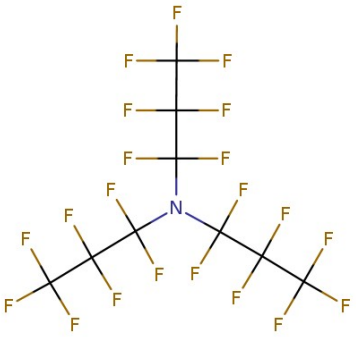
SUBSTANCE EVALUATION CONCLUSION and EVALUATION REPORT

for

Perfluamine

EC No 206-420-2

CAS RN 338-83-0



Evaluating Member State Competent Authority: Belgium

Dated: 13 November 2025

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2020

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

Further information on the substance evaluation process here:

https://echa.europa.eu/regulations/reach/evaluation/substance-evaluation

DISCLAIMER

This document has been prepared by the evaluating MSCA as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating MSCA nor any person acting on either of their behalf may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the outcome of the Substance Evaluation carried out by the evaluating MSCA. The document consists of two parts i.e. A) the conclusion and B) the evaluation report.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the Substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating MSCA. In case the evaluating MSCA proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating MSCA, it does not preclude other MSCAs or the European Commission from initiating regulatory risk management measures which they deem appropriate.

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Part A. Conclusion

In the conclusion (part A), the evaluating MSCA considers how the information on the Substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling.

Alternatively, the outcome of the evaluation may be that presently there is no need for regulatory follow-up at EU level if sufficient information on the potential hazards is available and all necessary measures for safe handling of the Substance are in place.

1. Scope of the evaluation

Perfluamine ("the Substance") was originally selected for substance evaluation to clarify potential risks resulting from the following initial concerns[1]:

- PBT/vPvB;
- Exposure of environment.

2. Overview of other processes / EU legislation

Table 1: Overview of other processes / EU legislation

No other processes	CCH	TPE	ARN	Previously on CoRAP	Annex VI (CLP)	Annex XVII (Restriction)	Candidate List/Annex XIV (Authorisation)
☐	☒	☒	☐	☐	☐	☐	☒

Other EU legislation	Previous legislation	Stockholm convention	Other
PPP/BPR	NONS/RAR	POP	
☐	☐	☐	☐

Dossier Evaluation follow-up:

Following its decision of 19 July 2017[2], ECHA noted that the registration dossier still did not comply with certain information requirements. ECHA performed a targeted compliance check (CCH) and considered it necessary to issue a new decision. In its Decision taken under Article 42(1) of the REACH Regulation of 14 July 2022[3], the following tests were required to be performed:

- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20./OECD TG 211) with the FZ-7941 (cell crude of FC-3283) composition of the registered substance;

[1] The justification document explains the grounds of the initial concerns that triggered the inclusion of the Substance in the CoRAP for further clarification under substance evaluation. When Substances are included in the CoRAP, they have not yet been evaluated and thus the concern is indicative. Consequently, further concerns may be identified during substance evaluation process.

[2] ECHA dissemination website – Dossier Evaluation status of perfluamine (CCH) https://echa.europa.eu/information-on-chemicals/dossier-evaluation-status/-/dislist/details/0b0236e18159c5bd (accessed 23 July 2024).

[3] ECHA dissemination website – Dossier Evaluation status of perfluamine (CCH) https://echa.europa.eu/information-on-chemicals/dossier-evaluation-status/-/dislist/details/0b0236e185ee57d8 (accessed 23 July 2024).

- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the FZ-7941 (cell crude of FC-3283) composition of the registered substance.

At the time of writing this Substance Evaluation Conclusion document, the studies were provided in a dossier update and the follow-up assessment is ongoing.

Testing proposal evaluation:

In the framework of Dossier Evaluation, ECHA performed a Testing Proposal Examination (TPE). In its decision of 14 July 2022[4], and in accordance with Article 40 of the REACH Regulation, the following tests were required to be performed by 21 January 2026:

- *In vivo* mammalian alkaline comet assay (test method: OECD TG 489) combined with *in vivo* mammalian erythrocyte micronucleus test (test method: OECD TG 474) in rats, or if justified, in mice, oral route (triggered by Annex I, Section 0.5 in conjunction with Annex IX, Section 8.4., column 2). For the comet assay the following tissues shall be analysed: liver, glandular stomach and duodenum;

- Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: EU B.56./OECD TG 443) by oral route, in rats (specifications listed in Final Decision);
- Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rabbit).

At the time of writing this Substance Evaluation Conclusion document, the studies were provided in a dossier update and the follow-up assessment is ongoing.

Candidate List / Annex XIV (Authorisation):

The Member State Committee (MSC) unanimously agreed via written procedure, which closed on 22 November 2024, that Perfluamine meets the criteria set out in Article 57 of REACH for identification as SVHC for its vPvB properties.

Under Articles 59(6) and 59(8) of REACH, Perfluamine has been included in the Candidate List on 21 January 2025, for eventual inclusion in Annex XIV to REACH[5].

3. Conclusion and regulatory follow-up action

The evaluation of the available information on Perfluamine has led the evaluating MSCA to the following conclusions:

[4] ECHA dissemination website – Dossier Evaluation status of perfluamine (TPE) https://echa.europa.eu/information-on-chemicals/dossier-evaluation-status/-/dislist/details/0b0236e1835aab26 (accessed 23 July 2024).
[5] ECHA dissemination website – Candidate List of substances of very high concern for Authorisation https://echa.europa.eu/candidate-list-table/-/dislist/details/0b0236e18a8c7fdb (accessed 03 February 2025).

Table 2: Conclusion and regulatory follow-up action for hazard-based concerns

Initial and additional hazard-based concern[6]	Conclusion on hazard-based concern	Regulatory follow-up action
Suspected PBT/vPvB	Concern confirmed. vP and vB criteria are met in accordance with Annex XIII of the REACH Regulation. Perfluamine has been identified as an SVHC for its vPvB properties (Article 57e).	Need for follow-up regulatory action at EU level. A general restriction proposal on PFAS also covering perfluamine has been submitted by other MSCAs.

Table 3: Additional hazard-based endpoints evaluated (outside scope of initial/additional concern)

Additional hazard-based endpoint	Conclusion	Regulatory follow-up action
Aquatic toxicity	Inconclusive.	Dossier evaluation follow-up assessment ongoing, no suggestion yet.
Acute toxicity	Concern removed (clarification of hazard/exposure). Based on the available data, Perfluamine is not acutely toxic.	No need for regulatory follow-up at EU level
Corrosion / Irritation	Concern removed (clarification of hazard/exposure). Based on the available data, Perfluamine is not irritating to the skin and not irritating to the eyes.	No need for regulatory follow-up at EU level
Sensitisation (skin)	Concern removed (clarification of hazard/exposure). Based on the available data, Perfluamine is not skin sensitizing.	No need for regulatory follow-up at EU level
Specific target organ toxicity (repeated)	Concern removed (clarification of hazard/exposure). Based on the available data, Perfluamine cannot be classified for repeated dose toxicity.	No need for regulatory follow-up at EU level
Mutagenicity	Inconclusive.	Dossier evaluation follow-up assessment ongoing, no suggestion yet.
Reproductive toxicity	Inconclusive.	Dossier evaluation follow-up assessment ongoing, no suggestion yet.

[6] Further information on the initial grounds for concern are provided within the published CoRAP updates and/or justification documents.
ECHA dissemination website – Substance evaluation – CoRAP
https://echa.europa.eu/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table/-/dislist/details/0b0236e180b8a7e5 (accessed 23 July 2024).

4. Need for regulatory follow-up actions at EU level

4.1 Harmonised Classification and Labelling

NA.

4.2 Identification as a substance of very high concern, SVHC (first step towards authorisation)

NA.

4.3 Restriction

A restriction proposal on the 'Per- and polyfluoroalkyl substances (PFAS)' has been submitted by five Member State Competent Authorities (MSCAs): Germany, Denmark, the Netherlands, Norway and Sweden. Perfluamine will be included in the scope of this restriction proposal.

At the time of writing the Substance Evaluation Conclusion document for Perfluamine, this restriction proposal was in the 'opinion development' phase.

4.4 Other EU-wide regulatory risk management measures

NA.

5. Currently no need for regulatory follow-up action at EU level

5.1 Regulatory follow-up actions already taken at EU level

During the Substance Evaluation process, a 'bioaccumulation in aquatic species via dietary exposure' study according to OECD TG 305 was requested. The obtained results from this study contributed to the argumentation on vPvB properties for perfluamine.

In the meantime, perfluamine has been identified as an SVHC because of its vPvB (Article 57e) properties. Perfluamine has been included in the Candidate List on 21 January 2025, for eventual inclusion in Annex XIV to REACH.

5.2 No need for regulatory follow-up actions at EU level

NA.

5.3. Other actions

NA.

5.4. No suggestion yet

Some concerns (aquatic toxicity, mutagenicity and reproductive toxicity) remain inconclusive as the dossier evaluation follow-up assessment is ongoing.

6. Tentative plan for follow-up actions

As indicated in Table 4, the following regulatory action(s) are proposed.

Indication of a tentative plan is not a formal commitment by the evaluating MSCA. A commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP (Classification, Labelling and Packaging) Annex VI dossier should be made via the Registry of Intentions.

Table 4: Follow-up actions

Follow-up action	Date for intention	Actor
Restriction.	Not applicable (Ongoing)	Germany, Denmark, the Netherlands, Norway and Sweden[7].

[7] ECHA dissemination website – Registry of restriction intentions until outcome - Per- and polyfluoroalkyl substances (PFAS) https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e18663449b (accessed 13 October 2025).

Part B. Substance evaluation report

In the substance evaluation report (part B), the document provides explanation how the evaluating MSCA assessed and drew the conclusions from the information available.

7. Overview of the Substance Evaluation Process

In accordance with Article 45(4) of the REACH Regulation, the evaluating MSCA evaluated the Substance (perfluamine) based on the information in the registration dossier(s) and on other relevant and available information.

Before concluding the substance evaluation, a Decision to request further information was issued according to Article 46 on 8 December 2021.

In this 'Decision on Substance Evaluation', the following study was requested on perfluamine to clarify the potential risk related to its potential PBT (Persistent, Bioaccumulative and Toxic) and/or vPvB (very Persistent and very Bioaccumulative) properties:[8]

- Bioaccumulation in aquatic species via dietary exposure (test method: Bioaccumulation in fish: aqueous and dietary exposure, EU C.13/ OECD TG 305) with the Substance:
    - under flow-through conditions, to ensure the two phases of uptake (test substance-spiked feed) and depuration (clean, untreated feed);
    - in addition the growth-corrected lipid-normalised kinetic BMF and the corresponding BCF must be determined.

After submission and evaluation of the requested study, the eMSCA (evaluating Member State Competent Authority) concluded that sufficient information was available for perfluamine in order to proceed with an identification as SVHC because of its vPvB (Article 57e) properties. A proposal for identification of an SVHC was submitted on 1 August 2024 and the process was completed by MSC agreement on 22 November 2024.

8. Substance identity

The information on the Substance, including identifiers and structural formula, can be found on the cover page. For more details see European Chemicals Agency, ECHA: https://chem.echa.europa.eu/

Synonyms:

Perfluorotripropylamine (acronym PTPA)

8.1. Type of Substance

Perfluamine is a mono-constituent substance, however it should be noted that the concentration level of its main constituent may occasionally be < 80% w/w.

[8] ECHA dissemination website – Substance evaluation – CoRAP https://echa.europa.eu/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table/-/dislist/details/0b0236e180b8a7e5 (accessed 23 July 2024).

8.2. Other relevant information

NA.

8.3. Analogue substance (read-across)

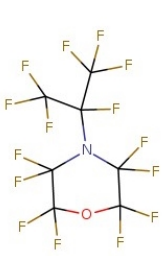
A read-across approach was used as supportive information for the persistence assessment of perfluamine; a justification on the read-across approach can be consulted in Annex II. The structurally related substances used in the read-across approach are listed in Table 5 and

Table 6.

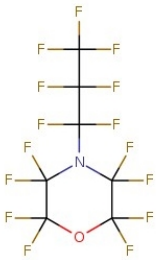
Table 5: Identity of structurally related substance 1

EC number:	473-390-7
Chemical name:	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
CAS number (in the EC inventory)[9]:	/
Index number in Annex VI of the CLP Regulation	NA
Molecular formula:	$C_7F_{15}NO$
Acronym	FC-770

Structural formula:



N/A



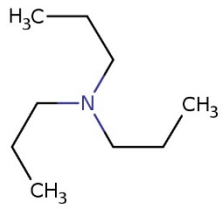
N/A

[9] This substance may have been described using CAS 1093615-61-2, Hydrofluoric acid, reaction products with 4-(1-methylethyl)morpholine.

Table 6: Identity of structurally related substance 2

EC number:	203-047-7
EC name:	tripropylamine
CAS number (in the EC inventory):	102-69-2
CAS number:	102-69-2
IUPAC names:	tripropylamine
Index number in Annex VI of the CLP Regulation	NA
Molecular formula:	$C_9H_{21}N$

Structural formula:



9. Physicochemical properties

Table 7 shows the overview of the physicochemical properties which are provided in the registration dossier of perfluamine.

Regarding the experimental Log K_{ow} 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_{ow} values. It is also not possible to quantitatively assess to what extent Log K_{ow} values of the read-across substances would deviate from the actual Log K_{ow} value of perfluamine.

The Log K_{ow} 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_{ow} 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_{ow} 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 7: Overview of physicochemical properties (registration dossier)

Property	Description of key information	Value	Reference (reliability as determined by the eMSCA)
Physical state at 20°C and 101.3 kPa	No guideline specified	Clear, colourless liquid	Unpublished study report, 2012a (Klimisch score 1)
Melting/freezing point	Summary data point only from company product technical data sheet	-50°C	Company data, 2001 (Klimisch score 4)
Boiling point	ASTM E1719-97 and ASTM D1120-94; deviations from OECD TG 103 Non-GLP	132°C (at 760 mm Hg)	Unpublished study report, 2011a (Klimisch score 2)
Vapour pressure	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, 2011a (Klimisch score 2)
Density	ASTM D4052-11; deviations from OECD TG 109 Non-GLP	1.8204 g/cm^3 (at 25°C)	Unpublished study report, 2011a (Klimisch score 2)
Water solubility	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)
Partition coefficient n-octanol/water (log value)	**Read-across as proposed in the registration dossier** *Test material - Lower limit: perfluoroheptanes CAS RN 1064698-16-3* *Test material - Upper limit: perfluorotributyl amines CAS RN: 1064698-37-8* *These generic identifiers have been reported in the registration dossier. No further information on the identity or composition of the test material was provided.* No guideline specified GLP: not specified	Log K_{ow} range = 5.3 – 6.1 (at 23°C)	Unpublished study report, 2012b (Klimisch score 4)
	QSAR (EPI Suite; KOWWIN v1.68)	Log K_{ow} = 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 'COSMO*therm* 2020' software. The output from the 'COSMO*therm* 2020' software was compared to the experimental physicochemical data originating from the ECHA database (Glüge and Scheringer, 2023). Perfluamine was also assessed by these authors. The output for the physicochemical properties from the 'COSMO*therm* 2020' software is provided in Table 8, together with the values from the registration dossier for comparison.

Table 8: Physicochemical properties of perfluamine calculated by 'COSMO*therm* 2020' software (Glüge and Scheringer, 2023; supplementary material), compared with values from the registration dossier

Property	Value calculated by 'COSMO*therm* 2020'	Value from registration dossier
Boiling point	137.51 °C	132 °C (Klimisch score 2)
Vapour pressure	388 Pa (at 20 °C)	516 Pa (at 20 °C) (Klimisch score 2)
Water solubility	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)
Partition coefficient n-octanol/water (log value)	Log_{10} K_{ow} = 7.28 (at 20 °C) (reliable)	**Read-across:** Log K_{ow} range = 5.3 – 6.1 (at 23 °C) (Klimisch score 4) **QSAR (EPI Suite; KOWWIN v1.68)** Log K_{ow} = 6.19
Partition coefficient octanol/air (log value)	Log_{10} K_{oa} = 2.23 (at 20 °C) (reliable)	**Read-across:** Log K_{oa} range = 0.1 – 1.0 (at 23 °C) (Klimisch score 4)
Partition coefficient organic carbon/water (log value)	Log_{10} K_{oc} = 5.18 (at 25 °C) (reliability cannot be assessed)	Log K_{oc} range = 4.4 - 5 (calculated at 20 °C) (Klimisch score 2)

The values for boiling point and vapour pressure are quite comparable for the 'COSMO*therm* 2020' calculation and the registration dossier. The water solubility calculated by COSMO*therm* is already very low, but the experimental value is even many times lower. A slight difference can be observed in the Log K_{ow} value, which is 7.28 in the COSMO*therm* calculation, and for which a range (5.3 to 6.1) was derived from read-across substances in the registration dossier. The Log K_{oa} and Log K_{oc} values calculated by COSMO*therm* 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). COSMO*therm* 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 'COSMO*therm* 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* $log_{10} K_{AW}$ *values for 21 per- and poly-fluoroalkyl substances were within one* log_{10} *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 COSMO*therm*, at least on these parameters, may be considered reliable. However, in terms of Log K_{oc} 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 Quantitative Structure Activity Relationship (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.

10. Manufacture and uses

10.1. Quantities

The estimated tonnage band (per year) of the Substance is 10 – 100 tonnes[10].

10.2. Overview of uses

Table 9: Overview of uses[11]

Main uses	Key information
Formulation or re-packing	– Formulation / Repackaging into smaller containers ○ Formulation / Repackaging into smaller containers at customer site ○ Repackaging into smaller containers
Uses at industrial sites	– Industrial end use ○ Industrial equipment charging and discharging and use in a closed system ○ Transfer non dedicated ○ Transfer dedicated ○ Industrial end use in closed system

[10] ECHA dissemination website - REACH Registration dossier of perfluamine https://chem.echa.europa.eu/100.005.837/dossier-list/reach/dossiers/active (accessed 20 October 2025).
[11] ECHA dissemination website - REACH Registration dossier of perfluamine (section Manufacture, use and exposure; Use and exposure information), 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).

11. Classification and labelling

Table 10: Classification and labelling of Perfluamine[12]

Harmonised classification (Annex VI of CLP)	Self-classification in registrations	Self-classification in C&L notifications
None	*FC-3283*	None
	Not classified	
	FZ-7941 (cell crude of FC-3283)	
	Acute Tox. 4, H302	
	Acute Tox. 3, H311	
	Eye Irrit. 2, H319	

12. 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 I of this conclusion document. The reliability of studies was assessed with Klimisch scores (Klimisch *et al*., 1997).

12.1. Degradation

12.1.1. Abiotic degradation

12.1.1.1. Hydrolysis

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

Therefore, hydrolysis is not considered to be a relevant degradation mechanism for perfluamine.

12.1.1.2. 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.

12.1.1.3. Phototransformation/photolysis

12.1.1.3.1. Phototransformation in air

[12] ECHA dissemination website - REACH Registration dossier of perfluamine (section Classification & Labelling and PBT assessment; GHS) 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).

Table 11: Studies on phototransformation in air

Method	Results	Remarks	Reference
No guideline specified Indirect photolysis with *OH radical initiation, direct photolysis Light source: mercury lamp	Degradation: 0% degradation after 60 minutes *(relative to trifluoromethane* *EC No: 200-872-4* *CAS RN: 75-46-7)* Half-life (DT_{50}): • *pentadecafluoro-triethylamine* *$N(C_2F_5)_3$* *(EC No: 206-632-5* *CAS RN: 359-70-6)* *> 1 380 years* Expected atmospheric lifetime > 2000 years (based on reactivity of perfluoroalkanes)	**Read-across** *Test material:* *pentadecafluoro-triethylamine* *EC No: 206-632-5* *CAS RN: 359-70-6* Klimisch score 2 Non-GLP	REACH Registration dossier: Unpublished study report, 1993
No guideline specified Computational methods; (Atmospheric) model calculations	Total lifetime: • perfluamine $N(C_3F_7)_3$ > 1 000 years • *pentadecafluoro-triethylamine* *$N(C_2F_5)_3$* *> 1 000 years* • *tris(perfluorobutyl)-amine* *$N(C_4F_9)_3$* *> 1 000 years* • *tris(undecafluoropent-yl)amine* *$N(C_5F_{11})_3$* *> 1 000 years*	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 *Test material:* *pentadecafluoro-triethylamine* *EC No: 206-632-5* *CAS RN: 359-70-6* *Test material:* *tris(perfluorobutyl)amine* *EC No: 206-223-1* *CAS RN: 311-89-7* *Test material:* *tris(undecafluoropentyl)-amine* *EC No: 206-421-8* *CAS RN: 338-84-1* Klimisch score 4	WMO (2019)

Method	Results	Remarks	Reference
		Non-GLP	
No guideline specified Measurement of gas-phase UV absorption spectra Measurement of UV photodissociation yields Experimental and computational methods	Total global atmospheric lifetime: • perfluamine $N(C_3F_7)_3$ 3 795 years • *pentadecafluoro-triethylamine* *$N(C_2F_5)_3$* *3 880 years* • *tris(perfluorobutyl)-amine* *$N(C_4F_9)_3$* *3 650 years*	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 *Test material:* *pentadecafluoro-triethylamine* *EC No: 206-632-5* *CAS RN: 359-70-6* *Test material:* *tris(perfluorobutyl)amine* *EC No: 206-223-1* *CAS RN: 311-89-7* Klimisch score 2 Non-GLP	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 scientific 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.

12.1.1.3.2. Phototransformation in water

Phototransformation in water is not experimentally tested for perfluamine.

12.1.1.3.3. Phototransformation in soil

Phototransformation in soil is not experimentally tested for perfluamine.

12.1.1.3.4. 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 12.1.1.3.1) 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_{50}) 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.

12.1.2. Biodegradation

12.1.2.1. Biodegradation in aqueous media or aqueous environment

12.1.2.1.1. 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 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.

12.1.2.1.2. Screening tests

Table 12: Screening tests for biodegradation in water

Method	Results	Remarks	Reference
Test type: ready biodegradability According to OECD TG 310: Ready Biodegradability – CO_2 in Sealed Vessels (Headspace Test) Test system: sewage, domestic, non-adapted Oxygen: aerobic	Degradation: 0 % degradation after 28 d (CO_2 evolution, measurement of inorganic carbon concentration, no significant difference with blanks)	**Read-across:** *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 473-390-7* Klimisch score 4 GLP	REACH Registration dossier: Unpublished study report, 2007a
Test type: BOD5 tests No guideline specified Trend analysis of several tests Oxygen: aerobic	Degradation: No biodegradation observed	**Read-across:** *Test material as described in the registration dossier: C_5-C_{18} PFOCs* *perfluorohexanes EC No: CAS RN: 1064697-81-9* *perfluoroheptanes EC No: / CAS RN: 1064698-16-3* *perfluorotributyl amines CAS RN: 1064698-37-8* *perfluoro-N-methylmorpholine EC No: 206-841-1 CAS RN: 382-28-5* *perfluoro-N-C1,3-alkyl morpholines CAS RN: 1093615-61-2* *perfluoro-C6,8-furans, pyrans and acyclic ethers EC No: / CAS RN: 1064698-52-7* Klimisch score 4 GLP: not specified	REACH Registration dossier: Unpublished study report, 2012c

Test type: ready biodegradability 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 Test system: effluent from a laboratory waste water treatment plant treating municipal sewage Oxygen: aerobic	Degradation: 0 – 10 % degradation after 28 d (DOC removal)	**Read-across:** *tripropylamine* *EC No: 203-047-7* *CAS RN: 102-69-2* Klimisch score 4 Non-GLP	REACH Registration dossier: Unpublished study report, 1990a
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)	**Read-across:** *tripropylamine* *EC No: 203-047-7* *CAS RN: 102-69-2* Klimisch score 4 Non-GLP	REACH Registration dossier: Unpublished study report, 1990b

Experimental studies on 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: $C_7F_{15}NO$) (Unpublished study report, 2007a). 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, 2007a; Klimisch score 4).

The second dataset contains a trend analysis for several BOD5 tests, performed with various perfluorinated organic compounds (PFOCs; C_5-C_{18}), **Error! Reference source not found.** (identified in the registration dossier with CAS RN: 1064697-81-9 – molecular formula: C_6F_{14}; CAS RN: 1064698-16-3 – molecular formula: C_7F_{16}; CAS RN: 1064698-37-8 – molecular formula: $C_{12}F_{27}N$; CAS RN: 382-28-5 – molecular formula: $C_5F_{11}NO$; CAS RN: 1093615-61-2 – molecular formula: $C_7F_{15}NO$; CAS RN: 1064698-52-7 – molecular formula: /) (Unpublished study report, 2012c). According to the registration dossier, no biodegradation was observed for these substances. 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 (Unpublished study report, 2012c).

The last two screening tests in Table 12 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) (Unpublished study report, 1990a). This ready biodegradability test was performed according to OECD TG 301 E. 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 (Unpublished study report, 1990a; Klimisch score 4). 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) (Unpublished study report, 1990b). The test duration was 41 days. This inherent biodegradability test was performed with a guideline equivalent to OECD TG 302 B. 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 (Unpublished study report, 1990b; Klimisch score 4). As the full study report is not available for this study, no additional information regarding validity criteria could be provided.
Based on all the available evidence under screening conditions, perfluamine is likely to have a low degradability, as the perfluorinated structural analogues described in this section (12.1.2.1.2), 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 II.

12.1.2.1.3. Simulation tests

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

12.1.2.2. Biodegradation in soil

Biodegradation in soil is not experimentally tested for perfluamine.

12.1.2.3. 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 perfluorooctanoic acid (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.

12.1.2.4. 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.

12.1.3. Field data

Field studies are not available with perfluamine.

12.1.4. Other information on degradation

12.1.4.1. 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).

12.1.4.2. 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_3).

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).

12.1.5. 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_2 evolution) for EC No 473-390-7 (Unpublished study report 2007a; Klimisch score 4). BOD5 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).

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, allow to conclude that perfluamine fulfils the P and vP criteria, based on a weight-of-evidence consideration.

12.2. Environmental distribution

12.2.1. 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_{oc} range was reported based on an equation from the Technical Guidance Document on Risk Assessment (non-GLP; Company data, 2012a; Klimisch score 2).

Table 13: Partition coefficient organic carbon/water

Method	Results	Remarks	Reference
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_{oc} 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	REACH Registration dossier: Company data, 2012a

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 'COSMO*therm* 2020' (see Table 8; Glüge and Scheringer, 2023) resulted in a Log_{10} K_{oc} value of 5.18 (at 25 °C) (reliability cannot be assessed).

With Log K_{oc} values ranging from 4.3 to 6.7, perfluamine can be considered to be hardly mobile or even immobile in the environment.

12.2.2. 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 x 10^8 Pa.m³/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_7F_{16}; upper limit: identified as 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 two compounds during the experimental tests, a Klimisch score of 4 is deemed appropriate in this case.

Table 14: Henry's Law Constant (HLC)

Method	Results	Remarks	Reference
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	**Read-across:** *Test material:* *Lower limit: perfluoroheptanes* *EC No: /* *CAS RN: 1064698-16-3* *Upper limit: perfluorotributyl amines* *EC No: 830-388-4* *CAS RN: 1064698-37-8* Klimisch score 4 GLP: not specified	REACH Registration dossier: Unpublished study report, 2012d

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. Based on the relatively high vapour pressure and HLC, perfluamine can be considered to be volatile.

12.2.3. 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 15: 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.

12.2.4. 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 8; Glüge and Scheringer, 2023) resulted in a Log_{10} K_{oa} value of 2.23 (at 20 °C) (reliable).

Table 16: Partition coefficient octanol/air

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

Table 17: Soil volatilisation half-lives

Method	Results	Remarks	Reference
US EPA Human Health Risk Assessment Protocol for Hazardous Waste Combustion Facilities (EPA530-R-05-006, Sept. 2005); Calculation method	Half-lives for volatilisation from soil: 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	REACH Registration dossier: 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.

12.2.5. Field data

Field studies are not available with perfluamine.

12.2.6. 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.

12.3. Data indicating potential for long-range transport

12.3.1. Potential for long-range transport

Monitoring data on Perfluamine in remote areas is not available.

Perfluamine meets the vP criterion (as explained in section 12.1.5). 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 12.1.1.3.1) 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 12.2.3), it is reasonable to conclude that perfluamine shows high potential for long-range atmospheric transport.

12.3.2. 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).

12.3.3. Conclusion on data indicating potential for long-range transport

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

12.4. Bioaccumulation

12.4.1. Bioaccumulation in aquatic organisms (pelagic & sediment organisms)

12.4.1.1. 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 7; 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 'COSMO*therm* 2020' software (Glüge and Scheringer, 2023) results in a Log_{10} K_{ow} value of 7.28 (reliable; see Table 8).

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).

12.4.1.2. 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.

12.4.1.3. Experimental information

Table 18: Aquatic bioaccumulation

Method	Results	Remarks	Reference
According to OECD TG 305: Bioaccumulation in Fish: Aqueous and Dietary Exposure – III: Dietary Exposure Bioaccumulation Fish Test *Lepomis macrochirus* Route of exposure: feed freshwater flow-through	BCF_{KgL}: 5 527 – 51 602 L/kg > 5 000 Depuration half-life: 42 d Minimal BMF values: BMF_{Kg}: 0.61 BMF_{KgL}: 2.19 $BMF_{5\%}$: 0.59	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 Klimisch score 2 GLP	REACH Registration dossier: 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 < 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 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 19.

Table 19: 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	*Lepomis macrochirus* 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 ± 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 ± 0.42 g (more details on fish length, weight and lipid level are provided in Table 20)
Depuration period	37 days
Fish weight at depuration end	6.86 ± 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: ≥ 7.1 mg/L (82 % of air saturation) throughout the test
Hardness	140 – 156 mg $CaCO_3$/L (control group)
Alkalinity	180 – 186 mg $CaCO_3$/L (control group)
Conductivity	332 – 366 µS/cm (control group)

The measured raw data from the study are shown in

Table 20.

Table 20: Experimental results (Unpublished study report, 2023)

day[a]	conc. test item in fish (ng/g)	fish length (mm)	fish weight (g)	fish lipid level[b] (%)	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.

[a] depuration day in parentheses
[b] 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 tracks were removed from test fish and test item concentrations were measured both in the gut tracks and in the rest of the fish. The concentration in the gut tracks appeared to be circa 6 times higher than in the rest of the fish, namely 55.9 ng/g in the gut tracks 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 12.4.1.5 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.

12.4.1.4. 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.

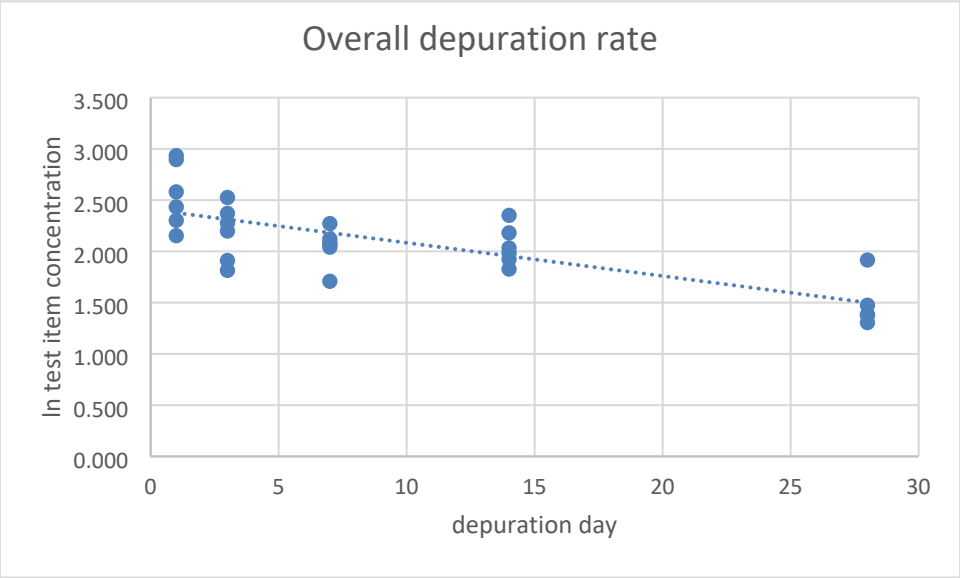


Figure 1: Determination of overall depuration rate constant k_2

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.

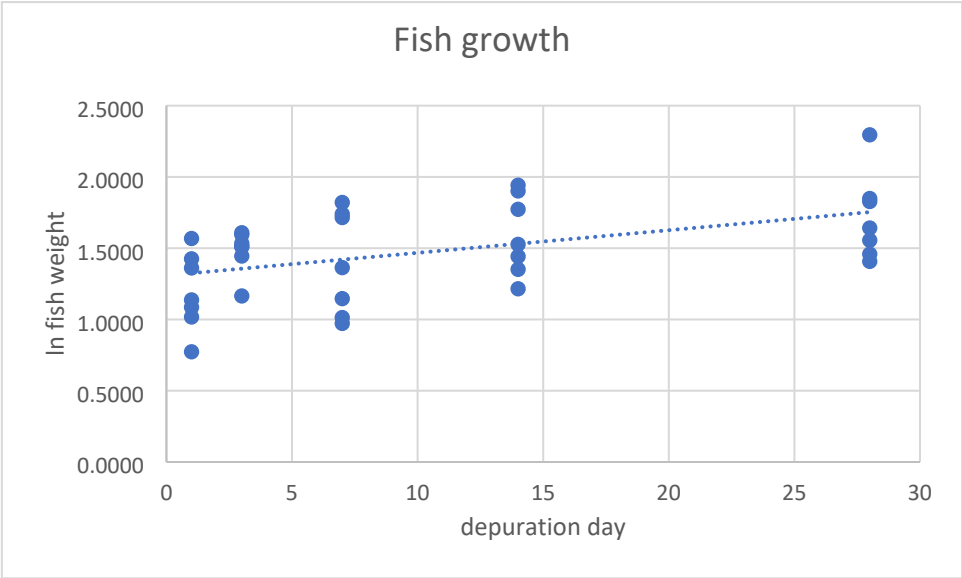


Figure 2: Determination of fish growth rate constant k_g

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.

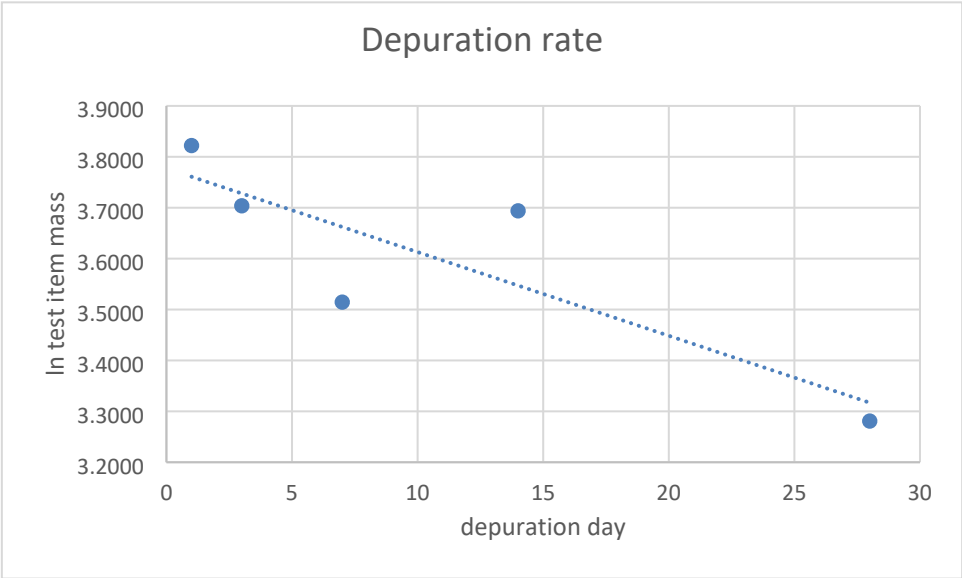


Figure 3: Determination of depuration rate constant k_{2g} based on test item mass

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 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_{KgL}.

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 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_{2gL} 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

Variable	Value
Mean weight at test start (g)	2.65
Uptake phase duration (days)	14
Growth rate, K_g (day^{-1})	0.0159
Log K_{ow}	6.19
K_{2g} (K_2 - K_g)	0.0165
Mean fish lipid uptake end or depuration start (fraction)	0.0465
Mean fish lipid depuration end (fraction)	0.0575
Depuration phase duration (days)	28
BMF_{g1}	

Interim Outputs

Variable	Value
Mean weight midpoint uptake phase (g)	3.265
Mean lipid content midpoint depuration phase	0.052
K_{2g1}	0.017

Outputs

Method 1			
inputs for K1	K1	BCF Est.	Ref.
weight	399.45	23277.8	Hayton and Barron (1990)
weight	558.49	32545.8	Erickson and McKim (1990a)
weight	548.75	31978.6	Barber *et al*. (1991)
weight	352.47	20540.3	Barber (2003) - observed
weight	572.78	33378.6	Barber (2001)
weight	108.28	6310.3	Streit and Siré (1993)
weight	434.94	25346.4	Erickson and McKim (1990b)
weight	356.09	20751.2	Sijm *et al*. (1995)
weight	414.19	24137.2	Barber (2003) - calibrated
log Kow	885.48	51601.5	Tolls and Sijm (1995)
log Kow	776.12	45228.6	Spacie and Hamelink (1982)
weight, log Kow	94.84	5526.9	Hendriks *et al*. (2001)
weight, log Kow	127.65	7439.0	Thomann (1989)

Method 2			
input	Estimated K1	BCF Est.	Ref.
K_{2g1}	610.15	35556.6	Brooke *et al*. (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.

12.4.1.5. 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 (α) of the test item, which reflects its relative absorption across the gut of the fish.

The equation for the calculation of α 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 $g_{food}/g_{fish}/d$ 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 µg test item/kg diet. However, using

this C_{food} value in combination with an I value of 0.0238 $g_{food}/g_{fish}/d$, leads to a calculated α of 1.86, a result that is per definition impossible (as this number is > 1). The derivation of a value for α 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 µg/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 µg/kg food is accepted because this is the lowest value that leads to an assimilation efficiency ≤ 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.

12.4.2. 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 Log K_{oa} ≥ 5 in combination with a Log K_{ow} ≥ 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 Log K_{ow} value of 6.19 (medium uncertainty) and a 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 Log K_{ow} value is higher than 2, but the 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 Log K_{ow} ≥ 2 and Log K_{oa} ≥ 5.

12.4.3. Field data

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

12.4.4. Conclusion on bioaccumulation

Perfluamine meets the bioaccumulation screening criterion for aquatic organisms (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 BCF_{KgL} range of 5 527 to 51 602 L/kg. Furthermore, a depuration half-life of 42 days was determined. Minimum estimations for the BMF_{Kg}, BMF_{KgL} and $BMF_{5\%}$ are 0.61, 2.19 and 0.59, respectively. Moreover, an alternative estimation based on an allometric relationship provides a 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 Log K_{ow} > 2, but a 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 (BCF > 5 000 L/kg).

12.5. Additional information on environmental fate properties

Table 21: Studies on radiative efficiency and global warming potential (GWP)

Method	Results	Remarks	Reference
High-resolution infrared spectrum obtained using a protocol following EPA method 320 Integrated IR cross-section and radiative forcing calculated using the approach of Pinnock *et al*. (1995) GWP calculated using the IPCC 4th Science Assessment Report method with updated CO_2 response and forcing	Radiative efficiency: 0.71 W/(m^2.ppbv) GWP_{100} (calculated for perfluamine): 8 690	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 Klimisch score 2 Non-GLP	REACH Registration dossier: Company data, 2012c
No guideline specified Computational methods; (Atmospheric) model calculations	GWP_{100}: • perfluamine $N(C_3F_7)_3$: 9 180 • *pentadecafluoro-triethylamine $N(C_2F_5)_3$: 10 610* • *tris(perfluorobutyl)-amine $N(C_4F_9)_3$ 8 420* • *tris(undecafluoropent-yl)amine $N(C_5F_{11})_3$ 7 520*	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 *Test material: pentadecafluoro-triethylamine* *EC No: 206-632-5* *CAS RN: 359-70-6* *Test material: tris(perfluorobutyl)amine* *EC No: 206-223-1* *CAS RN: 311-89-7* *Test material: tris(undecafluoropentyl)-amine* *EC No: 206-421-8* *CAS RN: 338-84-1* Klimisch score 4 Non-GLP	WMO (2019)
No guideline specified Measurement of infrared absorption	Radiative efficiency: • perfluamine $N(C_3F_7)_3$: 0.75 W/(m^2.ppb)	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0	Bernard *et al*. (2018)

Method	Results	Remarks	Reference
spectra	• *pentadecafluoro-triethylamine $N(C_2F_5)_3$: 0.61 W/(m².ppb)* • *tris(perfluorobutyl)-amine $N(C_4F_9)_3$ 0.87 W/(m².ppb)* • *tris(undecafluoropent-yl)amine $N(C_5F_{11})_3$ 0.95 W/(m².ppb)*	*Test material: pentadecafluoro-triethylamine EC No: 206-632-5 CAS RN: 359-70-6* *Test material: tris(perfluorobutyl)amine EC No: 206-223-1 CAS RN: 311-89-7* *Test material: tris(undecafluoropentyl)-amine EC No: 206-421-8 CAS RN: 338-84-1* Klimisch score 2 Non-GLP	
No guideline specified Measurement of gas-phase UV absorption spectra Measurement of UV photodissociation yields Experimental and computational methods	GWP_{100} (relative to CO_2): • perfluamine $N(C_3F_7)_3$: 8 700 • *pentadecafluoro-triethylamine $N(C_2F_5)_3$: 9 900* • *tris(perfluorobutyl)-amine $N(C_4F_9)_3$ 7 800*	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 *Test material: pentadecafluoro-triethylamine EC No: 206-632-5 CAS RN: 359-70-6* *Test material: tris(perfluorobutyl)amine EC No: 206-223-1 CAS RN: 311-89-7* Klimisch score 2 Non-GLP	Bernard *et al*. (2020)

The registration dossier mentions a calculation of GWP_{100} (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/(m².ppbv). A calculation method from the IPCC 4th Science Assessment Report was used, and a GWP_{100} 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_{100} 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_{100} 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^{-1} spectral region at 294 K using Fourier transform infrared spectroscopy at 1 cm^{-1} resolution, for four perfluoroamine compounds (among which perfluamine). The calculated radiative efficiencies were 0.61, 0.75, 0.87 and 0.95 W/(m^2.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_{100} values (relative to CO_2) of 9 900, 8 700 and 7 800 for pentadecafluorotriethylamine ($N(C_2F_5)_3$), perfluamine ($N(C_3F_7)_3$) and pris(perfluorobutyl)amine ($N(C_4F_9)_3$), respectively (Bernard *et al*., 2020; Klimisch score 2).

Conclusion:

Perfluamine is an atmospherically persistent potent greenhouse gas.

12.6. 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 henicosafluoroundecanoic acid (CAS RN: 2058-94-8; ECHA, 2012a), heptacosafluorotetradecanoic acid (CAS RN: 376-06-7; ECHA, 2012b), pentacosafluorotridecanoic acid (CAS RN: 72629-94-8; ECHA, 2012c), tricosafluorododecanoic 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.

12.7. 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, 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.

Several similar perfluorinated substances have already been identified as SVHC in the past.

13. Environmental hazard assessment

13.1. Aquatic compartment (including sediment)

13.1.1. Fish

13.1.1.1. Short-term toxicity to fish

Table 22: Short-term effects on fish

Method	Results	Remarks	Reference
Test type: Fish toxicity tests No guideline specified Trend analysis of several tests	96h LC_{50} > 750 mg/L (nominal) based on: mortality (slope of trendline equals to zero)	**Read-across:** *Test material:* *C_5-C_{18} PFOCs* *perfluorohexanes* *CAS RN: 1064697-81-9* *perfluoroheptanes* *CAS RN: 1064698-16-3* *perfluorotributyl amines* *CAS RN: 1064698-37-8* *perfluoro-N-methylmorpholine* *EC No: 206-841-1* *CAS RN: 382-28-5* *perfluoro-N-C1,3-alkyl morpholines* *CAS RN: 1093615-61-2* *perfluoro-C6,8-furans, pyrans and acyclic ethers* *CAS RN: 1064698-52-7* Klimisch score 4 GLP: not specified	REACH Registration dossier: Unpublished study report, 2012f

Method	Results	Remarks	Reference
According to OECD TG 203: Fish, Acute Toxicity Test; EU Method C.1: Acute Toxicity for Fish; ISO International Standard 7346-2; Guidance document on aquatic toxicity testing of difficult substances and mixtures, OECD series on testing and assessment number 23, December 14, 2000 *Danio rerio* freshwater semi-static	96h LC_{50} > 5.96 µg/L (estimated) based on: mortality	**Read-across:** *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* Klimisch score 2 GLP	REACH Registration dossier: Unpublished study report, 2007b
Equivalent or similar to ASTM-E729-80 *Pimephales promelas* freshwater static	96h LC_{50} > 5.96 µg/L (estimated) based on: mortality	**Read-across:** *Test material described in the registration dossier as follows:* *perfluoro-C6,8-furans, pyrans and acyclic ethers* *CAS RN: 1064698-52-7, FC-77* Klimisch score 2 Non-GLP	REACH Registration dossier: Unpublished study report, 1982

The registration dossier mentions three short-term toxicity tests on fish performed with read-across substances. Experimental studies with perfluamine are not available for this endpoint.

The first datapoint contains a trend analysis for several fish toxicity tests, performed with various PFOCs (C_5-C_{18}), specified in Table 22 (identified in the registration dossier with CAS RN: 1064697-81-9 – molecular formula: C_6F_{14}; CAS RN: 1064698-16-3 – molecular formula: C_7F_{16}; CAS RN: 1064698-37-8 – molecular formula: $C_{12}F_{27}N$; CAS RN: 382-28-5 – molecular formula: $C_5F_{11}NO$; CAS RN: 1093615-61-2 – molecular formula: $C_7F_{15}NO$; CAS RN: 1064698-52-7 – molecular formula: /). According to the registration dossier, no toxicity to fish was observed in the various studies at the limits of media solubility, as demonstrated by the slope of the trendline which equaled to zero (Unpublished study report, 2012f). A 96h LC_{50} > 750 mg/L (nominal, based on mortality) was reported. 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 appropriate in this case.

The second study was performed according to OECD TG 203 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: $C_7F_{15}NO$). 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 (Unpublished study report, 2007b; Klimisch score 2). In this acute toxicity test, no effects were observed with *Danio rerio* (previously named *Brachydanio rerio*; 96h LC_{50} > 5.96 µg/L (estimated, based on mortality)) up to the solubility limit.

The third study from the registration dossier was also performed with a read-across substance (identified in the registration dossier with CAS RN: 1064698-52-7 – molecular formula: /). This was a non-GLP study according to a non-OECD guideline (Unpublished study report, 1982; Klimisch score 2). In this acute toxicity test, no effects were observed with *Pimephales promelas* (96h LC_{50} > 5.96 µg/L (estimated, based on mortality)) up to the solubility limit.

Conclusion:

No effects were observed up to the solubility limit, therefore no acute toxicity to fish is expected.

13.1.1.2. Long-term toxicity to fish

There are currently no data available to conclude on the long-term toxicity to fish of perfluamine. A study according to OECD TG 210 has been requested under CCH on 19 July 2017.

13.1.1.3. Conclusion on toxicity to fish

There is currently not enough data available to conclude on the toxic properties to fish of perfluamine.

Long-term toxicity testing on fish (OECD TG 210) has been requested by means of CCH (CCH-D-2114600397-52-01/F).

The results of the study need to be awaited in order to be able to draw a definitive conclusion, therefore the toxic properties to fish of perfluamine remain currently inconclusive.

13.1.2. Aquatic invertebrates

13.1.2.1. Short-term toxicity to aquatic invertebrates

Table 23: Short-term effects on aquatic invertebrates

Method	Results	Remarks	Reference
According to OECD TG 202: Daphnia sp. Acute Immobilisation Test; EPA OPPTS 850.1010: Aquatic Invertebrate Acute Toxicity Test, Freshwater Daphnids; ASTM Stnd. E 729-96;	48h EC_{50} > 2.84 µg/L (meas. (arithm. mean)) based on: mobility 48h EC_{50} > 1 125 mg/L (nominal) based on: mobility	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 Klimisch score 1 GLP	REACH Registration dossier: Unpublished study report, 2012e

Guidance document on aquatic toxicity testing of difficult substances and mixtures, OECD series on testing and assessment Number 23 *Daphnia magna* freshwater static			

In the registration dossier, a short-term toxicity study on *Daphnia magna* performed with perfluamine is included (Unpublished study report, 2012e). In this acute immobilisation test (OECD TG 202; Klimisch score 1), no immobility and no toxicity was observed with *Daphnia magna* (48h EC_{50} > 2.84 µg/L (meas. (arithm. mean), based on mobility)) up to the solubility limit.

Conclusion:

No toxic effects were observed with perfluamine up to the solubility limit, therefore no acute toxicity to aquatic invertebrates is expected.

13.1.2.2. Long-term toxicity to aquatic invertebrates

Table 24: Long-term effects on aquatic invertebrates

Method	Results	Remarks	Reference
Equivalent or similar to OECD TG 211: *Daphnia magna* Reproduction Test *Daphnia magna* freshwater semi-static	21d NOEC = 5.96 µg/L (estimated) based on: reproduction	**Read-across:** *Test material described in the registration dossier as follows: perfluorotributyl amines* *CAS RN: 1064698-37-8* Klimisch score 2 Non-GLP	REACH Registration dossier: Unpublished study report, 1984

The registration dossier mentions a long-term toxicity test on aquatic invertebrates performed with a read-across substance. An experimental study with perfluamine is currently not available for this endpoint, but an OECD TG 211 is requested via CCH.

This non-GLP study (Unpublished study report, 1984) was performed according to a guideline equivalent or similar to OECD TG 211 (Klimisch score 2), with a read-across substance (identified in the registration dossier with CAS RN: 1064698-37-8 – molecular formula: $C_{12}F_{27}N$). In this reproduction test, no effects were observed with *Daphnia magna* (21d NOEC = 5.96 µg/L (estimated, based on reproduction)) up to the solubility limit.

Conclusion:

There is currently not enough data available to conclude on the long-term toxicity to aquatic invertebrates of perfluamine. A study according to OECD TG 211 has been requested under CCH on 19 July 2017.

13.1.2.3. Conclusion on toxicity to aquatic invertebrates

There is currently not enough data available to conclude on the toxic properties to aquatic invertebrates of perfluamine.

Long-term toxicity testing on aquatic invertebrates (OECD TG 211) is requested by means of CCH (CCH-D-2114600397-52-01/F).

The results of this study need to be awaited in order to be able to draw a definitive conclusion, therefore the toxic properties to aquatic invertebrates of perfluamine remain currently inconclusive.

13.1.3. Algae and aquatic plants

Table 25: Effects on algae

Method	Results	Remarks	Reference
According to OECD TG 201: Alga, Growth Inhibition Test *Raphidocelis subcapitata* (previously named *Pseudokirchneriella subcapitata, Selenastrum capricornutum)* freshwater static	72h EC_{50} > 5.96 µg/L (estimated) based on: growth rate 72h NOEC = 5.96 µg/L (estimated) based on: growth rate	**Read-across:** *Test material described in the registration dossier as follows:* *perfluoro-N-methylmorpholine* *CAS RN: 382-28-5* Klimisch score 2 GLP	REACH Registration dossier: Unpublished study report, 2012g
According to OECD TG 201: Alga, Growth Inhibition Test; EU Method C.3: Algal Inhibition Test; ISO 8692: Water Quality – Fresh Water Algal Growth Inhibition Test with *Scenedesmus subspicatus* and *Selenastrum capricornutum*; Guidance document	48h EC_{50} > 5.96 µg/L (estimated) based on: growth rate	**Read-across:** *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 473-390-7*	REACH Registration dossier: Unpublished study report, 2007c

Method	Results	Remarks	Reference
on aquatic toxicity testing of difficult substances and mixtures, OECD series on testing and assessment number 23, December 14, 2000 *Raphidocelis subcapitata* (previously named *Pseudokirchneriella subcapitata, Selenastrum capricornutum)* freshwater static		Klimisch score 2 GLP	
According to OECD TG 201: Freshwater Alga and Cyanobacteria, Growth Inhibition Test *Raphidocelis subcapitata* (previously named *Pseudokirchneriella subcapitata*, *Selenastrum capricornutum*) freshwater static	72h EL_{50} > 100 mg/L (nominal) based on: growth rate 72h NOE_rL = 100 mg/L (nominal) based on: growth rate	Test material: cell crude of perfluamine EC No: 206-420-2 CAS RN: 338-83-0 Klimisch score 1 GLP	REACH Registration dossier: Unpublished study report, 2022a

The registration dossier mentions three toxicity studies which studied the effects on algae.

The first study was performed according to OECD TG 201 (Unpublished study report, 2012g; Klimisch score 2), with a read-across substance (identified in the registration dossier with CAS RN: 382-28-5 – molecular formula: $C_5F_{11}NO$). In this algae growth inhibition test, no effects were observed with *Raphidocelis subcapitata* (72h EC_{50} > 5.96 µg/L (estimated, based on growth rate); 72h NOEC = 5.96 µg/L (estimated, based on growth rate)) up to the solubility limit.

The second study, also according to OECD TG 201 (Unpublished study report, 2007c; Klimisch score 2), was performed 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: $C_7F_{15}NO$). 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 study resulted in a 48h EC_{50} > 5.96 µg/L (estimated, based on growth rate). Thus, no effects were observed with *Raphidocelis subcapitata* up to the solubility limit.

The final study was recently performed with the cell crude of perfluamine, also according to OECD TG 201 (Unpublished study report, 2022a; Klimisch score 1). The cell crude of perfluamine showed no toxic effects to *Raphidocelis subcapitata* at a loading rate of 100 mg/L (72h EL_{50} > 100 mg/L (nominal, based on growth rate); 72h NOE_rL = 100 mg/L (nominal, based on growth rate)).

Conclusion:

No toxic effects were observed with the cell crude of perfluamine at a loading rate of 100 mg/L, therefore no toxicity to algae is expected.

13.1.4. Sediment organisms

NA.

13.1.5. Other aquatic organisms

NA.

13.2. Terrestrial compartment

NA.

13.3. Microbiological activity in sewage treatment systems

Table 26: Effects on micro-organisms

Method	Results	Remarks	Reference
According to OECD TG 209: Activated Sludge, Respiration Inhibition Test (Carbon and Ammonium Oxidation) freshwater static	30 minutes EC_{50} > 1 000 mg/L (nominal) based on: inhibition of total respiration 30 minutes NOEC = 1 000 mg/L (nominal) based on: inhibition of total respiration	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 Klimisch score 1 GLP	REACH Registration dossier: Unpublished study report, 2022b
Test type: Toxicity tests on micro-organisms No guideline specified Trend analysis of several tests	3h EC_{50} > 1 000 mg/L (nominal) based on: inhibition of total respiration (slope of trendline equals to zero)	**Read-across:** *Test material:* *C_5-C_{18} PFOCs* *perfluorohexanes* *CAS RN: 1064697-81-9* *perfluoroheptanes* *CAS RN: 1064698-16-3* *perfluorotributyl amines*	REACH Registration dossier: Unpublished study report, 2012h

Method	Results	Remarks	Reference
		CAS RN: 1064698-37-8 *perfluoro-N-methylmorpholine* *EC No: 206-841-1* *CAS RN: 382-28-5* *perfluoro-N-C1,3-alkyl morpholines* *CAS RN: 1093615-61-2* *perfluoro-C6,8-furans, pyrans and acyclic ethers* *CAS RN: 1064698-52-7* Klimisch score 4 Non-GLP	

In the registration dossier, two datapoints regarding the effects on microbiological activity in sewage treatment systems are available.

A first study testing the toxic effects on micro-organisms was performed with perfluamine (Unpublished study report, 2022b). In this respiration inhibition test (OECD TG 209; Klimisch score 1), no inhibition of microbiological activity in activated sludge was observed after 30 minutes at the highest tested concentration (30 minutes EC_{50} > 1 000 mg/L; 30 minutes NOEC = 1 000 mg/L (nominal, based on inhibition of total respiration)).

The last datapoint contains a trend analysis for several toxicity tests on micro-organisms, performed with various PFOCs (C_5-C_{18}), specified in Table 26 (identified in the registration dossier with CAS RN: 1064697-81-9 – molecular formula: C_6F_{14}; CAS RN: 1064698-16-3 – molecular formula: C_7F_{16}; CAS RN: 1064698-37-8 – molecular formula: $C_{12}F_{27}N$; CAS RN: 382-28-5 – molecular formula: $C_5F_{11}NO$; CAS RN: 1093615-61-2 – molecular formula: $C_7F_{15}NO$; CAS RN: 1064698-52-7 – molecular formula: /). According to the registration dossier, no toxicity to micro-organisms in activated sludge was observed in the various studies at the highest tested concentration of 1 000 mg/L, as demonstrated by the slope of the trendline which equaled to zero (Unpublished study report, 2012h). A 3h EC_{50} > 1 000 mg/L (nominal, based on inhibition of total respiration) was reported. 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 appropriate in this case.

Conclusion:

No toxic effects were observed with perfluamine at the highest tested concentration of 1 000 mg/L, therefore no toxicity to micro-organisms is expected.

13.4. PNEC derivation and other hazard conclusions

Not assessed.

13.5. Conclusions of the environmental hazard assessment and related classification and labelling

There is currently not enough data available to conclude on the environmental hazard assessment and related classification and labelling for perfluamine. Studies requested by means of CCH on fish and aquatic invertebrates need to be awaited in order to be able to draw a definitive conclusion.

14. Human health hazard assessment

14.1. Toxicokinetics

No information available.

14.2. Acute toxicity

14.2.1. Acute toxicity - oral

Table 27: Acute toxicity after oral administration

Method	Species, strain, sex, no/group	Remarks	Dose levels, duration of exposure	Results	Reference
According to OECD TG 401: Acute oral toxicity Gavage	Rat (albino Crl:CD (SD) BR) both sexes 5 animals/ sex/dose	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 No vehicle Klimisch score 2 GLP: not specified	Dose: 5 000 mg/kg bw Single exposure	LD_{50} > 5 000 mg/kg bw No mortality Clinical signs, bw and gross pathology examination: unaffected	REACH Registration dossier: Unpublished study report, 1994a
Test type: acute oral toxicity studies No guideline specified Trend analysis of several tests Gavage	Rat Strain, sex and nb of animals not specified	**Read-across:** *Test material as described in the registration dossier:* *C_5-C_{18} PFOCs* *perfluorohexanes* *CAS RN: 1064697-81-9* *perfluoroheptanes* *CAS RN: 1064698-16-3* *perfluorotributyl amines* *CAS RN: 1064698-37-8* *perfluoro-N-methylmorpholine* *EC No: 206-841-1* *CAS RN: 382-28-5* *perfluoro-N-C1,3-alkyl morpholines* *CAS RN: 1093615-61-2* *perfluoro-C6,8-furans, pyrans and*	Tested dose not specified Single exposure	LD_{50} > 2 000 mg/kg bw No mortality Clinical signs, bw and gross pathology examination: unaffected	REACH Registration dossier: Unpublished study report, 2012i

		acyclic ethers *CAS RN: 1064698-52-7* No vehicle Klimisch score 4 GLP: not specified			

In the registration dossier, two acute toxicity studies via the oral route are available.

The first study is an acute oral toxicity study according to OECD TG 401 (Unpublished study report, 1994a; Klimisch score 2). Perfluamine was administered in a single dose of 5 000 mg/kg bw to rats of both sexes via gavage (5 animals/sex/dose). No mortality occurred and no adverse effects were noted. Therefore, the study resulted in an LD_{50} larger than 5 000 mg/kg bw.

The second study contains a trend analysis for several acute oral toxicity studies, performed with various perfluorinated organic compounds (PFOCs; C_5-C_{18}), specified in Table 27 (identified in the registration dossier with CAS RN: 1064697-81-9 – molecular formula: C_6F_{14}; CAS RN: 1064698-16-3 – molecular formula: C_7F_{16}; CAS RN: 1064698-37-8 – molecular formula: $C_{12}F_{27}N$; CAS RN: 382-28-5 – molecular formula: $C_5F_{11}NO$; CAS RN: 1093615-61-2 – molecular formula: $C_7F_{15}NO$; CAS RN: 1064698-52-7 – molecular formula: /). According to the registration dossier, the LD_{50} value derived from these acute oral toxicity studies is larger than 2 000 mg/kg bw (Unpublished study report, 2012i). 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 appropriate in this case.

Conclusion:

Perfluamine is not acutely toxic via the oral route.

14.2.2. Acute toxicity - inhalation

Table 28: Acute toxicity via inhalation

Method	Species, strain, sex, no/group	Remarks	Dose levels, duration of expo-sure	Results	Reference
Test type: acute inhalation toxicity studies No guideline specified Trend analysis of several tests Vapour	Rat, guinea pig and mouse Strain, sex and nb of animals not specified	**Read-across:** *Test material as described in the registration dossier:* *C_5-C_{18} PFOCs* *perfluorohexanes* *CAS RN: 1064697-81-9* *perfluoroheptanes* *CAS RN: 1064698-16-3* *perfluorotributyl amines* *CAS RN: 1064698-37-8* *perfluoro-N-methylmorpholine* *EC No: 206-841-1*	Tested dose not specified Duration of exposure: 4 h in exposure chamber	LC_{50} > 17 mg/L air recalculated LC_{50} taking into account molecular weight of perfluamine: LC_{50} > 13.20 mg/L No mortality Clinical signs, bw and gross pathology	REACH Registration dossier: Unpublished study report, 2012j

Method	Species, strain, sex, no/group	Remarks	Dose levels, duration of expo-sure	Results	Reference
		CAS RN: 382-28-5 *perfluoro-N-C1,3-alkyl morpholines* *CAS RN: 1093615-61-2* *perfluoro-C6,8-furans, pyrans and acyclic ethers* *CAS RN: 1064698-52-7* Klimisch score 4 GLP: not specified		examination: unaffected	

Regarding acute inhalation toxicity, one dataset is available in the registration dossier which contains a trend analysis for several acute inhalation toxicity studies, performed with various perfluorinated organic compounds (PFOCs; C_5-C_{18}), specified in Table 28 (identified in the registration dossier with CAS RN: 1064697-81-9 – molecular formula: C_6F_{14}; CAS RN: 1064698-16-3 – molecular formula: C_7F_{16}; CAS RN: 1064698-37-8 – molecular formula: $C_{12}F_{27}N$; CAS RN: 382-28-5 – molecular formula: $C_5F_{11}NO$; CAS RN: 1093615-61-2 – molecular formula: $C_7F_{15}NO$; CAS RN: 1064698-52-7 – molecular formula: /). According to the registration dossier, the LC_{50} value derived from these acute inhalation toxicity studies is larger than 17 mg/L air (Unpublished study report, 2012j). When this value is recalculated taking into account the molecular weight of perfluamine, a LC_{50} value larger than 13.20 mg/L can be derived. 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 appropriate in this case.

Conclusion:

Perfluamine is not acutely toxic via inhalation.

14.2.3. Acute toxicity - dermal

No information.

14.2.4. Acute toxicity - other routes

Table 29: Acute toxicity via other routes

Method	Species, strain, sex, no/group	Remarks	Dose levels, duration of expo-sure	Results	Reference
Test type: acute toxicity studies – other routes No guideline specified Intraperitoneal	Rat (Charles River) both sexes 2 animals/ sex/dose	**Read-across:** *Test material as described in the registration dossier:* *reaction mass of 1,1,2,2,3,3,4,4,4-nonafluoro-N,N-bis(nonafluorobutyl)butan-1-amine and*	Doses: 15.4, 23.1, 34.6 g/kg bw Single exposure	LD_{50} > 34.6 g/kg bw recalculated LD_{50} taking into account molecular weight of perfluamine: LD_{50} > 26.87 g/kg	REACH Registration dossier: Unpublished study report, 1969

Method	Species, strain, sex, no/group	Remarks	Dose levels, duration of expo-sure	Results	Reference
injection		*1,1,2,2,3,3,4,4,4-nonafluoro-N-[1,1,2,3,3-hexafluoro-2-(trifluoromethyl)propyl]-N-(1,1,2,2,3,3,4,4,4-nonafluorobutyl)butan-1-amine* *EC No: 939-511-7* *CAS RN: 1064698-37-8* Klimisch score 4 GLP: not specified		bw No mortality Clinical signs: • Abnormal stance, hypoactivity and muscular weakness → ended after 50 minutes • Ruffled fur → decreased after 2 d. Bw gains: normal. Gross pathology: • Clear fluid in the abdominal cavity of all animals. • White soft ovoid masses attached to the mesentery near the blood vessels and/or free floating in the abdominal cavity. • Watery vacuoles found in the subcutaneous tissue of the ventral abdomen.	

Information is also available on acute toxicity via other routes, more specifically via intraperitoneal injection. The read-across substance "reaction mass of 1,1,2,2,3,3,4,4,4-nonafluoro-N,N-bis(nonafluorobutyl)butan-1-amine and 1,1,2,2,3,3,4,4,4-nonafluoro-N-[1,1,2,3,3-hexafluoro-2-(trifluoromethyl)propyl]-N-(1,1,2,2,3,3,4,4,4-nonafluorobutyl)butan-1-amine" (EC No: 939-511-7 – molecular formula: $C_{12}F_{27}N$) was administered to three groups of rats (2 animals of each sex) in dose groups of 15.4, 23.1 or 34.6 g/kg bw (single exposure) (Unpublished study report, 1969). Animals were observed daily during 14 days after exposure. An LD_{50}-value larger than 34.6 g/kg bw was derived from this study. When this value is recalculated taking into account the molecular weight of perfluamine, a LD_{50} value larger than 26.87 g/kg bw can be derived. Some clinical signs were noted; abnormal stance, hypoactivity and muscular weakness, which all ended after 50 minutes; and a ruffled fur which decreased after 2 days. There was no mortality and body weight gains were normal. During gross pathology, a clear fluid was present in the abdominal cavity of all animals, but no lesions could be observed. It is

however unclear which guideline was applied during this study, therefore a Klimisch score of 4 is appropriate in this case.

Conclusion:

Perfluamine is not acutely toxic via intraperitoneal injection.

14.2.5. Acute toxicity - conclusion

The Registrant(s) concluded that perfluamine is not acutely toxic.

Based on the available information, the eMSCA supports the conclusion that no classification is warranted for acute toxicity.

14.3. Corrosion/irritation

14.3.1. Skin irritation

Table 30: Studies on skin irritation

Method	Species, strain, sex, no/group	Remarks	Dose levels, duration of exposure	Results	Reference
According to OECD TG 404: Acute Dermal Irritation / Corrosion *In vivo*	Rabbit (NZW) both sexes 3 animals/ sex/dose	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 No vehicle Klimisch score 2 GLP: not specified	Amount applied: 0.5 mL Duration of exposure: 4 h Obs. period: 72 h Semi-occlusive Patch	Average primary dermal irritation scores: 0 Reversibility: no data	REACH Registration dossier: Unpublished study report, 1994b

The registration dossier includes one study on skin irritation (Unpublished study report, 1994b; Klimisch score 2) according to OECD TG 404, performed with rabbits *in vivo* (3 animals/sex/dose). Perfluamine was applied in an amount of 0.5 mL, in a semi-occlusive manner to the skin of the back of the animal. Exposure lasted 4 hours after which the patch was removed. Edema and erythema scores were noted after 4 hours (30 min after removal of patch), 24, 48 and 72 hours. Total dermal irritation scores were calculated by dividing erythema and edema scores by the number of test sites, at each observation time point. Average primary dermal irritation scores were zero at all time points.

Further testing is waived.

Conclusion:

Perfluamine is not irritating to the skin.

14.3.2. Eye irritation

Table 31: Studies on eye irritation

Method	Species, strain, sex, no/group	Remarks	Dose levels, duration of exposure	Results	Reference
According to OECD TG 405: Acute Eye Irritation / Corrosion *In vivo*	Rabbit (NZW) both sexes 3 animals/ sex/dose	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 No vehicle Klimisch score 2 GLP: not specified	Amount applied: 0.1 mL Obs. period: 72 h	Primary irritation score: 0 Cornea opacity score: 0 Iris score: 0 Conjunctivae score: 0 Reversibility: no data	REACH Registration dossier: Unpublished study report, 1994c

The registration dossier includes one study on eye irritation (Unpublished study report, 1994c; Klimisch score 2) according to OECD TG 405, performed with rabbits *in vivo* (3 animals/sex/dose). Perfluamine was applied in an amount of 0.1 mL. The exposure lasted for a few seconds during the application of the test material into the right eye. The untreated left eye served as control. Primary irritation, cornea opacity, iris and conjunctivae scores were noted after 24, 48 and 72 hours. All eye irritation scores were zero at all time points.

Further testing is waived.

Conclusion:

Perfluamine is not irritating to the eyes.

14.3.3. Conclusion on corrosion/irritation

The Registrant(s) concluded that perfluamine is not irritating to the skin and not irritating to the eyes.

Based on the available information, the eMSCA supports the conclusion that no classification is warranted for skin or eye irritation.

14.4. Sensitisation

14.4.1. Skin sensitisation

Table 32: Studies on skin sensitisation

Method	Species, strain, sex, no/group	Remarks	Dose levels, duration of exposure	Results	Reference
According to OECD TG 429: Skin Sensitisation: Local Lymph Node Assay; EU Method B.42: Skin Sensitisation: Local Lymph Node Assay; EPA OPPTS 870.2600: Skin Sensitisation *In vivo*	Mouse (CBA) female 5 animals/ group 1 control group + 1 treatment group No positive control evaluated in this study	**Read-across:** *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 473-390-7* Klimisch score 2 GLP	25 µL/ear of control (Milli-Q or Milli-U water) or 100 % of the undiluted test article by topical application onto both ears Duration of exposure: once per day for 3 d	Calculated median SI = 2.8	REACH Registration dossier: Unpublished study report, 2007d

The registration dossier includes one study on skin sensitisation (Unpublished study report, 2007d; Klimisch score 2) according to OECD TG 429 (local lymph node assay), performed with mice *in vivo*. The study was performed 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: $C_7F_{15}NO$). 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 animals received each day 25 µL/ear by pipette to the dorsal surface of both ears of a control (0 %) or a treatment item (100 %) of the undiluted test article; exposure lasted 3 days. The calculated median Stimulation Index (SI) was 2.8. A positive control was not evaluated in this study. According to the registration dossier, the positive control (hexylcinnamaldehyde) was tested regularly at another facility and the test method was hence considered to be valid.

Further testing is waived.

Conclusion:

Perfluamine is not skin sensitizing.

14.4.2. Respiratory sensitisation

NA.

14.4.3. Conclusion on sensitisation

The Registrant(s) concluded that perfluamine is not skin sensitizing.

Based on the available information, the eMSCA supports the conclusion that no classification is warranted for skin sensitization.

14.5. Specific target organ toxicity following repeated exposure

14.5.1. Repeated dose toxicity - oral

Table 33: Repeated dose toxicity after oral administration

Method	Species, strain, sex, no/group, dose levels, duration of exposure	Remarks	Results	Reference
Test type: Sub-chronic toxicity - oral According to OECD TG 408: Repeated Dose 90-Day Oral Toxicity Study in Rodents Gavage	Rat (Wistar) both sexes <u>Main study:</u> 10 animals/sex/dose; Doses: 0, 75, 300 and 1 200 mg/kg bw/d <u>Recovery study:</u> 5 animals/sex/dose; Doses: 0 and 1 200 mg/kg bw/d Duration of exposure: 13 w (7 d/w)	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 Vehicle: corn oil Klimisch score 1 GLP	NOAEL: 1 200 mg/kg bw/d See results below	REACH Registration dossier: Unpublished study report, 2019a
Test type: Short-term repeated dose toxicity – oral According to OECD TG 421: Reproduction/ Developmental Toxicity Screening Test Gavage	Rat (Wistar) both sexes 10 animals/sex/dose Doses: 0, 100, 300 and 1 000 mg/kg bw/d Duration of exposure: 28-29 d in M (up to and during the	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 No vehicle Klimisch score 1 GLP	NOAEL: 1 000 mg/kg bw/d NOAEL (reproduction): 1 000 mg/kg bw/d No mortality Clinical signs: no treatment-related effects observed (1 M of the mid dose showed abnormal gait at the end of mating period, this M didn’t	REACH Registration dossier: Unpublished study report, 2019b

Method	Species, strain, sex, no/group, dose levels, duration of exposure	Remarks	Results	Reference
	mating period) and 51-64 d in F (14 d prior to mating, during mating and gestation and at least 13 d after delivery), 40-54 d for F which failed to deliver		succeed to mate) Bw: at the highest dose: • In M: lower bwg (sign in several occasions during the study) however average bwg overall during the study was normal) • In F: mean bw slightly reduced (variation between 2 to 5 %) Food consumption: no effects observed Haematological examination: not performed Clinical biochemistry: serum level of T4 unaffected Macroscopic examination, organ weight and histopathology: no effects observed Oestrous cycle: no treatment-related effects observed Mating index, precoital interval, nb of implantation sites and fertility index, early postnatal pup development: unaffected	
Test type: Repeated dose toxicity – oral No guideline specified Gavage	Rat both sexes Strain and nb of animals not specified Duration of exposure: 28 d	**Read-across:** *Test material as described in the registration dossier: C_5-C_{18} PFOCs* *perfluorohexanes CAS RN: 1064697-81-9*	NOAEL > 1 000 mg/kg bw/d Recalculated NOAEL taking into account molecular weight of perfluamine: NOAEL > 1 306 mg/kg bw/d	REACH Registration dossier: Unpublished study report, 2012k

Method	Species, strain, sex, no/group, dose levels, duration of exposure	Remarks	Results	Reference
		perfluoroheptanes *CAS RN: 1064698-16-3* *perfluorotributyl amines* *CAS RN: 1064698-37-8* *perfluoro-N-methylmorpholine* *EC No: 206-841-1* *CAS RN: 382-28-5* *perfluoro-N-C1,3-alkyl morpholines* *CAS RN: 1093615-61-2* *perfluoro-C6,8-furans, pyrans and acyclic ethers* *CAS RN: 1064698-52-7* No vehicle Klimisch score 4 GLP: not specified	No mortality or histopathological abnormalities observed	

In the registration dossier, three repeated dose toxicity studies via the oral route are available.

Sub-chronic oral toxicity study in rats (Unpublished study report, 2019a)

Summary of the study results and relevant endpoints:

- *mortality and time to death:* no mortality occurred during the study period
- *body weight and body weight changes:*

Table 34: Body weight data (in g)

	Males				Females			
Dose level (in mg/kg bw/d)	0	75	300	1200	0	75	300	1200
Nb examined	15	10	10	15	15	10	10	15
D0	172.27	174.85	074.94	172.49	135.98	134.84	137.88	136.05
D28	301.91	305.49	303.16	303.03	193.55	195.58	194.58	190.98
D63	370.56	381.35	373.72	368.23	219.15	220.49	225.32	217.31
D90	402.51	410.81	402.89	394.15	234.45	232.94	237.59	224.39

BWG D 0 - 90	230.23	235.96	227.95	221.66	98.47	98.10	99.71	88.34**
Nb examined	5	/	/	5	5	/	/	5
D105	387.04	/	/	416.40	235.66	/	/	225.54
D118	395.24	/	/	424.56	236.96	/	/	227.32
BWG D 91 – 118	13.54	/	/	14.04	6.84	/	/	9.48

** : $p < 0.01$

- *description, severity, time of onset and duration of clinical signs:* no severe clinical signs were noted. Salivation was observed in 1, 3 and 1 males, resp. at 75, 300 and 1200 mg/kg bw/d and in 1 female exposed to 1200 mg/kg bw/d. Cataract was observed in 1 females at the highest dose.
- *ophthalmologic findings:* 1 w before the study's begin, persistent pupillary membrane was observed in 1, 1, 2 and 3 males and in 1, 0, 0 and 1 female, resp. at 0, 75, 300 and 1200 mg/kg bw/d. At the end of the study (D90), persistent pupillary membrane in 1 male of the control group and 1 male of the highest dose group. No other abnormalities were observed.
- *haematological findings:* significant changes were only observed for :

  Prothrombin time: 18.46, 17.85, 17.65* and 18.08 s in males, resp. at 0, 75, 300 and 1200 mg/kg bw/d (recovery groups : 19.72 and 19.70 s, resp. at 0 and 1200 mg/kg bw/d)

  Reticulocytes: 2.724, 2.256*, 2.327 and 2.293 % in females, resp. at 0, 75, 300 and 1200 mg/kg bw/d (recovery groups : 2.598 and 2.220 %, resp. at 0 and 1200 mg/kg bw/d)
- *clinical biochemistry findings:* significant difference was only observed for :

  Glucose plasma: 7.313, 6.939, 6.228* and 6.385* mmol/L in males, resp. at 0, 75, 300 and 1200 mg/kg bw/d (recovery groups : 7.896 and 7.968 mmol/L, resp. at 0 and 1200 mg/kg bw/d)
- *gross pathology findings:*

  Main groups: thymus discoloration (red) was noted but not significantly or dose related (7, 3, 3 and 7 in males and 6, 1, 3 and 1 in females, resp. at 0, 75, 300 and 1200 mg/kg bw/d). Same observation was observed for uterus which was swollen in 7, 5, 1 and 1 in females, resp. at 0, 75, 300 and 1200 mg/kg bw/d.

  Recovery groups: same trend was observed. Thymus discoloration was observed in 2 and 1 males and in 1 and 1 females, resp. at 0, 75, 300 and 1200 mg/kg bw/d. Uterus swollen was noted in 3 females of the control group and in 1 female of the highest dose.

  Other small changes were observed but all in only 1 animal.
- organ weight: see Table 35 and Table 36

Table 35: Organ weight in males (in g or %)

	Main group				Recovery group	
Dose level (in mg/kg bw/d)	0	75	300	1200	0	1200
FBW	399.57	397.82	389.44	373.03	381.30	410.60

		Main group				Recovery group	
Dose level (in mg/kg bw/d)		0	75	300	1200	0	1200
Adrenals	Abs	0.0599	0.0565	0.0516	0.0537	0.0460	0.0504
	Rela	0.1513	0.1419	0.1326	0.1437	0.1207	0.1227
Brain	Abs	2.080	2.073	2.055	2.059	2.032	2.146
	Rela	5.237	5.248	5.294	5.537	5.337	5.271
Heart	Abs	1.099	1.032	1.067	1.000	0.994	1.036
	Rela	2.766	2.591	2.735	2.683	2.614	2.526
Kidneys	Abs	2.163	2.074	2.127	1.989	2.074	2.122
	Rela	5.421	5.219	5.463	5.331	5.445	5.153
Liver	Abs	8.995	9.635	9.481	9.070	8.148	9.296
	Rela	22.48	24.24**	24.31**	24.34**	21.35	22.61
Spleen	Abs	0.6047	0.5802	0.5741	0.5825	05564	0.5972
	Rela	1.508	1.475	1.474	1.563	1.459	1.459
Thymus	Abs	0.3604	0.3607	0.3599	0.3399	0.3460	0.2990
	Rela	0.901	0.907	0.931	0.914	0.912	0.742
Thyroid	Abs	0.0168	0.0192	0.0191	0.0191	0.0186	0.0178
	Rela	0.0423	0.0486	0.0491	0.0511	0.0485	0.0438
Testes	Abs	3.722	3.551	3.683	3.651	3.466	3.806
	Rela	9.376	9.015	9.482	9.830	9.107	9.340
Epididymides	Abs	1.313	1.263	1.249	1.248	1.194	1.342
	Rela	3.309	3.204	3.226	3.345	3.135	3.302
Prostate	Abs	0.965	1.075	1.019	1.091	1.006	1.118
	Rela	2.435	2.722	2.620	2.929	2.639	2.730
Seminal vesicles	Abs	1.392	1.377	1.331	1.248	1.150	1.422
	Rela	3.519	3.482	3.413	3.344	3.016	3.459

** : $p < 0.01$

Table 36: Organ weight in females (g and %)

		Main group				Recovery group	
Dose level (in mg/kg bw/d)		0	75	300	1200	0	1200
FBW		221.79	221.42	227.59	219.76	225.26	216.12
Adrenals	Abs	0.0620	0.0552	0.0672	0.0611	0.0564	0.0552
	Rela	0.2810	0.2512	0.2949	0.2784	0.2514	0.2564
Brain	Abs	1.922	1.877	1.932	1.934	1.926	1.902
	Rela	8.696	8.491	8.500	8.814	8.560	8.838
Heart	Abs	0.736	0.688	0.704	0.987	0.724	0.678
	Rela	3.318	3.115	3.097	3.128	3.213	3.134
Kidneys	Abs	1.360	1.320	1.443	1.313	1.344	1.346
	Rela	6.137	5.982	6.341	5.978	5.970	6.229

Liver	Abs	5.362	5.424	5.534	5.223	5.372	5.270
	Rela	24.18	24.55	24.34	23.77	23.88	24.30
Spleen	Abs	0.4502	0.4132	0.4412	0.4167	0.4276	0.4560
	Rela	2.027	1.871	1.941	1.898	1.904	2.106
Thymus	Abs	0.3230	0.3083	0.3357	0.2783	0.2784	0.2650
	Rela	1.451	1.393	1.480	1.269	1.233	1.230
Thyroid	Abs	0.0142	0.0222	0.0160	0.0143	0.0132	0.0144
	Rela	0.0640	0.0997	0.0704	0.0648	0.0585	0.0669
Ovaries	Abs	0.0980	0.0944	0.1091	0.0952	0.1018	0.0914
	Rela	0.4418	0.4261	0.4817	0.4327	0.4535	0.4185
Uterus	Abs	0.8081	0.7686	0.4993*	0.5795	0.9284	0.5298*
	Rela	3.677	3.521	2.197*	2.648	4.133	2.443

* : $p < 0.05$

- *histopathology findings:*

  Mononuclear inflammation was observed in different organs (epididymides, heart, kidneys, liver, lungs, pancreas, prostate gland, stomach, trachea, urinary bladder). However, all these changes were observed in control and treated groups, without significant differences.

  Liver: see Table 37

Table 37: Liver's histopathological findings

		Males				Females			
Dose level (in mg/kg bw/d)		0	75	300	1200	0	75	300	1200
No visible lesions		8	1	0	0	3	6	8	3
Hypertrophy centrilobular	Inc.	0	9***	9***	10***	0	0	0	0
	Min.	0	7	2	6				
	Mild	0	2	7	4				
Vacuolation	Inc.	1	8**	6	5	0	0	0	0
Mononuclear inflammation	Inc.	2	4	6	0	7	4	2	7

** : $p < 0.01$; *** : $p < 0.001$

Reproduction/developmental toxicity screening test (Unpublished study report, 2019b)

Described in chapter 14.8.

Read-across: Repeated dose toxicity - oral (Unpublished study report, 2012k)

A trend analysis for repeated dose toxicity studies via oral route, performed with various perfluorinated organic compounds (PFOCs; C_5-C_{18}), specified in Table 33 (identified in the registration dossier with CAS RN: 1064697-81-9 – molecular formula: C_6F_{14}; CAS RN: 1064698-16-3 – molecular formula: C_7F_{16}; CAS RN: 1064698-37-8 – molecular formula: $C_{12}F_{27}N$; CAS RN: 382-28-5 – molecular formula: $C_5F_{11}NO$; CAS RN: 1093615-61-2 – molecular formula: $C_7F_{15}NO$; CAS RN: 1064698-52-7 – molecular formula: /). According to the registration dossier, the NOAEL derived from these repeated dose toxicity studies via oral route is larger than 1 000 mg/kg bw/d (Unpublished study report, 2012k). When this value is recalculated taking into account the molecular weight of perfluamine, a NOAEL larger than 1 306 mg/kg bw/d can be derived. No mortality or histopathological

abnormalities were observed. 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 appropriate in this case.

Conclusion:

Perfluamine does not show repeated dose toxicity after oral administration.

14.5.2. Repeated dose toxicity - inhalation

Table 38: Repeated dose toxicity via inhalation

Method	Species, strain, sex, no/group, dose levels, duration of exposure	Remarks	Results	Reference
Test type: Short-term repeated dose toxicity - inhalation No guideline specified Vapour	Rat (Sprague-Dawley) both sexes control group: 11 males + 5 females treatment group: 27 males + 15 females Doses: 0 and 7.28 mL/m^3 Duration of exposure: 6 w (5 d/w; 7 h/d)	**Read-across:** *Test material as described in the registration dossier:* *reaction mass of 1,1,2,2,3,3,4,4,4-nonafluoro-N,N-bis(nonafluorobutyl)butan-1-amine and 1,1,2,2,3,3,4,4,4-nonafluoro-N-[1,1,2,3,3-hexafluoro-2-(trifluoromethyl)propyl]-N-(1,1,2,2,3,3,4,4,4-nonafluorobutyl)butan-1-amine* *EC No: 939-511-7* *CAS RN: 1064698-37-8* Klimisch score 4 Non-GLP	NOAEL > 7.28 mL/m^3 Recalculated NOAEL taking into account molecular weight of perfluamine: NOAEL > 5.65 mL/m^3 No mortality and no clinical signs observed Bw: treatment-related effect observed (lower bwg for males) Hematology: no effects observed Clinical biochemistry: not examined Organ weight and macroscopic examination: no effects observed Histopathology: not examined	REACH Registration dossier: Unpublished study report, 1977
Test type: Sub-chronic toxicity – inhalation According to	Rat (Sprague-Dawley) both sexes 10	**Read-across:** *Test material as described in the registration dossier:* *reaction mass of*	NOAEL: 49 821 ppm Recalculated NOAEL taking into account molecular	REACH Registration dossier: Unpublished study report,

Method	Species, strain, sex, no/group, dose levels, duration of exposure	Remarks	Results	Reference
OECD TG 413: Subchronic Inhalation Toxicity: 90-Day Study Vapour	animals/sex/dose Doses: 0, 5 000, 15 000 and 50 000 ppm Duration of exposure: 13 w (5 d/w; 6 h/d)	*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* *EC No: 943-336-1* *CAS RN: 1064697-81-9* Klimisch score 2 GLP	weight of perfluamine: NOAEL: 77 070 ppm Mortality, clinical signs, bw, hematology and clinical biochemistry: no effects observed Organ weight and macroscopic examination: no effects observed Histopathology: no effects observed	1992a
Test type: Short-term repeated dose toxicity - inhalation Equivalent or similar to OECD TG 412: Subacute Inhalation Toxicity: 28-Day Study (*deviation:* rats were exposed for 11 days in total and not for 28 days) Vapour	Rat (Sprague-Dawley CD) both sexes 10 animals/sex/dose Doses: 0 and 50 129 ppm Duration of exposure: 5 d/w; 6 h/d; 11 days in total	**Read-across:** *Test material as described in the registration dossier:* *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* *EC No: 943-336-1* *CAS RN: 1064697-81-9* Klimisch score 2 GLP	NOAEL > 50 129 ppm Mortality, clinical signs and bw: no effects observed Hematology and clinical biochemistry: not examined Organ weight and macroscopic examination: no effects observed Histopathology: not examined	REACH Registration dossier: Unpublished study report, 1992b *Disregarded study*

In the registration dossier, three datapoints regarding repeated dose toxicity studies via inhalation are available.

Read-across: Short-term repeated dose toxicity - inhalation (Unpublished study report, 1977)

A non-guideline (non-GLP) short-term repeated dose toxicity study via inhalation is available in the registration dossier (Unpublished study report, 1977). Rats (both sexes)

were exposed to the read-across substance "reaction mass of 1,1,2,2,3,3,4,4,4-nonafluoro-N,N-bis(nonafluorobutyl)butan-1-amine and 1,1,2,2,3,3,4,4,4-nonafluoro-N-[1,1,2,3,3-hexafluoro-2-(trifluoromethyl)propyl]-N-(1,1,2,2,3,3,4,4,4-nonafluorobutyl)butan-1-amine" (EC No: 939-511-7 – molecular formula: $C_{12}F_{27}N$). A control group received a dose of 0 mL/m^3 and a treatment group received a dose of 7.28 mL/m^3 via inhalation (vapour). Exposure lasted 6 weeks (5 days per week; 7 hours per day). No mortality and no clinical signs were observed. No treatment-related effects were observed, expect for a lower body weight gain for males in the treatment group than for the control group. Gross pathology showed a mild degree of thickening of alveolar septa in some lung tissue samples, and showed a mild degree of focal fatty degeneration in some liver samples. However, the overall gross pathology can be considered as comparable for the treatment and the control group. The NOAEL derived from this repeated dose toxicity study via inhalation is larger than 7.28 mL/m^3. When this value is recalculated taking into account the molecular weight of perfluamine, a NOAEL larger than 5.65 mL/m^3 can be derived. It is however unclear which guideline was applied during this study, therefore a Klimisch score of 4 is appropriate in this case.

Read-across: Sub-chronic toxicity - inhalation (Unpublished study report, 1992a)

A sub-chronic toxicity study via inhalation was performed with rats (both sexes) according to OECD TG 413 (Unpublished study report, 1992a; Klimisch score 2). The read-across substance "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" (EC No: 943-336-1 – molecular formula: C_6F_{14}) was used as test material. 10 animals per sex per group were used; a control group received a dose of 0 ppm and the treatment groups received doses of 5 000, 15 000 and 50 000 ppm, respectively. Exposure lasted 13 weeks (5 days per week; 6 hours per day). No mortality and no treatment-related effects were observed for none of the examined parameters. The NOAEL derived from this repeated dose toxicity study via inhalation is 49 821 ppm. When this value is recalculated taking into account the molecular weight of perfluamine, a NOAEL of 77 070 ppm can be derived.

Read-across: Short-term repeated dose toxicity - inhalation (Unpublished study report, 1992b)

A short-term repeated dose toxicity study via inhalation was performed with rats (both sexes) equivalent or similar to OECD TG 412 (Unpublished study report, 1992b; Klimisch score 2). The study was however disregarded by the Registrant(s) due to major methodological deficiencies. Indeed, there is a deviation from the OECD TG 412, as rats were only exposed for 11 days in total (5 days per week; 6 hours per day) and not for 28 days as is stated in the guideline. The read-across substance "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" (EC No: 943-336-1 – molecular formula: C_6F_{14}) was used as test material. A control group received a dose of 0 ppm and a treatment group received a dose of 50 129 ppm via inhalation (vapour). No mortality and no treatment-related effects were observed for none of the examined parameters. A NOAEL > 50 129 ppm was derived from this repeated dose toxicity study via inhalation.

Conclusion:

Perfluamine does not show repeated dose toxicity via inhalation.

14.5.3. Repeated dose toxicity - dermal

No information available.

14.5.4. Conclusion on repeated dose toxicity

The Registrant(s) concluded that perfluamine cannot be classified for repeated dose toxicity.

Based on the available information, the eMSCA supports the conclusion that no classification is warranted for repeated dose toxicity.

14.6. Mutagenicity

14.6.1. Mutagenicity – *in vitro*

No information.

14.6.2. Mutagenicity – *in vivo*

No information.

14.6.3. Conclusion on mutagenicity

There is currently not enough data available to conclude on the mutagenic properties of perfluamine.

An *in vivo* mammalian alkaline comet assay (test method: OECD TG 489) combined with an *in vivo* mammalian erythrocyte micronucleus test (test method: OECD TG 474) in rats, or if justified, in mice, oral route, is requested by means of TPE (TPE-D-2114602382-61-01/F), and shall be submitted by 21 January 2026.

The results of this study need to be awaited in order to be able to draw a definitive conclusion, therefore the mutagenic properties of perfluamine remain currently inconclusive.

14.7. Carcinogenicity

No information available.

14.8. Toxicity to reproduction (effects on fertility and developmental toxicity)

14.8.1. Effects on fertility

Table 39: Toxicity to reproduction (fertility)

Method	Species, strain, sex, no/group, dose levels, duration of exposure	Remarks	Results	Reference
Test type: Screening test According to OECD TG 421: Reproduction / Developmental Toxicity Screening Test Gavage	Rat (Wistar) both sexes 10 animals/sex/dose Doses: 0, 100, 300 and 1 000 mg/kg bw/d Duration of exposure: 28-29 d in M (up to and during the mating period) and 51-64 d in F (14 d prior to mating, during mating and gestation and at least 13 d after delivery), 40-54 d for F which failed to deliver	Test material: perfluamine EC No: 206-420-2 CAS RN: 338-83-0 No vehicle Klimisch score 1 GLP	NOAEL (P0): 1 000 mg/kg bw/d NOAEL (F1): 1 000 mg/kg bw/d See results below	REACH Registration dossier: Unpublished study report, 2019b
Test type: Screening test According to OECD TG 421: Reproduction / Developmental Toxicity Screening Test Gavage	Rat (Sprague-Dawley) both sexes 10 animals/sex/dose Doses: 0, 100, 500 and 1 000 mg/kg bw/d Duration of exposure: • M: treated for 4 w (starting from 2 w before mating, until day prior to termination) • F: from 2 w	**Read-across:** *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 473-390-7* Vehicle: 0.5% Natrosol 250HX and 0.1% Tween 80 in Water Klimisch score 2	NOEL (P0): ≥ 1 000 mg/kg bw/d Recalculated NOEL taking into account molecular weight of perfluamine: NOEL > 1 306 mg/kg bw/d <u>P0:</u> Bw: • M: bwg and food consumption similar to control throughout the study period • F: bwg and food consumption	REACH Registration dossier: Unpublished study report, 2011b

Method	Species, strain, sex, no/group, dose levels, duration of exposure	Remarks	Results	Reference
	before mating until at least day 4 of lactation (until day prior to termination)	GLP	were lower during the first 2 w of exposure (sign. at the 2 highest doses). Abs. bw and food consumption were already slightly lower than control before exposure. During gestation and lactation, bwg and food consumption were similar to control. Mating performance, fertility, duration of gestation, litter size and survival, litter- and pup weights: no effects observed <u>F1:</u> No mortality observed Clinical signs: no effects observed Bw: pup weights similar to control	

<u>Reproduction/developmental toxicity screening test (Unpublished study report, 2019b)</u>

Summary of the study results and relevant endpoints:

For P adults (per dose):

- *time of death during the study and whether animals survived to termination:* no animal died during the study period
- *clinical observations:* no treatment-related effects observed
- *body weight data for parental animals:*

Table 40: Body weight data (in g)

		Males		Females	
		0	1000	0	1000
Pre mating period	D1	288	286	225	218
	D8	319	312	227	226
Mating period	D1	340	330	236	230
	D15	368	357		
Post coitum	D0			237	228
	D20			340	327
Lactation	D1			267	252*
	D13			304	294

* : $p < 0.05$

- *reproduction data:* mating and gestation index were 100 % in the control and the high dose groups. Fertility index was 80 % in the control and 100 % in the high dose group.
- *mean precoital time:* 1.9 and 2.2 d, resp. at 0 and 1 000 mg/kg bw/d
- *mean implantation sites:* 12.5 and 13.4, resp. at 0 and 1 000 mg/kg bw/d
- *duration of gestation:* 21.4 and 21.8 d, resp. at 0 and 1 000 mg/kg bw/d
- *haematological findings:* not examined
- *clinical biochemistry findings:*
    - total thyroxine (T4): 4.22 and 4.75 ug/dL in males, resp. at 0 and 1000 mg/kg bw/d
- *effects on sperm:* not examined
- *necropsy findings:*
    - M: 9 males in the control and 5 males in the high dose group did not exhibit abnormalities. One male in the control group exhibited exophthalmus. At the highest dose, 3 males had nodules on epididymides, 1 male exhibited agenesis of the right coagulating gland and misshaping of the left coagulating gland, 1 other male had an enlarged thyroid gland.
    - F: 5 females in the control and 9 females in the high dose group did not exhibit abnormalities. In the control group, 3 females exhibited isolated foci on mandibular lymph nodes, 1 female had a uterus containing fluid and one other female had a uterus containing fluid and a pale, discoloured thyroid gland. One female exposed to 1 000 mg/kg bw/d had discolouration of the adrenal glands.
- *organ weight:*

Table 41: Organ weight data (in g)

	Males		Females	
Dose level (in mg/kg bw/d)	0	1000	0	1000
FBW	347	338	292	291
Liver	8.45	8.17	11.60	12.01
Thyroids	0.016	0.017	0.015	0.014
Testes/Ovaries	3.27	3.43	0.127	0.118
Prostate gland	0.801	0.753		
Epididymides	1.085	1.130		
Seminal vesicles	1.256	1.256		

- *histopathological findings:*
    - M: 3 males in the control group and 4 males in the high dose group exhibited follicular hypertrophy of the thyroid gland, 1 male of the control and 1 of the highest dose group had inflammatory infiltrate in the prostate gland. Furthermore, 3 males of the highest dose group showed sperm granuloma in epididymides.
    - F: 1 female in the control group and 1 in the highest dose group exhibited hypertrophy of the thyroid gland, the uterus was dilated in 2 females of the control group, 4 females in the control group showed congested mandibular lymph nodes.

For pups/litters (per dose):

- *total litters:* 8 and 10, resp. at 0 and 1 000 mg/kg bw/d
- *developmental data:* viability and lactation index were not affected (viability index 100 % for the high dose group vs 99 % for the control group, lactation index 100 % for the high dose group vs 98 % for the control group)

Table 42: Developmental data

Dose level (in mg/kg bw/d)		0	1000
Living pups at first litter check	total	84	124
	mean	10.5	12.4
Dead pups at first litter check		0	0
% of postnatal loss		1.2	0.0
Living pups at D 4 P.P.	total	60	80
	mean	7.5	8.0
Living pups at D 13 P.P.	total	59	80
	mean	7.4	8.0

- *sex ratio:* 46/54 % of males/females in the control and the high dose groups.
- *mean pup weight by sex and with sexes combined:*

Table 43: Pups body weight data (in g)

Dose level (in mg/kg bw/d)		0	1000
PND 1	M	6.5	6.6
	F	6.3	6.3
	M + F	6.4	6.4
PND 4	M	10.3	9.9
	F	10.0	9.4
	M + F	10.1	9.6
PND 13	M	33.6	31.1
	F	33.3	30.0
	M + F	33.3	30.5

- *anogenital distance :*
    - M: 2.56 mm at the highest dose group vs. 2.66 mm in the control group.
    - F: 1.10 mm at the highest dose group vs. 1.08 mm in the control group.
- *clinical biochemistry findings:* total T4 (PND 14 – 16): 6.22 and 7.30 ug/dL in males, resp. at 0 and 1 000 mg/kg bw/d, and 5.61 and 6.48 ug/dL in females, resp. at 0 and 1 000 mg/kg bw/d.

Read-across: Reproduction/developmental toxicity screening test (Unpublished study report, 2011b)

A reproduction/developmental toxicity screening test via gavage was performed according to OECD TG 421 (Unpublished study report, 2011b; Klimisch score 2) 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: $C_7F_{15}NO$). 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 study was performed with rats (both sexes; 10 animals per sex per group). Doses of 0 (control), 100, 500 and 1 000 mg/kg bw/d of test material were administered to the animals. Exposure lasted 4 weeks for the males, starting from 2 weeks before mating (until day prior to termination), and for the females from 2 weeks before mating until at least day 4 of lactation (until day prior to termination). A decrease in body weight gain and food consumption was noted for the females of the P0 generation during the first 2 weeks of exposure (significant at the two highest doses), but during gestation and lactation body weight gain and food consumption recovered to values similar to the control. For males, body weight gain and food consumption were similar to the control throughout the study period. Mating performance, fertility, duration of gestation, litter size and survival, litter- and pup weights were unaffected. The F1 generation also showed no mortality, no clear clinical signs and pup weights similar to the control. The NOEL (no observed effect level) (P0) derived from this study on toxicity to reproduction is ≥ 1 000 mg/kg bw/d. When this value is recalculated taking into account the molecular weight of perfluamine, a NOEL > 1 306 mg/kg bw/d can be derived.

Conclusion:

There is currently not enough data available to conclude on the toxicity to reproduction (fertility) of perfluamine.

14.8.2. Developmental toxicity

Table 44: Toxicity to reproduction (developmental toxicity)

Method	Species, strain, sex, no/group, dose levels, duration of exposure	Remarks	Results	Reference
Test type: Developmental toxicity test According to OECD TG 414: Prenatal Developmental Toxicity Study Gavage	Rat (Wistar) female 22 animals/dose Doses: 0, 100, 300 and 1 000 mg/kg bw/d Duration of exposure: day 6 to day 20 post-coitum (included)	Test material: Perfluamine EC No: 206-420-2 CAS RN: 338-83-0 No vehicle Klimisch score 1 GLP	NOAEL (maternal animals): 1 000 mg/kg bw/d NOAEL (fetuses): 1 000 mg/kg bw/d See results below	REACH Registration dossier: Unpublished study report, 2019c

Prenatal developmental toxicity study (Unpublished study report, 2019c)

Summary of the study results and relevant endpoints:

- no mortality occurred during the study period
- *clinical observations:* no effects observed
- *body weight data:*
  - at gestational day (GD) 6 : 231, 234, 230 and 233 g, resp. at 0, 100, 300 and 1000 mg/kg bw/d
  - at GD 21: 330, 332, 331 and 333 g, resp. at 0, 100, 300 and 1000 mg/kg bw/d
- *food consumption:* no effects
- *clinical biochemistry findings:*
  - Thyroid Stimulating Hormone (TSH): 0.357, 0.316, 0.334 and 0.396 IU/mL, resp. at 0, 100, 300 and 1000 mg/kg bw/d
  - Total triiodothyronine (T3): 59.4, 55.1, 61.3 and 55.7 ng/dL, resp. at 0, 100, 300 and 1000 mg/kg bw/d
  - Total T4: 2.58, 2.40, 2.32 and 2.55 ug/dL, resp. at 0, 100, 300 and 1000 mg/kg bw/d
- no females aborted during the study and only one female exposed to 1000 mg/kg bw/d was non gravid.

- *mean resorptions:* early: 0.4, 0.4, 0.5 and 0.2, resp. at 0, 100, 300 and 1000 mg/kg bw/d. No late resorptions observed.
- *mean post implantation loss:* 0.4, 0.4, 0.5 and 0.3, resp. at 0, 100, 300 and 1000 mg/kg bw/d
- *necropsy findings:* no treatment-related effects observed
- *body weight:* FBW: 330, 332, 331 and 333 g, resp. at 0, 100, 300 and 1000 mg/kg bw/d
- *organ weight:* thyroid weight: 0.015, 0.016, 0.015 and 0.016 g, resp. at 0, 100, 300 and 1000 mg/kg bw/d
- *histopathological findings:* thyroid gland: follicular hypertrophy observed in 4, 3, 3 and 2 animals, resp. at 0, 100, 300 and 1000 mg/kg bw/d
- *mean number of live births:* 10.7, 10.8, 10.8 and 11.0, resp. at 0, 100, 300 and 1000 mg/kg bw/d
- *mean fetal weight:* 5.1, 5.1, 5.2 and 5.2 g, resp. at 0, 100, 300 and 1000 mg/kg bw/d
- *mean ano-genital distance (AGD):* 2.74, 2.72, 2.76 and 2.77 mm in males, and 1.25, 1.19, 1.23 and 1.27 mm in females, resp. at 0, 100, 300 and 1000 mg/kg bw/d
- *fetal malformation findings:* no treatment-related malformations observed.
    - external: 1 foetus of the control and 1 of the mid dose exhibited the lower jaw to be absent or small.
    - visceral: 1 foetus of the control group and 1 of the high dose group had aortic arch right-sided, and 1 foetus of the control group had situs inversus.
    - skeletal: 1 foetus of the control group had vertebral anomaly, 1 foetus of the control and 1 of the high dose had costal cartilage anomaly, 1 foetus of the low dose, 2 of the mid dose and 1 of the high dose exhibited bent limb bones, and 1 foetus of the mid dose had vertebral central anomaly.

Conclusion:

There is currently not enough data available to conclude on the developmental toxicity of perfluamine.

14.8.3. Conclusion on toxicity to reproduction (effects on fertility and developmental toxicity)

There is currently not enough data available to conclude on the toxicity to reproduction (effects on fertility and developmental toxicity) of perfluamine.

An extended one-generation reproductive toxicity study (test method: OECD TG 443) by oral route, in rats, is requested by means of TP (TPE-D-2114602382-61-01/F), and shall be submitted by 21 January 2026.

A pre-natal developmental toxicity study (test method: OECD TG 414) by oral route, in a second species (rabbit), is requested by means of TP (TPE-D-2114602382-61-01/F), and shall be submitted by 21 January 2026.

The results of these studies need to be awaited in order to be able to draw a definitive conclusion, therefore the endpoints regarding the toxicity to reproduction of perfluamine remain currently inconclusive.

14.9. Hazard assessment of physicochemical properties

Not assessed.

14.10. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

NA.

14.11. Conclusions of the human health hazard assessment and related classification and labelling

There is currently not enough data available to conclude on all the human health endpoints of perfluamine.

Based on the available information, the eMSCA supports the conclusion that no classification is warranted for perfluamine for acute toxicity, for skin or eye irritation, for skin sensitization, and for repeated dose toxicity.

Further studies regarding mutagenicity and regarding toxicity to reproduction (effects on fertility and developmental toxicity) have been requested by means of TPs. The results of these studies need to be awaited in order to be able to draw a definitive conclusion. Therefore, the human health endpoints regarding mutagenicity and regarding toxicity to reproduction (effects on fertility and developmental toxicity) remain currently inconclusive.

15. Endocrine disrupting (ED) properties assessment

Not assessed.

16. PBT/vPvB and PMT/vPvM assessment

16.1. 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_2 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.

Conclusion:

In conclusion, 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.

16.2. 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 'COSMO*therm* 2020' software (estimated Log_{10} 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_{KgL} 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_K 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).

Conclusion:

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.

16.3. Mobility

The registration dossier mentions a calculated Log K_{oc} range for perfluamine of 4.4 to 5 (Company data, 2012a; Klimisch score 2). Modelling with 'COSMO*therm* 2020' (Glüge and Scheringer, 2023) resulted in a Log_{10} K_{oc} value of 5.18 (at 25 °C) (reliability cannot be assessed).

Conclusion:

As both these calculated Log K_{oc} values do not meet the M criterion (as they are > 3) and do not meet the vM criterion (as they are > 2), it is concluded that perfluamine is not considered to be mobile.

16.4. Toxicity

Studies have been requested by means of CCH on fish and aquatic invertebrates. Studies regarding mutagenicity and regarding toxicity to reproduction (effects on fertility and developmental toxicity) have been requested by means of TPs.

Conclusion:

Toxicity endpoints remain currently inconclusive.

16.5. Conclusions of the PBT/vPvB/PMT/vPvM assessment and related classification and labelling

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, points 1.1.1 and 1.2.1 of the REACH Regulation.

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 1.1.2 and 1.2.2 of the REACH Regulation.

Perfluamine therefore 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).

17. Exposure assessment

17.1. Human health

17.1.1. Worker

NA.

17.2. Environment

NA.

18. Risk characterisation

18.1. Human health

18.1.1. Worker

NA.

18.2. Environment

NA.

19. References

Table 45: References

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20. Abbreviations

Table 46: Abbreviations

*	$p < 0.05$
**	$p < 0.01$
***	$p < 0.001$
Abs	absolute
AGD	ano-genital distance
Arithm.	arithmetic
B	Bioaccumulative
BASS	Bioaccumulation and Aquatic System Simulator
BCF	Bioconcentration factor
BMF	Biomagnification factor
BPR	Biocidal Products Regulation (EU) 528/2012
Bw	body weight
Bwg	body weight gain
CAS RN	Chemical Abstracts Service Registry Number
CCH	Compliance Check
C-F	carbon-fluorine
C-N	carbon-nitrogen
CLP	Classification, Labelling and Packaging
CMR	Carcinogenic, Mutagenic, toxic to Reproduction
CoRAP	Community Rolling Action Plan
D	day
DMEL	Derived Minimal Effect Level
DNEL	Derived No Effect Level
DOC	dissolved organic carbon
DT_{50}	dissipation half-life
EC	European Community
EC_{50}	concentration effective in producing 50 % of the maximal response
ECHA	European Chemicals Agency
ED	Endocrine Disruption
EL_{50}	effective loading causing 50 % of the maximal response
EPI	Estimation Programs Interface
eMSCA	evaluating Member State Competent Authority
EU	European Union
F	female

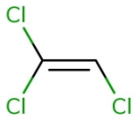
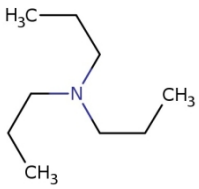
FBW	final body weight
FELS	Fish, early-life stage
FUP	Follow up evaluation (Dossier evaluation)
GC/MS	gas chromatography/mass spectrometry
GD	gestational day
GLP	Good Laboratory Practice
GWP	global warming potential
GWP_{100}	GWP on the 100-year time horizon
H	hours
HFPO-DA	2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, its salts and its acyl halides (covering any of their individual isomers and combinations thereof)
HLC	Henry's Law Constant
Inc.	incidence
IPCC	Intergovernmental Panel on Climate Change
K_{oa}	Partition coefficient octanol/air
K_{oc}	Partition coefficient organic carbon/water
K_{ow}	Partition coefficient n-octanol/water
LC_{50}	Lethal concentration causing 50 % death
LC-MS	Liquid Chromatography – Mass Spectrometry
LD_{50}	Lethal dose causing 50 % death
LMC	Laboratory of Mathematical Chemistry
Log K_{oa}	Partition coefficient octanol/air (log-value)
Log K_{oc}	Partition coefficient organic carbon/water (log-value)
Log K_{ow}	Partition coefficient n-octanol/water (log-value)
M	male
MCI	Molecular Connectivity Index
Meas.	measured
Min.	minimum
MSC	Member State Committee
MSCA	Member State Competent Authority
NA	Not Applicable
Nb or No	number
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NOEL	No Observed Effect Level
NOE_rL	No Observed Effect Level for Growth Rate
NONs	Notification Of New Substances
NZW	New Zealand White
Obs.	observation
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
PMT	Persistent, Mobile and Toxic
PND	post-natal day
PNEC	Predicted No Effect Concentration
POP	Persistent Organic Pollutants
P.P.	post-partum
PPP	Plant Protection Products regulation EC 1107/2009
PTPA	perfluorotripropylamine
QSAR	Quantitative Structure Activity Relationship
RAR	Risk Assessment Report
REACH	EU Regulation No 1907/2006 concerning Registration, Evaluation, Authorisation, and restriction of CHemicals
Rela	relative
Resp.	Respectively
SD	Sprague-Dawley

SI	Stimulation Index
SVHC	Substance of Very High Concern
TAR	Third Assessment Report
TCE	trichloroethylene
T3	triiodothyronine
T4	thyroxine
TG	Test Guideline
TPE	Testing Proposal Examination
TSH	Thyroid Stimulating Hormone
UNEP	United Nations Environment Program
US EPA	United States Environmental Protection Agency
vB	very Bioaccumulative
vP	very Persistent
vPvB	very Persistent and very Bioaccumulative
vPvM	very Persistent and very Mobile
vs.	versus
W	week
WMO	World Meteorological Organization

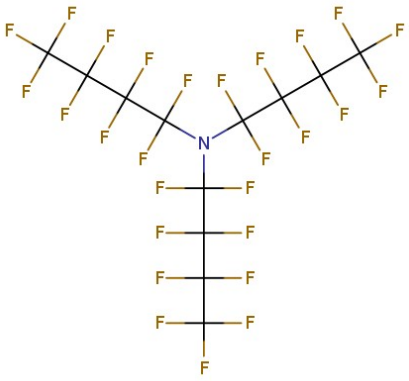
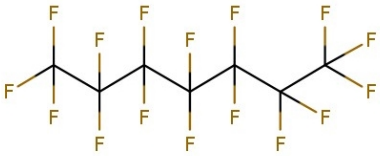
Annex I. Structural formulas

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[13].

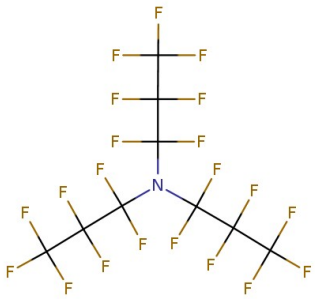
Table A1: Structural formulas corresponding to the CAS-numbers of read-across substances

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

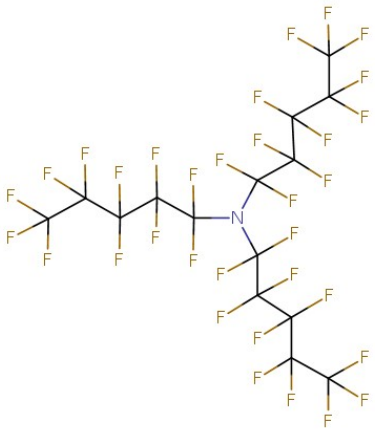
[13] Source: ECHA dissemination website https://echa.europa.eu/ (accessed 23 July 2024).

EC No: 206-203-2 **CAS RN: 307-55-1**	**Tricosafluorododecanoic acid**
	
EC No: 206-223-1 **CAS RN: 311-89-7**	**Tris(perfluorobutyl)amine**
	
EC No: 206-392-1 **CAS RN: 335-57-9**	**Perfluoroheptane**
	
EC No: 206-397-9 **CAS RN: 335-67-1**	**Pentadecafluorooctanoic acid**
	

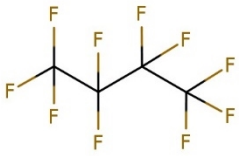
EC No: 206-420-2 **CAS RN: 338-83-0**	**Perfluamine**

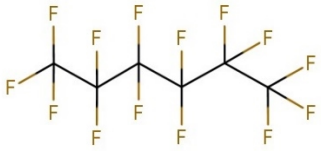
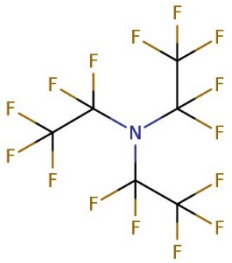
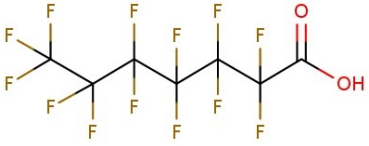


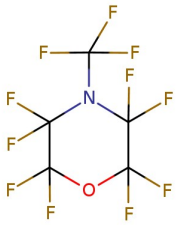
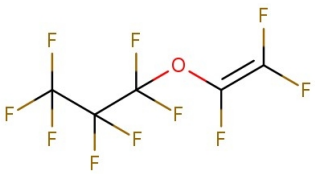
EC No: 206-421-8 **CAS RN: 338-84-1**	**Tris(undecafluoropentyl)amine**

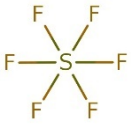
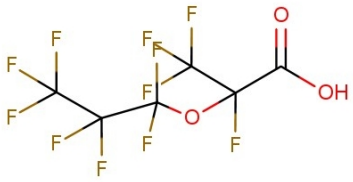


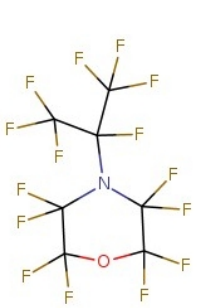
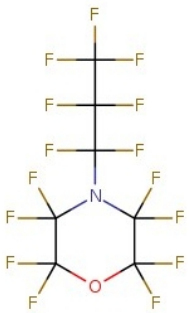
EC No: 206-580-3 **CAS RN: 355-25-9**	**Decafluorobutane**

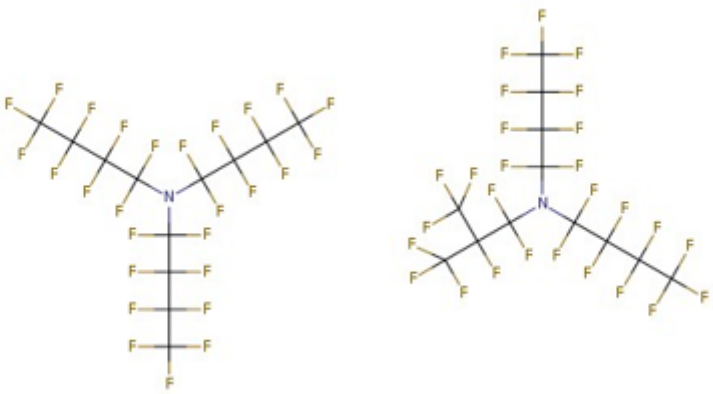
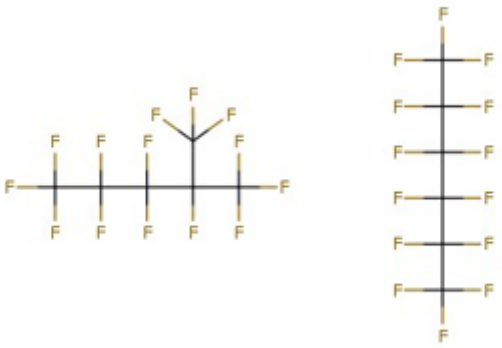


EC No: 206-585-0 **CAS RN: 355-42-0**	**Tetradecafluorohexane**
	
EC No: 206-587-1 **CAS RN: 355-46-4**	**Perfluorohexane-1-sulphonic acid and its salts**
	
EC No: 206-632-5 **CAS RN: 359-70-6**	**Pentadecafluorotriethylamine**
	
EC No: 206-798-9 **CAS RN: 375-85-9**	**Perfluoroheptanoic acid and its salts**
	

EC No: 206-803-4 **CAS RN: 376-06-7**	**Heptacosafluorotetradecanoic acid**
	
EC No: 206-841-1 **CAS RN: 382-28-5**	**2,2,3,3,5,5,6,6-octafluoro-4-(trifluoromethyl)morpholine**
	
EC No: 211-647-5 **CAS RN: 678-26-2**	**Dodecafluoropentane**
	
EC No: 216-600-2 **CAS RN: 1623-05-8**	**1,1,1,2,2,3,3-heptafluoro-3-[(trifluorovinyl)oxy]propane**
	

EC No: 218-165-4 **CAS RN: 2058-94-8**	**Henicosafluoroundecanoic acid**
	
EC No: 219-854-2 **CAS RN: 2551-62-4**	**Sulphur hexafluoride**
	
EC No: 231-635-3 **CAS RN: 7664-41-7**	**Ammonia, anhydrous**
NH_3	
EC No: 232-007-1 **CAS RN: 7783-54-2**	**Nitrogen trifluoride**
NF_3 No image available	
EC No: 236-236-8 **CAS RN: 13252-13-6**	**2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid**
	

EC No: 276-745-2 **CAS RN: 72629-94-8**	**Pentacosafluorotridecanoic acid**
	
EC No: 473-390-7 **CAS RN: /** (CAS RN: 1093615-61-2 may have been used to describe this substance)	**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**
 N/A  N/A	
CAS RN: /	**Perfluorobutane sulfonic acid and its salts**
No image available	
EC No: 908-198-9 **CAS RN: /** (**CAS RN: 1064698-** **16-3 may have been used to describe this substance)**	**Reaction mass of 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,7 heptadecafluoro-heptane and 1,1,1,2,2,3,3,4,4,5,6,6,6 tridecafluoro-5-(trifluoromethyl)hexane**
C_7F_{16} No image available	

EC No: 939-511-7 **CAS RN: /** Or EC No: 830-388-4 CAS RN: 1064698-37-8	**Reaction mass of 1,1,2,2,3,3,4,4,4-nonafluoro-*N,N*-bis(nonafluorobutyl)butan-1-amine and 1,1,2,2,3,3,4,4,4-nonafluoro-*N*-[1,1,2,3,3-hexafluoro-2-(trifluoromethyl)propyl]-*N*-(1,1,2,2,3,3,4,4,4-nonafluorobutyl)butan-1-amine**
	
EC No: 943-336-1 **CAS RN: /** (CAS RN: 1064697-81-9 may have been used to identify this substance)	**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**
	
EC No: not available **CAS RN: 1064698-52-7 (Octanoyl chloride, fluorinated, C8 cyclic ether fraction – this CAS number may have been used to describe the substance)**	**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 heptadecafluoro-heptane**
No image available	

Annex II. 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^3 (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_{ow} and Log K_{oc} 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[14].

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: $C_9F_{21}N$), while EC No 473-390-7 is a multi-constituent substance (molecular formula: $C_7F_{15}NO$), 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;

[14] 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

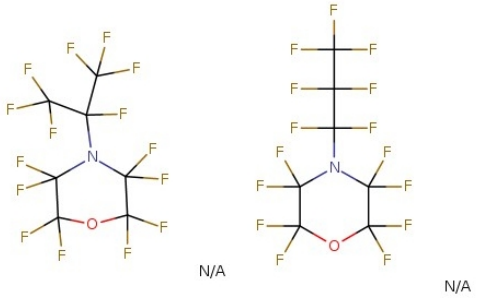
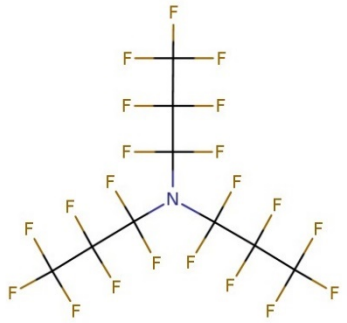
BIOWIN v4.11[15]). Both perfluamine and EC No 473-390-7 are considered to not biodegrade fast (BIOWIN 2), to have an ultimate biodegradation longer than months (BIOWIN 3), and to be not readily degradable (BIOWIN 6).

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_2 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.

[15] US EPA. (2012). EPI Suite™, v4.1., developed by US EPA, Washington DC, USA.

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

Chemical name	**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**	**perfluamine**
Substance identity		
EC number	473-390-7	206-420-2
CAS number (in the EC inventory)	/	338-83-0
Index number in Annex VI of the CLP Regulation	NA	NA
Molecular formula	$C_7F_{15}NO$	$C_9F_{21}N$
Structural formula	 N/A N/A	
Physico-chemical properties		
Physical state at 20 °C and 101.3 kPa	Liquid *(observation)*	Liquid *(observation)*
Melting / freezing point	-127 °C *(method similar to ASTM D97)*	-50 °C *(summary data point from company product technical data sheet)*

Chemical name	**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**	**perfluamine**
Boiling point	96 °C (at 101.5 kPa) *(EU Method A.2; OECD TG 103)*	132 °C (at 760 mm Hg) *(ASTM E1719-97 and ASTM D1120-94; deviations from OECD TG 103)*
Vapour pressure	50.6 mm Hg (6 750 Pa; at 20 °C) *(EU Method A.4; OECD TG 104)*	3.87 mm Hg (516 Pa; at 20 °C) *(ASTM E1719-97 and ASTM D1120-94; deviations from OECD TG 104)*
Density	1.80 g/cm^3 (at 20 °C) *(EU Method A.3; OECD TG 109)*	1.8204 g/cm^3 (at 25 °C) *(ASTM D4052-11; deviations from OECD TG 109)*
Water solubility	66.2 µg/L (at 23 °C) *(EPA OPPTS 830.7840 and OECD TG 105)*	Range = 0.0695 – 1.96 µg/L (at 23 °C) Average = 0.381 µg/L (at 23 °C) *(EPA OPPTS 830.7840)*
Partition coefficient n-octanol/water (log value)	Log P_{ow} = 5.7 (at 23 °C) *(calculation based on the individual n-octanol and water solubilities)*	Log K_{ow} = 6.19 (at 25 °C) *QSAR (EPI Suite; KOWWIN v1.68)*
Partition coefficient organic carbon/water (log value)	Log K_{oc} range = 4.26 - 5.16 Log K_{oc} average = 4.71 ± 0.45 *(calculation based on equation from Chapter 4 'Predominantly hydrophobics' in 'European Chemicals Bureau: Technical Guidance Document on Risk Assessment')*	Log K_{oc} range = ≥ 4.4 - ≤ 5 (calculated at 20 °C) *(calculation based on equation from Chapter 4 'Predominantly hydrophobics' in 'European Chemicals Bureau: Technical Guidance Document on Risk Assessment')*

Chemical name	**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**	**perfluamine**
Degradation		
BIOWIN 2	0.0000 (< 0.5) ➔ Does not biodegrade fast	0.0000 (< 0.5) ➔ Does not biodegrade fast
BIOWIN 3	0.2682 (< 2.25) ➔ Ultimate biodegradation longer than months	-1.0187 (< 2.25) ➔ Ultimate biodegradation longer than months
BIOWIN 6	0.0000 (< 0.5) ➔ Not readily degradable	0.0000 (< 0.5) ➔ Not readily degradable
Biodegradation in water: screening tests	*Ready biodegradability* 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 Degradation: 0 % degradation after 28 d (CO_2 evolution, measurement of inorganic carbon concentration, no significant difference with blanks) *(OECD TG 310)* ➔ Not readily biodegradable	NA

Perfluamine and tripropylamine

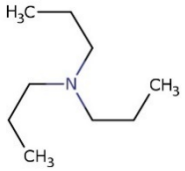
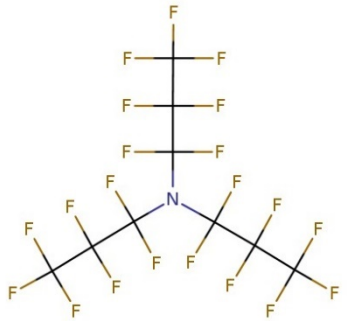
Perfluamine and tripropylamine (EC No 203-047-7) are both liquid substances and have a similar boiling point, and vapour pressure at 20 °C (Table A3). Water solubility is however extremely low for perfluamine, and much higher for tripropylamine. Log K_{ow} (P_{ow}) and Log K_{oc} values are much higher 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
Substance identity		
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	$C_9H_{21}N$	$C_9F_{21}N$
Structural formula		
Physico-chemical properties		
Physical state at 20 °C and 101.3 kPa	Liquid *(observation)*	Liquid *(observation)*

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

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

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.