

**Substance Name: Perfluamine**

**EC Number: 206-420-2**

**CAS Number: 338-83-0**

**MEMBER STATE COMMITTEE SUPPORT DOCUMENT  
FOR IDENTIFICATION OF**

**PERFLUAMINE**

**AS A SUBSTANCE OF VERY HIGH CONCERN  
BECAUSE OF ITS VPVB (ARTICLE 57E)  
PROPERTIES**

**Adopted on 22 November 2024**

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## ABBREVIATIONS

B: Bioaccumulative  
BASS: Bioaccumulation and Aquatic System Simulator  
BCF: Bioconcentration factor  
BMF: Biomagnification factor  
CMR: Carcinogenic, Mutagenic, toxic to Reproduction  
C-F: Carbon-fluorine  
C-N: Carbon-nitrogen  
D: Day  
DOC: Dissolved organic carbon  
DT<sub>50</sub>: Dissipation half-life  
EC: European Community  
ECHA: European Chemicals Agency  
EPI: Estimation Programs Interface  
GC/MS: Gas chromatography/mass spectrometry  
GWP: Global warming potential  
GWP<sub>100</sub>: GWP on the 100-year time horizon  
H: Hours  
HFPO-DA: 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, its salts and its acyl halides (covering any of their individual isomers and combinations thereof)  
HLC: Henry's Law Constant  
IPCC: Intergovernmental Panel on Climate Change  
K<sub>oa</sub>: Partition coefficient octanol/air  
K<sub>oc</sub>: Partition coefficient organic carbon/water  
K<sub>ow</sub>: Partition coefficient n-octanol/water  
LC-MS: Liquid Chromatography – Mass Spectrometry  
LMC: Laboratory of Mathematical Chemistry  
Log K<sub>oa</sub>: Partition coefficient octanol/air (log-value)  
Log K<sub>oc</sub>: Partition coefficient organic carbon/water (log-value)  
Log K<sub>ow</sub>: Partition coefficient n-octanol/water (log-value)  
MCI: Molecular Connectivity Index  
No: Number  
OECD: Organisation for Economic Co-operation and Development  
P: Persistent  
PBT: Persistent, Bioaccumulative and Toxic  
PFAS: Per- and polyfluoroalkyl substances  
PFC: Perfluorocarbon  
PFOA: Perfluorooctanoic acid / pentadecafluorooctanoic acid  
PFOC: Perfluorinated organic compound  
POP: Persistent Organic Pollutants  
REACH: EU Regulation No 1907/2006 concerning Registration, Evaluation, Authorisation, and restriction of Chemicals  
SVHC: Substance of Very High Concern  
TAR: Third Assessment Report  
TCE: Trichloroethylene  
TG: Test Guideline  
US EPA: United States Environmental Protection Agency  
vB: very Bioaccumulative  
vP: very Persistent  
vPvB: very Persistent and very Bioaccumulative  
WMO: World Meteorological Organization

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

**Substance name:** Perfluamine

**EC number:** 206-420-2

**CAS number:** 338-83-0

- Perfluamine is identified as very persistent and very bioaccumulative (vPvB) according to Article 57 (e) of Regulation (EC) No 1907/2006 (REACH).

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

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

#### Persistence

Based on a weight-of-evidence approach and considering assessment information in accordance with REACH Annex XIII Section 3.2.1.(d), it is concluded that perfluamine is very persistent due to its C-F bonds which cannot be broken under environmental conditions, and the abundant presence of fluorine atoms which shields the carbon skeleton from other transformation reactions. The C-N bonds of perfluamine are also shielded from chemical attack through 'pyramidal nitrogen inversion'.

Perfluamine is not expected to hydrolyse and is not expected to be affected by oxidation processes. Perfluamine is photochemically stable and persistent in the atmosphere with a total global atmospheric lifetime of 3 795 years (Klimisch score 2). Structurally similar substances (as specified in section 3.1.1.3.1) also have total atmospheric lifetimes or half-life in air of at least 1 000 years (Klimisch score 4 and 2). In addition, based on modelling data, perfluamine screens as potentially persistent or very persistent in the environment. This is supported by biodegradation screening studies performed with analogue substances, which resulted in no or very limited biodegradation. In an OECD TG 310 ready biodegradability study, 0% degradation was observed after 28 days (CO<sub>2</sub> evolution) for the analogue substance EC No 473-390-7 (Klimisch score 4). A study with the analogue substance tripropylamine (EC No 203-047-7) and according to OECD TG 301 E, resulted in 0 – 10 % degradation after 28 days (DOC removal) (Klimisch score 4). In a second study equivalent to OECD TG 302 B, tripropylamine was not degraded after 3 hours and after 21 days with each time 0% degradation (DOC removal). Based on these screening tests with analogue substances, perfluamine is concluded as not readily and not inherently biodegradable.

In summary, perfluamine is considered to be very persistent in all environmental compartments, as no indications are found that it can undergo abiotic or biotic degradation under relevant environmental conditions. Half-lives are expected to largely exceed the P and vP criteria (degradation half-life > 60 days in water, and degradation half-lives > 180 days in sediment or soil) of REACH Annex XIII Sections 1.1.1 and 1.2.1. Furthermore,

Annex XIII, point 3.2.1.(d) of the REACH Regulation requires that any relevant information for the assessment of the persistence of the substance be considered. Therefore, it is concluded that perfluamine fulfils the 'persistence' (P) and 'very persistent' (vP) criteria in accordance with the criteria and provisions set out in Annex XIII of REACH.

#### Bioaccumulation

Perfluamine meets the bioaccumulation screening criterion for aquatic organisms ( $\text{Log } K_{ow} > 4.5$ ). The experimental bioaccumulation study with *Lepomis macrochirus* via dietary exposure, according to OECD TG 305 (Klimisch score 2), indicates a potential for bioaccumulation of perfluamine with a long depuration half-life in fish of 42 days. Detailed analysis of the available test data from the study leads to  $\text{BCF}_{\text{kgL}}$  values for perfluamine ranging from 5 527 L/kg to 51 602 L/kg. Moreover, an alternative estimation based on an allometric relationship provides a  $\text{BCF}_k$  of 20 424 L/kg. All these BCF estimations exceed the very bioaccumulative (vB) criteria of REACH Annex XIII ( $\text{BCF} > 5\,000$  L/kg). This experimental dietary bioaccumulation study is given high weight in the weight of evidence assessment.

Experimental studies on bioaccumulation in terrestrial organisms are not available. However, it is noted that the screening criterion for bioaccumulation in air-breathing organisms is not met ( $\text{Log } K_{oa} < 5$ ).

Based on a weight-of-evidence, it is concluded that perfluamine meets the 'bioaccumulation' criterion (B) and the 'very bioaccumulative' criterion (vB) for aquatic organisms in accordance with REACH Annex XIII, points 1.1.2 and 1.2.2, of the REACH Regulation.

#### Conclusion

In conclusion, perfluamine meets the criteria for a vPvB substance in accordance with Annex XIII of the REACH Regulation, and thereby the substance fulfils the criteria set out in REACH Article 57 (e).

#### Summary of other considerations

Perfluamine shows high potential for long-range atmospheric transport based on atmospheric lifetimes or half-life in air of at least 1 000 years and it is identified in public literature as a potential POP substance. Furthermore, studies on radiative efficiency and global warming potential indicate that perfluamine is a potent greenhouse gas.

**Registration dossier submitted for the substance: Yes**

## Justification

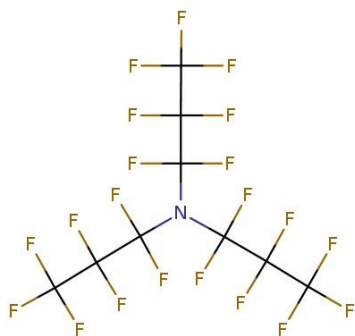
### 1. Identity of the substance and physical and chemical properties

#### 1.1 Name and other identifiers of the substance

**Table 1: Substance identity**

<b>EC number:</b>	206-420-2
<b>EC name:</b>	perfluamine
<b>CAS number (in the EC inventory):</b>	338-83-0
<b>CAS number:</b>	338-83-0
<b>IUPAC names:</b>	1,1,2,2,3,3,3-heptafluoro- <i>N,N</i> -bis(heptafluoropropyl)propan-1-amine; tris(1,1,2,2,3,3,3-heptafluoropropyl)amine
<b>Index number in Annex VI of the CLP Regulation</b>	NA
<b>Molecular formula:</b>	C <sub>9</sub> F <sub>21</sub> N
<b>Molecular weight:</b>	521.07 g/mole
<b>Synonyms:</b>	perfluorotripropylamine (acronym PTPA)

**Structural formula:**



## 1.2 Composition of the substance

**Name:** perfluamine

**Description:** As the name suggests, perfluamine (synonym: perfluorotripropylamine) consists of an amine in its center, to which three perfluorinated propyl groups are attached.

**Substance type:** mono-constituent

The substance that is subject to the "Substance of Very High Concern" (SVHC) proposal is a mono-constituent substance, however it should be noted that the concentration level of its main constituent may occasionally be < 80% w/w. The SVHC proposal also covers these types of compositions.

## 1.3 Identity and composition of degradation products/metabolites relevant for the SVHC assessment

NA.

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

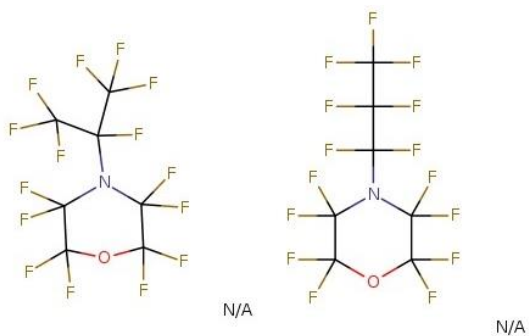
A read-across approach was used as supportive information for the persistence assessment of perfluamine; a justification on the read-across approach can be consulted in Annex 2.

The structurally related substances used in the read-across approach are listed in Table 2 and Table 3.

**Table 2: Identity of structurally related substance 1**

<b>EC number:</b>	473-390-7
<b>Chemical name:</b>	Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine
<b>CAS number (in the EC inventory)<sup>1</sup>:</b>	/
<b>Index number in Annex VI of the CLP Regulation</b>	NA
<b>Molecular formula:</b>	C <sub>7</sub> F <sub>15</sub> NO
<b>Acronym</b>	FC-770

<sup>1</sup> This substance may have been described using CAS 1093615-61-2, Hydrofluoric acid, reaction products with 4-(1-methylethyl)morpholine

**Structural formula:****Table 3: Identity of structurally related substance 2**

<b>EC number:</b>	203-047-7
<b>EC name:</b>	tripropylamine
<b>CAS number (in the EC inventory):</b>	102-69-2
<b>CAS number:</b>	102-69-2
<b>IUPAC names:</b>	tripropylamine
<b>Index number in Annex VI of the CLP Regulation</b>	NA
<b>Molecular formula:</b>	C <sub>9</sub> H <sub>21</sub> N

**Structural formula:**

## 1.5 Physicochemical properties

Table 4 shows the overview of the physicochemical properties which are provided in the registration dossier of perfluamine.

Regarding the experimental Log K<sub>ow</sub> range mentioned in the registration dossier, a Klimisch score of 4 is deemed appropriate as no specifications are given on the methods used for deriving the Log K<sub>ow</sub> values. It is also not possible to quantitatively assess to what extent Log K<sub>ow</sub> values of the read-across substances would deviate from the actual Log K<sub>ow</sub> value of perfluamine.

The Log K<sub>ow</sub> value of 6.19 provided by KOWWIN v1.68 in EPI Suite (EPIWEB v4.1; US EPA, 2012) is considered to be the most adequate estimation of the real Log K<sub>ow</sub> value because KOWWIN v1.68 uses a fragment constant methodology, in combination with correction factors, and the applied regression is based on a database of many thousands of reliably measured Log K<sub>ow</sub> values. This EPI Suite value is considered to have medium uncertainty as all the fragments in perfluamine are recognized by KOWWIN, and at least the validation set contains a compound with more than 9 carbon atoms without an attached hydrogen atom and a compound with more than 21 fluorine atoms. The molecular weight of perfluamine is within the range established for both the training set and the validation set.

**Table 4: Overview of physicochemical properties (registration dossier)**

Property	Description of key information	Value	Reference <sup>2</sup> (reliability as determined by the Belgian Competent Authority)
<b>Physical state at 20°C and 101.3 kPa</b>	No guideline specified Observation GLP	Clear, colourless liquid	Unpublished study report, 2012a (Klimisch score 1)
<b>Melting/freezing point</b>	Summary data point only from company product technical data sheet	-50 °C	Company data, 2001 (Klimisch score 4)
<b>Boiling point</b>	ASTM E1719-97 and ASTM D1120-94; deviations from OECD TG 103 Non-GLP	132 °C (at 760 mm Hg)	Unpublished study report, 2011 (Klimisch score 2)
<b>Vapour pressure</b>	ASTM E1719-97 and ASTM D1120-94; deviations from OECD TG 104 Non-GLP	3.87 mm Hg (516 Pa; at 20 °C)	Unpublished study report, 2011 (Klimisch score 2)
<b>Density</b>	ASTM D4052-11; deviations from OECD TG 109 Non-GLP	1.8204 g/cm <sup>3</sup> (at 25 °C)	Unpublished study report, 2011 (Klimisch score 2)
<b>Water solubility</b>	EPA OPPTS 830.7840 GLP	Range = 0.0695 – 1.96 µg/L (at 23 °C) Average = 0.381 µg/L (at 23 °C)	Unpublished study report, 2012a (Klimisch score 2)

<sup>2</sup> ECHA dissemination website - REACH Registration dossier of perfluamine  
[https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5\\_986d3118-514e-436c-bd20-19d66a4f37a5](https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5_986d3118-514e-436c-bd20-19d66a4f37a5)  
 (accessed 23 July 2024).

Property	Description of key information	Value	Reference <sup>2</sup> (reliability as determined by the Belgian Competent Authority)
Partition coefficient n-octanol/water (log value)	<p><b>Read-across as proposed in the registration dossier</b></p> <p><i>Test material - Lower limit: perfluoroheptanes</i> EC No: / CAS RN: 1064698-16-3</p> <p><i>Test material - Upper limit: perfluorotributyl amines</i> CAS RN: 1064698-37-8</p> <p><i>These generic identifiers have been reported in the registration dossier. No further information on the identity or composition of the test material was provided.</i></p> <p>No guideline specified GLP: not specified</p>	Log K <sub>ow</sub> range = 5.3 – 6.1 (at 23 °C)	Unpublished study report, 2012b (Klimisch score 4)
	QSAR (EPI Suite; KOWWIN v1.68)	Log K <sub>ow</sub> = 6.19	EPIWEB v4.1 (US EPA, 2012) (medium uncertainty)

Glüge and Scheringer (2023) evaluated physicochemical property data of various mono-constituent, neutral organic substances that are fully registered under the EU Regulation No 1907/2006 concerning Registration, Evaluation, Authorisation, and restriction of CHemicals (REACH), with 'COSMOtherm 2020' software. The output from the 'COSMOtherm 2020' software was compared to the experimental physicochemical data originating from the European Chemicals Agency (ECHA) database (Glüge and Scheringer, 2023). Perfluamine was also assessed by these authors. The output for the physicochemical properties from the 'COSMOtherm 2020' software is provided in Table 5, together with the values from the registration dossier for comparison.

**Table 5: Physicochemical properties of perfluamine calculated by 'COSMOtherm 2020' software (Glüge and Scheringer, 2023; supplementary material), compared with values from the registration dossier**

Property	Value calculated by 'COSMOtherm 2020'	Value from registration dossier
<b>Boiling point</b>	137.51 °C	132 °C (Klimisch score 2)
<b>Vapour pressure</b>	388 Pa (at 20 °C)	516 Pa (at 20 °C) (Klimisch score 2)
<b>Water solubility</b>	0.056 mg/L (at 20 °C)	Range = 0.00007 – 0.002 mg/L (at 23 °C) Average = 0.00038 mg/L (at 23 °C) (Klimisch score 2)

<b>Partition coefficient n-octanol/water (log value)</b>	Log <sub>10</sub> K <sub>ow</sub> = 7.28 (at 20 °C) (reliable)	<b>Read-across:</b> Log K <sub>ow</sub> range = 5.3 – 6.1 (at 23 °C) (Klimisch score 4)  <b>QSAR (EPI Suite; KOWWIN v1.68)</b>  Log K <sub>ow</sub> = 6.19
<b>Partition coefficient octanol/air (log value)</b>	Log <sub>10</sub> K <sub>oa</sub> = 2.23 (at 20 °C) (reliable)	<b>Read-across:</b> Log K <sub>oa</sub> range = 0.1 – 1.0 (at 23 °C) (Klimisch score 4)
<b>Partition coefficient organic carbon/water (log value)</b>	Log <sub>10</sub> K <sub>oc</sub> = 5.18 (at 25 °C) (reliability cannot be assessed)	Log K <sub>oc</sub> range = 4.4 - 5 (calculated at 20 °C) (Klimisch score 2)

The values for boiling point and vapour pressure are quite comparable for the 'COSMOtherm 2020' calculation and the registration dossier. The water solubility calculated by COSMOtherm is already very low, but the experimental value is even many times lower. A slight difference can be observed in the Log K<sub>ow</sub> value, which is 7.28 in the COSMOtherm calculation, and for which a range (5.3 to 6.1) was derived from read-across substances in the registration dossier. The Log K<sub>oa</sub> and Log K<sub>oc</sub> values calculated by COSMOtherm are higher than the values mentioned in the registration dossier.

COSMOLOGIC predictions utilise BIOVIA COSMOconf and BIOVIA COSMOtherm to estimate the physicochemical properties of a substance. Both programs use quantum chemistry calculations and are based on the COSMO-RS theory (Eckert and Klamt, 2002; Klamt, 1995). COSMOtherm has a solid scientific basis for the predictions, and a number of publications are available referring to this method as reliable.

As the calculation with 'COSMOtherm 2020' (Glüge and Scheringer, 2023) is not based on training sets of physical properties but based on calculated differences between the physicochemical interactions of a molecule dissolved in different solvents, the reliability of a prediction can be assessed on basis of the local performance of the model, i.e. how well structurally related substances are predicted. In terms of perfluamine, a comparison between predictions and experimental data on PFAS may be used to assess the performance of the model. For instance, Glüge and Scheringer (2023) states that "A very recent publication showed that COSMOtherm was not only superior to other estimation programs but also that the calculated log<sub>10</sub> K<sub>AW</sub> values for 21 per- and poly-fluoroalkyl substances were within one log<sub>10</sub> unit of the experimental data". Furthermore, Endo et al., (2023) found that "The partition coefficients between octanol and water, air and water, and octanol and air predicted by the PP-LFER models agreed with those predicted by the quantum chemically based model COSMOtherm, suggesting that both models are highly accurate for neutral PFAS and can fill the current large data gaps in partition property data". Based on these, the predictions by COSMOtherm, at least on these parameters, may be considered reliable. However, in terms of Log K<sub>oc</sub> prediction, as no structurally similar substances with experimental data were found to support the prediction, it is not possible to assess the reliability of the prediction on this parameter.

The EPI Suite QSAR method with medium uncertainty (KOWWIN v1.68) is used as reference value throughout this Annex XV report, given the fact that KOWWIN v1.68 represents a transparent approach whose suitability can easily be checked, and that the given prediction is considered to be acceptable.

## 2. Harmonised classification and labelling

There is no harmonised classification available for perfluamine according to Annex VI of Regulation (EC) No. 1272/2008 (CLP Regulation).

The following hazard classes are contained in self-classifications notified to the CLP inventory<sup>3</sup>:

- Acute Tox. 4: H302, Harmful if swallowed;
- Acute Tox. 3: H311, Toxic in contact with skin;
- Eye Irrit. 2: H319, Causes serious eye irritation;
- Not classified.

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<sup>3</sup> ECHA dissemination website - C&L Inventory database for perfluamine  
<https://echa.europa.eu/nl/information-on-chemicals/cl-inventory-database/-/discli/details/14691> (accessed 23 July 2024).

### 3. Environmental fate properties

Structural formulas corresponding to the CAS-numbers of read-across substances, mentioned in study reports or in public literature, are provided in Annex 1. Reliabilities of studies were assessed with Klimisch scores (Klimisch *et al.*, 1997).

#### 3.1 Degradation

##### 3.1.1 Abiotic degradation

###### 3.1.1.1 Hydrolysis

A hydrolysis study has not been performed with perfluamine. However, based on the chemical structure, which does not contain hydrolysable functionalities, perfluamine is not expected to hydrolyse. Furthermore, perfluamine is highly insoluble in water.

It is also noted that perfluamine does not contain functional groups for which hydrolysis can be estimated by the QSAR model HYDROWIN v2.00 of the Estimation Programs Interface (EPI) Suite tool (United States Environmental Protection Agency (US EPA), 2012).

Based on the information above, hydrolysis is not considered to be a relevant degradation mechanism for perfluamine.

###### 3.1.1.2 Oxidation

Experimental data on oxidation of perfluamine is not available.

Taking into account its perfluorinated character, it is expected that under environmental conditions perfluamine is oxidatively very recalcitrant and that degradation by such process is highly unlikely.

###### 3.1.1.3 Phototransformation/photolysis

###### 3.1.1.3.1 Phototransformation in air

**Table 6: Studies on phototransformation in air**

Method	Results	Remarks	Reference
No guideline specified  Indirect photolysis with *OH radical initiation, direct photolysis  Light source:	Degradation: 0% degradation after 60 min. (relative to trifluoromethane EC No: 200-872-4 CAS RN: 75-46-7)  Half-life (DT <sub>50</sub> ):	<b>Read-across</b> <i>Test material:</i> <i>pentadecafluoro-triethylamine</i> EC No: 206-632-5 CAS RN: 359-70-6  Klimisch score 2	ECHA dissemination website <sup>4</sup> : Unpublished study report, 1993

<sup>4</sup> ECHA dissemination website - REACH Registration dossier of perfluamine [https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5\\_986d3118-514e-436c-bd20-19d66a4f37a5](https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5_986d3118-514e-436c-bd20-19d66a4f37a5) (accessed 23 July 2024).

Method	Results	Remarks	Reference
mercury lamp	<ul style="list-style-type: none"> <li><i>pentadecafluoro-triethylamine</i> <math>N(C_2F_5)_3</math>, (EC No: 206-632-5 CAS RN: 359-70-6)</li> </ul> <p>&gt; 1 380 years</p> <p>Expected atmospheric lifetime &gt; 2000 years (based on reactivity of perfluoroalkanes)</p>	Non-GLP	
<p>No guideline specified</p> <p>Computational methods; (Atmospheric) model calculations</p>	<p>Total lifetime:</p> <ul style="list-style-type: none"> <li>perfluamine <math>N(C_3F_7)_3</math>: &gt; 1 000 years</li> <li><i>pentadecafluoro-triethylamine</i> <math>N(C_2F_5)_3</math>: &gt; 1 000 years</li> <li><i>tris(perfluorobutyl)-amine</i> <math>N(C_4F_9)_3</math> &gt; 1 000 years</li> <li><i>tris(undecafluoropentyl)amine</i> <math>N(C_5F_{11})_3</math> &gt; 1 000 years</li> </ul>	<p>Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0</p> <p><i>Test material:</i> <i>pentadecafluoro-triethylamine</i> EC No: 206-632-5 CAS RN: 359-70-6</p> <p><i>Test material:</i> <i>tris(perfluorobutyl)amine</i> EC No: 206-223-1 CAS RN: 311-89-7</p> <p><i>Test material:</i> <i>tris(undecafluoropentyl)-amine</i> EC No: 206-421-8 CAS RN: 338-84-1</p> <p>Klimisch score 4</p> <p>Non-GLP</p>	WMO (2019)
<p>No guideline specified</p> <p>Measurement of gas-phase UV absorption spectra</p> <p>Measurement of UV photodissociation yields</p> <p>Experimental and computational methods</p>	<p>Total global atmospheric lifetime:</p> <ul style="list-style-type: none"> <li>perfluamine <math>N(C_3F_7)_3</math>: 3 795 years</li> <li><i>pentadecafluoro-triethylamine</i> <math>N(C_2F_5)_3</math>: 3 880 years</li> <li><i>tris(perfluorobutyl)-amine</i> <math>N(C_4F_9)_3</math> 3 650 years</li> </ul>	<p>Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0</p> <p><i>Test material:</i> <i>pentadecafluoro-triethylamine</i> EC No: 206-632-5 CAS RN: 359-70-6</p> <p><i>Test material:</i> <i>tris(perfluorobutyl)amine</i> EC No: 206-223-1 CAS RN: 311-89-7</p> <p>Klimisch score 2</p> <p>Non-GLP</p>	Bernard et al. (2020)

A non-guideline (non-GLP) study performed with a structurally similar substance, pentadecafluorotriethylamine, (CAS RN: 359-70-6; molecular formula:  $N(C_2F_5)_3$ ) on phototransformation in air is available in the registration dossier (Unpublished study report, 1993). Pentadecafluorotriethylamine showed no degradation after 60 minutes, relative to trifluoromethane (CAS RN: 75-46-7; molecular formula:  $CHF_3$ ). Based on the known reactivity of perfluoroalkanes, the atmospheric lifetime of pentadecafluorotriethylamine was expected to be > 2 000 years (Klimisch score 2). The dissipation half-life ( $DT_{50}$ ) was calculated to be > 1 380 years for pentadecafluorotriethylamine.

Pentadecafluorotriethylamine is a close structural analogue of perfluamine, differing only in the absence of one difluoromethylene group in each perfluoroalkyl side chain. The reactivity of pentadecafluorotriethylamine and perfluamine towards hydroxyl radical-induced photodegradation is thus expected to be very similar. Given the fact that the structurally similar substance pentadecafluorotriethylamine showed no direct phototransformation in air, therefore also no phototransformation in air and no UV absorbance is expected for perfluamine, in the range relevant for the lower atmosphere. Perfluamine is thus expected to have a similar atmospheric lifetime > 2 000 years and a similar dissipation half-life ( $DT_{50}$ ) > 1 380 years (Unpublished study report, 1993).

The World Meteorological Organization (WMO), in its report 'Scientific Assessment on Ozone Depletion' (WMO, 2019) assembled a large appendix containing several parameters (amongst others total lifetimes) of numerous substances of interest. Total lifetime is defined as the combination of the total atmospheric lifetime (including tropospheric and stratospheric loss), and the lifetimes due to ocean and soil uptake (WMO, 2019; Klimisch score 4). Total lifetimes were reported to be > 1 000 years for several perfluoroamines (perfluamine ( $N(C_3F_7)_3$ ), CAS RN: 338-83-0; pentadecafluorotriethylamine ( $N(C_2F_5)_3$ ), CAS RN: 359-70-6; tris(perfluorobutyl)amine ( $N(C_4F_9)_3$ ), CAS RN: 311-89-7; tris(undecafluoropentyl)amine ( $N(C_5F_{11})_3$ ), CAS RN: 338-84-1). In general, perfluorocarbons (PFCs) are extremely stable in the atmosphere. For comparison, perfluorobutane (decafluorobutane; CAS RN: 355-25-9; molecular formula:  $C_4F_{10}$ ) and perfluoropentane (dodecafluoropentane; CAS RN: 678-26-2; molecular formula:  $C_5F_{12}$ ) have total lifetimes of 2 600 and 4 100 years, respectively (WMO, 2019; IPCC, 2001). It is stated in the Third Assessment Report (TAR) of the Intergovernmental Panel on Climate Change (IPCC) that "*PFCs are far from a steady state between sources and sinks, and even small emissions will contribute to radiative forcing over the next several millennia*" (IPCC, 2001).

In public literature, a non-guideline (non-GLP) study performed with three structurally similar perfluoroamines (pentadecafluorotriethylamine, CAS RN: 359-70-6; perfluamine, CAS RN: 338-83-0; tris(perfluorobutyl)amine, CAS RN: 311-89-7) is available (Bernard *et al.*, 2020). Various experimental and computational methods were applied, among which measurements of gas-phase UV absorption spectra and measurements of UV photodissociation yields. UV absorption spectra were measured over the 200 – 350 nm wavelength range. UV absorption occurred between 200 and 300 nm for pentadecafluorotriethylamine, and between 200 and 250 nm for perfluamine and tris(perfluorobutyl)amine. Computational methods used in this study demonstrated that atmospheric loss of perfluoroamines due to reaction with the OH radical was negligible.

The  $O(^1D)$  reaction and UV photolysis loss processes were used in 2-D atmospheric model simulations to calculate total global atmospheric lifetimes. Perfluamine (molecular formula:  $N(C_3F_7)_3$ ) had a total global atmospheric lifetime of 3 795 years. The structurally similar compounds pentadecafluorotriethylamine (molecular formula:  $N(C_2F_5)_3$ ) and tris(perfluorobutyl) amine (molecular formula:  $N(C_4F_9)_3$ ) had comparable total global atmospheric lifetimes of 3 880 and 3 650 years, respectively. The three perfluoroamines for which results are available (including perfluamine) thus all have total global atmospheric lifetimes > 3 500 years, and are therefore atmospherically persistent

(Bernard *et al.*, 2020; Klimisch score 2).

It is also noted that perfluamine does not contain functional groups that allow the QSAR model AOP v1.92 of the EPI Suite tool (US EPA, 2012) to estimate a reaction rate constant or a half-life for reaction with hydroxyl radicals or ozone.

As an overall conclusion, perfluamine is considered to be persistent in the atmosphere.

#### **3.1.1.3.2 Phototransformation in water**

Phototransformation in water is not experimentally tested for perfluamine.

#### **3.1.1.3.3 Phototransformation in soil**

Phototransformation in soil is not experimentally tested for perfluamine.

#### **3.1.1.4 Conclusion on abiotic degradation**

Perfluamine is not expected to hydrolyse and is not expected to be affected by oxidation processes.

Total and atmospheric lifetimes have been calculated for perfluamine, and structurally similar substances, in public literature. The highest derived atmospheric lifetime is a total global atmospheric lifetime of 3 795 years for perfluamine (Bernard *et al.*, 2020; Klimisch score 2). Structurally similar substances (as specified in section 3.1.1.3.1) also have total atmospheric lifetimes of at least 1 000 years (WMO, 2019; Klimisch score 4). Pentadecafluorotriethylamine, a structurally similar substance to perfluamine, had a dissipation half-life (DT<sub>50</sub>) in air > 1 380 years (Unpublished report, 1993). Based on all the evidence, perfluamine is therefore considered to be persistent in the atmosphere.

Regarding phototransformation in water and soil, no experimental information is available with perfluamine.

As an overall conclusion, abiotic degradation is not expected to be a significant route of transformation for perfluamine.

### **3.1.2 Biodegradation**

#### **3.1.2.1 Biodegradation in aqueous media or aqueous environment**

##### **3.1.2.1.1 Estimated data**

The EPI Suite tool (EPIWEB v4.1; US EPA, 2012) includes several BIOWIN models that provide degradation timeframes for primary and ultimate degradation of chemicals. According to the Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11 (ECHA, 2023), the combination of estimates from BIOWIN 2, 3 and 6 can be used as screening criteria that indicate whether compounds are potentially (very) persistent. If the BIOWIN 2 or 6 score is less than 0.5 in combination with a BIOWIN 3 score less than 2.25, one can conclude that the evaluated substance is potentially (very) persistent.

The following BIOWIN estimates can be retrieved for perfluamine (BIOWIN v4.11; US EPA, 2012):

- BIOWIN 2: 0.0000 (< 0.5) → Does not biodegrade fast
- BIOWIN 3: -1.0187 (< 2.25) → Ultimate biodegradation longer than months
- BIOWIN 6: 0.0000 (< 0.5) → Not readily degradable

The estimated values are far below the screening criteria, which provides a strong indication that perfluamine is potentially persistent (P) or very persistent (vP).

It is to be noted that not so many fluorinated compounds are represented in the training sets of the various BIOWIN models. The training set of the BIOWIN 2 model contains only 2 fluorinated compounds, namely Fluridone (CAS RN 59756-60-4) and 2-fluorophenol (CAS RN 367-12-4). The training set of the BIOWIN 3 model contains only 3 fluorinated compounds with either 1 fluorine atom or 1 trifluoromethyl group. The training set of the BIOWIN 6 model contains substantially more fluorinated compounds (>15), many of which are polyfluorinated substances. Furthermore, BIOWIN 6 includes a coefficient for the fluorine [-F] fragment which is not included in BIOWIN 2 and 3. In that sense, BIOWIN 6 provides a stronger indication of the persistent character of perfluamine than BIOWIN 2 and 3. It is also noted that in BIOWIN 2 and 3 some, but not all of the fluorine atoms of perfluamine are covered by the fragments specifically containing fluorine. In these two models, the twelve fluorine atoms on the secondary carbons are represented (in addition to the molecular weight parameter) as a part of the fragment "Carbon with 4 single bonds & no hydrogens" similarly as would be counted any other (non-hydrogen) atom which has a single bond with a carbon atom matching to this fragment. Nonetheless, the BIOWIN estimations can still be used as a piece of evidence in the weight-of-evidence approach, and the estimations underpin that perfluamine screens as potentially (v)P, and that the biodegradability potential is very low.

### 3.1.2.1.2 Screening tests

**Table 7: Screening tests for biodegradation in water**

Method	Results	Remarks	Reference
Test type: ready biodegradability  According to OECD TG 310: Ready Biodegradability – CO <sub>2</sub> in Sealed Vessels (Headspace Test)  Test system: sewage, domestic, non-adapted  Oxygen: aerobic	Degradation: 0 % degradation after 28 d  (CO <sub>2</sub> evolution, measurement of inorganic carbon concentration, no significant difference with blanks)	<b>Read-across:</b> <i>Test material described in the registration dossier as follows:</i> <i>perfluoro-N-C1,3-alkyl morpholines</i> <i>CAS RN: 1093615-61-2,</i> <i>FC-770</i>  <i>Note: the acronym FC-770 is associated to the substance identified with EC 473-390-7</i>	ECHA dissemination website <sup>5</sup> : Unpublished study report, 2007

<sup>5</sup> ECHA dissemination website - REACH Registration dossier of perfluamine [https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5\\_986d3118-514e-436c-bd20-19d66a4f37a5](https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5_986d3118-514e-436c-bd20-19d66a4f37a5) (accessed 23 July 2024).

Method	Results	Remarks	Reference
		Klimisch score 4 GLP	
<p>Test type: BOD5 tests No guideline specified</p> <p>Trend analysis of several tests</p> <p>Oxygen: aerobic</p>	Degradation: No biodegradation observed	<p><b>Read-across:</b> <i>Test material as described in the registration dossier: C<sub>5</sub>-C<sub>18</sub> PFOCs</i></p> <p><i>Perfluorohexanes</i> EC No: CAS RN: 1064697-81-9</p> <p><i>perfluoroheptanes</i> EC No: / CAS RN: 1064698-16-3</p> <p><i>perfluorotributyl amines</i> CAS RN: 1064698-37-8</p> <p><i>perfluoro-N-methylmorpholine</i> EC No: 206-841-1 CAS RN: 382-28-5</p> <p><i>perfluoro-N-C1,3-alkyl morpholines</i> CAS RN: 1093615-61-2</p> <p><i>perfluoro-C6,8-furans, pyrans and acyclic ethers</i> EC No: / CAS RN: 1064698-52-7</p> <p>Klimisch score 4</p> <p>GLP: not specified</p>	ECHA dissemination website <sup>3</sup> : Unpublished study report, 2012c
<p>Test type: ready biodegradability</p> <p>According to EEC Directive 79-831 Annex V, C.3: Biodegradation according to modified OECD Screening Test; OECD TG 301 E: Ready biodegradability: modified OECD Screening Test</p>	Degradation: 0 – 10 % degradation after 28 d (DOC removal)	<p><b>Read-across:</b> <i>tripropylamine</i> EC No: 203-047-7 CAS RN: 102-69-2</p> <p>Klimisch score 4</p> <p>Non-GLP</p>	ECHA dissemination website <sup>6</sup> : Unpublished study report, 1990a

<sup>6</sup> ECHA dissemination website - REACH Registration dossier of Tripropylamine [https://chem.echa.europa.eu/100.002.771/dossier-view/72dcf028-b4c4-4dc8-81cf-76aa9a10054f/d609c5b0-2991-4f27-b7f4-7b709749b16d\\_d609c5b0-2991-4f27-b7f4-7b709749b16d](https://chem.echa.europa.eu/100.002.771/dossier-view/72dcf028-b4c4-4dc8-81cf-76aa9a10054f/d609c5b0-2991-4f27-b7f4-7b709749b16d_d609c5b0-2991-4f27-b7f4-7b709749b16d) (accessed 23 July 2024).

Method	Results	Remarks	Reference
Test system: effluent from a laboratory waste water treatment plant treating municipal sewage  Oxygen: aerobic			
Test type: inherent biodegradability  According to EC Directive 79-831 Annex V, Part C, Level 1: Biodegradation "Zahn-Wellens Test"; equivalent to OECD TG 302 B: Inherent biodegradability: Zahn-Wellens / EMPA Test  Test system: activated sludge, domestic, non-adapted  Oxygen: aerobic	Degradation:  0 % after 3 h  0 % after 21 d  24 % after 27 d  79 % after 33 d  100 % after 41 d  (DOC removal)	<b>Read-across:</b> <i>tripropylamine</i> <i>EC No: 203-047-7</i> <i>CAS RN: 102-69-2</i>  Klimisch score 4  Non-GLP	ECHA dissemination website <sup>4</sup> : Unpublished study report, 1990b

Experimental studies regarding biodegradation in water are not available for perfluamine.

The registration dossier of perfluamine mentions two screening tests for biodegradation in water, performed with read-across substances.

The first screening test was performed according to Organisation for Economic Co-operation and Development Test Guideline (OECD TG) 310 with a structurally similar substance, described with various identifiers: the name perfluoro-N-C1,3-alkyl morpholines, FC-770 and CAS RN: 1093615-61-2 (CAS name: *Hydrofluoric acid, reaction products with 4-(1-methylethyl)morpholine*, molecular formula: C<sub>7</sub>F<sub>15</sub>NO). The acronym FC-770 is used to identify the substance associated to EC No 473-390-7, *Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine*. Therefore, the test material is expected to correspond to EC No 473-390-7. The substance showed no degradation after 28 days (measurement of inorganic carbon concentration, compared to blanks). Therefore, it can be considered to be not readily biodegradable. As the full study report is not available for this study, no additional information regarding validity criteria could be provided (Unpublished study report, 2007; Klimisch score 4).

The second dataset contains a trend analysis for several BOD<sub>5</sub> tests, performed with various perfluorinated organic compounds (PFOCs; C<sub>5</sub>-C<sub>18</sub>), specified in Table 7 (identified in the registration dossier with CAS RN: 1064697-81-9 – molecular formula: C<sub>6</sub>F<sub>14</sub>; CAS RN: 1064698-16-3 – molecular formula: C<sub>7</sub>F<sub>16</sub>; CAS RN: 1064698-37-8 – molecular formula: C<sub>12</sub>F<sub>27</sub>N; CAS RN: 382-28-5 – molecular formula: C<sub>5</sub>F<sub>11</sub>NO; CAS RN: 1093615-61-2 – molecular formula: C<sub>7</sub>F<sub>15</sub>NO; CAS

RN: 1064698-52-7 – molecular formula: /). According to the registration dossier, no biodegradation was observed for these substances (Unpublished study report, 2012c). It is however unclear which guidelines and test systems were applied during the tests with these various compounds, therefore a Klimisch score of 4 is deemed appropriate in this case.

The last two screening tests are read-across from tripropylamine (EC No 203-047-7 – molecular formula:  $C_9H_{21}N$ ) and are described in the registration dossier of tripropylamine. As tripropylamine is a non-fluorinated tertiary propylamine, this is a structural analogue, and thus useful for comparison of ready biodegradability with perfluamine.

The first screening test in the registration dossier of tripropylamine resulted in 0-10 % degradation after 28 days (measured as dissolved organic carbon (DOC) removal). This ready biodegradability test was performed according to OECD TG 301 E (Unpublished study report, 1990a; Klimisch score 4). The initial test substance concentration was 28 mg/L tripropylamine. The pass criterion of 70 % biodegradation measured as DOC removal is, with a percentage of 0-10 %, therefore not met. Tripropylamine is thus not readily biodegradable. As the full study report is not available for this study, no additional information regarding validity criteria could be provided.

The second screening test in the registration dossier of tripropylamine resulted in 0 % degradation after 3 hours, and 0 % even after 21 days (measured as DOC removal). The test duration was 41 days. This inherent biodegradability test was performed with a guideline equivalent to OECD TG 302 B (Unpublished study report, 1990b; Klimisch score 4). Measured initial tripropylamine concentration was 445 mg/L DOC. It must be noted that after an extended lag phase, 100 % degradation was reached after 41 days. Nevertheless, the pass criterion of 70 % mineralisation measured as DOC removal within 7 days is, with 0 % after 21 days, not met. Tripropylamine is thus not inherently biodegradable. As the full study report is not available for this study, no additional information regarding validity criteria could be provided.

Based on all the evidence under screening conditions, perfluamine is likely to have a low degradability, as the perfluorinated structural analogues described in this section (3.1.2.1.2), and thus it is expected to be not readily biodegradable and not inherently biodegradable. Tripropylamine is a non-fluorinated tertiary propylamine, and has been demonstrated in screening tests to be both not readily biodegradable and not inherently biodegradable. Perfluamine is expected to degrade less than tripropylamine in conditions similar to the inherent test. A read-across approach was used as supportive information for the persistence assessment of perfluamine; a justification on the read-across approach can be consulted in Annex 2.

### **3.1.2.1.3 Simulation tests**

No simulation tests in water or sediment are available with perfluamine.

### **3.1.2.2 Biodegradation in soil**

Biodegradation in soil is not experimentally tested for perfluamine.

### 3.1.2.3 Biodegradation by microbial communities

Studies on biodegradation by microbial communities are not available for perfluamine in public literature.

Liou *et al.* (2010) studied the susceptibility of PFOA (CAS RN: 335-67-1; molecular formula:  $C_8HF_{15}O_2$ ) to microbial metabolic attack (Klimisch score 2).

A first preliminary screening experiment, to test whether the different microbial communities would use PFOA as an electron acceptor, was conducted using five different inoculum sources (municipal wastewater treatment plant, industrial site sediment, agricultural soil, soil from a first fire training area, and soil from a second fire training area), and three different electron donors (acetate, ethanol, and  $H_2$  gas). No evidence was found that microbial communities used PFOA as an electron acceptor.

A second experiment examined the potential reductive defluorination, metabolism, and cometabolism of PFOA. The municipal wastewater treatment plant inoculum was used with 100 ppm PFOA ( $^{14}C$ -labelled; high purity (99.9 %)) as electron acceptor and 10 mM acetate as electron donor. After 110 days, no loss of PFOA was detectable and no  $^{14}CO_2$  was produced. It was also examined whether PFOA could be used as an electron donor or be co-metabolised during five terminal electron-accepting processes (aerobic respiration, nitrate reduction, iron reduction, sulfate reduction, and methanogenesis). Again, the municipal wastewater treatment plant inoculum was used with 100 ppm or 100 ppb PFOA (high purity). The treatments were the inoculum with or without acetate as electron donor (10 mM), and electron acceptors were  $O_2$ /nitrate, iron oxide, sulfate, or  $CO_2$ . Also here, no significant decrease in PFOA concentration was observed in any of the treatments.

In a last experiment, the municipal wastewater treatment plant inoculum was used with 100 ppm or 100 ppb PFOA (high purity). An electron acceptor (0.4 mM TCE (trichloroethylene; CAS RN: 79-01-6; molecular formula:  $C_2HCl_3$ )) and an electron donor (acetate (10 mM) and lactate (40 mM)) were supplied to the experiment. A decrease in PFOA concentration was only observed in the 100 ppb PFOA treatment after 65 days of incubation, thus only with co-metabolism of PFOA during reductive de-chlorination of TCE. Extensive analysis by Liquid Chromatography – Mass Spectrometry (LC-MS) however failed to confirm the presence of transformation products. No decrease in PFOA concentration was observed for the 100 ppm PFOA treatment (Liou *et al.*, 2010).

Therefore, it can be concluded that PFOA could not be biodegraded by the microbial communities present in the studied systems under the different conditions used in the study. This suggests low biodegradability of PFOA which could also be applicable to perfluamine.

### 3.1.2.4 Conclusion on biodegradation

In EPI Suite estimated BIOWIN values are all far below the screening criteria, which indicates that perfluamine is potentially (v)P.

Furthermore, screening studies with analogue substances demonstrate that PFOCs (such as perfluamine) are not readily biodegradable. A first ready biodegradability screening test according to OECD TG 310 (Unpublished study report 2007a; Klimisch score 4), performed with EC No 473-390-7, showed 0 % degradation after 28 days ( $CO_2$  evolution). Secondly, a trend analysis for several BOD5 tests (Unpublished study report 2012c; Klimisch score 4), performed with various PFOCs ( $C_5$ - $C_{18}$ ), showed no biodegradation.

Screening studies with tripropylamine (EC No: 203-047-7) are also available. A first OECD TG 301 E study resulted in 0 – 10 % degradation after 28 days (DOC removal) (Unpublished study report, 1990a; Klimisch score 4). Therefore, tripropylamine is not readily biodegradable. For a second study equivalent to OECD TG 302 B, 0 % degradation was reported after 3 hours, and 0 % degradation after 21 days (DOC removal) (Unpublished study report, 1990b; Klimisch score 4). Therefore, it is also not inherently biodegradable. As tripropylamine is a non-fluorinated tertiary propylamine, this is a structural analogue, and thus useful for comparison of ready biodegradability with perfluamine.

Another perfluorinated substance, namely PFOA, has been studied on its potential for biodegradation by microbial communities (Liou *et al.*, 2010; Klimisch score 2). No evidence was found that microbial communities used PFOA as an electron acceptor. Tests at conditions favourable for processes such as reductive defluorination, metabolism, and cometabolism could also not lead to an alteration of the chemical structure of PFOA.

Altogether, based on a weight-of-evidence consideration, it can be concluded that perfluamine, like other PFOCs, is very persistent.

### 3.1.3 Field data

Field studies are not available with perfluamine.

### 3.1.4 Other information on degradation

#### 3.1.4.1 Carbon-fluorine (C-F) bond

Perfluamine is a PFAS of which the structure consists of covalent carbon-fluorine (C-F) bonds. The C-F bond is considered to be the strongest in organic chemistry, which leads to a unique structure and stability for PFAS substances that contain these bonds (Zhang *et al.*, 2022).

Hiyama *et al.* (2013) stated that “A C-F bond is the strongest among halogen-carbon bonds: heat of formation of a C-F bond is 456-486 kJ/mol; that of a C-Cl bond is roughly 350 kJ/mol, comparable to a C-H bond of 356-435 kJ/mol. The strong bond energy of C-F bonds contributes to the high thermal and oxidative stabilities of organofluorine compounds”. Fluorine is also associated with the highest electronegativity of all the elements in the periodic table. For comparison, fluorine has an electronegativity of 3.98, while hydrogen, bromine and chlorine all have lower electronegativities of 2.20, 2.96 and 3.16 (Kirsch, 2013).

The high polarity of the carbon-fluorine bond is described by O’Hagan (2008): “Fluorine is the most electronegative element in the periodic table. When bound to carbon it forms the strongest bonds in organic chemistry and this makes fluorine substitution attractive for the development of pharmaceuticals and a wide range of speciality materials. Although highly polarised, the C-F bond gains stability from the resultant electrostatic attraction between the polarised  $C^{\delta+}$  and  $F^{\delta-}$  atoms. This polarity suppresses lone pair donation from fluorine and in general fluorine is a weak coordinator”.

The highly stable C-F bonds cause PFAS substances to be chemically inert, inaccessible for environmental degradation processes like oxidation, and complex to be degraded by microorganisms (Roesch *et al.*, 2022). Perfluoroalkyl chemicals in general resist biotransformation and defluorination under natural conditions. Reasons for this are, amongst others, the unavailability of the necessary enzymatic systems in nature, high

strength of the C-F bonds, and absence of structures that are susceptible to electrophilic or nucleophilic attack, in order to be degraded by microorganisms (Liu and Avendaño, 2013).

#### 3.1.4.2 Pyramidal nitrogen inversion

The carbon-nitrogen (C-N) bonds of perfluamine are shielded from chemical attack by a phenomenon called 'pyramidal nitrogen inversion'. Pyramidal inversion is described as a rapid oscillation of the atom and substituents, with the molecule or ion passing through a planar transition state (Lehn, 1970). This mechanism typically occurs in compounds with a pyramidal molecule, such as ammonia (ammonia, anhydrous; CAS RN: 7664-41-7; molecular formula: NH<sub>3</sub>).

Morgan and Leyden (1970) described the kinetics of the nitrogen inversion of three tertiary amines in aqueous acid solution, demonstrating that this mechanism also takes place in compounds containing an amine group (such as perfluamine).

#### 3.1.4.3 Identification of other perfluorinated substances as vPvB

Several other perfluorinated substances have already been assessed in the framework of the REACH Regulation and have been identified as SVHC because of their very persistent and very bioaccumulative (vPvB) properties, such as heneicosfluoroundecanoic acid (CAS RN: 2058-94-8; ECHA, 2012a), heptacosfluorotetradecanoic acid (CAS RN: 376-06-7; ECHA, 2012b), pentacosfluorotridecanoic acid (CAS RN: 72629-94-8; ECHA, 2012c), tricosfluorododecanoic acid (CAS RN: 307-55-1; ECHA, 2012d), perfluorohexane-1-sulphonic acid and its salts (CAS RN: 355-46-4; ECHA, 2017), perfluoroheptanoic acid and its salts (CAS RN: 375-85-9; ECHA, 2022a), and reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine (EC No 473-390-7; ECHA, 2022b).

The following perfluorinated substances were identified in the framework of the REACH Regulation to be of equivalent level of concern to Carcinogenic, Mutagenic, toxic to Reproduction (CMR) and Persistent, Bioaccumulative and Toxic (PBT)/vPvB substances: 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, its salts and its acyl halides (covering any of their individual isomers and combinations thereof) (HFPO-DA; CAS RN: 13252-13-6; ECHA, 2019a), and perfluorobutane sulfonic acid and its salts (EC No: 799-977-0; ECHA, 2019b), with also an emphasis on their vP properties in the support documents.

### 3.1.5 Conclusion on degradation

As perfluamine almost entirely consists of strong covalent C-F bonds (Zhang *et al.*, 2022; Hiyama *et al.*, 2013; Kirsch, 2013; O'Hagan, 2008), its degradation will be very limited or negligible (Roesch *et al.*, 2022; Liu and Avendaño, 2013), resulting in a stable substance that cannot be broken down under relevant environmental conditions. Furthermore, the C-N bonds of perfluamine are shielded from chemical attack through 'pyramidal nitrogen inversion' (Lehn, 1970; Morgan and Leyden, 1970).

A total global atmospheric lifetime of 3 795 years has been reported for perfluamine (Bernard *et al.*, 2020; Klimisch score 2). Structurally similar substances (as specified in section 3.1.1.3.1) also have total atmospheric lifetimes and half-lives in air of at least 1 000 years (WMO, 2019; Klimisch score 4 and Unpublished report, 1993; Klimisch score 2).

Screening tests for biodegradation, performed with analogue substances, demonstrate the non-biodegradability of PFOCs. In an OECD TG 310 ready biodegradability study, 0% degradation was observed after 28 days (CO<sub>2</sub> evolution) for EC No 473-390-7 (Unpublished study report 2007a; Klimisch score 4). BOD<sub>5</sub> tests are available for several read-across substances, in which no biodegradation was observed for none of these substances (Unpublished study report 2012c; Klimisch score 4). Screening studies with tripropylamine (EC No: 203-047-7) are also available. A first OECD TG 301 E study resulted in 0 – 10 % degradation after 28 days (DOC removal) (Unpublished study report, 1990a; Klimisch score 4). Therefore, tripropylamine is not readily biodegradable. For a second study equivalent to OECD TG 302 B, 0 % degradation was reported after 3 hours, and 0 % degradation after 21 days (DOC removal) (Unpublished study report, 1990b; Klimisch score 4). Therefore, perfluamine is also expected to be not inherently biodegradable under similar conditions.

Perfluamine, like other PFOCs, is thus not readily and not inherently biodegradable. Another perfluorinated substance, namely PFOA, was also demonstrated to be microbiologically inert (Liou *et al.*, 2010; Klimisch score 2). Moreover, several other perfluorinated substances have already been assessed in the framework of the REACH Regulation and have been identified as SVHC because of their vPvB properties (ECHA, 2012a; 2012b; 2012c; 2012d; 2017; 2022a; 2022b), or to be of equivalent level of concern to CMR and PBT/vPvB substances (ECHA, 2019a; 2019b).

Thus, the structural properties of perfluamine, the extremely high total global atmospheric lifetime and the high atmospheric half-life, the fact that no or very limited biodegradation was observed in screening tests performed with read-across substances, and the fact that several similar perfluorinated substances have already been identified as SVHC (and concluded to fulfil the P and vP criteria as part of the justifications for SVHC), altogether allow to conclude that perfluamine fulfils the P and vP criteria, based on a weight-of-evidence consideration.

## 3.2 Environmental distribution

### 3.2.1 Adsorption/desorption

The adsorption capacity of perfluamine on organic carbon is not measured experimentally. In absence of experimental data, one may try to assess the adsorption capacity via indirect approaches. In the registration dossier, a Log K<sub>oc</sub> range was reported based on an equation from the Technical Guidance Document on Risk Assessment (non-GLP; Company data, 2012a; Klimisch score 2).

**Table 8: Partition coefficient organic carbon/water**

Method	Results	Remarks	Reference <sup>7</sup>
Calculation based on equation from Chapter 4 'Predominantly hydrophobics' in 'European Chemicals Bureau: Technical Guidance Document on Risk Assessment'	Partition coefficient organic carbon/water:  Log K <sub>oc</sub> range = ≥ 4.4 - ≤ 5 (calculated at 20 °C)	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0  Klimisch score 2  Non-GLP	ECHA dissemination website: Company data, 2012a

<sup>7</sup> ECHA dissemination website - REACH Registration dossier of perfluamine [https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5\\_986d3118-514e-436c-bd20-19d66a4f37a5](https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5_986d3118-514e-436c-bd20-19d66a4f37a5) (accessed 23 July 2024).

In this way, a calculated Log  $K_{oc}$  range of 4.4 to 5 was reported.

The KOCWIN v2.00 model in EPI Suite (US EPA, 2012) provides two approaches to estimate the Log  $K_{oc}$  value: one method is based on the Molecular Connectivity Index (MCI), while in the second method the Log  $K_{oc}$  is derived from the Log  $K_{ow}$  value. The MCI method leads to an estimated Log  $K_{oc}$  of 6.7, while the Log  $K_{ow}$  method results in a lower Log  $K_{oc}$  value, namely 4.3. Perfluamine is within the applicability domain (molecular weight and fragment domain). However, the training set does not include poly- or perfluorinated substances. Therefore, both Log  $K_{oc}$  values derived from the MCI method and the Log  $K_{ow}$  method can be considered to have high uncertainty. Modelling with 'COSMOtherm 2020' (see Table 5; Glüge and Scheringer, 2023) resulted in a Log<sub>10</sub>  $K_{oc}$  value of 5.18 (at 25 °C) (reliability cannot be assessed).

### 3.2.2 Volatilisation

In order to assess the volatilisation potential, a reliable Henry's Law Constant (HLC) is needed. Because the vapour pressure and the water solubility are experimentally measured, it is possible to estimate a range for the HLC in a reliable way. Based on a vapour pressure of 516 Pa and a water solubility range of 70 to 1 960 ng/L, with an accepted average value of 381 ng/L, one can calculate a dimensionless HLC range of 56 300 to 1 580 000, with an average value of 290 000. This corresponds with an average value of  $7.06 \times 10^8$  Pa.m<sup>3</sup>/mole. Thus, in field conditions the equilibrium air/water points towards the air compartment.

In the registration dossier, a HLC range of 140 000 to 166 000 was derived for perfluamine (Unpublished study report, 2012d), using the experimental values of two read-across substances (lower limit: identified as perfluoroheptanes - CAS RN: 1064698-16-3 – molecular formula: C<sub>7</sub>F<sub>16</sub>; upper limit: identified as perfluorotributyl amines - CAS RN: 1064698-37-8 – molecular formula: C<sub>12</sub>F<sub>27</sub>N). As it is unclear which guidelines and test systems were applied for the two compounds during the experimental tests, a Klimisch score of 4 is deemed appropriate in this case.

**Table 9: Henry's Law Constant (HLC)**

Method	Results	Remarks	Reference <sup>8</sup>
No guideline specified  Range defined by using experimental HLCs of two similar substances	HLC range = 140 000 – 166 000 dimensionless at 23 °C and 760 mm Hg	<b>Read-across:</b> <i>Test material:</i>  <i>Lower limit:</i> <i>perfluoroheptanes</i> <i>EC No: /</i> <i>CAS RN: 1064698-16-3</i>  <i>Upper limit:</i> <i>perfluorotributyl amines</i> <i>EC No: 830-388-4</i> <i>CAS RN: 1064698-37-8</i>  Klimisch score 4  GLP: not specified	ECHA dissemination website: Unpublished study report, 2012d

<sup>8</sup> ECHA dissemination website - REACH Registration dossier of perfluamine  
[https://chem.echa.europa.eu/100.005.837/dossier-view/3016abee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5\\_986d3118-514e-436c-bd20-19d66a4f37a5](https://chem.echa.europa.eu/100.005.837/dossier-view/3016abee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5_986d3118-514e-436c-bd20-19d66a4f37a5) (accessed 23 July 2024).

In EPI Suite, the HLC is estimated with the HENRYWIN v3.20 model (US EPA, 2012; Klimisch score 2). In this model two methodologies are presented, namely a first one based on 'bond contributions' and a second one based on 'group contributions'. For perfluamine only the bond contribution methodology provides a value as coefficients are missing for some fragments in the group contributions methodology. The bond contribution method estimates a dimensionless HLC of 15 400. This value is lower than the values based on experimental measurements and on read-across. This lower value is triggered by an assumed water solubility of 28 µg/L, which is at least one order of magnitude higher than experimentally measured water solubilities. The prediction provided on basis of the bond contribution method is an extrapolation, and there are no similar substances in the training set. Therefore, this predicted EPI Suite value has high uncertainty.

The average HLC of 290 000 is in the same order of magnitude as the HLC range derived via read-across.

### 3.2.3 Distribution modelling

One approach to assess the distribution of perfluamine into the various environmental compartments is given by the Level III Fugacity Model from EPI Suite (EPIWEB v4.1; US EPA, 2012). This Fugacity Model predicts the partitioning of a chemical in an evaluative environment. That means that the model assumes steady-state conditions but not equilibrium conditions.

**Table 10: Distribution modelling for perfluamine (Level III Fugacity Model; EPIWEB v4.1; US EPA, 2012)**

Release	Air	Water	Soil	Sediment
Equal	1.15 %	1.3 %	0.42 %	97.1 %
Only to air	99.9 %	0.000017 %	0.13 %	0.0013 %
Only to water	0.041 %	1.32 %	0.000055 %	98.6 %
Only to soil	57 %	0.001 %	42.9 %	0.075 %

It should be noted that model predictions are defined by the structure of the compartments and the parameters of connection between those compartments. Nevertheless, the environmental distribution modelling described above demonstrates that mass distribution of perfluamine may occur to all environmental compartments.

### 3.2.4 Other distribution data

The partition coefficient  $K_{oa}$  is not experimentally measured.

In EPI Suite, the Log  $K_{oa}$  value is estimated via the KOAWIN v1.10 model (US EPA, 2012). This model simply uses the estimated values for Log  $K_{ow}$  (6.19) and the logarithm of the dimensionless HLC (Log  $K_{aw}$  = 4.187; Log  $K_{oa}$  = Log  $K_{ow}$  - Log  $K_{aw}$ ). The model estimates a Log  $K_{oa}$  of 2.003. This predicted EPI Suite value has high uncertainty, as it is partly based on the HENRYWIN v3.20 prediction, which also has high uncertainty.

In the registration dossier (Company data, 2012b), a calculated Log  $K_{oa}$  range of 0.1 to 1.0 was mentioned for perfluamine, based on the HLC and the Log  $K_{ow}$  range derived from two read-across substances (lower limit: perfluoroheptanes - CAS RN: 1064698-16-3 – molecular formula:  $C_7F_{16}$ ; upper limit: perfluorotributyl amines - CAS RN: 1064698-37-8 – molecular formula:  $C_{12}F_{27}N$ ). As it is unclear which guidelines and test systems were applied for the derivation of the ranges for these two read-across compounds, a Klimisch score of 4 is deemed appropriate. Modelling with 'COSMOtherm 2020' (see Table 5; Glüge and Scheringer, 2023) resulted in a Log<sub>10</sub>  $K_{oa}$  value of 2.23 (at 20 °C) (reliable).

**Table 11: Partition coefficient octanol/air**

Method	Results	Remarks	Reference <sup>9</sup>
No guideline specified  Calculation based on HLC range and Log K <sub>ow</sub> range of two similar substances  $K_{oa} = K_{ow}/K_{aw}$	Partition coefficient octanol/air:  K <sub>oa</sub> range = 1.2 – 9.3 Log K <sub>oa</sub> range = 0.1 – 1.0 (at 23 °C)	<b>Read-across:</b> <i>Test material:</i>  <i>Lower limit:</i> <i>perfluoroheptanes</i> <i>EC No: /</i> <i>CAS RN: 1064698-16-3</i>  <i>Upper limit:</i> <i>perfluorotributyl amines</i> <i>CAS RN: 1064698-37-8</i>  Klimisch score 4  GLP: not specified	ECHA dissemination website: Company data, 2012b

**Table 12: Soil volatilisation half-lives**

Method	Results	Remarks	Reference <sup>10</sup>
US EPA Human Health Risk Assessment Protocol for Hazardous Waste Combustion Facilities (EPA530-R-05-006, Sept. 2005); Calculation method	<u>Half-lives for volatilisation from soil:</u>  Agricultural soil: 25.6 h  Natural grassland: 1.6 h  Industrial soil: 1.6 h	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0  Klimisch score 2  Non-GLP	ECHA dissemination website: Company data, 2013

According to calculations mentioned in the registration dossier (Company data, 2013; Klimisch score 2), performed according to a US EPA calculation method, volatilisation half-lives for perfluamine are 25.6 hours from agricultural soil and 1.6 hours from natural grassland and industrial soil.

### 3.2.5 Field data

Field studies are not available with perfluamine.

<sup>9</sup> ECHA dissemination website - REACH Registration dossier of perfluamine  
[https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5\\_986d3118-514e-436c-bd20-19d66a4f37a5](https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5_986d3118-514e-436c-bd20-19d66a4f37a5) (accessed 23 July 2024).

<sup>10</sup> ECHA dissemination website - REACH Registration dossier of perfluamine  
[https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5\\_986d3118-514e-436c-bd20-19d66a4f37a5](https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5_986d3118-514e-436c-bd20-19d66a4f37a5) (accessed 23 July 2024).

### 3.2.6 Conclusion on environmental distribution

The values of various physical properties of perfluamine were estimated. These values will determine the distribution of the test substance into environmental compartments. A property that can be determined in a reliable way is the HLC, as both vapour pressure and water solubility of perfluamine are experimentally measured. The dimensionless value is assessed to be in the range of 56 300 to 1 580 000, with an accepted average value of 290 000. A calculated Log  $K_{oc}$  range of 4.4 to 5 was reported for perfluamine (Company data, 2012a; Klimisch score 2). The Log  $K_{oa}$  is estimated via read-across to be in the range of 0.1 to 1 (Company data, 2012b; Klimisch score 4).

The Level III Fugacity Model from EPI Suite (US EPA, 2012; Klimisch score 2) demonstrates that in steady-state circumstances, perfluamine will partition to the different compartments, depending on the route of emission that is chosen.

The registration dossier contains calculated half-lives for volatilisation of the test substance from soil, more specifically 25.6 h, 1.6 h and 1.6 h for agricultural soil, natural grassland and industrial soil, respectively.

## 3.3 Data indicating potential for long-range transport

### 3.3.1 Potential for long-range transport

Monitoring data on Perfluamine in remote areas is not available.

Perfluamine meets the vP criterion (as explained in section 3.1.5). Total and atmospheric lifetimes and half-lives in air have been calculated for perfluamine, and structurally similar compounds, in public literature. The highest derived atmospheric lifetime is a total global atmospheric lifetime of 3 795 years for perfluamine (Bernard *et al.*, 2020; Klimisch score 2). Structurally similar substances (as specified in section 3.1.1.3.1) also have total atmospheric lifetimes and half-life in air of at least 1 000 years (WMO, 2019; Klimisch score 4 and unpublished report, 1993; Klimisch score 2). Perfluamine is therefore considered to be atmospherically persistent. In combination with the prediction that perfluamine also distributes to the air compartment according to the Level III Fugacity model (section 3.2.3), it is reasonable to conclude that perfluamine shows high potential for long-range atmospheric transport.

### 3.3.2 Persistent Organic Pollutants (POP)

Scheringer *et al.* (2012) summarised a list of potential Persistent Organic Pollutants (POP) substances, defined as chemicals exceeding the Annex D criteria of the Stockholm Convention ("POP group"), and a list of chemicals strongly exceeding the Annex D criteria of the Stockholm Convention ("very-POP group"). Perfluamine is included as potential POP and potential very POP substance in both lists (table S2 and table S3 in Scheringer *et al.*, 2012; supporting material).

### 3.3.3 Conclusion on data indicating potential for long-range transport

Perfluamine shows high potential for long-range atmospheric transport and is identified in public literature as a potential POP substance.

## 3.4 Bioaccumulation

### 3.4.1 Bioaccumulation in aquatic organisms (pelagic & sediment organisms)

#### 3.4.1.1 Screening information

The Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11 (ECHA, 2023; section R.11.4.1.2.1) points out that if the Log  $K_{ow}$  of a substance is greater than 4.5, this substance is potentially (very) bioaccumulative for aquatic organisms.

The Log  $K_{ow}$  is not experimentally determined for perfluamine, but in the registration dossier a Log  $K_{ow}$  range of 5.3 - 6.1 is proposed based on read-across from two substances (see Table 4; Unpublished study report, 2012b; Klimisch score 4 (as full study reports are not available)). The KOWWIN v1.68 module of the EPI Suite tool (US EPA, 2012) predicts a value for Log  $K_{ow}$  of 6.19. This EPI Suite value is considered to have medium uncertainty as all the fragments in perfluamine are recognized by KOWWIN, and at least the validation set contains a compound with more than 9 carbon atoms without an attached hydrogen atom and a compound with more than 21 fluorine atoms. The molecular weight of perfluamine is within the range established for both the training set and the validation set. Therefore, KOWWIN v1.68 represents a transparent approach whose suitability can easily be checked, and the prediction is considered to be acceptable. Further, it is noted that analyses with 'COSMOtherm 2020' software (Glüge and Scheringer, 2023) results in a Log<sub>10</sub>  $K_{ow}$  value of 7.28 (reliable; see Table 5).

#### **Conclusion:**

The Log  $K_{ow}$  value derived in EPI suite of 6.19 (US EPA, 2012; medium uncertainty) shows that the Log  $K_{ow}$  threshold of 4.5 is exceeded. Perfluamine therefore meets the screening criterion set out in the PBT Guidance (REACH Chapter R.11; ECHA, 2023) for aquatic organisms as being potentially 'bioaccumulative' (B) and/or 'very bioaccumulative' (vB) (i.e. Log  $K_{ow}$  > 4.5).

#### 3.4.1.2 QSAR estimations

QSAR models were run in order to estimate the bioaccumulation potential of perfluamine.

At this moment, the BCFBAF v3.01 module of the EPI Suite tool is not recommended for highly fluorinated substances, as the maximum number of fluorine atoms in training set compounds is 8 (appendix F, BCFBAF User guide; US EPA, 2012), while perfluamine contains 21 fluorine atoms. None of the BCF models in VEGA (VEGA HUB, 2022) can be applied due to a lack of similar substances in the training sets. The BCF baseline model of CATALOGIC, developed by the Laboratory of Mathematical Chemistry (LMC, 2022), cannot be used either, as perfluamine is out of the structural and mechanistic domains.

#### **Conclusion:**

Therefore, it is concluded that at the moment QSAR estimations do not provide sufficiently reliable information on the bioaccumulation potential of perfluamine.

## 3.4.1.3 Experimental information

**Table 13: Aquatic bioaccumulation**

Method	Results	Remarks	Reference <sup>11</sup>
According to OECD TG 305: Bioaccumulation in Fish: Aqueous and Dietary Exposure – III: Dietary Exposure Bioaccumulation Fish Test  <i>Lepomis macrochirus</i>  Route of exposure: feed  freshwater  flow-through	BCF <sub>KgL</sub> : 5 527 – 51 602 L/kg > 5 000  Depuration half-life: 42 d  Minimal BMF values: BMF <sub>Kg</sub> : 0.61 BMF <sub>KgL</sub> : 2.19 BMF <sub>5%</sub> : 0.59	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0  Klimisch score 2  GLP	ECHA dissemination website: Unpublished study report, 2023

A bioaccumulation study on aquatic organisms according to OECD TG 305 (OECD, 2012) is available in the registration dossier (Unpublished study report, 2023; Klimisch score 2). Such study can in principle be carried out with aqueous exposure or dietary exposure. In view of the very low water solubility (381 ng/L at 23 °C), and the high volatility (516 Pa at 20 °C) of perfluamine, the study was performed with dietary exposure. A Klimisch score of 2 is considered appropriate for this dietary study, as not all the validity criteria listed in the OECD TG 305 are fulfilled (page 26-27; OECD, 2012). More specifically the criteria in paragraph 113, bullet points 3 and 4, relating to the variation of the test item concentration in the diet and the homogeneity of the diet are not met. Further, it is noted that increase in fish weight and increase in lipid content of the fish were substantial in the study, triggering uncertainty on the precise values of the half-life and the bioconcentration factor (BCF) of perfluamine in fish. However, the results of the dietary study are considered to be reliable, and their interpretation is concluded to be indisputable as the uncertainty relating to the exposure conditions does not have an impact on the data from the depuration phase. Therefore, the study is assigned with a Klimisch score of 2. The calculated half-life and the BCF are derived only from depuration phase data. These values clearly exceed the thresholds ( $5\,527 < \text{BCF} < 51\,602$  L/kg and half-life = 42 days).

The laboratory that performed the dietary study has tried to achieve consistent exposure conditions throughout the whole duration of the test. Several preliminary trials were conducted to examine what would be the best way to prepare the fish diet and what nominal test item concentration should be applied in order to get test item levels in fish that can be reliably monitored during the depuration phase. These trials indicated that diets should be freshly prepared for each feeding event because maintaining steady concentrations in fortified diets proved to be difficult when stored during longer periods. Mixing the test item with diet should also be carried out overnight at low temperature. Further, it was observed that the test item leached out from the fortified diet once it was brought into contact with water. For this reason, five additional leaching trials were conducted in order to verify quantitatively how fast leaching into water takes place. These

<sup>11</sup> ECHA dissemination website - REACH Registration dossier of perfluamine  
[https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5\\_986d3118-514e-436c-bd20-19d66a4f37a5](https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5_986d3118-514e-436c-bd20-19d66a4f37a5)  
 (accessed 23 July 2024).

trials pointed out that when water was added to dry diets, the amount of test substance detected declined sharply in the first few minutes, but afterwards losses were much less precipitous. Apparently, a kind of equilibrium is established in the small vials used in the preliminary trials. Based on these observations, it was concluded that the fortified diet needed to be pre-wetted prior to delivery to the test system in order to achieve an effective and relatively steady test item concentration in the food.

In order to further optimise the definitive study, a preliminary non-GLP pilot study was conducted to find an appropriate nominal test item concentration in the diet. This pilot study was conducted with a nominal perfluamine concentration of 250 µg/kg food. Both the uptake phase and the depuration phase lasted 14 days. It was observed that the time it took between adding the fortified diet to the test water, and fish actually eating the food, could vary a lot. Some fish consumed the food almost instantaneously, while for others it could take up to 5 minutes. In a separate experiment, pre-wetted food was brought into contact with test water and it appeared that after 5 minutes the test item concentration decreased from 250 µg/kg food to circa 1 µg/kg food. This indicates that the leaching rate constant for the test substance at the start of a feeding event could be greater than 1/minute. This is an exceptionally high leaching rate but there seemed to be no practical way to avoid this leaching. This observation points out that how fast fish eat the food, determines to a large extent their actual exposure level. A small variation in the time during which fish consume their food can cause a huge fluctuation in their actual exposure. Consequently, the determination of a biomagnification factor (BMF) can be associated with substantial uncertainty. Nevertheless, the pilot study demonstrated that with a nominal test item concentration of 250 µg/kg food, test item concentrations in fish tissues could reliably be monitored. This pilot study already indicated that depuration of perfluamine from fish occurs very slowly.

The definitive bioaccumulation study with dietary exposure was carried out according to a protocol based on procedures outlined in OECD TG 305 (OECD, 2012). The study was performed with freshwater in a flow-through apparatus using *Lepomis macrochirus* (common name: bluegill). The test substance was not radiolabeled because specific chemical analysis by gas chromatography/mass spectrometry (GC/MS) was considered to be effective. The uptake period was 14 days, with fish only being sampled at the end. A 37-day depuration phase followed with fish being sampled on days 1, 3, 7, 14, 28 and 37. On day 37, only fish weight was measured and not the test substance concentration in fish.

The test conditions in the study are further described in Table 14.

**Table 14: Test conditions (Unpublished study report, 2023)**

Apparatus	Uptake phase: 127 L Teflon-lined stainless steel aquaria with 80 L of dilution water Depuration phase: 54 L stainless steel aquaria with 45 L of dilution water Continuous-flow diluter delivering 6 exchanges/day
Test organism	<i>Lepomis macrochirus</i> Common name: bluegill 90 fish in the treatment group 90 fish in the control group
# of replicates/sampling event	6 or 7
Diet	Commercially prepared Aquamax Starter from Purina amended with cod liver oil (0.5%)  Mean percent lipids in diet: - Control group: 18.1 ± 0.26 %

	- Treatment group: $18.7 \pm 0.38$ %  Diet: approximately 2 to 3 % of body weight (wet weight)  Initial feed rate: based on weight measurements of a sample of fish from the stock population collected on day 0
Nominal test item concentration	250 µg/kg food Purity 95.5 % No radiolabelling
Vehicles	Methyl tert-butyl ether, MTBE (20 mg/mL) Dimethylformamide, DMF (1.25 % (v/v))
Uptake period	14 days
Fish weight at uptake initiation	$2.65 \pm 0.42$ g (more details on fish length, weight and lipid level are provided in Table 15)
Depuration period	37 days
Fish weight at depuration end	$6.86 \pm 2.61$ g
Loading rate	3.0 g/L
Temperature	21.3 – 22.5 °C
pH	8.1 – 8.5
Dissolved oxygen level	7.1 – 8.5 mg/L  Dissolved oxygen: $\geq 7.1$ mg/L (82 % of air saturation) throughout the test
Hardness	140 – 156 mg CaCO <sub>3</sub> /L (control group)
Alkalinity	180 – 186 mg CaCO <sub>3</sub> /L (control group)
Conductivity	332 – 366 µS/cm (control group)

The measured raw data from the study are shown in Table 15.

**Table 15: Experimental results (Unpublished study report, 2023)**

day <sup>a</sup>	conc. test item in fish (ng/g)	fish length (mm)	fish weight (g)	fish lipid level <sup>b</sup> (%)	mass test item in fish (ng)
0	0	61.17	2.65	3.06	0
14	10.9	64.14	3.88	4.65	42.3
15 (1)	13.4	64.86	3.41	(4.69)	45.7
17 (3)	9.14	67.43	4.44	(4.76)	40.6
21 (7)	7.86	65.86	4.27	(4.90)	33.6
28 (14)	7.89	68.71	5.09	(5.17)	40.2
42 (28)	4.56	72.29	5.83	(5.75)	26.6
51 (37)	n.a.	73.33	6.86	6.16	n.a.

<sup>a</sup> depuration day in parentheses

<sup>b</sup> values in parentheses are interpolated assuming exponential lipid increase

It is important to note that fish growth was considerable in this study. It is likely explained by the high feeding rate (approximately 2 to 3 % of body weight). The mean fish weight at the start was 2.65 g, while at the end of the depuration phase (after 51 days) the mean fish weight rose to 6.86 g. Not only the fish weight, but also their lipid content increased from 3.06 % at the start of the study to 6.16 % at the end of depuration.

In general, OECD TG 305 (OECD, 2012) advises that "*the feeding rate should be selected such that fast growth and large increase of lipid content are avoided*", since these phenomena could complicate the interpretation of the test results and could jeopardize the reliability of BCFs or BMFs calculated from these data. OECD TG 305 (Annex 5, section 7; OECD, 2012) describes how to take into account growth dilution in the calculation of the growth-corrected kinetic BCF ( $BCF_{kg}$ ), and this approach will be applied here. As pointed out in Annex 5, section 8 of OECD TG 305 (OECD, 2012), BCFs from aqueous exposure tests must be reported relative to a default fish lipid content of 5%. For tests with dietary exposure, normalisation to 5% lipid content is mentioned in the test guideline in paragraph 162 which is referring to Annex 5 (OECD, 2012). However, it remains unclear how this perfluorinated substance partitions between lipid and non-lipid tissues in fish, and probably the test substance does not primarily accumulate in lipid based on the following information. It is noted that at the end of the uptake phase (day 14), the gut tracts were removed from test fish and test item concentrations were measured both in the gut tracts and in the rest of the fish. The concentration in the gut tracts appeared to be circa 6 times higher than in the rest of the fish, namely 55.9 ng/g in the gut tracts versus 9.59 ng/g in the rest of the fish. This observation points out that accumulation is only partially in lipid tissues, and that applying lipid normalisation could lead to an underestimation of the extent of bioaccumulation. Consequently, it is not clear whether applying lipid normalisation is appropriate for the determination of a BCF for perfluamine.

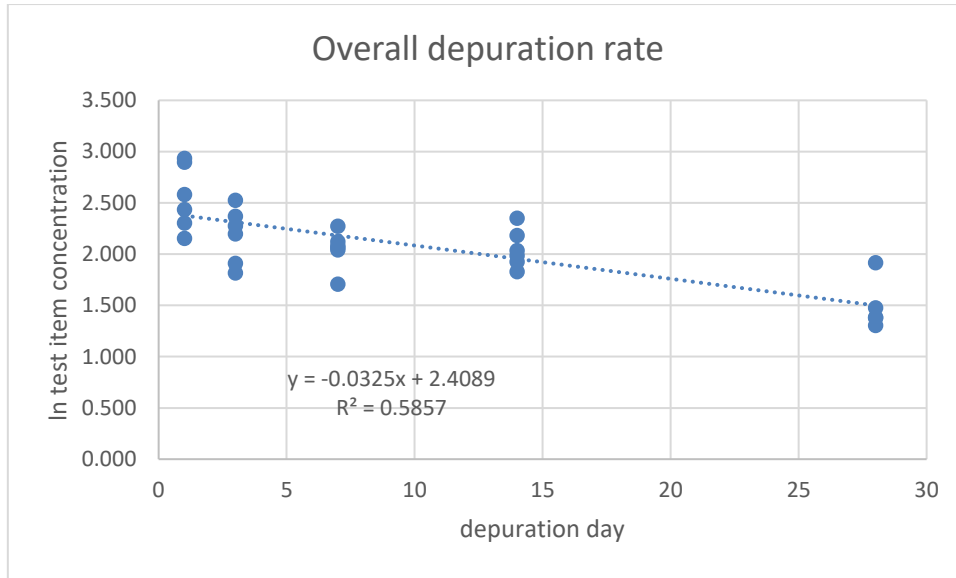
Finally, the actual exposure of fish at the various feeding events is quite uncertain as leaching of test substance out of the diet under the conditions of the definitive test is fast and variable, and thus difficult to assess accurately. This uncertain element will have an adverse impact on the reliability of BMF estimations (see section 3.4.1.5 Derivation of relevant biomagnification factors (BMFs) for further details), but it does not impact the BCF estimations as the uptake rate constant  $k_1$  is not experimentally measured.

#### 3.4.1.4 Derivation of relevant bioconcentration factors (BCFs)

Because the study was carried out with dietary exposure, it is not possible to determine a steady-state  $BCF_{ss}$ . Only a growth-corrected kinetic BCF ( $BCF_{kg}$ ) can be derived based on the measured depuration rate constant  $k_2$  and an estimated uptake rate constant  $k_1$ .

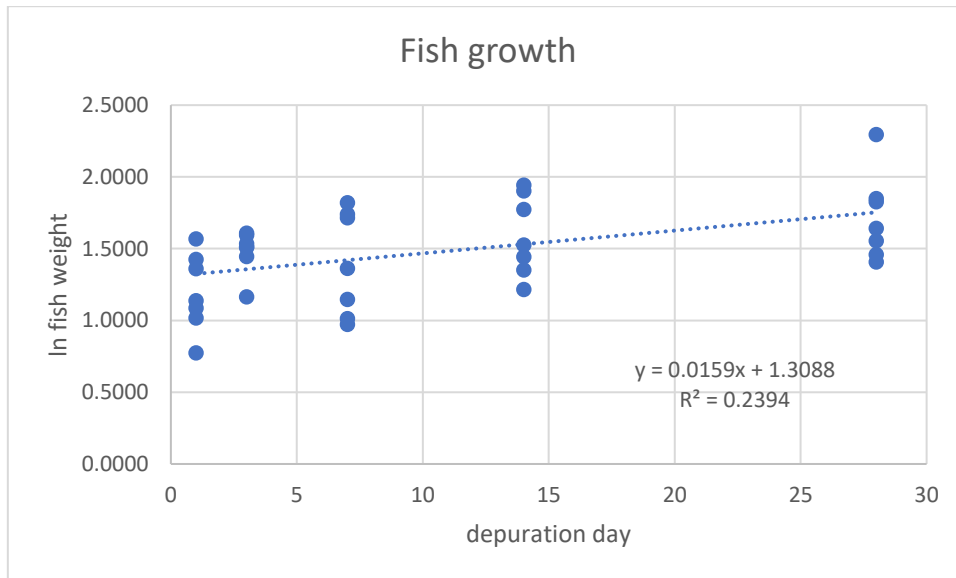
As already noted in the preceding paragraph, fish growth in the study was substantial and must be accounted for in order to derive an unbiased depuration rate constant. In Annex 5, section 7 of the OECD TG 305 (page 59-60; OECD, 2012), two mathematical approaches are described to do this, namely the 'subtraction method' and the 'mass based method'. Both methods were applied in order to estimate the growth-corrected depuration rate constant  $k_{2g}$  as accurately as possible.

In the subtraction method, the calculated growth rate constant  $k_g$  is subtracted from the measured 'overall' depuration rate constant  $k_2$  to give the 'corrected' depuration rate constant  $k_{2g}$  ( $k_{2g} = k_2$  minus  $k_g$ ). An overall depuration rate constant  $k_2$  of 0.0325/d is found via linear regression of the natural logarithm of the concentration values versus time. In this way, also an average concentration in the fish ( $C_{0,d}$ ) at the end of the 14 day uptake period of 11.1 ng/g fish is derived.



**Figure 1: Determination of overall depuration rate constant  $k_2$**

It is noted that fish growth in this study was not only substantial, but also that fish grew much more during the uptake phase than in the depuration phase, and that fish growth in the treatment group deviated significantly from fish growth in the control group. Because the overall depuration rate constant is derived from test item levels in the depuration phase of the treatment group, fish growth data from the treatment group only, and only during depuration and not during the whole experiment were used. The growth rate constant  $k_g$  derived for the treatment group in the depuration phase is 0.0159/d.

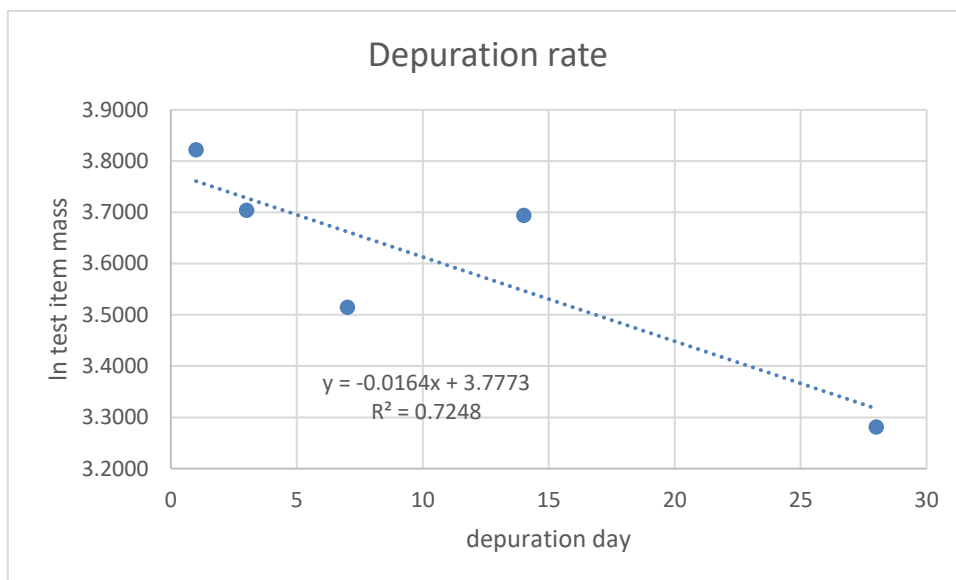


**Figure 2: Determination of fish growth rate constant  $k_g$**

Consequently, applying the subtraction method provides a growth-corrected depuration rate constant  $k_{2g}$  of 0.0166/d (= 0.0325/d minus 0.0159/d).

A growth-corrected depuration rate constant can also be derived via the mass based method. In this method, the raw data from the depuration phase are used on a mass basis rather than on a concentration basis. In principle, one should match each individual

measured test item concentration with that fish's weight. Because concentrations and weights were not measured for the same fish, the average values for the various sampling events are used instead. Following this method, a growth-corrected depuration rate constant of 0.0164/d is obtained.



**Figure 3: Determination of depuration rate constant  $k_{2g}$  based on test item mass**

The growth-corrected depuration rate constants, that are estimated by these two methods (0.0166/d and 0.0164/d), are very well in line with each other. The average of the two values, 0.0165/d, is concluded to be the most suitable estimate of the depuration rate constant  $k_{2g}$  and this value was used in the determination of the  $BCF_{Kg}$ . It is noted that a first-order depuration rate constant of 0.0165/d corresponds to a half-life in fish of 42 days. Such a remarkably long half-life for a relatively small organism as bluegill provides a strong indication of the bioaccumulative property of perfluamine in aquatic organisms.

In order to determine a kinetic  $BCF_{Kg(L)}$ , it is necessary to estimate the uptake rate constant ( $k_1$ ) for the situation where the fish had been exposed to the test substance via water. As indicated in annex 8 of OECD TG 305 (OECD, 2012), such an estimation relies on several assumptions that can be summarized as follows:

- the uptake from the water would follow first order kinetics;
- the uptake rate can be correlated with fish weight and/or the substance  $\text{Log } K_{ow}$ ;
- factors like molecular size have little effect;
- the training set of the database should be representative for the test substance.

A straightforward way to estimate a  $k_1$  value is to utilise the spreadsheet that is published in conjunction with the OECD TG 305 (OECD, 2012). In this spreadsheet, three methods are developed to estimate a BCF; the first two are based on the determination of an uptake rate constant  $k_1$ , and the third one based on the determination of a  $BMF_{Kg(L)}$ .

In the first method, 13 QSAR equations are provided that allow to estimate a  $k_1$  and the corresponding  $BCF_{Kg(L)}$ . The estimations are based on fish weight or on the  $\text{Log } K_{ow}$  of the test item or on both. It is noted that the estimated values for  $k_1$  vary a lot. The lowest value is 94.84 L/kg/d (Hendriks *et al.*, 2001), while the highest value is 885.48 L/kg/d (Tolls and Sijm, 1995) (see Figure 4). In the spreadsheet, normalisation to 5% lipid content is applied by default, leading to a  $k_{2g(L)}$  of 0.01716/d. It remains questionable

whether this normalisation is appropriate for this perfluorinated substance, as discussed in Section 3.4.1.3 above. Applying lipid normalisation leads to estimated  $BCF_{KgL}$  values for perfluamine in a range from 5 527 to 51 602 L/kg. Not applying lipid normalization would lead to even greater estimated  $BCF_{Kg}$  values, namely in a range from 5 748 to 53 666 L/kg.

It is recognised that there is uncertainty relating to the applicability of the underlying training sets for the various QSAR methods. Nevertheless, it is noted that even the least conservative estimate results in a  $BCF_{KgL}$  of 5 527 L/kg, a value that still exceeds the bioaccumulative (B) and very bioaccumulative (vB) criteria ( $BCF > 2\ 000$  for B and  $BCF > 5\ 000$  L/kg for vB) in accordance with Annex XIII of the REACH Regulation for aquatic organisms.

In the second method,  $k_1$  is estimated according to the QSAR approach based on the growth-corrected and lipid normalized  $k_{2gL}$  value as proposed by Brooke *et al.* (2012). The estimated  $k_1$  is 610.15 L/kg/d, resulting in a normalised kinetic  $BCF_{KgL}$  of 35 557 L/kg.

The third method in the spreadsheet relies on the derived BMF and its applicability is unknown for other species than carp. It is considered that the estimated BMF might be accompanied by high uncertainty, and therefore this method is not considered appropriate to derive a BCF for this case.

Inputs		Outputs			
Variable	Value	Method 1			
Mean weight at test start (g)	2.65	inputs for K1	K1	BCF Est.	Ref.
Uptake phase duration (days)	14	weight	399.45	23277.8	Hayton and Barron (1990)
Growth rate, $K_g$ (day <sup>-1</sup> )	0.0159	weight	558.49	32545.8	Erickson and McKim (1990a)
Log $K_{OW}$	6.19	weight	548.75	31978.6	Barber <i>et al.</i> (1991)
$K_{2g}$ ( $K_2 - K_g$ )	0.0165	weight	352.47	20540.3	Barber (2003) - observed
Mean fish lipid uptake end or depuration start (fraction)	0.0465	weight	572.78	33378.6	Barber (2001)
Mean fish lipid depuration end (fraction)	0.0575	weight	108.28	6310.3	Streit and Siré (1993)
Depuration phase duration (days)	28	weight	434.94	25346.4	Erickson and McKim (1990b)
$BMF_{FI}$		weight	356.09	20751.2	Sijm <i>et al.</i> (1995)
		weight	414.19	24137.2	Barber (2003) - calibrated
Interim Outputs		log Kow	885.48	51601.5	Tolls and Sijm (1995)
Variable	Value	log Kow	776.12	45228.6	Spacie and Hamelink (1982)
Mean weight midpoint uptake phase (g)	3.265	weight, log Kow	94.84	5526.9	Hendriks <i>et al.</i> (2001)
Mean lipid content midpoint depuration phase	0.052	weight, log Kow	127.65	7439.0	Thomann (1989)
$K_{2gI}$	0.017	Method 2			
		input	Estimated K1	BCF Est.	Ref.
		$K_{2gI}$	610.15	35556.6	Brooke <i>et al.</i> (2012)

**Figure 4: OECD TG 305 spreadsheet (OECD, 2012) in support of the BCF determination**

A last method to determine an uptake rate constant  $k_1$  value is mentioned in Annex 5 of OECD TG 305 (Equation A5.7; OECD, 2012). The following allometric relationship is presented there:  $k_1 = 520 * (\text{fish wet weight})^{-0.32}$ . At the end of the uptake phase, the mean fish weight was 3.88 g. Based on this fish weight, the  $k_1$  is estimated to be 337 L/kg/d. Combining this  $k_1$  value with the accepted  $k_{2g}$  value of 0.0165/d, leads to a  $BCF_{Kg}$  of 20 424 L/kg. This value also largely exceeds the vB criterion of REACH Annex XIII ( $BCF > 5\ 000$  L/kg) for aquatic organisms.

### 3.4.1.5 Derivation of relevant biomagnification factors (BMFs)

In studies where fish are exposed to a test item via their diet, kinetic biomagnification factors are derived ( $BMF_K$ ). The equations to be used in the determination of a  $BMF_K$  are elaborated in annex 7, section 3 of OECD TG 305 (OECD, 2012). In a first step, one needs to calculate the chemical assimilation efficiency ( $\alpha$ ) of the test item, which reflects its relative absorption across the gut of the fish.

The equation for the calculation of  $\alpha$  is the following:  $\alpha = (C_{0,d} * k_2) / ((I * C_{food}) * (1 - e^{-k_2 t}))$  (Equation A7.1; OECD, 2012), and its value must result in a number between 0 and 1. It is noted that in this case, ideally there should be little uncertainty on the correctness of the values for  $C_{0,d}$  (= test item concentration in fish at the start of the depuration phase),  $k_2$  (= overall depuration rate constant) and  $t$  (= uptake period). On the contrary, in this study the effective  $C_{food}$  (= test item concentration in the diet as eaten by fish) is uncertain because of the unpredictable leaching rate of the test item once the food is administered.  $C_{food}$  is not directly measured, only indirectly estimated via preliminary trials. Further, the term  $I$  (= food ingestion rate constant) continuously diminishes during the uptake phase, because the amount of food is kept constant while fish weight increased by 46% in 14 days. In the study report, a feeding rate  $I$  of  $0.0238 \text{ g}_{food}/\text{g}_{fish}/\text{d}$  is mentioned. This value probably reflects the rate at the end of the uptake phase.

Based on results from preliminary leaching tests, the study authors claim that the effective  $C_{food}$  concentration in the definitive study was  $22.1 \text{ } \mu\text{g}$  test item/kg diet. However, using this  $C_{food}$  value in combination with an  $I$  value of  $0.0238 \text{ g}_{food}/\text{g}_{fish}/\text{d}$ , leads to a calculated  $\alpha$  of 1.86, a result that is per definition impossible (as this number is  $> 1$ ). The derivation of a value for  $\alpha$  greater than 1 demonstrates that at least the assumption for the  $C_{food}$  value is not correct. Consequently, it is considered that the BMF derived by the study authors ( $BMF_{KgL} = 16.5$ ), is an overestimation of the true BMF.

In order to come to a more accurate estimation of the BMF, it is deemed appropriate to determine a range of  $C_{food}$  values in which the actual test item concentration during uptake in the definitive study could have been found. In the full study report, it is mentioned that the amended dry diet stored in the freezer at the end of the uptake phase had a mean concentration of  $95.3 \text{ } \mu\text{g}/\text{kg}$  food. This  $C_{food}$  value is accepted as a realistic upper limit of the range. As the lower limit of the  $C_{food}$  range, a value of  $41.4 \text{ } \mu\text{g}/\text{kg}$  food is accepted because this is the lowest value that leads to an assimilation efficiency  $\leq 1$ . Based on this range of  $C_{food}$ -values, the assimilation efficiency would be between 0.43 and 1.00, and this in turn leads to uncorrected  $BMF_K$ -values between 0.31 and 0.73 ( $BMF_K = I * \alpha / k_2$ ).

As pointed out in Annex 7, section 3 of OECD TG 305 (OECD, 2012), the effect of growth dilution must also be accounted for. The equation for the growth corrected kinetic BMF becomes  $BMF_{Kg} = I * \alpha / k_{2g}$  (Equation A7.5; OECD, 2012), leading to estimated  $BMF_{Kg}$  values of between 0.61 and 1.42.

It is noted that the preferred endpoint according to OECD TG 305 (OECD, 2012) is not only a growth-, but also a lipid corrected-kinetic BMF ( $BMF_{KgL}$ ). However, as elaborated in the Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11 (ECHA, 2023; section R.11.4.1.2.3), based on recent publications it remains questionable whether lipid content correction for both fish and diet are appropriate from a regulatory perspective. Taking into account the diet lipid content, renders the estimated BMF value to be much more dependent on the actual feeding conditions in the laboratory study, and thus less reproducible and less standardised.

If diet lipid correction is nevertheless implemented, the derived  $BMF_{KgL}$  with a lipid correction factor ( $L_c$ ) of 0.278 (5.2%/18.7%) would be between 2.19 and 5.11.

Another, and probably more relevant, metric to quantify the bioaccumulation potential is to normalise the  $BMF_{Kg}$  to fish with 5% lipid content ( $BMF_{5\%}$ ). The fish lipid content during depuration increased substantially, and it is deemed appropriate to use the mean of the

lipid levels at the start (4.65%), and the end (5.75%) of the depuration phase. This leads to a normalisation factor of 0.96 (5%/5.2%) and normalised kinetic  $BMF_{5\%}$  values between 0.59 and 1.36.

Biomagnification of perfluamine in aquatic organisms can be quantified via several metrics. Because of the high uncertainty on the effective test item concentration in the food as eaten by fish, it is not possible to present reliable single value for these metrics. That is why, it is deemed more appropriate to present a range of values wherein the 'true' BMF is expected to be found. The minimum estimations for the  $BMF_{Kg}$ ,  $BMF_{KgL}$  and  $BMF_{5\%}$  are 0.61, 2.19 and 0.59, respectively.

### **Conclusion:**

It is concluded, based on the results of the bioaccumulation study in aquatic organisms (OECD TG 305; Unpublished study report, 2023; Klimisch score 2) via dietary exposure, that the depuration half-life in fish amounts to 42 days thus indicating a high bioaccumulation potential of perfluamine in bluegill. Minimum estimations for the  $BMF_{Kg}$ ,  $BMF_{KgL}$  and  $BMF_{5\%}$  are 0.61, 2.19 and 0.59, respectively. The  $BCF_{KgL}$  estimated according to the OECD TG 305 spreadsheet (OECD, 2012) is in the range 5 527 - 51 602 L/kg. Moreover, an alternative estimation based on an allometric relationship provides a  $BCF_K$  of 20 424 L/kg. As all these BCF estimations exceed the vB criterion of REACH Annex XIII ( $BCF > 5\ 000$  L/kg), it is considered appropriate to identify perfluamine as a vB substance for aquatic organisms.

### **3.4.2 Bioaccumulation in terrestrial organisms (soil dwelling organisms, vertebrates)**

According to the PBT guidance (REACH Chapter R.11; ECHA, 2023), an efficiently absorbed, non-biotransformed neutral organic substance with a  $\text{Log } K_{oa} \geq 5$  in combination with a  $\text{Log } K_{ow} \geq 2$  has the potential to biomagnify in vertebrates of the terrestrial food chains and air-breathing marine wildlife, as well as in humans.

With an estimated  $\text{Log } K_{ow}$  value of 6.19 (medium uncertainty) and a  $\text{Log } K_{oa}$  range (via read-across) of 0.1 to 1.0 (Klimisch score 4), perfluamine does not meet the screening criteria for bioaccumulation in air-breathers.

In this case, further assessment was not considered to be necessary at this stage, as aquatic bioaccumulation testing already demonstrated that perfluamine has a high potential for bioaccumulation (vB).

### **Conclusion:**

It can be concluded that the  $\text{Log } K_{ow}$  value is higher than 2, but the  $\text{Log } K_{oa}$  value is considerably less than 5 for perfluamine. Therefore, based on available QSAR predictions and read-across, perfluamine does not fulfil both the screening criteria for bioaccumulation in air-breathing organisms of  $\text{Log } K_{ow} \geq 2$  and  $\text{Log } K_{oa} \geq 5$ .

### **3.4.3 Field data**

Field and/or biomonitoring data relating to perfluamine is not available.

### 3.4.4 Conclusion on bioaccumulation

Perfluamine meets the bioaccumulation screening criterion for aquatic organisms ( $\text{Log } K_{ow} > 4.5$ ). The experimental bioaccumulation study via dietary exposure, according to OECD TG 305 (OECD, 2012) on *Lepomis macrochirus* performed with perfluamine, resulted in a  $\text{BCF}_{K_{GL}}$  range of 5 527 to 51 602 L/kg. Furthermore, a depuration half-life of 42 days was determined. Minimum estimations for the  $\text{BMF}_{K_{G}}$ ,  $\text{BMF}_{K_{GL}}$  and  $\text{BMF}_{5\%}$  are 0.61, 2.19 and 0.59, respectively. Moreover, an alternative estimation based on an allometric relationship provides a  $\text{BCF}_K$  of 20 424 L/kg. The results of this experimental study allow to conclude that perfluamine qualifies as B and vB for aquatic organisms.

With a  $\text{Log } K_{ow} > 2$ , but a  $\text{Log } K_{oa} < 5$ , perfluamine does not fulfil the screening criteria for bioaccumulation in air-breathing organisms.

Based on a weight-of-evidence consideration, taking all lines of evidence into account, it can be concluded that perfluamine fulfils the B- and vB-criteria of REACH Annex XIII ( $\text{BCF} > 5\,000$  L/kg).

## 3.5 Additional information on environmental fate properties

**Table 16: Studies on radiative efficiency and global warming potential (GWP)**

Method	Results	Remarks	Reference
<p>High-resolution infrared spectrum obtained using a protocol following EPA method 320</p> <p>Integrated IR cross-section and radiative forcing calculated using the approach of Pinnock <i>et al.</i> (1995)</p> <p>GWP calculated using the IPCC 4th Science Assessment Report method with updated <math>\text{CO}_2</math> response and forcing</p>	<p>Radiative efficiency:</p> <p>0.71 W/(m<sup>2</sup>.ppbv)</p> <p><math>\text{GWP}_{100}</math> (calculated for perfluamine):</p> <p>8 690</p>	<p>Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0</p> <p>Klimisch score 2</p> <p>Non-GLP</p>	<p>ECHA dissemination website<sup>12</sup>: Company data, 2012c</p>
<p>No guideline specified</p> <p>Computational methods; (Atmospheric)</p>	<p><math>\text{GWP}_{100}</math>:</p> <ul style="list-style-type: none"> <li>perfluamine <math>\text{N}(\text{C}_3\text{F}_7)_3</math>: 9 180</li> </ul>	<p>Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0</p> <p><i>Test material:</i></p>	<p>WMO (2019)</p>

<sup>12</sup> ECHA dissemination website - REACH Registration dossier of perfluamine [https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5\\_986d3118-514e-436c-bd20-19d66a4f37a5](https://chem.echa.europa.eu/100.005.837/dossier-view/3016ebee-8713-4719-80bd-0bdc213a7341/986d3118-514e-436c-bd20-19d66a4f37a5_986d3118-514e-436c-bd20-19d66a4f37a5) (accessed 23 July 2024).

Method	Results	Remarks	Reference
model calculations	<ul style="list-style-type: none"> <li>• <i>pentadecafluoro-triethylamine</i> <math>N(C_2F_5)_3</math>: 10 610</li> <li>• <i>tris(perfluorobutyl)-amine</i> <math>N(C_4F_9)_3</math> 8 420</li> <li>• <i>tris(undecafluoropentyl)amine</i> <math>N(C_5F_{11})_3</math> 7 520</li> </ul>	<p><i>pentadecafluoro-triethylamine</i> EC No: 206-632-5 CAS RN: 359-70-6</p> <p>Test material: <i>tris(perfluorobutyl)amine</i> EC No: 206-223-1 CAS RN: 311-89-7</p> <p>Test material: <i>tris(undecafluoropentyl)-amine</i> EC No: 206-421-8 CAS RN: 338-84-1</p> <p>Klimisch score 4</p> <p>Non-GLP</p>	
<p>No guideline specified</p> <p>Measurement of infrared absorption spectra</p>	<p>Radiative efficiency:</p> <ul style="list-style-type: none"> <li>• perfluamine <math>N(C_3F_7)_3</math>: 0.75 W/(m<sup>2</sup>.ppb)</li> <li>• <i>pentadecafluoro-triethylamine</i> <math>N(C_2F_5)_3</math>: 0.61 W/(m<sup>2</sup>.ppb)</li> <li>• <i>tris(perfluorobutyl)-amine</i> <math>N(C_4F_9)_3</math> 0.87 W/(m<sup>2</sup>.ppb)</li> <li>• <i>tris(undecafluoropentyl)amine</i> <math>N(C_5F_{11})_3</math> 0.95 W/(m<sup>2</sup>.ppb)</li> </ul>	<p>Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0</p> <p>Test material: <i>pentadecafluoro-triethylamine</i> EC No: 206-632-5 CAS RN: 359-70-6</p> <p>Test material: <i>tris(perfluorobutyl)amine</i> EC No: 206-223-1 CAS RN: 311-89-7</p> <p>Test material: <i>tris(undecafluoropentyl)-amine</i> EC No: 206-421-8 CAS RN: 338-84-1</p> <p>Klimisch score 2</p> <p>Non-GLP</p>	Bernard <i>et al.</i> (2018)
<p>No guideline specified</p> <p>Measurement of gas-phase UV absorption spectra</p> <p>Measurement of UV photodissociation yields</p> <p>Experimental and computational methods</p>	<p>GWP<sub>100</sub> (relative to CO<sub>2</sub>):</p> <ul style="list-style-type: none"> <li>• perfluamine <math>N(C_3F_7)_3</math>: 8 700</li> <li>• <i>pentadecafluoro-triethylamine</i> <math>N(C_2F_5)_3</math>: 9 900</li> <li>• <i>tris(perfluorobutyl)-amine</i></li> </ul>	<p>Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0</p> <p>Test material: <i>pentadecafluoro-triethylamine</i> EC No: 206-632-5 CAS RN: 359-70-6</p> <p>Test material: <i>tris(perfluorobutyl)amine</i> EC No: 206-223-1</p>	Bernard <i>et al.</i> (2020)

Method	Results	Remarks	Reference
	$N(C_4F_9)_3$ 7 800	CAS RN: 311-89-7  Klimisch score 2  Non-GLP	

The registration dossier mentions a calculation of GWP<sub>100</sub> (global warming potential (GWP) on the 100-year time horizon) for perfluamine (Company data, 2012c). The atmospheric lifetime of pentadecafluorotriethylamine (CAS RN: 359-70-6; molecular formula:  $N(C_2F_5)_3$ ) was taken from the study in section 3.1.1.3.1 (read-across; Unpublished study report, 1993), in which an atmospheric lifetime > 2 000 years was obtained. The radiative efficiency was set at 0.71 W/(m<sup>2</sup>.ppbv). A calculation method from the IPCC 4th Science Assessment Report was used, and a GWP<sub>100</sub> of 8 690 could be calculated for perfluamine (Company data, 2012c; Klimisch score 2).

The WMO, in its report 'Scientific Assessment on Ozone Depletion' (WMO, 2019) assembled a large appendix containing several parameters (amongst others global warming potentials) of numerous substances of interest (WMO, 2019; Klimisch score 4). GWP<sub>100</sub> values were reported to be 10 610, 9 180, 8 420 and 7 520 for pentadecafluorotriethylamine ( $N(C_2F_5)_3$ ; CAS RN: 359-70-6), perfluamine ( $N(C_3F_7)_3$ ; CAS RN: 338-83-0), tris(perfluorobutyl)amine ( $N(C_4F_9)_3$ ; CAS RN: 311-89-7) and tris(undecafluoropentyl)amine ( $N(C_5F_{11})_3$ ; CAS RN: 338-84-1). For comparison, carbon tetrafluoride (CAS RN: 75-73-0; molecular formula:  $CF_4$ ), nitrogen trifluoride (CAS RN: 7783-54-2; molecular formula:  $NF_3$ ) and sulphur hexafluoride (CAS RN: 2551-62-4; molecular formula:  $SF_6$ ) have GWP<sub>100</sub> values of 6 630, 15 750 and 23 500, respectively (WMO, 2019).

In public literature, a non-guideline (non-GLP) study is available (Bernard *et al.*, 2018), which measured infrared absorption spectra over the 500 – 4 000 cm<sup>-1</sup> spectral region at 294 K using Fourier transform infrared spectroscopy at 1 cm<sup>-1</sup> resolution, for four perfluoroamine compounds (among which perfluamine). The calculated radiative efficiencies were 0.61, 0.75, 0.87 and 0.95 W/(m<sup>2</sup>.ppb) for pentadecafluorotriethylamine ( $N(C_2F_5)_3$ ; CAS RN: 359-70-6), perfluamine ( $N(C_3F_7)_3$ ; CAS RN: 338-83-0), tris(perfluorobutyl)amine ( $N(C_4F_9)_3$ ; CAS RN: 311-89-7) and tris(undecafluoropentyl)amine ( $N(C_5F_{11})_3$ ; CAS RN: 338-84-1), respectively (Bernard *et al.*, 2018; Klimisch score 2). Calculations were performed taking into account atmospherically well-mixed conditions and a + 10 % stratospheric temperature correction.

A study from the same institution goes further with the data from Bernard *et al.* (2018) and combines the radiative efficiencies above with newly derived atmospheric lifetimes (previously discussed in section 3.1.1.3.1; Bernard *et al.*, 2020). These combined results lead to estimated GWP<sub>100</sub> values (relative to CO<sub>2</sub>) of 9 900, 8 700 and 7 800 for pentadecafluorotriethylamine ( $N(C_2F_5)_3$ ), perfluamine ( $N(C_3F_7)_3$ ) and tris(perfluorobutyl)amine ( $N(C_4F_9)_3$ ), respectively (Bernard *et al.*, 2020; Klimisch score 2).

### **Conclusion:**

Perfluamine is an atmospherically persistent potent greenhouse gas.

### **3.6 Conclusion on environmental fate properties**

The structural properties of perfluamine, the extremely high total global atmospheric lifetime, the fact that no or very limited biodegradation in water was observed in screening tests performed with read-across substances, and the fact that several similar perfluorinated substances have already been identified as SVHC (and concluded to fulfil the P and vP criteria as part of the justifications for SVHC), altogether allow to conclude that perfluamine fulfils the P and vP criteria.

Perfluamine distributes to the different environmental compartments, as is indicated by distribution modelling, and has been identified as a potential POP substance in public literature.

Perfluamine qualifies as B and vB for aquatic organisms due to the results from the experimental bioaccumulation study via dietary exposure, according to OECD TG 305. This experimental study demonstrated that all derived BCF-values, using various calculation methods, exceeded the vB criterion of 5 000 L/kg.

Perfluamine has extremely high values for GWP and is an atmospherically persistent potent greenhouse gas.

## **4. Human health hazard assessment**

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

## **5. Environmental hazard assessment**

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

## 6. Conclusions on the SVHC Properties

### 6.1 CMR assessment

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

### 6.2 PBT and vPvB assessment

#### 6.2.1 Assessment of PBT/vPvB properties

##### 6.2.1.1 Persistence

The C-F bond is considered to be the strongest in organic chemistry (Zhang *et al.*, 2022; Hiyama *et al.*, 2013; Kirsch, 2013; O'Hagan, 2008), and degradation of these C-F bonds will be very limited or negligible (Roesch *et al.*, 2022; Liu and Avendaño, 2013). The C-N bonds are also shielded from chemical attack through 'pyramidal nitrogen inversion' (Lehn, 1970; Morgan and Leyden, 1970). Therefore, perfluamine is a stable substance that cannot be broken down under relevant environmental conditions.

Perfluamine is not expected to hydrolyse and is not expected to be affected by oxidation processes.

A total global atmospheric lifetime of 3 795 years has been reported for perfluamine (Bernard *et al.*, 2020; Klimisch score 2). Structurally similar substances (as specified in section 3.1.1.3.1) also have total atmospheric lifetimes or half-lives in air of at least 1 000 years (WMO, 2019; Klimisch score 4). Perfluamine is therefore considered to be atmospherically persistent.

In EPI Suite estimated BIOWIN values are all far below the screening criteria, which indicates that perfluamine is potentially (v)P.

Screening tests for biodegradation, performed with analogue substances, demonstrate the non-biodegradability of PFOCs. In an OECD TG 310 ready biodegradability study, 0 % degradation was observed after 28 days (CO<sub>2</sub> evolution) for EC No 473-390-7 (Unpublished study report 2007a; Klimisch score 4). A study with tripropylamine (EC No: 203-047-7) according to OECD TG 301 E, resulted in 0 – 10 % degradation after 28 days (DOC removal) (Unpublished study report, 1990a; Klimisch score 4). For a second study equivalent to OECD TG 302 B with tripropylamine, 0 % degradation was reported after 3 hours, and 0 % degradation after 21 days (DOC removal) (Unpublished study report, 1990b; Klimisch score 4). Therefore, perfluamine is expected to be not readily and inherently biodegradable under similar conditions.

Several other perfluorinated substances have already been assessed in the framework of the REACH Regulation and have been identified as SVHC because of their vPvB properties (ECHA, 2012a; 2012b; 2012c; 2012d; 2017; 2022a; 2022b), such as henicosafluoroundecanoic acid (CAS RN: 2058-94-8), heptacosafuorotetradecanoic acid (CAS RN: 376-06-7), pentacosafuorotridecanoic acid (CAS RN: 72629-94-8), tricosafuorododecanoic acid (CAS RN: 307-55-1), perfluorohexane-1-sulphonic acid and its salts (CAS RN: 355-46-4), perfluoroheptanoic acid and its salts (CAS RN: 375-85-9), and reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine (EC No 473-390-7).

The following perfluorinated substances were identified in the framework of the REACH Regulation to be of equivalent level of concern to CMR and PBT/vPvB substances (ECHA, 2019a; 2019b): HFPO-DA (CAS RN: 13252-13-6), and perfluorobutane sulfonic acid and its salts (EC No: 799-977-0), with also an emphasis on their vP properties in the support documents.

Based on the assessment above, and considering a weight-of-evidence approach, it is concluded that perfluamine meets the P and vP criteria in accordance with Annex XIII of REACH.

#### 6.2.1.2 Bioaccumulation

The Log  $K_{ow}$  is not experimentally determined for perfluamine, but a Log  $K_{ow}$  range of 5.3 - 6.1 has been derived based on read-across with two substances (Unpublished study report, 2012b; Klimisch score 4). This Log  $K_{ow}$  range is supported by modelling with the EPI Suite tool (estimated Log  $K_{ow}$  = 6.19; US EPA, 2012; medium uncertainty) and analyses with 'COSMOtherm 2020' software (estimated Log<sub>10</sub>  $K_{ow}$  = 7.28; Glüge and Scheringer, 2023; reliable). Perfluamine thus meets the bioaccumulation screening criterion for aquatic organisms (Log  $K_{ow}$  > 4.5).

The experimental bioaccumulation study in aquatic organisms (OECD TG 305; Unpublished study report, 2023; Klimisch score 2), via dietary exposure, has demonstrated that the depuration half-life in fish amounts to 42 days. The BCF<sub>K<sub>GL</sub></sub> estimated according to the OECD TG 305 spreadsheet is in the range 5 527 – 51 602 L/kg. Moreover, an alternative estimation based on an allometric relationship provided a BCF<sub>K</sub> of 20 424 L/kg. As all these BCF values exceed the vB criterion of 5 000 L/kg, it can be concluded that perfluamine is a vB substance for aquatic organisms in accordance with REACH Annex XIII.

Experimental studies on bioaccumulation in terrestrial organisms are not available. However, it is noted that the screening criterion for bioaccumulation in air-breathing organisms is not met (Log  $K_{oa}$  < 5).

Considering the results of the experimental study (BCF values exceeding the vB criterion of 5 000 L/kg), it is concluded that perfluamine meets the B and vB criteria in accordance with Annex XIII, points 1.2.1 and 1.2.2 of the REACH Regulation.

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

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

##### Persistence

Based on a weight-of-evidence approach and considering assessment information in accordance with REACH Annex XIII Section 3.2.1.(d), it is concluded that perfluamine is very persistent due to its C-F bonds which cannot be broken under environmental conditions, and the abundant presence of fluorine atoms which shields the carbon skeleton from other transformation reactions. The C-N bonds of perfluamine are also shielded from chemical attack through 'pyramidal nitrogen inversion'.

Perfluamine is not expected to hydrolyse and is not expected to be affected by oxidation processes. Perfluamine is photochemically stable and persistent in the atmosphere with a total global atmospheric lifetime of 3 795 years (Klimisch score 2). Structurally similar substances (as specified in section 3.1.1.3.1) also have total atmospheric lifetimes or half-life in air of at least 1 000 years (Klimisch score 4 and 2). In addition, based on modelling data, perfluamine screens as potentially persistent or very persistent in the environment. This is supported by biodegradation screening studies performed with analogue substances, which resulted in no or very limited biodegradation. In an OECD TG 310 ready biodegradability study, 0% degradation was observed after 28 days (CO<sub>2</sub> evolution) for the analogue substance EC No 473-390-7 (Klimisch score 4). A study with the analogue substance tripropylamine (EC No 203-047-7) and according to OECD TG 301 E, resulted in 0 – 10 % degradation after 28 days (DOC removal) (Klimisch score 4). In a second study equivalent to OECD TG 302 B, tripropylamine was not degraded after 3 hours and after 21 days with each time 0% degradation (DOC removal). Based on these screening tests with analogue substances, perfluamine is concluded as not readily and not inherently biodegradable.

In summary, perfluamine is considered to be very persistent in all environmental compartments, as no indications are found that it can undergo abiotic or biotic degradation under relevant environmental conditions. Half-lives are expected to largely exceed the P and vP criteria (degradation half-life > 60 days in water, and degradation half-lives > 180 days in sediment or soil) of REACH Annex XIII Sections 1.1.1 and 1.2.1. Furthermore, Annex XIII, point 3.2.1.(d) of the REACH Regulation requires that any relevant information for the assessment of the persistence of the substance be considered. Therefore, it is concluded that perfluamine fulfils the 'persistence' (P) and 'very persistent' (vP) criteria in accordance with the criteria and provisions set out in Annex XIII of REACH.

#### Bioaccumulation

Perfluamine meets the bioaccumulation screening criterion for aquatic organisms (Log K<sub>ow</sub> > 4.5). The experimental bioaccumulation study with *Lepomis macrochirus* via dietary exposure, according to OECD TG 305 (Klimisch score 2), indicates a potential for bioaccumulation of perfluamine with a long depuration half-life in fish of 42 days. Detailed analysis of the available test data from the study leads to BCF<sub>K<sub>g</sub>L</sub> values for perfluamine ranging from 5 527 L/kg to 51 602 L/kg. Moreover, an alternative estimation based on an allometric relationship provides a BCF<sub>K</sub> of 20 424 L/kg. All these BCF estimations exceed the very bioaccumulative (vB) criteria of REACH Annex XIII (BCF > 5 000 L/kg). This experimental dietary bioaccumulation study is given high weight in the weight of evidence assessment.

Experimental studies on bioaccumulation in terrestrial organisms are not available. However, it is noted that the screening criterion for bioaccumulation in air-breathing organisms is not met (Log K<sub>oa</sub> < 5).

Based on a weight-of-evidence, it is concluded that perfluamine meets the 'bioaccumulation' criterion (B) and the 'very bioaccumulative' criterion (vB) for aquatic organisms in accordance with REACH Annex XIII, points 1.1.2 and 1.2.2, of the REACH Regulation.

#### Conclusion

In conclusion, perfluamine meets the criteria for a vPvB substance in accordance with Annex XIII of the REACH Regulation, and thereby the substance fulfils the criteria set out in REACH Article 57 (e).

### Summary of other considerations

Perfluamine shows high potential for long-range atmospheric transport based on atmospheric lifetimes or half-life in air of at least 1 000 years and it is identified in public literature as a potential POP substance. Furthermore, studies on radiative efficiency and global warming potential indicate that perfluamine is a potent greenhouse gas.

### **6.3 Assessment under Article 57(f)**

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

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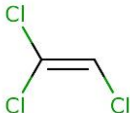
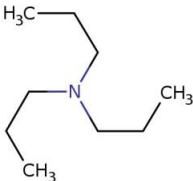
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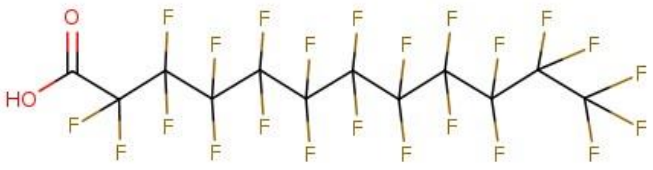
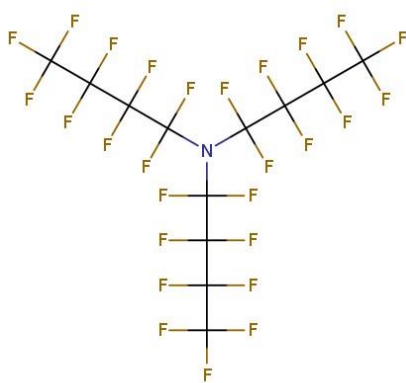
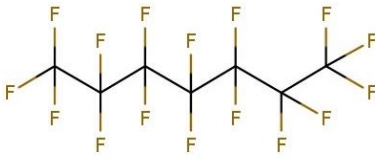
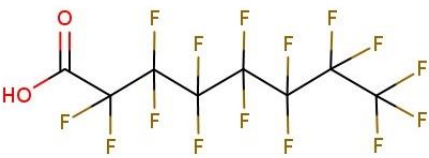
## Annex 1: Structural formulas

Table A1 provides an overview of the structural formulas corresponding to the CAS-numbers of read-across substances, mentioned in study reports or in public literature.<sup>13</sup>

**Table A1: Structural formulas corresponding to the CAS-numbers of read-across substances**

<b>EC No: 200-872-4</b> <b>CAS RN: 75-46-7</b>	<b>Trifluoromethane</b>
	
<b>EC No: 200-896-5</b> <b>CAS RN: 75-73-0</b>	<b>Carbon tetrafluoride</b>
	
<b>EC No: 201-167-4</b> <b>CAS RN: 79-01-6</b>	<b>Trichloroethylene</b>
	
<b>EC No: 203-047-7</b> <b>CAS RN: 102-69-2</b>	<b>Tripropylamine</b>
	

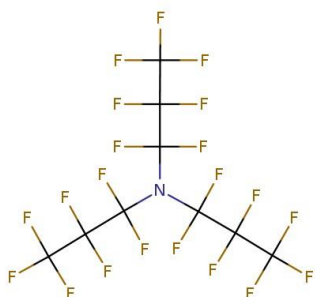
<sup>13</sup> Source: ECHA dissemination website <https://echa.europa.eu/> (accessed 23 July 2024).

<b>EC No: 206-203-2</b> <b>CAS RN: 307-55-1</b>	<b>Tricosafluorododecanoic acid</b>
 <p>The image shows the chemical structure of Tricosafluorododecanoic acid. It consists of a dodecanoic acid chain (12 carbons) where all hydrogen atoms are replaced by fluorine atoms. The carboxylic acid group is shown on the left, with the carbonyl oxygen in red and the hydroxyl group in red. The rest of the chain is a long hydrocarbon chain with 11 methylene groups and two terminal methyl groups, all fully fluorinated.</p>	
<b>EC No: 206-223-1</b> <b>CAS RN: 311-89-7</b>	<b>Tris(perfluorobutyl)amine</b>
 <p>The image shows the chemical structure of Tris(perfluorobutyl)amine. It features a central nitrogen atom (N) bonded to three perfluorobutyl groups. Each perfluorobutyl group is a four-carbon chain where all hydrogen atoms are replaced by fluorine atoms. The structure is shown in a perspective view, with the nitrogen atom at the center and the three chains extending outwards.</p>	
<b>EC No: 206-392-1</b> <b>CAS RN: 335-57-9</b>	<b>Perfluoroheptane</b>
 <p>The image shows the chemical structure of Perfluoroheptane. It is a seven-carbon chain where all hydrogen atoms are replaced by fluorine atoms. The structure is shown in a perspective view, with the carbon chain forming a zig-zag shape and fluorine atoms attached to each carbon.</p>	
<b>EC No: 206-397-9</b> <b>CAS RN: 335-67-1</b>	<b>Pentadecafluorooctanoic acid</b>
 <p>The image shows the chemical structure of Pentadecafluorooctanoic acid. It consists of an octanoic acid chain (8 carbons) where all hydrogen atoms are replaced by fluorine atoms. The carboxylic acid group is shown on the left, with the carbonyl oxygen in red and the hydroxyl group in red. The rest of the chain is a long hydrocarbon chain with 6 methylene groups and two terminal methyl groups, all fully fluorinated.</p>	

EC No: 206-420-2

CAS RN: 338-83-0

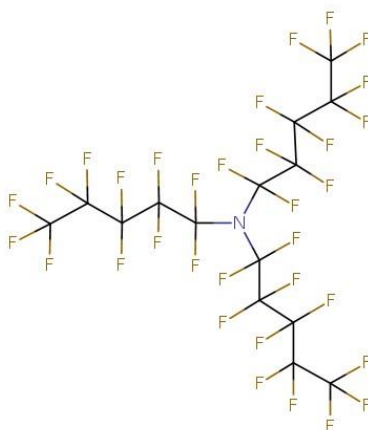
Perfluamine



EC No: 206-421-8

CAS RN: 338-84-1

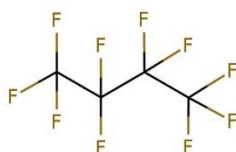
Tris(undecafluoropentyl)amine

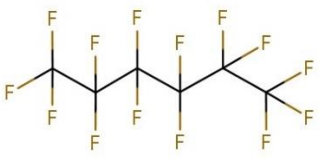
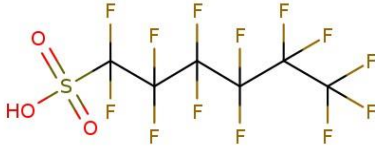
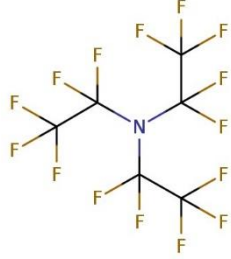
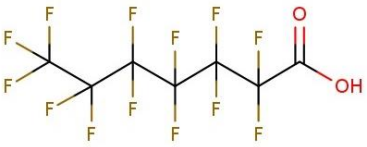


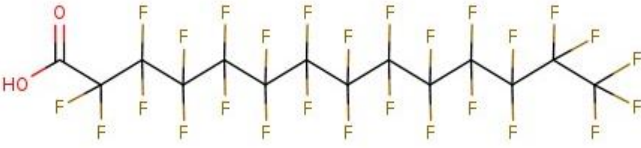

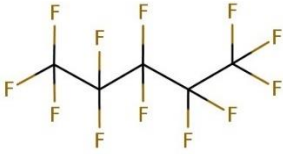
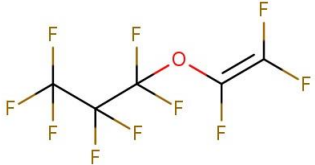
EC No: 206-580-3

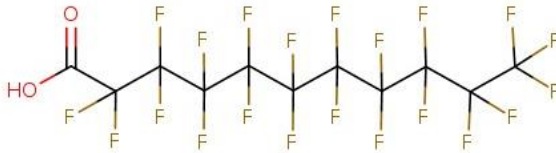
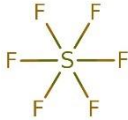
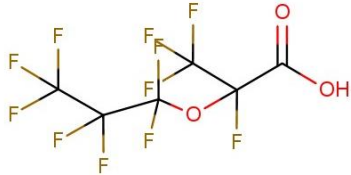
CAS RN: 355-25-9

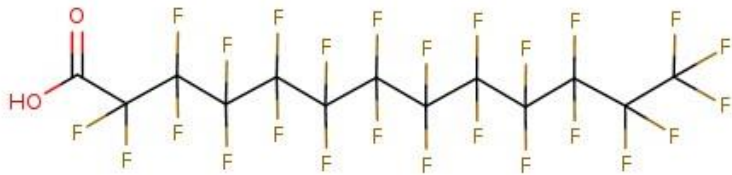
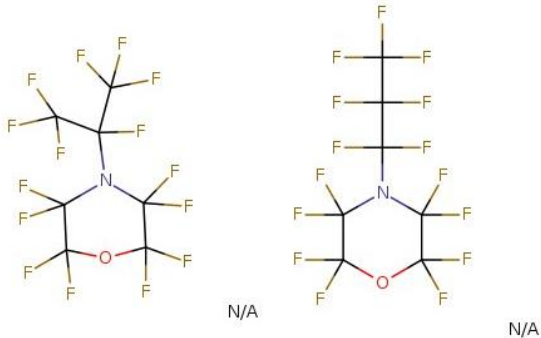
Decafluorobutane



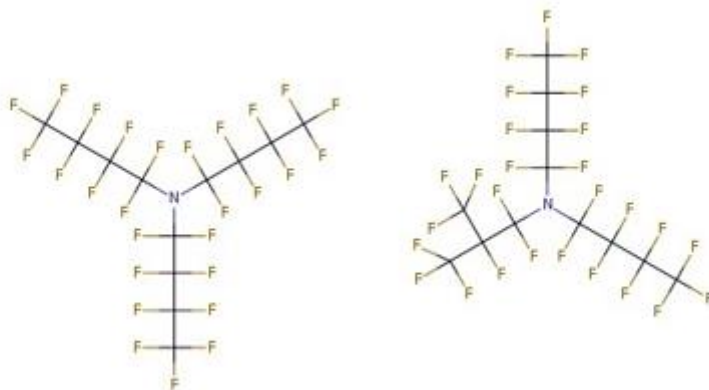
<b>EC No: 206-585-0</b> <b>CAS RN: 355-42-0</b>	<b>Tetradecafluorohexane</b>
 <p>The image shows the skeletal structure of tetradecafluorohexane, a six-carbon chain where every carbon atom is bonded to two fluorine atoms, resulting in a total of 14 fluorine atoms.</p>	
<b>EC No: 206-587-1</b> <b>CAS RN: 355-46-4</b>	<b>Perfluorohexane-1-sulphonic acid and its salts</b>
 <p>The image shows the skeletal structure of perfluorohexane-1-sulphonic acid. It consists of a six-carbon chain with two fluorine atoms on each carbon, and a sulfonic acid group (-SO<sub>3</sub>H) attached to the first carbon.</p>	
<b>EC No: 206-632-5</b> <b>CAS RN: 359-70-6</b>	<b>Pentadecafluorotriethylamine</b>
 <p>The image shows the skeletal structure of pentadecafluorotriethylamine, a central nitrogen atom bonded to three ethyl groups, where every carbon atom in the ethyl groups is bonded to two fluorine atoms, resulting in a total of 15 fluorine atoms.</p>	
<b>EC No: 206-798-9</b> <b>CAS RN: 375-85-9</b>	<b>Perfluoroheptanoic acid and its salts</b>
 <p>The image shows the skeletal structure of perfluoroheptanoic acid, a seven-carbon chain with two fluorine atoms on each carbon, and a carboxylic acid group (-COOH) attached to the first carbon.</p>	

<b>EC No: 206-803-4</b> <b>CAS RN: 376-06-7</b>	<b>Heptacosfluorotetradecanoic acid</b>
 <p>The image shows the chemical structure of Heptacosfluorotetradecanoic acid. It consists of a long, straight hydrocarbon chain with 14 carbon atoms. The first carbon is part of a carboxylic acid group (HO-C=O). The remaining 13 carbon atoms are fully substituted with fluorine atoms, resulting in a total of 27 fluorine atoms in the molecule.</p>	
<b>EC No: 206-841-1</b> <b>CAS RN: 382-28-5</b>	<b>2,2,3,3,5,5,6,6-octafluoro-4-(trifluoromethyl)morpholine</b>
 <p>The image shows the chemical structure of 2,2,3,3,5,5,6,6-octafluoro-4-(trifluoromethyl)morpholine. It is a six-membered ring containing one nitrogen atom and one oxygen atom. The ring carbons are substituted with fluorine atoms: C2 and C3 have two fluorine atoms each, C5 and C6 have two fluorine atoms each, and C4 has one fluorine atom. A trifluoromethyl group (-CF<sub>3</sub>) is attached to the nitrogen atom.</p>	
<b>EC No: 211-647-5</b> <b>CAS RN: 678-26-2</b>	<b>Dodecafluoropentane</b>
 <p>The image shows the chemical structure of Dodecafluoropentane. It is a five-carbon chain where every carbon atom is bonded to two fluorine atoms, resulting in a total of 12 fluorine atoms.</p>	
<b>EC No: 216-600-2</b> <b>CAS RN: 1623-05-8</b>	<b>1,1,1,2,2,3,3-heptafluoro-3-[(trifluorovinyl)oxy]propane</b>
 <p>The image shows the chemical structure of 1,1,1,2,2,3,3-heptafluoro-3-[(trifluorovinyl)oxy]propane. It consists of a three-carbon propane chain. The first carbon is bonded to three fluorine atoms. The second carbon is bonded to two fluorine atoms. The third carbon is bonded to two fluorine atoms and is also bonded to an oxygen atom. The oxygen atom is part of a trifluorovinyl group (-O-CF=CF<sub>2</sub>).</p>	

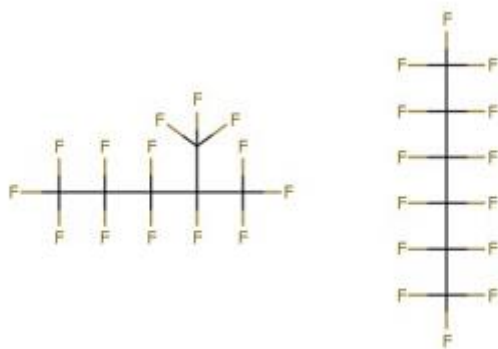
<b>EC No: 218-165-4</b> <b>CAS RN: 2058-94-8</b>	<b>Henicosafuoroundecanoic acid</b>
	
<b>EC No: 219-854-2</b> <b>CAS RN: 2551-62-4</b>	<b>Sulphur hexafluoride</b>
	
<b>EC No: 231-635-3</b> <b>CAS RN: 7664-41-7</b>	<b>Ammonia, anhydrous</b>
$\text{NH}_3$	
<b>EC No: 232-007-1</b> <b>CAS RN: 7783-54-2</b>	<b>Nitrogen trifluoride</b>
$\text{NF}_3$ No image available	
<b>EC No: 236-236-8</b> <b>CAS RN: 13252-13-6</b>	<b>2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid</b>
	

<b>EC No: 276-745-2</b> <b>CAS RN: 72629-94-8</b>	<b>Pentacosafuorotridecanoic acid</b>
	
<b>EC No: 473-390-7</b> <b>CAS RN: /</b> (CAS RN: 1093615-61-2 may have been used to describe this substance)	<b>reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine</b>
	
<b>CAS RN: /</b>	<b>Perfluorobutane sulfonic acid and its salts</b>
<p style="text-align: center;">No image available</p>	
<b>EC No: 908-198-9</b> <b>CAS RN: /</b> (CAS RN: 1064698-16-3 may have been used to describe this substance)	<b>Reaction mass of 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,7 heptafluoro-heptane and 1,1,1,2,2,3,3,4,4,5,6,6,6 tridecafluoro-5-(trifluoromethyl)hexane</b>
<p style="text-align: center;">C<sub>7</sub>F<sub>16</sub></p> <p style="text-align: center;">No image available</p>	

<p><b>EC No: 939-511-7</b></p> <p><b>CAS RN: /</b></p> <p>Or</p> <p>EC No: 830-388-4</p> <p>CAS RN: 1064698-37-8</p>	<p><b>Reaction mass of 1,1,2,2,3,3,4,4,4-nonafluoro-<i>N,N</i>-bis(nonafluorobutyl)butan-1-amine and 1,1,2,2,3,3,4,4,4-nonafluoro-<i>N</i>-[1,1,2,3,3-hexafluoro-2-(trifluoromethyl)propyl]-<i>N</i>-(1,1,2,2,3,3,4,4,4-nonafluorobutyl)butan-1-amine</b></p>
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<p><b>EC No: 943-336-1</b></p> <p><b>CAS RN: /</b></p> <p>(CAS RN: 1064697-81-9 may have been used to identify this substance)</p>	<p><b>Reaction mass of 1,1,1,2,2,3,3,4,4,5,5,6,6,6-tetradecafluoro-hexane and 1,1,1,2,2,3,3,4,5,5,5-undecafluoro-4-(trifluoromethyl)pentane</b></p>
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<b>EC No: not available</b> <b>CAS RN: 1064698-52-7</b> <b>(Octanoyl chloride, fluorinated, C8 cyclic ether fraction – this CAS number may have been used to describe the substance)</b>	<b>Reaction mass of 2,2,3,3,4,4,5-heptafluoro-5-(1,1,2,2,3,3,4,4,4-nonafluorobutyl)tetrahydrofuran and 2,2,3,3,4,4,5,5,6-nonafluoro-6-(7,7,8,8,9,9,9 heptafluoropropyl)tetrahydro-2H-pyran and 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,7 heptafluoroheptane</b>
No image available	

## Annex 2: Justification on read-across approach

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

A read-across approach was used as supportive information for the persistence assessment of perfluamine (EC No 206-420-2). Matrices with relevant information on physico-chemical and environmental fate properties of read-across substances are provided below.

### Perfluamine and reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine (EC No 473-390-7)

Perfluamine and reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine (EC No 473-390-7) are both liquid substances. They have a similar boiling point (but higher for perfluamine), and the same density of 1.8 g/cm<sup>3</sup> (Table A2). The vapour pressure is high for both substances, therefore both substances can be considered as volatile. But with a vapour pressure of 6 750 Pa (at 20 °C), EC No 473-390-7 can be described as highly volatile. Log K<sub>ow</sub> and Log K<sub>oc</sub> values are comparable for both substances. Water solubilities are low for both substances. But with a water solubility of 0.381 µg/L (at 23 °C), perfluamine can be considered to have a very low water solubility. This lower water solubility suggests a lower bioavailability of perfluamine as compared to EC No 473-390-7. EC No 473-390-7 has been identified as a substance of very high concern because of its vPvB (Article 57e) properties (ECHA, 2022).

Perfluamine and EC No 473-390-7 both have a central nitrogen atom in their molecules; perfluamine in a tertiary amine form, and EC No 473-390-7 in a morpholine form. They are structurally similar substances, as they both have fluorine atoms completely enveloping the carbon skeleton thereby shielding it from any attack by microorganisms. These observations strongly suggest that both substances will not be biodegradable. Perfluamine is a mono-constituent substance (molecular formula: C<sub>9</sub>F<sub>21</sub>N), while EC No 473-390-7 is a multi-constituent substance (molecular formula: C<sub>7</sub>F<sub>15</sub>NO), containing two carbon atoms and six fluorine atoms less than perfluamine, but having an extra oxygen atom. No hydrogen atoms are present in either substance. Both substances are neutral chemicals and have no ionizable groups.

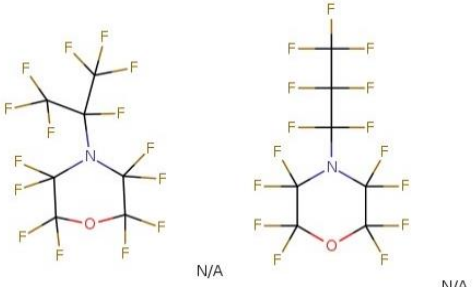
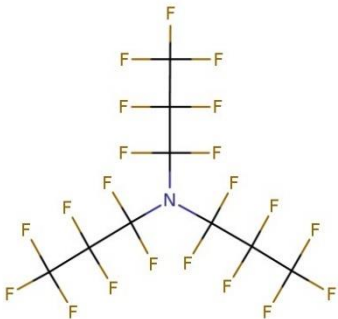
Both substances have the C-N bond in common. For perfluamine, this is associated with an electronegative effect on the nitrogen, reducing its ammonium forming capacity. Due to steric hindrance, the C-N bond will also hardly be available for micro-organisms. This is supported by the BIOWIN estimates that were found via the EPI Suite tool (EPIWEB v4.1; US EPA, 2012; BIOWIN v4.11). Both perfluamine and EC No 473-390-7 are considered to not biodegrade fast (BIOWIN 2), to have an ultimate biodegradation longer than months (BIOWIN 3), and to be not readily degradable (BIOWIN 6).

It is to be noted that not so many fluorinated compounds are represented in the training sets of the various BIOWIN models. The training set of the BIOWIN 2 model contains only 2 fluorinated compounds, namely Fluridone (CAS RN 59756-60-4) and 2-fluorophenol (CAS RN 367-12-4). The training set of the BIOWIN 3 model contains only 3 fluorinated compounds with either 1 fluorine atom or 1 trifluoromethyl group. The training set of the

BIOWIN 6 model contains substantially more fluorinated compounds (>15), many of which are polyfluorinated substances. Furthermore, BIOWIN 6 includes a coefficient for the fluorine [-F] fragment which is not included in BIOWIN 2 and 3. In that sense, BIOWIN 6 provides a stronger indication of the persistent character of perfluamine than BIOWIN 2 and 3. It is also noted that in BIOWIN 2 and 3 some, but not all of the fluorine atoms of perfluamine are covered by the fragments specifically containing fluorine. In these two models, the twelve fluorine atoms on the secondary carbons are represented (in addition to the molecular weight parameter) as a part of the fragment "Carbon with 4 single bonds & no hydrogens" similarly as would be counted any other (non-hydrogen) atom which has a single bond with a carbon atom matching to this fragment. Nonetheless, the BIOWIN estimations can still be used as a piece of evidence in the weight-of-evidence approach, and the estimations underpin that perfluamine screens as potentially (v)P, and that the biodegradability potential is very low.

A screening test according to OECD TG 310 is available for perfluoro-N-C1,3-alkyl morpholines, CAS RN: 1093615-61-2, FC-770. The acronym FC-770 is associated with the substance identified with EC No 473-390-7. The test resulted in 0 % degradation after 28 days (CO<sub>2</sub> evolution, measurement of inorganic carbon concentration). Based on the absence of biodegradation in the screening test for EC No 473-390-7, perfluamine is likely to have a low degradability as the perfluorinated structural analogue EC No 473-390-7. Due to their similar physico-chemical properties and common functional groups, a read-across approach is considered to be relevant between perfluamine and EC No 473-390-7 for the persistence assessment.

**Table A2: Matrix of physico-chemical properties and environmental fate properties for EC No 473-390-7 and EC No 206-420-2 relevant to justify the read-across approach**

<b>Chemical name</b>	<b>reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine</b>	<b>perfluamine</b>
<b>Substance identity</b>		
<b>EC number</b>	473-390-7	206-420-2
<b>CAS number (in the EC inventory)</b>	/	338-83-0
<b>Index number in Annex VI of the CLP Regulation</b>	NA	NA
<b>Molecular formula</b>	C <sub>7</sub> F <sub>15</sub> NO	C <sub>9</sub> F <sub>21</sub> N
<b>Structural formula</b>		
<b>Physico-chemical properties</b>		
<b>Physical state at 20 °C and 101.3 kPa</b>	Liquid ( <i>observation</i> )	Liquid ( <i>observation</i> )

<b>Chemical name</b>	<b>reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine</b>	<b>perfluamine</b>
<b>Melting / freezing point</b>	-127 °C <i>(method similar to ASTM D97)</i>	-50 °C <i>(summary data point from company product technical data sheet)</i>
<b>Boiling point</b>	96 °C (at 101.5 kPa) <i>(EU Method A.2; OECD TG 103)</i>	132 °C (at 760 mm Hg) <i>(ASTM E1719-97 and ASTM D1120-94; deviations from OECD TG 103)</i>
<b>Vapour pressure</b>	50.6 mm Hg (6 750 Pa; at 20 °C) <i>(EU Method A.4; OECD TG 104)</i>	3.87 mm Hg (516 Pa; at 20 °C) <i>(ASTM E1719-97 and ASTM D1120-94; deviations from OECD TG 104)</i>
<b>Density</b>	1.80 g/cm <sup>3</sup> (at 20 °C) <i>(EU Method A.3; OECD TG 109)</i>	1.8204 g/cm <sup>3</sup> (at 25 °C) <i>(ASTM D4052-11; deviations from OECD TG 109)</i>
<b>Water solubility</b>	66.2 µg/L (at 23 °C) <i>(EPA OPPTS 830.7840 and OECD TG 105)</i>	Range = 0.0695 – 1.96 µg/L (at 23 °C) Average = 0.381 µg/L (at 23 °C) <i>(EPA OPPTS 830.7840)</i>
<b>Partition coefficient n-octanol/water (log value)</b>	Log P <sub>ow</sub> = 5.7 (at 23 °C) <i>(calculation based on the individual n-octanol and water solubilities)</i>	Log K <sub>ow</sub> = 6.19 (at 25 °C) <i>QSAR (EPI Suite; KOWWIN v1.68)</i>
<b>Partition coefficient organic carbon/water (log value)</b>	Log K <sub>oc</sub> range = 4.26 - 5.16 Log K <sub>oc</sub> average = 4.71 ± 0.45	Log K <sub>oc</sub> range = ≥ 4.4 - ≤ 5 <i>(calculated at 20 °C)</i>

<b>Chemical name</b>	<b>reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine</b>	<b>perfluamine</b>
	<i>(calculation based on equation from Chapter 4 'Predominantly hydrophobics' in 'European Chemicals Bureau: Technical Guidance Document on Risk Assessment')</i>	<i>(calculation based on equation from Chapter 4 'Predominantly hydrophobics' in 'European Chemicals Bureau: Technical Guidance Document on Risk Assessment')</i>
<b>Degradation</b>		
<b>BIOWIN 2</b>	0.0000 (< 0.5) → Does not biodegrade fast	0.0000 (< 0.5) → Does not biodegrade fast
<b>BIOWIN 3</b>	0.2682 (< 2.25) → Ultimate biodegradation longer than months	-1.0187 (< 2.25) → Ultimate biodegradation longer than months
<b>BIOWIN 6</b>	0.0000 (< 0.5) → Not readily degradable	0.0000 (< 0.5) → Not readily degradable
<b>Biodegradation in water: screening tests</b>	<p><i>Ready biodegradability</i></p> <p>Test material described in the registration dossier as follows: perfluoro-N-C1,3-alkyl morpholines, CAS RN: 1093615-61-2, FC-770 Note: the acronym FC-770 is associated to the substance identified with EC No 473-390-7</p> <p>Degradation: 0 % degradation after 28 d (CO<sub>2</sub> evolution, measurement of inorganic carbon concentration, no significant difference with blanks)</p> <p><i>(OECD TG 310)</i></p> <p>→ Not readily biodegradable</p>	NA

### Perfluamine and tripropylamine

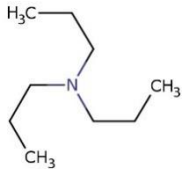
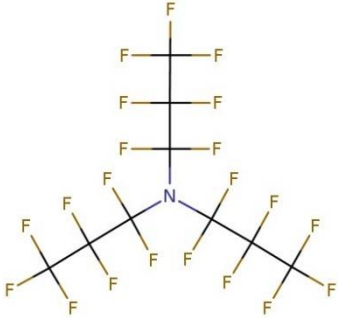
Perfluamine and tripropylamine (EC No 203-047-7) are both liquid substances and have a similar boiling point, and vapour pressure at 20 °C (Table A3). Water solubility is however extremely low for perfluamine, and much higher for tripropylamine. Log  $K_{ow}$  ( $P_{ow}$ ) and Log  $K_{oc}$  values are much higher for perfluamine than for tripropylamine. Density is also higher for perfluamine than for tripropylamine. These diverging physico-chemical properties are completely explainable by the fact that perfluamine is a perfluorinated compound, while tripropylamine is a structurally similar but non-fluorinated compound. The purpose here was to compare the behaviour of the C-N bonds in both structures, knowing that tripropylamine does not contain any fluorine atoms, whereas perfluamine does contain fluorine atoms.

Tripropylamine is a non-fluorinated tertiary propylamine, which is a structural analogue, and thus useful for comparison of ready biodegradability with perfluamine. Both perfluamine (perfluorotripropylamine) and tripropylamine have three propyl groups attached to a central N atom. The difference thus being that perfluamine (molecular formula:  $C_9F_{21}N$ ) is fully fluorinated and does not contain any hydrogen atoms, while tripropylamine (molecular formula:  $C_9H_{21}N$ ) contains carbon atoms bound to hydrogen atoms only. No fluorine atoms are present in this substance.

As the C-F bond is considered to be the strongest in organic chemistry, one would expect that degradation, in the hypothetical situation that degradation could take place, would occur at the C-N bonds of the structure of perfluamine. The read-across hypothesis is that the analogue substance without C-F bonds serves as best-case for predictions of persistence. The persistence of the target substance (i.e. perfluamine) is predicted to be higher than that of the analogue substance.

As tripropylamine (which is non-fluorinated) has been demonstrated in screening tests to be both not readily biodegradable and not inherently biodegradable, then perfluamine (of which its structural formula shows its tendency to be persistent, as it is fully fluorinated) will also not be readily or inherently biodegradable under conditions similar to these screening tests, and the C-N bonds of the structure will not be broken.

**Table A3: Matrix of physico-chemical properties and environmental fate properties for EC No 203-047-7 and EC No 206-420-2 relevant to justify the read-across approach**

Chemical name	tripropylamine	perfluamine
<b>Substance identity</b>		
EC number	203-047-7	206-420-2
CAS number (in the EC inventory)	102-69-2	338-83-0
Index number in Annex VI of the CLP Regulation	NA	NA
Molecular formula	C <sub>9</sub> H <sub>21</sub> N	C <sub>9</sub> F <sub>21</sub> N
Structural formula		
<b>Physico-chemical properties</b>		
Physical state at 20 °C and 101.3 kPa	Liquid <i>(observation)</i>	Liquid <i>(observation)</i>

<b>Chemical name</b>	<b>tripropylamine</b>	<b>perfluamine</b>
<b>Melting / freezing point</b>	Test waived	-50 °C <i>(summary data point from company product technical data sheet)</i>
<b>Boiling point</b>	156.4 °C (at 1 013 hPa) <i>(OECD TG 103)</i>	132 °C (at 760 mm Hg) <i>(ASTM E1719-97 and ASTM D1120-94; deviations from OECD TG 103)</i>
<b>Vapour pressure</b>	430 Pa (at 20 °C) 2 230 Pa (at 50 °C) <i>(weight-of-evidence; company standard method)</i>	3.87 mm Hg (516 Pa; at 20 °C) <i>(ASTM E1719-97 and ASTM D1120-94; deviations from OECD TG 104)</i>
<b>Density</b>	0.7557 g/cm <sup>3</sup> (at 20 °C) <i>(German standard DIN 51757)</i>	1.8204 g/cm <sup>3</sup> (at 25 °C) <i>(ASTM D4052-11; deviations from OECD TG 109)</i>
<b>Water solubility</b>	444 mg/L (at 20 °C) <i>(OECD TG 105; EU Method A.6)</i>	Range = 0.0695 – 1.96 µg/L (at 23 °C) Average = 0.381 µg/L (at 23 °C) <i>(EPA OPPTS 830.7840)</i>
<b>Partition coefficient n-octanol/water (log value)</b>	Log P <sub>ow</sub> = 0.9 (at 25 °C; pH = 7.5) <i>(OECD TG 117; EU Method A.8)</i>	Log K <sub>ow</sub> = 6.19 (at 25 °C) <i>QSAR (EPI Suite; KOWWIN v1.68)</i>
<b>Partition coefficient organic carbon/water (log value)</b>	Log K <sub>oc</sub> = 2.17 (at 25 °C; pH = 5-8) <i>(calculation method determining the K<sub>oc</sub> for charged molecules according to Franco &amp; Trapp)</i>	Log K <sub>oc</sub> range = ≥ 4.4 - ≤ 5 (calculated at 20 °C) <i>(calculation based on equation from Chapter 4 'Predominantly hydrophobics' in 'European Chemicals Bureau: Technical Guidance Document on Risk Assessment')</i>

Chemical name	tripropylamine	perfluamine
<b>Degradation</b>		
<b>Biodegradation in water: screening tests</b>	<p><i>Ready biodegradability</i> Test material: tripropylamine</p> <p>Degradation: 0 – 10 % degradation after 28 d (DOC removal)</p> <p><i>(EEC Directive 79-831 Annex V, C.3; OECD TG 301 E)</i></p> <p>→ Not readily biodegradable</p> <hr/> <p><i>Inherent biodegradability</i> Test material: tripropylamine</p> <p>Degradation:</p> <p>0 % after 3 h</p> <p>0 % after 21 d</p> <p>24 % after 27 d</p> <p>79 % after 33 d</p> <p>100 % after 41 d</p> <p>(DOC removal)</p> <p><i>(EC Directive 79-831 Annex V, Part C, Level 1; OECD TG 302 B)</i></p> <p>→ Not inherently biodegradable</p>	NA

### Overall conclusion on the read-across approach for the persistence assessment

The read-across approach explained above can be used as supportive information for the persistence assessment of perfluamine, as the substances have similar physicochemical properties, and are expected to resist degradation as a result of structural similarity.

Based on the absence of biodegradation in the screening test for EC No 473-390-7, perfluamine is likely to have a low degradability as the perfluorinated structural analogue EC No 473-390-7. Due to their similar physico-chemical properties and common functional groups, a read-across approach is considered to be relevant between perfluamine and EC No 473-390-7 for the persistence assessment.

Tripropylamine is a non-fluorinated tertiary propylamine, and has been demonstrated in screening tests to be both not readily biodegradable and not inherently biodegradable. Perfluamine is expected to degrade less than tripropylamine in conditions similar to the inherent test. Therefore, perfluamine will also not be readily or inherently biodegradable under conditions similar to these screening tests, and the C-N bonds of the structure will not be broken.

All pieces of evidence regarding these analogue substances can be used in a read-across approach as supportive information for the persistence assessment of perfluamine.

## References for Annex 2

ECHA. (2022). Member State Committee Support Document for identification of reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine as a substance of very high concern because of its vPvB (Article 57e) properties.  
<https://echa.europa.eu/documents/10162/91ea9d72-6a36-91fe-bd98-f5ba5331011f>

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