 1.7(Bathurst)		
	Caribou (whole)/ vegetation	12.4± 5.5(Porcupine) 7.2± 3.8(Bathurst)		
	Wolf (whole)/ Caribou (whole)	1.7± 0.2(Porcupine) 2.1± 0.2(Bathurst)		
Swedish dairy cattle farm, Backa Gård in Kårsta	silage, barley/Swedish red (*Bos taurus*)muscle	1.1	2	Vestergren *et al.* 2013
	silage, barley/Swedish red (*Bos taurus*)liver	10.4		
	silage, barley/Swedish red (*Bos taurus*)blood	4.6		

Table 13: TMFs for PFDA in a remote terrestrial food chain (from two different locations)

Location	Species (tissue)	TMF	Reliability	Reference
Porcupine in northern Yukon Territory and Bathurst in the Northwest Territories of Canada	Wolf (liver)/ caribou (liver)/ lichen	7.1± 0.4(Porcupine) 5.1 ± 0.3(Bathurst)	2	Müller *et al.* 2011
	Wolf (whole)/ caribou (whole)/ lichen	2.6± 0.1(Porcupine) 2.3 ± 0.1(Bathurst)		
	Wolf (whole)/ caribou (whole)/ vegetation	2.3± 0.1(Porcupine) 2.3± 0.2(Bathurst)		

Conclusion: The terrestrial BMF and TMF of PFDA are greater than one for the remote arctic food chain lichen – caribou – wolf, indicating trophic biomagnification. Caribou are a major human food source in numerous arctic communities. This food-chain may also be considered comparable to the pasture-cow food-chain in temperate regions. A study conducted with cattle from a Swedish dairy cattle farm confirms these findings. The results suggest that long-chain PFCAs have a relatively high potential for transfer to milk and beef from the diet of dairy cows.

3.3.4. Summary and discussion of bioaccumulation

BCF values range between 450 and 2700 for carcass, liver and blood. Conclusions on bioaccumulation should be based on whole body values and carcass is seen as a good approximation for whole body. Based on the BCF of carcass PFDA does not bioaccumulate in fish. However, as shown in this report, PFDA does not accumulate in lipid but rather binds to protein and membrane phospholipids, therefore the carcass or whole-body BCF values are less relevant. Based on the BCF value in the blood of rainbow trout (2700±350), PFDA can be considered bioaccumulative.

BAFs vary considerably for PFDA. Whole body BAF values from water breathing animals range from 714 to 7943. Tissue specific BAFs are up to 158489. The majority of data supports that PFDA is bioaccumulative.

The BMF values for gill breathing organisms like fish as predators range between 0.1 and 4.4. The expected[4] high water solubility of PFDA may enable fish and mussels to quickly excrete this substance via gill permeation, facilitated by the high water throughput whereas air-breathing homeotherms are unable to efficiently eliminate PFDA to avoid accumulation. For predator-prey relationships, including seals, beluga whales, dolphins and polar bears, available data are indicating bioaccumulation (BMFs 2.4-87). BMFs range from 2.4 – 8.8 based on estimated whole body values. These data support the conclusion that PFDA is bioaccumulative.

In the same manner as BMFs also TMFs are lower when gill breathing organisms are top predators of the investigated food chain (TMF 0.39 – 3.67). When air breathing animals are top predators in the food chains, all studies indicate trophic magnification of PFDA (2.2 – 12.1) referring to either whole body measurements or estimated whole body values.

[4] Based on the data of the analogue PFOA, see Annex I.

The terrestrial BMF and TMF of PFDA are greater than one for the remote Arctic food chain lichen – caribou – wolf as well as for cattle from a Swedish dairy cattle farm. TMFs range between 2.3 and 2.6 based on estimated whole body. BMFs range between 1.7 and 12.4 based on estimated whole body. The results from the Swedish dairy cattle farm suggest that long-chain PFCAs have a relatively high potential for transfer to milk and beef from the diet of dairy cows. Caribou are a major human food source in numerous arctic communities. This food-chain may also be considered comparable to the pasture-cow food-chain in temperate regions.

Many field analyses are based on tissue or serum samples. Problems with respect to sampling and laboratory constraints increase with increasing body size of predators at the top of the food chain. If the mass fraction is known, whole body values may be estimated for the organism. This has been conducted in some of the studies, especially concerning mammalian top predators. TMFs and BMFs based on whole body values should be preferred, as utilization of serum or organ specific concentrations may be overestimative. The extrapolation to whole body burdens may however include some unquantifiable uncertainties (Houde *et al.* 2006). It is very complex and laborious to obtain all information needed to calculate whole body concentrations for larger animals. If not all information is available, uncertainties are introduced. Nevertheless, all BMFs and TMFs including air-breathing animals and based on whole body estimations are well above 1 and thus indicate biomagnification and trophic magnification.

With the exception of the study by Xu *et al.* (2014) and Vestergren *et al.* (2013) sampling was conducted in different years all around the millennial. The time laps were three to four years. Some uncertainty may therefore exist due to varying environmental concentrations in the different years. Many of the studies have been conducted in remote regions were the variation of the environmental concentration may be expected to be lower than in urban areas with possible point sources of emissions. In polar bears, PFDA concentrations increased gradually from 1984 to 2006 with a doubling time of 12.4 years and an annual increase of 5.6% in east Greenland (Rigét *et al.* 2013). In the same study ringed seals showed an annual increase of 7.9% (doubling time 8.7 years) and 6.5% (doubling time 10.7 years) in west and east Greenland, respectively. A similar annual increase of 4.3% in polar bears in east Greenland was reported by Dietz *et al.* (2008). Butt *et al.* (2007) reported a doubling time of 11.0 to 11.7 years for arctic ring seals sampled between 1992-2005. Smithwick *et al.* (2006) reported a doubling time of 4.2 and 6.7 between 1972-2002. Between 1997 and 2008 Lake Ontario Lake Trout showed an annual increase of 0.06% (Gewurtz *et al.* 2012). Considering the time laps of the sampling years and comparing these with the time trends reported for PFDA the variation due to sampling in different years is probably less pronounced than the variation between individual animals.

In contrast to many other chemicals PFCAs do not accumulate in storage lipids. Therefore, the customary approach to normalise all values to a certain lipid portion is not straightforward. A protein-normalisation has been conducted in one study. This seems reasonable as it has been observed that PFCAs accumulate especially in protein rich tissue. A protein normalisation of all B- values in this dossier is however not feasible as the fractions of protein are unknown for the organisms that were investigated with regard to accumulation of PFCAs. Additionally, the fraction of protein content may vary considerably between different organisms. Therefore, a generalised approach with respect to protein-normalisation does not seem reasonable. Furthermore, PFCAs do not only tend to bind to proteins but also to membrane phospholipids (Ng and Hungerbühler, 2014). Depending on the individual PFCA and its physico-chemical properties, PFCAs do not exclusively bind to proteins.

The data summarised above is in high accordance with the bioaccumulation data on the other long chained PFCAs (for details, see the Support Documents of PFOA and the C_{11}-C_{14}-PFCAs (European Chemicals Agency, 2013b, 2012a, 2012b, 2012c, 2012d) and

Figures A1-A3 in Annex I). Altogether these data show a regular pattern of bioaccumulation which depends on the chain-length of the perfluorinated alkyl chain.

In addition to the information on bioaccumulation in environmental species, data on laboratory mammals and humans provide evidence on the bioaccumulative behaviour (see Section 4 for further details).

4. Human health hazard assessment

4.1. Toxicokinetics (absorption, distribution, metabolism and elimination)

4.1.1. Non-human information

4.1.1.1. Absorption

No data for PFDA has been found, but based on other toxicokinetic data for PFDA (Ohmori *et al.* 2003) and data for other PFCAs, such as PFOA and APFO (US EPA, 2005, US HHS, 2015), it can be assumed that PFDA is well absorbed in laboratory animals following oral and inhalation exposure, and to a lesser extent following dermal exposure.

4.1.1.2. Distribution

Several animal studies in rats, mice, rainbow trout, seals, whales and gulls demonstrate that PFAAs 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 and Hungerbühler, 2013 and 2014).

While liver and blood are primary sites of accumulation for PFAAs, some variability exists among different species and different PFAA derivatives (depending *e.g.* on the carbon chain length) with the kidneys and bladder being also important distribution sites (Ng and Hungerbühler, 2014). However, unlike neutral hydrophobic organic chemicals, PFAAs do not accumulate in fat tissues (storage lipids) owing to their water and oil/grease repellent properties. The two prevailing hypotheses to explain the substantial bioaccumulation of PFAAs currently relate to association to phospholipids and interaction with proteins such as serum albumin in blood, L-FABP in both liver and kidney, and renal organic anionic transport proteins (Ng and Hungerbühler, 2014).

The concentrations of PFCAs (PFDA, PFNA, PFOA or PFHpA) in serum and liver in rats were determined 5 days after injection (20 mg/kg bw, i.p.) (Kudo *et al.* 2001). Significant differences were observed between different PFCAs, with a tendency of higher serum concentrations of PFCAs with longer carbon chain lengths as compared to PFCAs with shorter carbon chain lengths. The concentration of PFDA in serum was approximately (estimated from graphical presentation) 35 µg/ml serum in males and 45 µg/ml serum in females, and 120 µg/g liver and 140 µg/g liver in male and female rats respectively. In contrast to PFDA, large differences in serum and liver concentrations between female and male rats were observed for PFOA and PFNA, where the concentrations in females were lower.

In a study by Vanden Heuvel *et al.* (1991) in rats, the liver contained the highest concentration of PFDA-derived ^{14}C at all investigated time points up to 28 days in both males (2.7% of [^{14}C]PFDA-derived dose per gram tissue after 28 days) and females (4.0% of [^{14}C]PFDA-derived dose per gram tissue after 28 days). Lower concentrations were observed in plasma (0.32% and 0.74 % of [^{14}C]PFDA-derived dose per gram tissue after 28 days in males and females, respectively) followed by the kidneys (0.27% and 1.12 % in males and females, respectively) after a single i.p. dose (9.4 µmol/kg, 5 mg/kg) [1-^{14}C]PFDA.

4.1.1.3. Metabolism

The metabolism of [1-^{14}C]PFDA was examined in male and female rats for 28 days after a single i.p. dose (9.4 µmol/kg, 5 mg/kg) (Vanden Heuvel *et al.* 1991). Only the parent compound of PFDA was excreted in urine and bile and no urinary or biliary metabolites of PFDA were detected in either sex. Moreover, the daily urinary excretion of fluoride in

male and female rats before and after PFDA treatment was similar, suggesting that the parent compound is not defluorinated. The results therefore demonstrate a lack of biotransformation of PFDA in male and female rats.

4.1.1.4. Elimination

In a comparative study by Ohmori *et al.* (2003), an elimination half-life in serum of 39.9 days in male and 58.6 days in female Wistar rats after a single i.v. dose of 48.64 µmol/kg bw PFDA was reported. For comparison, the serum half-lives of PFNA in males and females were 29.6 and 2.4 days respectively, while the half-lives of PFOA for males and females were 5.6 and 0.1 days, respectively. The role of urinary excretion in plasma clearance, renal clearance, was determined and the total clearance rate for PFDA was found to be extremely low, 5.2 ml/(day/kg) in male rats and 5.3 ml/(day/kg) in female rats. Ranking PFCAs according to the rate of renal clearance in this study resulted in the following order: PFHpA>PFOA>PFNA≈PFDA in male rats, and PFHpA≥PFOA>PFNA>PFDA in female rats. The total clearance was significantly correlated with the renal clearance rate (r^2=0.98). Organic anion transport proteins are reported to play a key role in PFCAs (C_4 to C_{10}) renal tubular reabsorption (Han *et al.* 2012) and the rate of renal excretion of PFCAs has been demonstrated to be regulated by testosterone and is determined by carbon chain length (Kudo *et al.* 2001).

Kudo *et al.* (2001) reported that the elimination of PFDA in urine was 0.2% of the dose within 120 hours in male rats (after i.v. injection) compared to 92%, 55% and 2% for PFHpA, PFOA and PFNA respectively. Faecal elimination was instead demonstrated to be a major route for PFDA in both male and female rats in contrast to the shorter perfluorinated fatty acids (PFHpA, PFOA). More than 4% of the injected dose of PFDA was eliminated within 120 hours.

A sex difference in the faecal elimination of PFDA was observed with 51% and 24% of the administered ^{14}C being recovered in the faeces of male and female rats, respectively, by 28 days post-treatment after a single i.p. dose (9.4 µmol/kg, 5 mg/kg) of [1-^{14}C]PFDA (Vanden Heuvel *et al.* 1991). Half-life for whole body elimination of [^{14}C]PFDA-derived radioactivity was 23 days in males and 43 days in females. Less than 5% of the administered dose in both males and females was excreted in the urine in both males and females over the same 28 days period. The concentration of ^{14}C derived from PFDA in blood was also higher in female rats and the PFDA-derived radioactivity was eliminated more slowly in females with a half-life of 29 days compared to 22 days in male rats.

The following behaviour of PFDA and other PFCAs can be observed based on the toxicokinetic studies.

- Comparing the C_7 to C_{10} PFCAs, there is an association between increasing carbon chain length and slower plasma clearance in both male and female rats (*cf.* Table 14).
- The gender variability in elimination half-lives in rats is smaller for PFDA than for PFOA and PFNA.
- Faecal elimination was observed as a major route for elimination in rats for PFDA in contrast to PFOA and PFNA where renal excretion is a major elimination pathway.

RAC, in their opinion on the harmonised classification of PFDA and its ammonium (PFD-A) and sodium (PFD-S) salts, concluded that "*PFDA (and its salts) and PFOA/APFO possess physicochemical and toxicokinetic properties which are similar or in the same range*" (European Chemicals Agency, 2015a).

4.1.2. Human information (including bioaccumulation in humans)

4.1.2.1. Absorption

There are no studies on absorption of PFDA in humans. However, elevated serum concentrations of perfluorochemicals 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 of other PFCAs, as well as on abundant findings of PFDA and other PFCAs in human blood, it can be assumed that PFDA is well absorbed after oral and inhalation exposure and to a lesser extent following dermal exposure.

4.1.2.2. Levels of PFDA in human body fluids

Exposure

There are two important sources of exposure of per- and polyfluoroalkyl substances (PFASs) such as PFDA to the general population, namely via food and drink intake (Haug *et al.* 2010a and 2010b) and through exposure to house dust (Huber *et al.* 2011, Ericson Jogsten *et al.* 2012, Bohlin-Nizzetto *et al.* 2015). Food intake is assumed to be a main source of exposure of the general population to long-chain PFCAs (Vestergren *et al.* 2012). PFDA has been detected in among others fish, cereals, milk and dairy products, meat and meat products (Haug *et al.* 2010a and 2010b).

Workers may be exposed to higher levels, for example when using high amounts of fluorinated ski waxes (Nilsson *et al.* 2010, Freberg *et al.* 2010).

General population

PFDA has been detected in various body fluids such as serum, cord blood and human breast milk (Bjermo *et al.* 2013, Glynn *et al.* 2012 and 2015, Gützkow *et al.* 2012, Haug *et al.* 2010, Kärrman *et al.* 2013, Liu *et al.* 2011, Mørck *et al.* 2015, Schecter *et al.* 2012, TemaNord, 2013).

In a study with blood sampled 2011-2012 from 270 adults in Sweden (age 18-80 years), the median serum concentration of PFDA was 0.39 ng/mL (P5-P95 range 0.19-0.84) (Bjermo *et al.* 2013). Men had higher serum levels than women (adjusted mean 0.36 vs 0.30 ng/ml), which may be due at least in part to elimination of this and other PFAAs during breastfeeding. Age was positively correlated to the serum levels of PFDA, suggesting an ongoing bioaccumulation process. The mean level among 61-80 years old was 48 % higher compared to the age group 18-40 years. The study also showed a positive correlation between PFDA levels and fish intake.

Similar levels have been found in Norway; the mean serum level of PFDA in 175 samples was 0.46 ng/ml (range 0.070-1.8) (Haug *et al.* 2010b). Consumption of fish and shrimps was significantly correlated to the serum levels of PFDA.

PFDA serum concentrations in Danish children and mothers were reported by Mørck *et al.* 2015. For 116 children and 143 mothers, median human PFDA serum concentrations were reported as 0.32 ng/mL and 0.28 ng/mL respectively, similar to levels found in other reported studies. In the study it was concluded that the levels of PFASs in the plasma increased with increasing age of the mothers. The levels in the children are somewhat higher than in the mothers which is believed to be due to higher exposure to *e.g.* dust and soil, and that the children have lower storage capacity compared to the mothers.

Several studies in the Swedish health related biomonitoring program have generated

data on PFDA in the general population. The medium serum level in more recent samples (2013) is around 0.2 ng/mL which is a decrease from the levels in 2010 (http://www.imm.ki.se/Datavard). In contrast, a temporal trend analysis from 1996 to 2010 in primiparous women in Sweden three weeks after delivery showed increasing levels of PFDA in serum with 3.8% increase per year (Glynn *et al.* 2012). In a follow-up study in 2015, a levelling off of the increasing trend of PFDA is observed (Glynn *et al.* 2015).

Professional workers

A study on occupational exposure of professional ski waxers (n=8) showed blood concentrations of PFDA much higher (up to 80-fold) than in the general population, the highest value was 24 ng/mL in whole blood, corresponding to approximately 48 ng/mL in serum (Nilsson *et al.* 2010). Monthly blood samples were collected before the ski season, *i.e.* preseason, then at four FIS World Cup competitions in cross country skiing, and finally during an unexposed 5-month post-season period. The PFDA levels in technicians with lower initial levels of PFDA (≤10 ng/mL) increased from pre-season to post-season. There was a significant association between number of years in the profession and blood levels of PFDA, indicating bioaccumulation.

In a Norwegian study, serum samples from 13 professional male ski waxers were collected at three occasions (Freberg *et al.* 2010). The first blood sample was drawn at the end of season I (spring), the second at the beginning of season II (autumn) and the third at the end of season II (spring). The median serum concentrations of PFDA were similar at all samplings; 7.5 ng/ml (range: 2.1-28 ng/ml); 6.8 ng/ml (range: 1.7-28 ng/ml) and 6.8 ng/ml (range: 2.3-27 ng/ml), respectively. There was only a slight decrease in serum levels during the 8 months between end of season I and start of season II, suggesting a long elimination half-life for PFDA. Also in this study a statistically significant positive association between years exposed as a ski waxer and concentration of PFDA in serum was observed.

4.1.2.3. Gestational and lactational transfer

PFDA has been detected in serum, cord blood and human breast milk, demonstrating gestational and lactational transfer (Berg *et al.* 2014, Bjermo *et al.* 2013, Glynn *et al.* 2012 and 2015, Gützkow *et al.* 2012, Haug *et al.* 2010, Kärrman *et al.* 2013, Kim *et al.* 2011, Liu *et al.* 2011, Mørck *et al.* 2015, Schecter *et al.* 2012, TemaNord, 2013).

In a study from Norway including 123 pairs of maternal and cord plasma samples, the median PFDA concentration in cord plasma (0.04 ng/ml, range: 0.04-0.18) was 57 % of the corresponding concentration in maternal plasma (0.07 ng/ml, range: 0.04-1.14) (Gützkow *et al.* 2012). The concentrations of PFDA were below the detection limit in some of the samples which precluded further statistical analyses. In a Chinese study including 50 pairs of maternal and cord serum samples, the median PFDA concentration in cord serum (0.226 ng/mL) was 39% of the corresponding concentration in maternal serum (0.585 ng/mL) and there was a high correlation between PFDA concentrations in matched maternal and cord serum (Liu *et al.* 2011). In general, it was observed that the transfer efficiency values for different PFCAs decreased in the order PFOA>PFNA>PFDA as has also been reported previously (Kim *et al.* 2011).

Parity was shown to affect serum levels of PFDA (Berg *et al.* 2014). When compared to nulliparous women, parous women had lower concentrations of PFDA. Although the study could not separate the effect of breastfeeding from parity, it is clear that breast milk is an important mechanism for elimination of long-chain PFAS (Brantsæter *et al.* 2013). In a Norwegian study, breastfeeding for more than 4 months was significantly associated with lower maternal serum levels of PFDA (Haug *et al.* 2010).

The levels of PFDA in breast milk are low however compared to the serum levels. In a Swedish study where PFDA was analysed in 50 matched milk and serum samples from primiparous women collected 2004-2011, PFDA was detected in 22 % of the milk samples at levels between 0.021 and 0.097 ng/mL. Serum levels were between 0.390 and 1.01 ng/mL although detected in only 20% of the serum samples (Kärrman *et al.* 2013). As discussed in the RAC opinion on the harmonised classification of PFDA and its ammonium (PFD-A) and sodium (PFD-S) salts, PFDA is detected in breast milk in several studies but the levels may vary depending on region.

In conclusion, PFDA can be transferred to the foetus through the placenta. Furthermore, PFDA has been detected in human breast milk and breast-feeding is thus one exposure route for PFDA in infants.

4.1.2.4. Distribution in the human body

PFASs do not tend to accumulate in fat tissue. PFOA displays the highest concentrations in liver, blood, lung and kidney (European Chemicals Agency, 2013b) and other PFASs can be expected to show similar distribution. Only little data can be found for PFDA; Pérez *et al.* (2013) reports on the detection of PFDA in brain, lung and kidney. In that study, 99 samples of autopsy tissues (brain, liver, lung, bone and kidney) from 20 individuals (28-83 yrs) from Tarragona in Spain were analysed. In particular brain contained high concentrations of PFDA; PFDA was detectible in 70% of the samples, with a median value of 12.4 ng/g wet weight (range <2.94 – 204 ng/g).

4.1.2.5. Elimination

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, including PFDA and other PFAAs. 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 PFAAs than the other groups and therefore the three other groups were combined. A reason for the lower levels in younger women is that menstrual bleeding, pregnancy and lactation are important elimination routes in addition to the major elimination via urine.

For most PFAAs, very good correlations ($p < 0.05$) were observed between the blood and urine concentrations. The weakest correlations were observed for PFUnA ($p > 0.05$), which is the longest chain-length PFCA that could be routinely detected in urine (detection frequency 98%), and for the branched isomer 3m-PFOA, which was only detected in 23% of samples (versus >75% for all other PFOA isomers). Among all urine samples, the predominant PFAAs (median values were reported and normalised by urinary volume) were PFOS (25 ng/L), followed by PFOA (19 ng/L), PFNA (1.7 ng/L), PFHxS (1.1 ng/L), PFHpA (0.82 ng/L), PFUnA (0.30 ng/L), and PFDA (0.22 ng/L).

Based on literature data and strong associations between urinary and blood concentrations (except PFUnA), renal clearance was assumed to be the major pathway for human elimination of the PFAAs, thus, CL_{total} was set equal to CL_{renal} (mL/day/kg). However, considering that menstrual clearance is an important clearance pathway for PFAAs in young females, menstrual clearance was estimated and added to renal clearance for calculation of CL_{total} in young females, using the same rate previously estimated for Japanese women (0.029 mL/day/kg). This estimated menstrual clearance is lower than CL_{renal} for most PFAAs and was considered a reasonable estimate because it is in the range of CL_{renal} for PFHxS and PFOS, which are two PFAAs that were significantly lower in younger females. Although other clearance mechanisms are acknowledged, they

are believed to be minor and were not accounted for experimentally (albeit, faecal elimination might be important for some longer chain (> C_{10}) PFAAs).

The estimated geometric mean elimination half-lives for the young female group and the combined male and older female group for PFDA were 4.0 and 7.1 years, respectively. Corresponding values for PFHpA, PFOA, PFNA and PFUnDA are included in Table 14 in section 4.1.3. The authors stated that these estimated half-lives should be viewed as upper limits due to the possibility that there might be other elimination routes than via the urine and menstrual bleeding.

In conclusion, renal clearance is the major elimination pathway in humans for PFDA but it can be expected that faecal excretion becomes more important for PFCAs longer than C_{10}. In younger women, menstrual clearance is another important clearance pathway. Estimated geometric mean elimination half-lives for PFDA in young females and in the group of males and older females are 4.0 and 7.1 years, respectively. Corresponding values for the shorter (PFNA) and longer (PFUnA) homologues are 1.7 y/3.2 y and 4.0 y/7.4 y.

4.1.2.6. Bioaccumulation in humans

Taken together, there is strong evidence that PFDA bioaccumulates in humans.

- PFDA is present in quantifiable amounts in blood serum from the general population.
- Humans have very long elimination half-lives for PFDA (several years).
  - Estimated average elimination half-lives in the general population are between 4.0 and 7.1 years, depending on sex and age.
- In professional ski waxers with comparatively high exposure to PFDA during the winter season, serum levels of PFDA decreased only slightly during 8 months between end of season and start of next season indicating slow elimination.
- Positive associations between years exposed as a ski waxer and concentration of PFDA in serum have been observed.
- In the general population, age is positively associated with serum levels of PFDA.
- Men have higher serum levels of PFDA than women, which may be due at least in part to elimination of this and other PFAAs during menstruation, pregnancy and breastfeeding.
- High protein binding to albumin, L-FABP and renal anionic transporters, as well as partitioning to membrane phospholipids, are plausible mechanisms for the slow elimination of PFDA, as for other PFCAs.

4.1.3. Conclusion on toxicokinetics and bioaccumulation in humans

The toxicokinetics of PFDA have been observed in available studies to be similar to PFOA and PFNA. This was also stated in the RAC opinion (European Chemicals Agency, 2015a) on the harmonised classification of PFDA and its ammonium (PFD-A) and sodium (PFD-S) salts (*"PFDA (and its salts) and PFOA/APFO possess physicochemical and toxicokinetic properties which are similar or in the same range"*). It may therefore be assumed that PFDA is well absorbed following oral and inhalation exposure, and to a lesser extent following dermal exposure. PFDA is present in human blood of the general population and elevated concentrations are seen following specific exposures such as in professional ski waxers, which remain high over a very long timespan although the high exposure is ceased. In experimental animals (rats) PFDA accumulates preferentially in the liver and

in serum. As for PFOA, PFDA may also distribute to kidneys. There are no indication that PFDA is metabolised.

PFDA can be transferred to the foetus via the placenta. The concentration in cord blood has been shown to be approximately half of the concentration in mother's blood. Further, parturition has been shown to decrease serum levels of PFDA.

PFDA is present in human breast milk. The concentration is lower than in serum (5-10 % of serum concentrations), but breast-feeding is nevertheless one source of PFDA in infants. Gestational and lactational exposure is of special concern as the foetus and newborn babies may be more vulnerable to exposure to toxic substances.

Urinary excretion is the primary route of elimination for PFDA, although faecal excretion becomes more important for PFCAs longer than C_{10}. In younger females menstrual bleeding is another important elimination pathway. Humans show a considerably slower elimination of PFDA compared to rats (22-59 days), with average half-lives in humans around 4-7 years. The reason for this phenomenon is not fully understood; in addition to allometric reasons the difference might be attributed to *e.g.* different expression and amounts of renal anionic transporter proteins. Albumin, fatty acid binding protein and renal anionic transporters, i.e. proteins that have been shown in animal studies to affect the distribution and elimination of PFDA and other PFCAs, are found in humans as well.

Available half-lives of PFCAs in humans and in rat, mice, pig and monkey are presented in Table 14 below. These data show that the potential bioaccumulation differs significantly across different species and gender. Variation within species/sex groups may be due to test conditions, such as dosing scheme (exposure route, single versus repeated dose). The half-lives of PFCAs generally increase with increasing chain-length. The half-life of PFDA in human serum is ≥ 4 years, whereas the same parameter in rats varies between 22 and 59 days.

It may also be valuable to compare data for PFDA with those for the longer and shorter homologous PFCAs, in particular when coming from the same study where identical methods have been used. In the study by Zhang *et al.* (2013), estimated geometric mean elimination half-lives for PFDA in young females and in the group of males and older females are 4.0 and 7.1 years, respectively. Corresponding values for the shorter PFOA and PFNA are 1.7 y/1.2 y and 1.7 y/3.2 y respectively while for the longer PFUnDA the values are 4.0 y/7.4 y, similar to PFDA.

Table 14: Half-lives of PFCAs in humans and other species.

Number of C/F-atoms	Name	Species 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: 9.2h, F: 1.8h [a] M: 6.4h, F: 1.0h [b]	M: 13h, F: 2.9h [c] M: 16h, F: 3.1h [d] M: 5.2h, F: 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]		
6/11	PFHxA	M: 1.0h, F: 0.42h [h] M: 2.2h, F: 2.7h [i] M: 2.7h, F: 2.4h [j] M: 2.8h, F: 2.3h [k] M: 1.7h, F: 0.5h [l] M: 1.5h, F: 0.7h [m]		M, F: 4.1d [n]	M: 5.3h, F: 2.4h [h]			
7/13	PFHpA	M: 2.4h, F: 1.2h [o]		M, F: 74d [p]			1.5y AM, 1.0y GM, 1.6y M [q]	1.2y AM, 0.82y GM, 0.79y M [q]
8/15	PFOA	M: 5.6d, F: 0.08d [o] M: 13d [r] M: 9.1d [s]	M: 22d, F: 16d [t]	M, F: 236d [u]	M: 21d, F: 33d [v] M: 20d [x] M: 21d [y]	M, F: 1.4y AM, 1.3y GM, 1.3y M [z]	2.3y AM, 1.7y GM, 2.0y M [q]	2.8y AM, 1.2y GM, 1.8y M [q]
9/17	PFNA	M: 30d, F: 2.4d [o] M: 41d [r] M: 47d, F: 2.1d [A] M: 42d [B] M: 24d, F: 32d [C] M: 28d [D]	M: 34d, F: 26d [E] M: 228d, F: 69d [F]				2.5y AM, 1.7y GM, 1.5y M [q]	4.3y AM, 3.2y GM, 3.5y M [q]
10/19	PFDA	M: 40d, F: 59d [o] M: 22d, F: 29d [G] M: 23d, F: 43d [H]					4.5y AM, 4.0y GM, 4.2y M [q]	12y AM, 7.1y GM, 9.2y M [q]
11/21	PFUnDA						4.5y AM, 4.0y GM, 4.4y M [q]	12y AM, 7.4y GM, 9.2y M [q]

[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 half-life calculated from two blood samples 7-11 d apart
[h] Data from Chengelis et al., 2009. Mean β-phase of two compartment model with first-order elimination, single IV dose of 10 mg/kg
[i] 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

[j] 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
[k] 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
[l] Data from Gannon et al., 2011. Mean β-phase of one compartment model with first-order elimination, single oral dose of 2 mg/kg
[m] Data from Gannon et al., 2011. Mean β-phase of one compartment model with first-order elimination, single oral dose of 100 mg/kg
[n] Data from Numata et al., 2014. Mean β-phase of two compartment model with first-order elimination, 21d exposure to 48 µg/kg dw in diet
[o] 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
[p] Data from Numata et al., 2014. Mean β-phase of two compartment model with first-order elimination, 21d exposure to 10.2 µg/kg dw in diet
[q] 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
[r] Data from Benskin et al., 2009. β-phase elimination rate, single oral dose, 0.5 mg/kg
[s] Data from De Silva et al., 2009. β-phase elimination rate, repeated dose, 12 week exposure to 0.40 mg/kg in diet
[t] 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
[u] Data from Numata et al., 2014. Mean β-phase of two compartment model with first-order elimination, 21d exposure to 22.4 µg/kg dw in diet
[v] Data from Butenhoff et al., 2004. Mean β-phase of non-compartment model with first-order elimination, single IV dose of 10 mg/kg
[x] 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
[y] 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
[z] Data from Olsen et al., 2007. Mean β-phase of non-compartment model with first-order elimination, periodic blood samples collected over 5 years
[A] Data from De Silva et al., 2009. β-phase elimination rate, repeated dose, 12 week exposure to 0.54 mg/kg in diet
[B] 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
[C] 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
[D] 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
[E] 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
[F] 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
[G] Data from Vanden Heuvel et al., 1991. First-order elimination, single i.p. dose of 5 mg/kg (blood elimination)
[H] Data from Vanden Heuvel et al., 1991. First-order elimination, single i.p. dose of 5 mg/kg (whole body elimination)

5. Environmental hazard assessment

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

6. Conclusions on the SVHC Properties

6.1. CMR assessment

In accordance with Article 37(4) of the CLP Regulation, the Committee for Risk Assessment (RAC) at RAC-35 (December 2015) has adopted an opinion that PFDA and its sodium and ammonium salts meet the criteria for classification as toxic for reproduction Repr. 1B, H360Df ("May damage the unborn child. Suspected of damaging fertility"). It is foreseen that this proposal for harmonised classification and labelling will be voted on by the REACH Committee in September 2016 for inclusion in the 10th ATP to CLP.

Therefore, PFDA and its sodium and ammonium salts meet the criteria of Article 57(c) of Regulation (EC) 1907/2006 (REACH Regulation).

6.2. PBT and vPvB assessment

6.2.1. Assessment of PBT/vPvB properties

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

6.2.1.1. Persistence

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

In general, the persistence of PFDA can be explained by the shielding effect of the fluorine atoms, blocking *e.g.* nucleophilic attacks to the carbon chain. High electronegativity, low polarizability and high bond energies make highly fluorinated alkanes the most stable organic compounds. It is not expected that the carboxylic group in PFCAs alters this persistence of these chemicals. The persistence of six PFCAs (PFOA/APFO, PFNA and C_{11}-C_{14} PFCAs) (P and vP) was already confirmed by the Member State Committee (see Table 1) (European Chemicals Agency, 2012a-d, 2013a-b, 2015b).

Therefore, based on the knowledge of the stability of the C-F bond and the read-across approach with PFOA, PFNA and C_{11}-C_{14} PFCAs it is concluded that PFDA is not degraded 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

Due to its expected notable water solubility, PFDA is, like the other PFCAs expected to be quickly excreted in fish via gill permeation. Hence, bioconcentration in gill-breathing organisms is not the most relevant endpoint to consider, as reflected by the differences between bioaccumulation data for gill- and air-breathing organisms. Field studies show that air-breathing organisms are more likely to bioaccumulate PFDA and other PFCAs compared to gill-breathing organisms. Based on the BCF values for PFDA it cannot be excluded that PFDA is bioaccumulative in fish: BCF values range from 450 to 2700 for carcass, liver and blood. Conclusions on bioaccumulation should be based on whole body values and carcass is seen as a good approximation for whole body. Based on the BCF of

carcass PFDA does not bioaccumulate in fish. However, as shown in this report, PFDA does not accumulate in lipid but rather binds to protein and membrane phospholipids, therefore the carcass or whole-body BCF values are less relevant. Based on the BCF value in the blood of rainbow trout (2700±350), PFDA can be considered bioaccumulative.

Annex XIII (section 3.2.2) defines information which shall be taken into account in the assessment and can be used to draw conclusions on the assessment even when the numerical criterion is not applicable. Such data are, for example, data on the bioaccumulation potential in terrestrial species, such as elevated levels in endangered species. PFDA was found in terrestrial species as well as in endangered species as shown for the polar bear and the beluga whale. These findings indicate a bioaccumulation potential.

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 assessed into account. For PFDA, gestational and lactational exposure in humans has been shown, which is of special concern as the foetus and newborn babies are highly vulnerable to exposure by xenobiotic substances. On top of that, data from human body fluids clearly provide quantitative proof of the bioaccumulation of PFDA; elimination half-lives in humans are ≥ 4 years. In addition, recent studies, taking into account relevant confounding factors, show that PFDA blood concentrations in humans increase with increasing age.

Finally, Annex XIII (section 3.2.2 (c)) foresees that the potential for biomagnification in food chains of a substance is assessed. The available field data provide evidence that bioaccumulation and trophic magnification do occur in certain food webs in the environment. For PFDA, field studies provide trophic magnification factors (TMFs) or biomagnification factors (BMFs) in aquatic and terrestrial food chains. When air breathing organisms are the top predators in these food chains, biomagnification could be demonstrated by calculation of TMFs and BMFs to be > 1 in several food chains, for example for wolves, dolphins and beluga whales.

The data summarised above is in high accordance with the bioaccumulation data on the other PFCAs. Altogether these show a regular pattern of bioaccumulation which depends on the chain-length of the perfluorinated alkyl chain (see Annex I for read-across as part of the weight-of evidence approach).

Conclusion:

1. PFDA accumulates in humans.
    a. PFDA is present in human blood of the general population. PFDA has also been detected in human brain, lungs and kidney.
    b. Elimination half-lives are ≥ 4 years, which is longer than for PFNA and PFOA (see Table 14).
    c. PFDA levels increase with age after adjusting for relevant confounding factors.

2. There is evidence that PFDA preferentially bioaccumulates in air-breathing mammals, including endangered species and humans.
    a. BMFs range from 2.4 to 8.8 based on estimated whole body values in marine food web.
    b. TMFs range from 2.2 to 12.1 referring to either whole body measurements or estimated whole body values in marine wood web.

3. For part of the aquatic food chains investigated, PFDA accumulates in water-breathing animals.
    a. BCFs range from 450 (carcass) to 2700 (in blood).
    b. whole body BAFs range from 714 to 7943.

c. whole body BMFs range from 0.21 to 4.4.
d. whole body TMFs range from 0.39 to 3.67 in aquatic piscivorous food webs.

4. The bioaccumulation data on PFDA in environmental species, in laboratory mammals and in humans are consistent with the data on other long-chain perfluorinated carboxylic acids. Recent mechanistic bioconcentration models explain the substantial bioaccumulation of PFCAs by taking into account the observed pattern of animal tissue distribution, the relationship between chain length and bioaccumulation and the species and gender-specific variation in elimination half-life.

To conclude, taken all available information together in a weight-of-evidence approach, the elimination half-lives from humans and other mammals show that PFDA bioaccumulates. The available field data also indicate that bioaccumulation and trophic magnification occur in certain food webs in the environment. The data on PFDA are in line with the expected regular pattern of fate properties of the already assessed PFOA/APFO, PFNA and C_{11}-C_{14} PFCAs. Therefore, it is considered that the B criterion of REACH Annex XIII is fulfilled. Whether the vB criterion is fulfilled has not been assessed.

6.2.1.3. Toxicity

There is evidence based on the RAC opinion on PFDA and its sodium and ammonium salts that these substances meet the criteria for classification as toxic for reproduction in accordance with Article 57 (c) of the REACH Regulation. It is foreseen that this proposal for harmonised classification and labelling will be voted on by the REACH Committee in September 2016 for inclusion in the 10th ATP to CLP.

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

6.2.2. Summary and overall conclusions on the PBT and vPvB properties

In conclusion, PFDA and its sodium and ammonium salts are identified as PBT substances according to Art. 57(d) 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.

Table 15: Comparison with Annex XIII criteria of REACH

	Annex XIII	PFDA	Conclusion
P/vP	P Half-life: a) in marine water > 60 days, or b) in fresh- or estuarine water > 40 days, or c) in marine sediment > 180 days, or d) in fresh- or estuarine water sediment > 120 days, or e) in soil > 120 days vP Half-life: a) in marine, fresh- or estuarine water > 60 days, or b) in marine, fresh- or estuarine water sediment > 180 days, or c) in soil > 180 days	No simulation test available => read-across to PFOA: All studies of PFOA demonstrate the extremely high persistence of the compound. No environmental half-life could be determined during duration of the studies => Persistence (vP) of PFOA, PFNA and C_{11}-C_{14} PFCAs was confirmed by Member State Committee. Furthermore, the high stability of the C-F bond strengthens the arguments on PFDA persistency.	P/vP

B	Assessment of B or vB properties Results from a bioconcentration or bioaccumulation study in aquatic species; ▪ A substance fulfils the bioaccumulation criterion (B) when the bioconcentration factor in aquatic species is higher than 2 000. ▪ A substance fulfils the 'very bioaccumulative' criterion (vB) when the bioconcentration factor in aquatic species is higher than 5 000. (b) Other information on the bioaccumulation potential provided that its suitability and reliability can be reasonably demonstrated, such as: ▪ Results from a bioaccumulation study in terrestrial species; ▪ Data from scientific analysis of human body fluids or tissues, such as blood, milk, or fat; ▪ Detection of elevated levels in biota, in particular in endangered species or in vulnerable populations, compared to levels in their surrounding environment; ▪ Results from a chronic toxicity study on animals; ▪ Assessment of the toxicokinetic behaviour of the substance; (c) Information on the ability of the substance to biomagnify in the food chain, where possible expressed by biomagnification factors or trophic magnification factors.	• Based on the BCF values it cannot be excluded that PFDA bioaccumulates. • BAF values from water breathing animals range between 714 and 7943. • BMF values for gill breathing organisms range between 0.21 and 4.4. • BMFs including air breathing animals range between 2.4 and 8.8 based on estimated whole body values. • TMF values for gill breathing organisms range between 0.39 and 3.67. • When air breathing animals are top predators TMFs range between 2.2 and 12.1 referring to either whole body measurements or estimated whole body values. • Protein corrected TMFs range between 0.39 and 6.99. • Terrestrial BMFs and TMFs range between 1.7 and 12.4 and 2.3-2.6, respectively, based on estimated whole body values. • PFCAs have a high potential for transfer to milk and beef from the diet of dairy cows. • PFDA is present in quantifiable amounts in blood serum from the general population. • Humans have long elimination half-lives for PFDA, ≥4 years in blood serum. • Estimated average half-lives in the general population are 4-7.1 years depending	B (vB not assessed)

		on sex and age. • In professional ski waxers, with comparatively high exposure to PFDA during the winter season, serum levels of PFDA decreased only slightly during 8 months between end of season and start of next season. • Positive associations between years exposed as a ski waxer and concentration of PFDA in serum have been observed. • Age is positively associated with serum levels of PFDA.	
T	a) NOEC < 0.01 mg/L, or b) Classified as carcinogenic (cat. 1or 2), mutagenic (cat. 1 or 2), or toxic for reproduction (cat. 1, 2 or 3), or c) Classified as STOT RE cat. 1 or 2	RAC opinion: Repr. 1B It is foreseen that the harmonised classification and labelling proposal will be voted on by the REACH Committee in September 2016.	T

PART II

7. Registration and C&L notification status

7.1. Registration status

There is yet no registration dossier for PFDA or its salts and thus no information about tonnage or uses in the EU. PFDA was planned for registration on November 30th, 2010 (three pre-registrations at >1000 tonnes/year), May 31st, 2013 (two pre-registrations 100-1000 tonnes/year), and May 31st, 2018 (three pre-registrations at 10-100 tonnes/year, and 11 pre-registrations at 1-10 tonnes/year). Ammonium nonadecafluorodecanoate is pre-registered with envisaged registration deadlines on May 31st, 2013 (two pre-registrations) and May 31st, 2018 (two pre-registrations at 10-100 tonnes/year, and five pre-registrations at 1-10 tonnes/year). Sodium nonadecafluorodecanoate has no pre-registrations. Further, PFDA or its salts are not registered in the SPIN database.

7.2. CLP notification status

Table 16: CLP notifications (EC No 206-400-3)

	CLP Notifications[5]
Number of aggregated notifications	6
Total number of notifiers	31

8. Total tonnage of the substance

No data available, there is no registration dossier for PFDA.

9. Information on uses of the substance

9.1. Overview of uses

Perfluoroalkyl substances are in general prepared via electrochemical fluorination or telomerization (Buck *et al.* 2011). Both odd- and even-numbered PFCAs may be prepared from either process and it is not clear if PFDA is preferably synthesised by a specific route. PFDA has been used as plasticiser, lubricant, surfactant, wetting agent and corrosion inhibitor (ChemSec, 2014). PFDA derivatives are also used and are important sources of PFDA in the environment (indirect sources, *i.e.* degradation of precursors to form PFDA). Wang *et al.* (2014) estimated the global cumulative emission of PFDA 2003-2015 in between 4 and 93 tonnes which includes both direct and indirect sources. The importance of indirect sources for release of long-chain PFCAs including PFDA is also concluded by Cousins *et al.* (2011).

Since 2002, there has been a trend amongst global manufacturers to replace long-chain PFCAs, PFSAs and their potential precursors with chemicals containing shorter

[5] C&L Inventory database, http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database (accessed 8 June 2016).

perfluoroalkyl chains, with non-perfluoroalkyl products, or switching to non-chemical techniques. Regarding substitutions to other fluorinated chemicals, C_{9-14} PFCAs can be replaced with shorter chain fluorinated substances based on C_4 or C_6 chemistry that cannot transform into PFDA (OECD, 2013; FluoroCouncil, 2013). As surfactants used for processing aids in the production of fluoropolymers, polyfluoroalkyl ether carboxylic acids have been introduced as viable alternatives to long-chain PFCAs, although this particular use has historically been most relevant for the C_8 (PFOA) and C_9 (PFNA) analogues.

9.2. Occurrence in mixtures and articles

PFDA has been detected in various water and stain resistant textiles. A German study from 2012 (Zangl *et al.* 2012) analysed different perfluorinated substances in workwear for paramedics, pilots and firefighters. The levels varied but PFDA was detected in many of the samples with highest concentrations around 30 µg/m^2.

The US EPA has analysed 116 products (articles and chemical products) to determine the extractable content of C_5 to C_{12} PFCAs (US EPA, 2009). PFDA was detected in almost 70 of these products.

A recent study on perfluoroalkyl and polyfluoroalkyl substances in consumer products shows that PFDA is present in nanosprays and impregnation sprays, outdoor textiles, carpets, gloves, leather, paper-based food contact materials and ski waxes (Kotthoff *et al.* 2015). High concentrations were found in paper-based food contact materials (max 489 µg/kg) and ski waxes (max 1840 µg/kg). In a Norwegian study on the detection of PFASs in outdoor textiles and gear, PFDA was detected in 3 out of 18 analysed products (Hanssen *et al.* 2015). In another recent study from the Nordic Council of Ministers, PFDA was detected in table cloths and sandwich paper (Blom and Hanssen, 2015).

9.3. Occurrence in the environment

In the environment PFDA is ubiquitously distributed which is confirmed by findings of this substance for example in surface waters, wastewater treatment plants (effluent and sludge), landfill leachates, snow and biota (*e.g.* polar bear) (Table 17).

Table 17: Occurrence of PFDA in the environment

Location	Concentration	Reference
Canadian Arctic lakes (5 locations)	1.1-19 ng/L (mean values)	Stock *et al.*, 2007
River Elbe (3 locations)	0.24-0.85 ng/L	Ahrens et al., 2010
Wastewater treatment plants (effluent, 6 plants), New York State	3-35 ng/L (mean values, 3 plants) <2.5 ng/L (limit of quantification, 3 plants)	Sinclair and Kannan, 2006
Wastewater treatment plants (sludge, 6 plants), Denmark	1.2-32 µg/kg dry weight (found in all plants)	Bossi *et al.*, 2008
Landfill leachates (22 landfill sites), Germany	<0.21-55.1 ng/L	Busch *et al.*, 2010
Snow (e.g. High Tatras, Slovakia, 2 samples)	0.137 and 0.183 ng/L	Greenpeace, 2015
Polar bear (several studies/locations)	6-103 ng/g wet weight	Butt *et al.*, 2010

10. Information on structure of the supply chain

No data available.

11. Additional information

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

Seven entries of long-chain PFCAs have already been included into the Candidate List (Table 1). 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. Determining the technical feasibility of an alternative for a specific use however requires expertise of the detailed function (UNEP, 2014). In addition, long-chain PFCAs are currently being replaced by shorter perfluoroalkyl chains or with non-perfluoroalkyl products (see below).

11.2. Alternatives

Since 2002, there has been a trend amongst global manufacturers to replace long-chain PFCAs and their potential precursors with chemicals containing shorter perfluoroalkyl chains or with non-perfluoroalkyl products. In general, C_9-C_{14} PFCAs can be replaced with shorter chain fluorinated substances based on C_4 or C_6 chemistry that cannot transform into PFDA (OECD, 2013; FluoroCouncil, 2013).

There are three types of alternatives to long-chain PFCAs (FluoroCouncil, 2013):

- substances with shorter per- or polyfluorinated chains,
- non-fluorine-containing substances, and
- non chemical techniques

Table 18: Alternatives to long-chain PFCAs including PFDA[a]

Alternative substances	Uses
6:2 Fluorotelomer-based chemicals	Replaces especially their higher homologues
Perfluorobutane sulfonyl fluoride (PFBS) or substances based on C-4 perfluorocompounds	Replaces chemicals based on perfluorooctane sulfonyl fluoride
Mono- and polyfluorinated alkyl ether carboxylic acids	Fluoropolymer manufacturing
Fluorinated oxetanes	
Other fluorinated polymers	
Fatty alcohol polyglycol ether sulphate	Levelling and wetting agents
Silicone polymers	Impregnation of textiles, leather and carpets

Sulfosuccinates	Wetting agent for paints and coatings
Propylated aromatics (naphthalenes and biphenyls)	Water repelling agents for *e.g.* corrosion protection systems, marine paints, resins, printing inks, electrical, electronical and mechanical applications
Other hydrocarbon surfactants	Photographic industry
Stearamidomethyl pyridine chloride	Impregnation of textiles, leather and carpets

[a] OECD, 2013; Fluorocouncil, 2013; Swedish Chemicals Agency, 2015

The technical and economic feasibility of an alternative is heavily influenced by the specific requirements of the user (a company, an industry or sector) of the alternative and the conditions prevailing in the country where the user operates. In addition, determining the technical feasibility of an alternative requires detailed information about the performance of the alternative for a specific use and the expertise to assess this information (UNEP, 2014). 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.

International activities

USA

US EPA has initiated the 2010/15 PFOA Stewardship Program with eight major companies (including some European companies) which target PFOA, precursor chemicals and higher homologue chemicals. The industry committed voluntarily to reduce global facility emissions and product content on a global basis by 95 percent no later than 2010, and to work toward eliminating emissions and product content of these chemicals by 2015. The latest report for 2013 and 2014, released in January 2015, shows that the companies were on track to reach the program's goal (US EPA, 2015).

On January 15, 2015, US EPA proposed a Significant New Use Rule (SNUR) under the Toxic Substances Control Act to require manufacturers (including importers) of some long-chain PFAS chemicals, including as part of articles, and processors of these chemicals to notify EPA at least 90 days before starting or resuming new uses of these chemicals in any products. This notification would allow EPA the opportunity to evaluate the new use and, if necessary, take action to prohibit or limit the activity. The SNUR is effective from July 15, 2016 (available at: https://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2015-0810-0001).

CANADA

The government of Canada is planning to implement regulations to prohibit manufacture, use, sale, offer for sale, import and export of the group of PFOA, as well as long chain (C9-C20) perfluorocarboxylic acids (PFCAs) and their salts and precursors. In January 2014 Environment Canada launched a public consultation on a proposed risk management measure for PFOA, its salts, and its precursors and long-chain (C_9-C_{20}) PFCAs, their salts and their precursors (Environment Canada, 2014). Proposed regulations were published April 4, 2015 and subject to a 75-day public comment period

where the received comments will be considered in the final regulations scheduled for publication in 2016.

11.3. Existing EU legislation

Based on current knowledge there are yet no EU legislation that specifically regulates PFDA. Once PFDA is included in Annex VI of the CLP legislation (as Repr. 1B), this will affect several other legislations such as the Toys Directive. After inclusion in Entry 30 of Annex XVII of REACH the presence in consumer products will also be regulated.

12. Previous assessments by other authorities

Long-chain perfluorinated chemicals including PFDA have in general been screened in the context of the more detailed assessments of the common perfluorooctyl sulfonate (PFOS) and perfluorooctanoic acid (PFOA). For example, Environment Canada performed an ecological screening of long-chain (C_9-C_{20}) perfluorocarboxylic acids, their salts and their precursors in 2012 and it is concluded in a weight of evidence approach that they are persistent and accumulate and biomagnify in terrestrial and marine mammals (Environment Canada, 2012).

There are no assessments known on PFDA specifically by other authorities.

References for Part I

Benskin, J. P., De Silva, A. O., Martin, L. J., Arsenault, G., McCrindle, R., Riddell, N., Mabury, S. A., Martin, J. W. (2009). Disposition of perfluorinated acid isomers in Sprague-dawley rats; part 1: single dose. *Environ. Toxicol. Chem*. **28**, 542-554.

Berg, V., Nøst, T. H., Huber, S., Rylander, C., Hansen, S., Veyhe, A. S., Fuskevåg, O. M., Odland, J. Ø., Sandanger, T. M. (2014). Maternal serum concentrations of per- and polyfluoroalkyl substances and their predictors in years with reduced production and use. *Environ. Internat.* **69**, 58-66.

Bjermo, H., Darnerud, P. O., Pearson, M., Enghardt Barbieri, H., Lindroos, A. K., Nälsén, C., Lindh, C. H., Jönsson, B. A. G., Glynn, A. (2013). Serum concentrations of perfluorinated alkyl acids and their associoations with diet and personal characteristics among Swedish adults. *Mol. Nutr. Food Res.* **57**, 2206-2215.

Bohlin-Nizzetto, P., Hanssen, L., Herzke, D. (2015). PFASs in house dust. Norwegian Institute for Air Research, NILU OR 29/2015.

Borgå, K., Kidd, K. A., Muir, D. C., Berglund, O., Conder, J. M., Gobas, F. A., Kucklick, J., Malm, O., Powell, D. E. (2012). Trophic magnification factors: Considerations of ecology, ecosystems and study design. *Integr. Environ. Assess. Manag.* **8**(1):64-84.

Brace, N. O. (1962). Long chain alkanoic and alkenoic acids with perfluoroalkyl terminal segments. *J. Org. Chem.* 4491-4498.

Brantsæter, A.L., Whitworth, K. W., Ydersbond, T. A., Haug, L. S., Knutsen, H. K., Thomsen, C., Meltzer, H. M., Becher, G., Sabaredzovic, A., Hoppin, J. A., Eggesbø, M., Longnecker, M. P. (2013). Determinants of plasma concentrations of perfluoroalkyl substances in pregnant Norwegian women. *Environ. Int.* **54**, 74-84.

Butenhoff, J. L., Kennedy, G. L. Jr., Hinderliter, P. M., Lieder, P. H., Jung, R., Hansen, K. J., Gorman, G. S., Noker, P. E., Thomford, P. J. (2004). Pharmacokinetics of perfluorooctanoate in cynomolgus monkeys. *Toxicol. Sci.* **82**, 394-406.

Butt, C. M., Mabury, S. A., Kwan, M., Wang, X., Muir, D. C. (2008). Mar. Spatial trends of perfluoroalkyl compounds in ringed seals (Phoca hispida) from the Canadian Arctic. *Environ. Toxicol. Chem.* **27**(3):542-553.

Butt. C. M., Muir, D. C. G., Stirling, I., Kwan, M., Mabury, S. A. (2007). Rapid response of arctic ringed seals to changes in perfluoroalkyl production. *Environ. Sci. Technol*. **41**, 42-49.

Chang, S.-C., Das, K., Ehresman, D. J., Ellefson, M. E., Gorman, G. S., Hart, J. A., Noker, P. E., Tan, Y.-M., Lieder, P. H., Lau, C., Olsen, G. W., Butenhoff, J. L. (2008). Comparative pharmacokinetics of perfluorobutyrate in rats, mice, monkeys, and humans and relevance to human exposure via drinking water. *Toxicol. Sci.* **104**, 40-53.

Chengelis, C. P., Kirkpatrick, J. B., Myers, N. R., Shinohara, M., Stetson, P. L., Sved, D. W. (2009). Comparison of the toxicokinetic behavior of perfluorohexanoic acid (PFHxA) and nonafluorobutane-1-sulfonic acid (PFBS) in cynomolgus monkeys and rats. *Reprod. Toxicol.* **27**, 400-406.

Conder, J. M., Gobas, F. A. P. C., Borga, K., Muir, D. C. G., Powell, D. E. (2012). Use of trophic magnification factors and related measures to characterize bioaccumulation potential of chemicals. *Integr. Environ. Assess. Manag*.:n/a.

De Silva, A. O., Benskin, J. P., Martin, L. J., Arsenault, G., McCrindle, R., Riddell, N., Martin, J. W., Mabury, S. A. (2009). Disposition of perfluorinated acid isomers in Sprague-Dawley rats; part 2: Subchronic dose. *Environ. Toxicol. Chem.* **28**, 555-567.

Dietz, R., Bossi, R., Rigét, F. F., Sonne, C., Born, E. W. (2008). Increasing perfluoroalkyl contaminants in east Greenland polar bears (Ursus maritimus): A new toxic threat to the arctic bears. *Environ. Sci. Technol.* **42**, 2701-2707.

Drouillard, K. G., Norstrom, R. J. (2000). Dietary absorption efficiencies and toxicokinetics of polychlorinated biphenyls in ring doves following exposure to arochlor mixtures. *Environ. Toxicol. Chem.* **19**, 2707–2714.

ECETOC (2014). Special Report 18 – Information to be considered in a weight-of-evidence-based PBT/vPvB assessment of chemicals (Annex XIII of REACH). Available at: http://www.ecetoc.org/publications/special-reports/

Ehrlich, G., Jöhncke, U., Drost, W., Schulte, C. (2011). Problems faced when evaluating the bioaccumulation potential of substances under REACH. *Integr. Environ. Assess. Manage.* **7**(4), 550-558.

Ericson Jogsten, I., Nadal, M., van Bavel, B., Lindström, G., Domingo J. L. (2012). Per- and polyfluorinated compounds (PFSs) in house dust and indoor air in Catalonia, Spain: Implications for human exposure. *Environ. Internat.* **39**, 172-180.

European Chemicals Agency (2012a). Member State Committee support document for identification of henicosafluoroundecanoic acid (EC Number: 218-165-4; CAS Number: 2058-94-8) as a substance of very high concern because of its vPvB properties. Available at: http://echa.europa.eu/documents/10162/01986fb8-ede8-4458-b54e-12ff8a534b98

European Chemicals Agency (2012b). Member State Committee support document for identification of tricosafluorododecanoic acid (EC Number: 206-203-2; CAS Number: 307-55-1) as a substance of very high concern because of its vPvB properties. Available at: http://echa.europa.eu/documents/10162/0d5abffa-6bbf-40c7-b6b1-1ca3736cf570

European Chemicals Agency (2012c). Member State Committee support document for identification of pentacosafluorotridecanoic acid (EC Number: 276-745-2; CAS Number: 72629-94-8) as a substance of very high concern because of its vPvB properties. Available at: http://echa.europa.eu/documents/10162/3fd11ee9-6925-475f-b328-d224d45219a4

European Chemicals Agency (2012d). Member State Committee support document for identification of heptacosafluorotetradecanoic acid (EC Number: 206-803-4; CAS Number: 376-06-7) as a substance of very high concern because of its vPvB properties. Available at: http://echa.europa.eu/documents/10162/997efe1b-0564-4ca1-a012-bab93e518f25

European Chemicals Agency (2013a). Member State Committee support document for identification of ammonium pentadecafluorooctanoate (APFO) (EC Number: 223-320-4; CAS Number: 3825-26-1) as a substance of very high concern because of its CMR and PBT properties. Available at: http://echa.europa.eu/documents/10162/5e2c1e53-be98-4104-8b96-9cd88655a92a

European Chemicals Agency (2013b). Member State Committee support document for identification of pentadecafluorooctanoic acid (PFOA) (EC Number: 206-397-9; CAS Number: 335-67-1) as a substance of very high concern because of its CMR and PBT properties. Available at: http://echa.europa.eu/documents/10162/8059e342-1092-410f-bd85-80118a5526f5

European Chemicals Agency (2015a). Committee for Risk Assessment. RAC Opinion proposing harmonised classification and labelling at EU level of Nonadecafluorodecanoic acid (PFDA) [1] and its ammonium (PFD-A) [2] and sodium (PFD-S) [3] salts, Nonadecafluorodecanoic acid [1], ammonium nonadecafluorodecanoate [2], sodium nonadecafluorodecanoate [3], EC numbers: 206-4003 [1], 221-470-5 [2], - [3], CAS numbers: 335-76-2 [1], 3108-42-7 [2], 3830-45-3 [3]. Available at: http://echa.europa.eu/documents/10162/40352a80-661e-4c75-8a37-e82e2064b435

European Chemicals Agency (2015b). Member State Committee support document for identification of perfluorononan-1-oic acid and its sodium and ammonium salts (EC numbers: 206-801-3, not applicable, not applicable, CAS numbers: 375-95-1, 21049-39-8, 4149-60-4) as substances of very high concern because of their toxic for reproduction and PBT properties. Available at: http://echa.europa.eu/documents/10162/48ae5fe3-9436-4a10-a533-ed642b92ce47

European Chemicals Agency (2015c). CLH report, Proposal for Harmonised Classification and Labelling for Nonadecafluorodecanoic Acid (PFDA) and its ammonium and sodium salts (EC Numbers: 206-400-3 [1], 221-470-5 [2], - [3], CAS Numbers: 335-76-2 [1], 3108-42-7 [2], 3830-45-3 [3]. Available at: http://echa.europa.eu/documents/10162/3e08ce73-4b1a-444f-ac15-2c130616341c

Fisk, A. T., Hobson, K. A., Norstrom, R. J. (2001). Influence of chemical and biological factors on trophic transfer of persistent organic pollutants in the northwater polynyamarine food web. *Environ. Sci. Technol.* **35**, 732–738.

Freberg, B. I., Haug, L. S., Olsen, R., Daae, H. L., Hersson, M., Thomsen, C., Thorud, S., Becher, G., Molander, P., Ellingsen, D. G. (2010). Occupational exposure to airborne perfluorinated compounds during professional ski waxing. *Environ. Sci. Technol.* **44**, 7723-7728.

Furdui, V. I., Stock, N. L., Ellis, D. A., Butt, C. M., Whittle, D. M., Crozier, P. W., Reiner, E. J., Muir, D. C. G., Mabury, S. A. (2007). Spatial distribution of perfluoroalkyl contaminants in lake trout from the Great Lakes. *Environ. Sci. Technol.* **41**, 1554-1559.

Gannon, S. A., Johnson, T., Nabb, D. L., Serex, T. L., Buck, R. C., Loveless, S. C. (2011). Absorption, distribution, metabolism, and excretion of [1-^{14}C]-perfluorohexanoate ([^{14}C]-PFHx) in rats and mice. *Toxicology* **283**, 55-62.

Gewurtz, S. B., De Silva, A. O., Backus, S. M., McGoldrick, D. J., Keir, M. J., Small, J., Melymuk, L., Muir, D. C. G. (2012). Perfluoroalkyl contaminants in Lake Ontario Lake Trout: Detailed examination of current status and long-term trends, *Environ. Sci. Technol*. **46**, 5842-5850.

Glynn, A., Benskin, J., Lignell, S., Gyllenhammar, I., Aune, M., Cantillana, T., Darnerud, P. O., Sandblom, O. (2015). Temporal trends of perfluoroalkyl substances in pooled serum samples from first-time mothers in Uppsala 1997-2014. Report to the Swedish EPA.

Glynn, A., Berger, U., Bignert, A., Ullah, S., Aune, M., Lignell, S., Darnerud, P. O. (2012). Perfluorinated alkyl acids in blood serum from primiparous women in Sweden: Serial sampling during pregnancy and nursing, and temporal trends 1996-2010. *Environ. Sci. Technol.* **46**, 9071-9079.

Gützkow, K. B., Haug, L. S., Thomsen, C., Sabaredzovic, A., Becher, G., Brunborg, G. (2012). Placental transfer of perfluorinated compounds is selective - A Norwegian mother and child sub-cohort study. *Int. J. Hyg. Environ. Health* **215**, 216-219.

Han, X., Nabb, D. L., Russell, M. H., Kennedy, G. L., Rickard, R. W. (2012). Renal elimination of perfluorocarboxylates (PFCAs). *Chem. Res. Toxicol.* **25**, 35-46.

Hare, E. F., Shafrin, E. G., Zisman, W. A. (1954). Properties of films of adsorbed fluorinated acids. *J. Phys. Chem.* **58**(3), 236-239.

Haug, L. S., Salihovic, S., Jogsten I. E., Thomsen, C., van Bavel, B., Lindstrom, G., *et al.* (2010a). Levels in food and beverages and daily intake of perfluorinated compounds in Norway. *Chemosphere* **80**, 1137-1143.

Haug, L. S., Thomsen, C., Brantsaeter, A., Kvalem, H., Haugen, M., Becher, G., *et al.* (2010b). Diet and particularly seafood are major sources of perfluorinated compounds in humans. *Environ. Internat.* **36**, 772-778.

Hickie BE, Mackay D & de Koning J (1999). Lifetime pharmacokinetic model for hydrophobic contaminants in marine mammals. *Environ. Toxicol. Chem.* **18** (11), 2622-33.

Higgins, C. P., McLeod, P. B., MacManus-Spencer, L. A., Luthy, R. G. (2007). Bioaccumulation of perfluorochemicals in sediments by the aquatic oligochaete Lumbriculus variegatus. *Environ. Sci. Technol.* **41**, 4600-4606.

Hop, H., Borga, K., Wing, G., Lars, G., Janneche, K., Skaare, U. (2002). Food web magnification of persistent organic pollutants in poikilotherms and homeotherms from the

Barents Sea. *Environ. Sci. Technol.* **36**, 2589-2597.

Hori, H., Yamamoto, A., Kutsuna, S. (2005). Efficient Photochemical Decomposition of Long-Chain Perfluorocarboxylic Acids by Means of an Aqueous/Liquid CO2Biphasic System. *Environ. Sci. Technol.* **39**, 7692-7697.

Houde, M., Bujas, T. A., Small, J., Wells, R. S., Fair, P. A., Bossart, G. D., Solomon, K. R., Muir, D. C. (2006). Biomagnification of perfluoroalkyl compounds in the bottlenose dolphin (Tursiops truncatus) food web. *Environ. Sci. Technol.* **40**, 4138-4144.

Huber, S., Haug, L. S., Schlabach, M. (2011). Per- and polyfluorinated compounds in house dust and indoor air from northern Norway – A pilot study. *Chemosphere* **84**, 1686–1693.

Inoue, Y., Hashizume, N., Yoshida, T., Murakami, H., Suzuki, Y., Koga, Y., Takeshige, R., Kikushima, E., Yakata, N., Otsuka, M. (2012). Comparison of Bioconcentration and Biomagnification Factors for Poorly Water-Soluble Chemicals Using Common Carp (Cyprinus carpio L.). *Arch. Environ. Contam. Toxicol.* **63**, 241-248.

Kaiser, M. A., Larsen, B. S., Kao, C-P., Buck, R. C. (2005). Vapor pressures of perfluorooctanoic, -nonanoic, -decanoic, -undecanoic, and -dodecanoic acids. *J. Chem. Eng. Data* **50**, 1841–1843.

Kärrman, A., Davies, J., Salihovic, S. (2013). PFAAs in matched milk and serum samples from *primipara* women. Report to the Swedish EPA. Available at: http://www.diva-portal.org/smash/get/diva2:710702/FULLTEXT01.pdf

Kauck, E. A.; Diesslin, A. R. (1951). Some Properties of Perfluorocarboxylic Acids. *Ind. Eng. Chem.* **43**(10), 2332–2334.

Kelly, B. C., Gobas, F. A. P. C., McLachlan, M. S. (2004). Intestinal absorption and biomagnification of organic contaminants in fish, wildlife, and humans. *Environ. Toxicol. Chem.* **23**, 2324-2336.

Kelly, B. C., Ikonomou, M. G., Blair, J. D., Surridge, B., Hoover, D., Grace, R., Gobas, F. A. P. C. (2009). Perfluoroalkyl Contaminants in an Arctic Marine Food Web: Trophic Magnification and Wildlife Exposure. *Environ. Sci. Technol*. **43**(11), 4037-4043.

Kim, S.-K., Lee, K. T., Kang, C. S., Tao, L., Kannan, K., Kim, K.-R., Kim, C.-K., Lee, J. S., Park, P. S., Yoo, Y. W., Ha, J. Y., Shin, Y.-S., Lee, J.-H. (2011). Distribution of perfluorochemicals between sera and milk from th esame mothers and implications for prenatal and postnatal exposures. *Environ. Pollut*. **159**, 169-174.

Kudo, N., Bandai, N., Suzuki, E., Katakura, M., Kawashima, Y. (2000). Induction by perfluorinated fatty acids with different carbon chain length of peroxisomal beta-oxidation in the liver of rats. *Chem-Biol. Interact.* **124**(2), 119-132.

Kudo, N., Suzuki, E., Katakura, M., Ohmori, K., Noshiro, R., Kawashima, Y. (2001). Comparison of the elimination between perfluorinated fatty acids with different carbon chain length in rats. *Chem-Biol. Interact.* **134**(2), 203-216.

Labadie, P., Chevreuil, M. (2011). Partitioning behaviour of perfluorinated alkyl contaminants between water, sediment and fish in the Orge River (nearby Paris, France). Environ. Pollut. 159(2), 391-397.

Lambert, N., Rostock, C., Bergfald, B., Bjorvik, L.M. (2011). Identifiying POP candidates fot the Stockholm Convention. TA-2871/2011.

Liu, J., Li, J., Liu, Y., Chan, H. M., Zhao, Y., Cai, Z., Wu, Y. (2011). Comparison on gestation and lactation exposure of perfluorinated compounds for newborns. *Environ. Intern*. **37**, 1206-1212.

Loi, E. I., Yeung, L. W., Taniyasu, S., Lam, P. K., Kannan, K., Yamashita, N. (2011). Trophic magnification of poly- and perfluorinated compounds in a subtropical food web. *Environ. Sci. Technol.* **45**(13), 5506-5513.

Lou, I., Wambaugh, J. F., Lau, C., Hanson, R. G., Lindstrom, A. B., Strynar, M. J., Zehr,

R. D., Setzer, R. W., Barton, H. A. (2009). Modeling single and repeated dose pharmacokinetics of PFOA in mice. *Toxicol. Sci.* **107**, 331-341.

Martin, J. W., Mabury, S. A., Solomon, K. R., Muir, D. C. (2003a). Bioconcentration and tissue distribution of perfluorinated acids in rainbow trout (Oncorhynchus mykiss). *Environ. Toxicol. Chem.* **22**(1), 196-204.

Martin, J. W., Mabury, S. A., Solomon, K. R., Muir, D. C. (2003b). Dietary accumulation of perfluorinated acids in juvenile rainbow trout (Oncorhynchus mykiss). *Environ. Toxicol. Chem.* **22**(1), 189-195.

Martin, J. W., Whittle, D. M., Muir, D. C., Mabury, S. A. (2004). Perfluoroalkyl contaminants in a food web from Lake Ontario. *Environ. Sci. Technol.* **38**(20), 5379-5385.

Mørck, T. A., Nielsen, F., Nielsen, J. K. S., Siersma, V. D., Grandjean, P., Knudsen, L. E. (2015). PFAS concentrations in plasma samples from Danish school children and their mothers. *Chemosphere* **129**, 203-209.

Moroi, Y., Yano, H., Shibata, O., Yonemitsu, T. (2001). Determination of acidity constants of perfluoroalkanoic acids. *Bull. Chem. Soc. Jpn.* **74**, 667-672.

Müller, C. E., De Silva, A. O., Small, J., Williamson, M., Wang, X., Morris, A., Katz, S., Gamberg, M., Muir, D. C. (2011). Biomagnification of Perfluorinated Compounds in a Remote Terrestrial Food Chain: Lichen-Caribou-Wolf. *Environ. Sci. Technol.* **45**(20), 8665-8673.

National Institute of Technology and Evaluation (2007). Biodegradation and Bioconcentration of Exisiting Chemical Substances under the Chemical Substances Control Law. Information on the chemical published in the Official Bulletin of Economy,Trade and Industry.

Ng, C. A., Hungerbühler, K. (2013). Bioconcentration of perfluorinated alkyl acids: How important is specific binding? *Environ. Sci. Technol*. **47**, 7214-7223.

Ng, C. A., Hungerbühler, K. (2014). Bioaccumulation of perfluorinated alkyl acids: observations and models. *Environ. Sci. Technol.* **48**, 4637−4648.

Nilsson, H., Kärrman, A., Westberg, H., Rotander, A., van Bavel, B., Lindström, G. (2010). A time trend study of significantly elevated perfluorocarboxylate levels in humans after using fluorinated ski wax. *Environ. Sci. Technol.* **44**, 2150-2155.

Numata, J., Kowalczyk, J., Adolphs, J., Ehlers, S., Schafft, H., Fuerst, P., Müller-Graf, C., Lahrssen-Wiederholt, M., Greiner, M. (2014). Toxicokinetics of seven perfluoroalkyl sulfonic and carboxylic acids in pigs fed a contaminated diet. *J. Agr. Food. Chem.* **62**, 6861-6870.

Ohmori, K., Kudo, N., Katayama, K., Kawashima, Y. (2003). Comparison of the toxicokinetics between perfluorocarboxylic acids with different carbon chain length. *Toxicology* **184**, 135-140.

Olsen, G. W., Burris, J. M., Ehresman, D. J., Froehlich, J. W., Seacat, A. M., Butenhoff, J. L., Zobel, L. R. (2007). Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. *Environ. Health Persp*. **115**, 1298-1305.

Pérez, F., Nadal, M., Navarro-Ortega, A., Fàbrega, F., Domingo, J. L., Barceló, D., Farré, M. (2013). Accumulation of perfluoroalkyl substances in human tissues. *Environ. Int.* **59**, 354-362.

Rich, C. D., Blaine, A. C., Hundal, L., Higgins, C. P. (2015). Bioaccumulation of perfluoroalkyl acids by earthworms (Eisenia fetida) exposed to contaminated soils. *Environ. Sci. Technol.* **49**(2), 881-888.

Rigét, F., Bossi, R., Sonne, C., Vorkamp, K., Dietz, R. (2013). Trends of perfluorochemicals in Greenland ringed seals and polar bears: Indications of shifts to

decreasing trends. *Chemosphere* **93**, 1607-1614.

Schecter, A., Malik-Bass, N., Calafat, A. M., Kato, K., Colacino, J. A., Gent, T. L., Hynan, L. S., Harris, T. R., Malla, S., Birnbaum, L. (2012). Polyfluoroalkyl compounds in Texas children from birth through 12 years of age. *Environ. Health Persp.* **120**(4), 590-594.

Siegemund, G., Schwertfeger, W., Feiring, A., Smart, B., Behr, F., Vogel, H., McKusick, B. (2000). Fluorine Compounds, Organic, Ullmann's Encyclopedia of Industrial Chemistry. Wiley-VCH Verlag GmbH & Co. KGaA.

Smithwick, M., Norstrom, R. J., Mabury, S. A., Solomon, K., Evans, T. J., Stirling, I., Taylor, M. K., Muir, D. C. G. (2006). Temporal trends of perfluoroalkyl contaminants in polar bears (*Ursus maritimus*) from two locations in the North American Arctic, 1972–2002. *Environ. Sci. Technol*. **40**, 1139–1143.

Stasinakis, A. S., Petalas, A. V., Mamais, D., Thomaidis, N. S. (2008). Application of the OECD 301F respirometric test for the biodegradability assessment of various potential endocrine disrupting chemicals. *Bioresource Technol.* **99**, 3458-3467.

Tatum-Gibbs, K., Wambaugh, J. F., Das, K. P., Zehr, R. D., Strynar, M. J., Lindstrom, A. B., Delinsky, A., Lau, C. (2011). Comparative pharmacokinetics of perfluorononanoic acid in rat and mouse. *Toxicology* **281**, 48-55.

TemaNord (2013). Per- and polyflourinated substances substances in the nordic countries.

Tomy, G. T., Pleskach, K., Ferguson, S. H., Hare, J., Stern, G., Macinnis, G., Marvin, C. H., Loseto, L. (2009). Trophodynamics of some PFCs and BFRs in a western Canadian Arctic marine food web. *Environ. Sci. Technol.* **43**(11), 4076-4081.

Upham BL, Deocampo ND, Wurl B & Trosko JE (1998): Inhibition of gap junctional intercellular communication by perfluorinated fatty acids is dependent on the chain length of the fluorinated tail. Int.J.Cancer 78 (4), 491-5.

US EPA (2005). Draft Risk Assessment of the Potential Human Health Effects Associated With Exposure to Perfluorooctanoic Acid and Its Salts (PFOA). Available at: http://www.epa.gov/nscep.

US HHS (2015). Draft Toxicological profile for perfluoroalkyls. Available at: http://www.atsdr.cdc.gov/toxprofiles/tp200.pdf

Vanden Heuvel, J. P., Kuslikis, B. I., Van Rafelghem, M. J., Peterson, R. E. (1991). Disposition of perfluorodecanoic acid in male and female rats. *Toxicol. Appl. Pharm.* **107**(3), 450-459.

Vestergren, R., Berger, U., Glynn, A., Cousins, I. T. (2012). Dietary exposure to perfluoroalkyl acids for the Swedish population in 1999, 2005 and 2010. *Environ. Int.* **49**, 120-127.

Vestergren, R., Orata, F., Berger, U., Cousins, I. T. (2013). Bioaccumulation of perfluoroalkyl acids in dairy cows in a naturally contaminated environment. *Environ. Sci. Pollut. R.* **20**(11), 7959-7969.

Vierke, L., Berger, U., Cousins, I. T. (2013). Estimation of the acid dissociation constant of perfluoroalkyl carboxylic acids through an experimental investigation of their water-to-air transport. *Environ. Sci. Technol.* **47**, 11032-11039.

Wang, Z., MacLeod, M., Cousins, I. T., Scheringer, M., Hungerbühler, K. (2011). Using COSMOtherm to predict physicochemical properties of poly- and perfluorinated alkyl substances (PFASs). *Environ. Chem.* **8**, 389-398.

Xu, J., Guo, C.-S., Zhang, Y., Meng, W. (2014). Bioaccumulation and trophic transfer of perfluorinated compounds in a eutrophic freshwater food web. *Environ. Pollut.* **184**, 254-261.

Zhang, Y., Beesoon, S., Zhu, L., Martin, J. W. (2013). Biomonitoring of perfluoroalkyl acids in human urine and estimates of biological half-life. *Environ. Sci. Technol.* **47**,

10619-10627.

Zhao, S., Zhu, L., Liu, L., Liu, Z., Zhang, Y. (2013). Bioaccumulation of perfluoroalkyl carboxylates (PFCAs) and perfluoroalkane sulfonates (PFSAs) by earthworms (Eisenia fetida) in soil. Environ. Pollut. **179**, 45-52.

References for part II

Ahrens, L., Gerwinski, W., Theobald, N., Ebinghaus, R. (2010). Sources of polyfluoroalkyl compounds in the North Sea, Baltic Sea and Norwegian Sea: Evidence from their spatial distribution in surface water. *Marine pollution bulletin*, **60**, 255-260.

Blom, C., Hanssen, L. (2015). Analysis of per- and polyfluorinated substances in articles. Nordic Council of Ministers. Available at: http://norden.diva-portal.org/smash/get/diva2:808634/FULLTEXT04.pdf

Bossi, R., Strand, J., Sortkjær, O., Larsen, M. M. (2008). Perfluoroalkyl compounds in Danish wastewater treatment plants and aquatic environments. *Environ. Internat.* **34**, 443-450.

Buck, R. C., Franklin, J., Berger, U., Conder, J. M., Cousins, I. T., de Voogt, P., Jensen, A. A., Kannan, K., Mabury, S. A., van Leeuwen, S. P. (2011). Perfluoroalkyl and polyfluoroalkyl substances in the environment: terminology, classification, and origins. *Integr. Environ. Assess Manag.* **7**, 513-541.

Busch, J., Ahrens, L., Sturm, R., Ebinghaus, R. (2010). Polyfluoroalkyl compounds in landfill leachates. *Environ. Pollut.* **158**, 1467-1471.

Butt, C. M., Berger, U., Bossi, R., Tomy, G. T. (2010). Levels and trends of poly-and perfluorinated compounds in the arctic environment. *Sci. Total Environ.* **408**, 2936-2965.

Chemsec (International Chemical Secretariat). The new SIN List substances. October 2014.

Cousins, I. T., Kong, D., Vestergren, R. (2011). Reconciling measurement and modelling studies of the sources and fate of perfluorinated carboxylates. *Environ. Chem.* **8**, 339-354.

Environment Canada (2014). Consultation document. Proposed risk management measure for perfluorooctanoic acid (PFOA) its salts, and its precursors and long-chain (C_9-C_{20}) perfluorocarboxylic acids (PFCAs), their salts, and their precursors. Available at: http://www.ec.gc.ca/ese-ees/2A11BA77-C816-4199-8407-0AF38E0E7965/Consultation%20Document_PFOA-PFCA_EN.pdf

Environment Canada (2012). Ecological Screening Assessment Report. Long-chain (C9-C20) perfluorocarboxylic acids, their salts and their precursors. Available at: http://www.ec.gc.ca/ese-ees/CA29B043-86E4-4308-BBC0-5CE163FEAC40/PFCAs_EN.pdf

FluoroCouncil (2013). Recent developments on alternatives to long-chain PFAS. Ppt-presentation held by Kai Schubert for Richard Holt, 20 November 2013.

Greenpeace (2015). Footprints in the snow. Hazardous PFCs in remote locations around the globe. Available at: http://www.greenpeace.org/sweden/Global/sweden/miljogifter/dokument/2015/Footprints%20in%20the%20snow%20-%20Detox%20Outdoor.pdf

Hanssen, L., Herzke, D. (2015). Investigation of outdoor textiles and gear with respect to determine the content of ionic perfluorinated substances (PFASs). Norwegian Institute for Air Research, NILU OR 4/2015.

Kotthoff, M., Müller, J., Jürling, H., Schlummer, M., Fiedler, D. (2015). Perfluoroalkyl and polyfluoroalkyl substances in consumer products. *Environ. Sci. Pollut. Res.* **22**, 14546-14559.

OECD (2013). OECD/UNEP Global PFC Group, Synthesis paper on per- and polyfluorinated chemicals (PFCs), Environment, Health and Safety, Environment Directorate, OECD.

Sinclair, E., Kannan, K. (2006). Mass Loading and Fate of Perfluoroalkyl Surfactants in Wastewater Treatment Plants. *Environ. Sci. Technol.* **40**(5), 1408-1414.

Stock, N. L., Furdui, V. I., Muir, D. C., Mabury, S. A. (2007). Perfluoroalkyl contaminants in the Canadian Arctic: evidence of atmospheric transport and local contamination.

Environ. Sci. Technol. **41**(10), 3529-3536.

Swedish Chemicals Agency (2015). Occurrence and use of highly fluorinated substances and alternatives. Available at: http://www.kemi.se/global/rapporter/2015/report-7-15-occurrence-and-use-of-highly-fluorinated-substances-and-alternatives.pdf

UNEP (2014). Draft report of the assessment of alternatives to perfluorooctane sulfonic acid, its salts and perfluorooctane sulfonyl fluoride.

US EPA (2009). Perfluorocarboxylic Acid Content in 116 Articles of Commerce. EPA/600/R-09/033.

US EPA (2015). 2010/2015 PFOA Stewardship Program – 2014 Annual Progress Reports. Available at: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/20102015-pfoa-stewardship-program

Wang, Z., Cousins, I. T., Scheringer, M., Buck, R. C., Hungerbühler, K. (2014). *Environ. Int.* **70**, 62-75.

Zangl, S., Blepp, M., Marquardt, M., Moch, K., Wirth, O., Homburg, B., Temme, C. (2012). Nationale Umsetzung des Stockholmer Übereinkommens zu persistenten organischen Schadstoffen (POPs) - PBDE und PFOS in Erzeugnissen und im Recyclingkreislauf Reprt No. UBA-FB 001661, Project No. FKZ 371063415.

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 read-across and categories" similarities may be due to a common functional group, common precursor or breakdown products, constant pattern in changing potency or common constituents or chemical class.

Category definition and its members

Category Hypothesis

The substances in the category are perfluorinated carboxylic acids (PFCAs) with C_8-C_{10} carbon chain lengths. The compounds in the category differ only in the number of carbon atoms in the fluorinated carbon chain. Thus, the PFCAs belong to the same chemical class and contain not only a common functional group but are highly similar according to their chemical structure. The substances are thus expected to behave in a predictable manner and the category approach can therefore be used for read-across in a weight-of-evidence approach in the PBT assessment.

Category members

In Table A.1 the chemical structures of PFOA, PFNA and PFDA are displayed. All contain a carboxylic acids group and a perfluorinated carbon chain. The compounds differ only in the number of carbon atoms within the fluorinated carbon chain.

Table A.1: CAS-Numbers and similarity of chemical structures of C_8-C_{10} PFCAs

Name	Abbreviation	CAS-No	IUPAC Name	Chemical structure
PFOA	C_8-PFCA	335-67-1	Pentadecafluorooctanoic acid	F F F F F F F O F F F F F F F F OH
PFNA	C_9-PFCA	375-95-1	Heptadecafluorononanoic acid	F F F F F F F F O F F F F F F F F F OH
PFDA	C_{10}-PFCA	335-76-2	Nonadecafluorodecanoic acid	F F F F F F F F F O F F F F F F F F F F OH

The C_{11}-C_{14} PFCAs are considered as supporting substances to the category. They are included in Table A.2 to illustrate the regular pattern in the physicochemical properties, and have previously been identified as substances of very high concern for their vPvB properties.

Purity / Impurities

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

Category justification

The structural similarities between the C_8-C_{10} PFCAs, including the supporting substances C_{11}-C_{14} PFCAs, with a common functional group and differing only in the carbon chain length lead to similar chemical and physicochemical properties. Comparing the experimental and estimated data, it is clear that the behaviour of the PFCAs follows a regular pattern (Tables A.2-A.3 and Figures A1-A3).

Dissociation of PFCAs in aqueous media

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

Physicochemical properties and partition coefficients of C_8-C_{10} PFCAs and some salts

The experimental determination of partition coefficients is difficult because of the surface active properties of the ionic PFCAs. The presence of ionic PFCAs depends on the dissociation of PFCAs in aqueous media. Nevertheless, there are models available, *e.g.* COSMOtherm, calculating partitioning coefficients of neutral PFCAs. COSMOtherm is a quantum chemistry-based method that requires no specific calibration. This calibration would be difficult because of missing measured data of PFCAs. Therefore COSMOtherm is expected to be able to estimate properties for PFASs. Studies have shown that properties estimated with COSMOtherm show good agreement with the experimental data for a number of per- and polyfluorinated chemicals, *e.g.* PFOA (Arp *et al.* 2006; Wang *et al.* 2011)). Again, whether neutral PFCAs are present in aqueous media depends in the dissociation of the acids. Air-water as well as octanol-water partition coefficients are of course different for PFCAs with 8 to 10 carbon atoms but they show a clear increasing, trend with chain length (see Table A.2 below, (Wang *et al.* 2011)). This can be explained by the increasing molecular volume with each additional CF_2-unit. The trend of the fate of PFCAs with chain length is supported by information on sorption of PFCAs on sediment. Sorption increases with increasing chain length (Higgins and Luthy, 2006) also under environmental conditions (Ahrens *et al.* 2010) (Table A.2).

Concluding remarks

To conclude, all data in Table A.2 are consistent with the hypothesis that the PFCAs behaviour follow a regular trend across the category which can be used in a weight-of-evidence approach in the PBT assessment. For the bioaccumulation assessment specifically, the data (Table A.3 and Figures A1-A3) show a bioaccumulation potential which depends on the chain-length of the perfluorinated alkyl chain.

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

Abbreviation	**C_8-PFCA**			**C_9-PFCA**	**C_{10}-PFCA**	**C_{11}-PFCA**	**C_{12}-PFCA**	**C_{13}-PFCA**	**C_{14}-PFCA**
Acronym	PFOA	APFO	NaPFO	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
IUPAC Name	**Octanoic acid, pentadecaflu oro-**	**ammonium pentadeca-fluoro-octanoate**	**pentadeca octanoic acid sodium salt**	**Nonanoic acid, heptadeca-fluoro-**	**Decanoic acid, nonadeca-fluoro-**	**Undecanoic acid, heneicosa-fluoro-**	**Dodecanoic acid, tricosafluoro -**	**Tridecanoic acid, pentacosa-fluoro-**	**Tetradecanoi c acid, heptacosa-fluoro-**
Chemical Structure	$CF_3(CF_2)_6$-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	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	414.09	431.1		464.08	514.08	564.0909	614.0984	664.1059	714.11
Partitioning Coefficient log K_{OW}	5.30 (calc., COSMOtherm (temp. not specified) Wang *et al.* 2011)			5.9 (calc., COSMOtherm, Wang *et al.* 2011)	6.5 (calc., COSMOtherm, Wang *et al.* 2011)	7.2 (calc., COSMOtherm, Wang *et al.* 2011)	7.8 (calc., COSMOtherm, Wang *et al.* 2011)	8.25 (calc., COSMOtherm, Wang *et al.* 2011)	8.90 (calc., COSMOtherm, Wang *et al.* 2011)
log K_{OA}	7.23 (calc., COSMOtherm, Wang *et al.* 2011)			7.50 (calc., COSMOtherm, Wang *et al.* 2011)	7.77 (calc., COSMOtherm, Wang *et al.* 2011)	8.08 (calc., COSMOtherm, Wang *et al.* 2011)	8.36 (calc., COSMOtherm, Wang *et al.* 2011)	8.63 (calc., COSMOtherm, Wang *et al.* 2011)	8.87 (calc., COSMOtherm, Wang *et al.* 2011)
log K_{AW}	-1.93 (calc., COSMOtherm, Wang *et al.* 2011)			-1.58 (calc., COSMOtherm, Wang *et al.* 2011)	-1.27 (calc., COSMOtherm, Wang *et al.* 2011)	-0.92 (calc., COSMOtherm, Wang *et al.* 2011)	-0.58 (calc., COSMOtherm, Wang *et al.* 2011)	-0.38 (calc., COSMOtherm, Wang *et al.* 2011)	0.03 (calc., COSMOtherm, Wang *et al.* 2011)
Dissociation constant	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)	<1.6 (Vierke *et al.* 2013)			
Partition coefficients log K_d (sediment and overlapping dissolved phase)	0.04 (Ahrens *et al.* 2010)*			0.6 (Ahrens *et al.* 2010) *	1.8 (Ahrens *et al.* 2010) *	3.0 (Ahrens *et al.* 2010) *			

Abbreviation	**C_8-PFCA**			**C_9-PFCA**	**C_{10}-PFCA**	**C_{11}-PFCA**	**C_{12}-PFCA**	**C_{13}-PFCA**	**C_{14}-PFCA**
Acronym	PFOA	APFO	NaPFO	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
Log Koc (sediment organic carbon-normalised distribution coefficient)	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	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)		5.14 g/L at 25°C (Kauck and Diesslin, 1951)	1.2E-4 g/L; pH 1 at 25°C 9.0E-4 g/L; pH 2 at 25°C 8.5E-3 g/L; pH 3 at 25°C 0.056 g/L; pH 4 at 25°C 0.14 g/L; pH 5 at 25°C 0.16 g/L; pH 6-10 at 25°C (calculated) (European Chemicals Agency, 2012a)	2.9E-5 g/L pH 1 at 25°C 2.2E-4 g/L pH 2 at 25°C 2.0E-3 g/L pH 3 at 25°C 0.014 g/L pH 4 at 25°C 0.034 g/L pH 5 at 25°C 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) (European Chemicals Agency, 2012b)	7.3E-6 g/L; pH 1 at 25 °C 5.5E-5 g/L; pH 2 at 25 °C 5.1E-4 g/L; pH 3 at 25 °C 3.5E-3 g/L; pH 4 at 25 °C 8.6E-3 g/L; pH 5 at 25 °C 0.0100 g/L; pH 6-10 at 25 °C (calculated) (European Chemicals Agency, 2012c)	1.9E-6 g/L; pH 1 at 25°C 1.4E-5 g/L; pH 2 at 25°C 1.3E-4 g/L; pH 3 at 25°C 9.3E-4 g/L; pH 4 at 25°C 2.2E-3 g/L; pH 5 at 25°C 2.6E-3 g/L; pH 6-10 at 25°C (calculated) (European Chemicals Agency, 2012d)
Vapour pressure	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)			3.1 to 99.97 kPa (129.6 to 218.9 °C) (calculated) (Kaiser, 2005)	0.6 to 99.97 kPa (112 to 237.7°C) (calculated) (European Chemicals Agency, 2012a)	1.25 Pa at 25°C (calculated) (European Chemicals Agency, 2012b)	0.48 Pa at 25°C (calculated) (European Chemicals Agency, 2012c)	0.18 Pa at 25 °C (calculated) (European Chemicals Agency, 2012d)

Abbreviation	**C_8-PFCA**			**C_9-PFCA**	**C_{10}-PFCA**	**C_{11}-PFCA**	**C_{12}-PFCA**	**C_{13}-PFCA**	**C_{14}-PFCA**
Acronym	PFOA	APFO	NaPFO	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
	Stability**								
Phototransformation in water DT50	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 ion ($S_2O_8^{2-}$) in water	No photodegradation tested under relevant env. Conditions 100 % after 12 h by use of persulfate ion ($S_2O_8^{2-}$) in water	No photodegradation tested under relevant env. Conditions 77% after 12 h by use of persulfate ion ($S_2O_8^{2-}$) in water			
Hydrolysis DT50	>97 yr			No hydrolysis tested under relevant env. conditions; 97% (absence of $S_2O_8^{2-}$) and 100% (by use of $S_2O_8^{2-}$) after 6 h in 80°C water					
Direct photolysis		No photo-degradation							
indirect photolysis		No photo-degradation (H_2O_2; synthethic humic water, Fe_2O_3) estimated half-life > 349 days (Fe_2O_3)							
ready biodegradability screening test	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 elimination by metabolic processes, mineralization or adsorption								

Abbreviation	**C_8-PFCA**			**C_9-PFCA**	**C_{10}-PFCA**	**C_{11}-PFCA**	**C_{12}-PFCA**	**C_{13}-PFCA**	**C_{14}-PFCA**
Acronym	PFOA	APFO	NaPFO	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
Biodegradation in soil, sediment	No degradation detected								

*pH of the water samples analysed 7.1-8.3 Temp.: 15.3 – 17.7 °C
** for reference see European Chemicals Agency 2012a-d, 2013a-b, 2015b.

Table A.3: Information on BCF, BAF, BMF and TMF relevant to justify read-across in the B assessment

Abbreviation	**C_8-PFCA**	**C_9-PFCA**	**C_{10}-PFCA**	**C_{11}-PFCA**	**C_{12}-PFCA**	**C_{13}-PFCA**	**C_{14}-PFCA**
Acronym	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA	PFTeDA
Reference	European Chemicals Agency (2013b)	European Chemicals Agency (2015b)	This document	European Chemicals Agency (2012a)	European Chemicals Agency (2012b)	European Chemicals Agency (2012c)	European Chemicals Agency (2012d)
BCF							
Rainbow trout (carcass)	4.5 ± 0.6	-	450 ± 62	2700 ± 400	18000 ± 2700	-	23000 ± 5300
Rainbow trout (blood)	27 ± 9.7	-	2700±350	11000 ±1400	40000 ± 4500	-	30000 ± 4200
Rainbow trout (liver)	8.0 ± 0.59	-	1100 ± 180	4900 ± 770	18000 ± 2900	-	30000 ± 6000
Carp (whole)	3.2-94	-	-	2300-3700	10000-16000	-	16000-17000
BAF	0.038-292	39-3981	714-158489	1409-1000000	10000-5011872	-	15857-19294
BMF	0.02-125	0.13-111	0.1-87	0.21-353	0.1-156	0.35-3.4	0.33-8.5
TMF	0.2-13	1.9-7.0	0.39-12.1	0.75-10.2	0.7-5.87	2.45	0.23-3.05

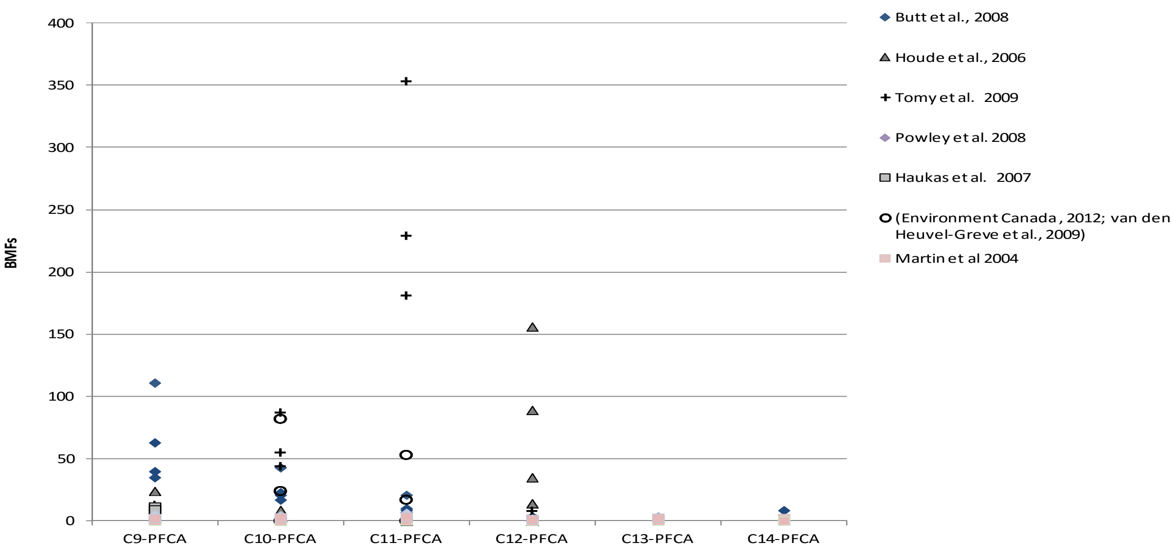


Figure A1: Biomagnification factors (BMFs) for C_9-C_{14} PFCA.

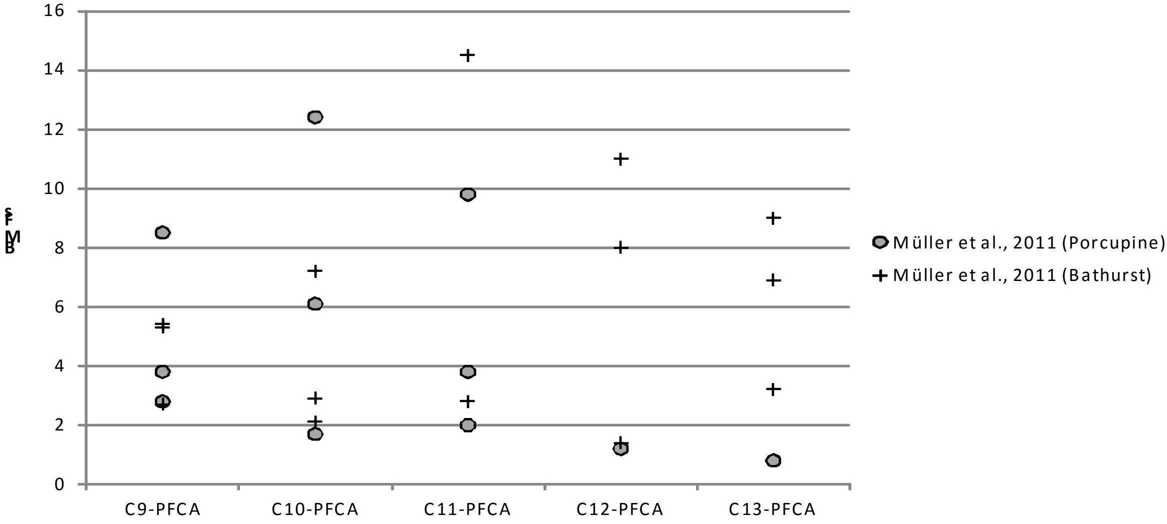


Figure A2: BMFs for C_9-C_{13} PFCAs in a remote terrestrial food chain from two different locations (whole body, Müller *et al.* 2011). The study is reliable (reliability 2). For further discussion on the study, see the Support Document of, *e.g.* C_{11} PFCA (European Chemicals Agency, 2012a).

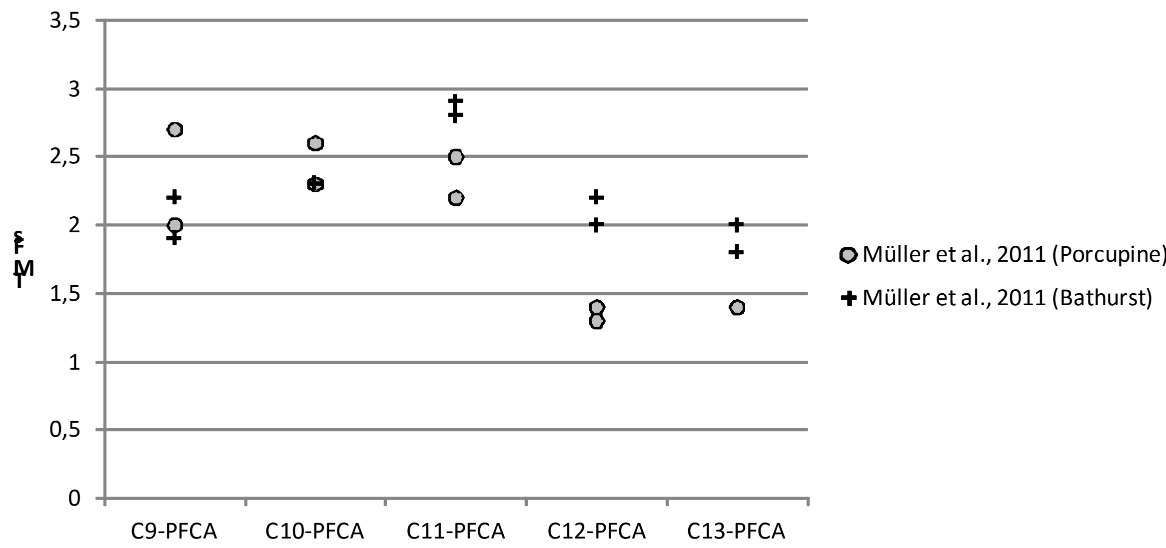


Figure A3: TMFs for C_9-C_{13} PFCAs in a remote terrestrial food chain from two different locations (whole-body, Müller *et al.* 2011). The study is reliable (reliability 2).

References for Annex I

Ahrens, L., Taniyasu, S., Yeung, L. W., Yamashita, N., Lam, P. K., Ebinghaus, R. (2010). Distribution of polyfluoroalkyl compounds in water, suspended particulate matter and sediment from Tokyo Bay, Japan. *Chemosphere* **79**, 266-272.

Arp, H. P., Niederer, C., Goss, K. U. (2006). Predicting the partitioning behavior of various highly fluorinated compounds. *Environ. Sci. Technol.* **40**, 7298-7304.

Brace, N. O. (1962). Long chain alkanoic and alkenoic acids with perfluoroalkyl terminal segments. *J. Org. Chem.* **27**, 4491-4498.

European Chemicals Agency (2012a). Member State Committee support document for identification of henicosafluoroundecanoic acid (EC Number: 218-165-4; CAS Number: 2058-94-8) as a substance of very high concern because of its vPvB properties. Available at: http://echa.europa.eu/documents/10162/01986fb8-ede8-4458-b54e-12ff8a534b98

European Chemicals Agency (2012b). Member State Committee support document for identification of tricosafluorododecanoic acid (EC Number: 206-203-2; CAS Number: 307-55-1) as a substance of very high concern because of its vPvB properties. Available at: http://echa.europa.eu/documents/10162/0d5abffa-6bbf-40c7-b6b1-1ca3736cf570

European Chemicals Agency (2012c). Member State Committee support document for identification of pentacosafluorotridecanoic acid (EC Number: 276-745-2; CAS Number: 72629-94-8) as a substance of very high concern because of its vPvB properties. Available at: http://echa.europa.eu/documents/10162/3fd11ee9-6925-475f-b328-d224d45219a4

European Chemicals Agency (2012d). Member State Committee support document for identification of heptacosafluorotetradecanoic acid (EC Number: 206-803-4; CAS Number: 376-06-7) as a substance of very high concern because of its vPvB properties. Available at: http://echa.europa.eu/documents/10162/997efe1b-0564-4ca1-a012-bab93e518f25

European Chemicals Agency (2013a). Member State Committee support document for identification of ammonium pentadecafluorooctanoate (APFO) (EC Number: 223-320-4; CAS Number: 3825-26-1) as a substance of very high concern because of its CMR and PBT properties. Available at: http://echa.europa.eu/documents/10162/5e2c1e53-be98-4104-8b96-9cd88655a92a

European Chemicals Agency (2013b). Member State Committee support document for identification of pentadecafluorooctanoic acid (PFOA) (EC Number: 206-397-9; CAS Number: 335-67-1) as a substance of very high concern because of its CMR and PBT properties. Available at: http://echa.europa.eu/documents/10162/8059e342-1092-410f-bd85-80118a5526f5

European Chemicals Agency (2015b). Member State Committee support document for identification of perfluorononan-1-oic acid and its sodium and ammonium salts (EC numbers: 206-801-3, not applicable, not applicable, CAS numbers: 375-95-1, 21049-39-8, 4149-60-4) as substances of very high concern because of their toxic for reproduction and PBT properties. Available at: http://echa.europa.eu/documents/10162/48ae5fe3-9436-4a10-a533-ed642b92ce47

Higgins, C. P., Luthy, R. G. (2006). Sorption of perfluorinated surfactants on sediments. *Environ. Sci. Technol.* **40**, 7251-7256.

Kaiser, M. A., Larsen, B. S., Kao, C-P., Buck, R. C. (2005). Vapor pressures of perfluorooctanoic, -nonanoic, -decanoic, -undecanoic, and -dodecanoic acids. *J. Chem. Eng. Data* **50**, 1841–1843.

Kauck, E. A.; Diesslin, A. R. (1951). Some Properties of Perfluorocarboxylic Acids. *Ind. Eng. Chem.* **43**(10), 2332–2334.

López-Fontán, J. L., Sarmiento, F., Schulz, P. C. (2005). The aggregation of sodium perfluorooctanoate in water. *Colloid. Polym. Sci.* **283**, 862-871.

Moroi, Y., Yano, H., Shibata, O., Yonemitsu, T. (2001). Determination of acidity constants of perfluoroalkanoic acids. *Bull. Chem. Soc. Jpn.* **74**, 667-672.

Müller, C. E., De Silva, A. O., Small, J., Williamson, M., Wang, X., Morris, A., Katz, S., Gamberg, M., Muir, D. C. (2011). Biomagnification of Perfluorinated Compounds in a Remote Terrestrial Food Chain: Lichen-Caribou-Wolf. *Environ. Sci. Technol.* **45**(20), 8665-8673.

Nielsen, C. J. (2012). PFOA Isomers, salts and precursors - Literature study and evaluation of physico-chemical properties. CTCC, Department of Chemistry, University of Oslo, Klif project no: 3012013.

Vierke, L., Berger, U., Cousins, I. T. (2013). Estimation of the acid dissociation constant of perfluoroalkyl carboxylic acids through an experimental investigation of their water-to-air transport. *Environ. Sci. Technol.* **47**, 11032-11039.

Wang, Z., MacLeod, M., Cousins, I. T., Scheringer, M., Hungerbühler, K. (2011). Using COSMOtherm to predict physicochemical properties of poly- and perfluorinated alkyl substances (PFASs). *Environ. Chem.* **8**, 389-398.

Ylinen, M., Kojo, A., Hanhijarvi, H., Peura, P. (1990). Disposition of perfluorooctanoic acid in the rat after single and subchronic administration. *Bull. Environ. Contam. Toxicol.* **44**, 46-53.