Environmental risk evaluation report: Perfluoro(2-ethoxy-2-fluoroethoxy)-acetic acid, ammonium salt [EEA-NH_4] (CAS no. 908020-52-0)

Chief Scientist’s Group report

April 2023

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Dr Robert Bradburne
Chief Scientist

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Executive summary

There is growing regulatory concern at international level about the emissions of per- and polyfluoroalkyl substances (PFAS) to the environment. This is due to their extreme persistence, which could lead to long-term exposure of both people and wildlife. High levels of exposure to certain PFAS has also been shown to cause harmful effects in humans and some have been declared to be ‘Persistent Organic Pollutants’ (POPs) under the United Nations Environment Programme (UNEP) Stockholm Convention.

The UK Government is developing an action plan to address the concerns arising from PFAS. As a contribution to this work, the Environment Agency informally reviewed several PFAS that are known to be used at two UK production facilities. The substance reviewed in this evaluation report is ammonium difluoro[1,1,2,2-tetrafluoro-2-(pentafluoroethoxy)-ethoxy]acetate, also known as perfluoro[(2-ethoxy-2-fluoroethoxy)acetic acid], ammonium salt or EEA-NH$_4$ (CAS number 908020-52-0).

EEA-NH$_4$ is a PFAS belonging to the group of perfluoroether carboxylic acids. It is imported to the UK from Japan at a supply level of 10 to 100 tonnes/year and used as a surfactant in the aqueous polymerization process to produce polytetrafluoroethylene (PTFE) at a single site. PTFE is used to make a wide range of articles; EEA-NH$_4$ may be present in PTFE polymers at very low concentrations so may be released during the polymer processing stage as well as from articles.

The Environment Agency has identified publicly available information on the regulatory status, uses, physico-chemical properties, environmental fate and (eco)toxicity of EEA-NH$_4$ and has reviewed this information for reliability. Further information has also been sought from the UK supplier. The data have then been used to conduct an environmental hazard and risk assessment. Human health hazards have only been reviewed in so far as they are relevant for the environmental assessment. Potential risks to people following environmental exposure have not been addressed.

EEA-NH$_4$ is not readily biodegradable and there is no evidence that it degrades significantly via abiotic mechanisms. In addition, there is no information on degradation rates or half-lives available from simulation studies. By analogy with other PFAS, EEA-NH$_4$ is considered to be very persistent (vP). Although experimental data are available to indicate that bioconcentration in fish is likely to be low, it is not possible to draw a conclusion on the bioaccumulation potential of EEA-NH$_4$ in air-breathing organisms in the absence of data on the human clearance time or better predictive methods. EEA-NH$_4$ is not acutely toxic to aquatic organisms, but it is self-classified for human health as Reprotoxic Category 2 by the UK supplier and so is considered toxic (T). Further information is needed to evaluate bioaccumulation (B) in air-breathing organisms before a PBT assessment can be concluded.

Draft criteria have been proposed by the EU to identify chemicals that are persistent, mobile and toxic (PMT) or very persistent and very mobile (vPvM). EEA-NH_4 is likely to meet the draft PMT/vPvM criteria, suggesting that it might be hazardous for groundwaters and has the potential for long distance transport.

An exposure assessment provided by the UK supplier has identified a risk characterisation ratio above 1 for marine surface waters (and sediments) due to emissions from the production of fluoropolymers at a single site. This suggests that there may be a potentially unacceptable level of risk to the marine environment. However, the environmental predicted no effect concentration (PNEC) is an unbounded value based on aquatic ecotoxicity studies which show no acute toxic effects at the highest concentrations tested. The risk characterisation ratio is therefore a “less than” value, which means it could be below 1. No risks have been identified for other environmental compartments or life cycle stages based on risk characterisation ratios.

A number of recommendations are made to the UK supplier of EEA-NH_4 to improve their registration data package to allow a more robust assessment of the environmental hazards and risks posed by EEA-NH_4. This report, along with others in this series, will be used by the Environment Agency to inform the UK Government action plan on PFAS and the PFAS Regulatory Management Options Analysis (RMOA) being conducted under the UK REACH Regulation.

Introduction

There is growing regulatory concern at international level about the emissions of per- and polyfluoroalkyl substances (PFAS) to the environment. This is due to their extreme persistence, which could lead to long-term exposure of both people and wildlife. High levels of exposure to certain PFAS has also been shown to cause harmful effects in humans and some have been declared to be ‘Persistent Organic Pollutants’ (POPs) under the United Nations Environment Programme (UNEP) Stockholm Convention.

The UK Government is developing an action plan to address the concerns arising from PFAS. As a contribution to this work, the Environment Agency informally reviewed several substances that are being used at two known UK production facilities, namely AGC Chemicals Europe Ltd of Thornton Cleveleys, Lancashire and F2 Chemicals Ltd of Preston, Lancashire. Based on information provided by these UK Companies, a provisional list of PFAS for further consideration was drawn up. This included the following eight substances which were, at the time, registered at more than 1 tonne per year under the EU REACH Regulation[1] and subsequently also under UK REACH. Additionally a potential substitute for perfluorooctanesulfonic acid (PFOS, which is a known POP) that had been identified from UK surface water monitoring data. All of the substances chosen for further evaluation are listed below:

- **Ammonium difluoro[1,1,2,2-tetrafluoro-2-(pentafluoroethoxy)ethoxy]acetate - also known as perfluoros[(2-ethoxy-2-fluoroethoxy)acetic acid], ammonium salt or EEA-NH_4 (CAS no. 908020-52-0)**
- Trideca-1,1,1,2,2,3,3,4,4,5,5,6,6-fluorohexane - also known as 1H-perfluorohexane or 1H-PFHx (CAS no. 355-37-3)
- 3,3,4,4,5,5,6,6,6-Nonafluorohexene - also known as perfluorobutylethylene or PFBE (CAS no. 19430-93-4)
- 1,1,1,2,2,3,3-Heptafluoro-3-[(trifluorovinyl)oxy]propane - also known as perfluoro(propyl vinyl ether) or PPVE (CAS no. 1623-05-8)
- 1,1,1,2,2,3,3,4,5,5,5-Undecafluoro-4-(trifluoromethyl)pentane - also known as perfluoroisohexane or PFiHx (CAS no. 355-04-4)
- Perflunafene - also known as perfluorodecalin or PFD (CAS no. 306-94-5)

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[1] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) - see: https://ec.europa.eu/environment/chemicals/reach/reach_en.htm

- Hexafluoropropene or HFP (CAS no. 116-15-4)
- Octafluoropropane - also known as perfluoropropane or PFP (CAS no. 76-19-7)

The additional substance also being considered is:

- 6:2 Chlorinated polyfluorinated ether sulfonate, 6:2 Cl-PFESA - also known as ‘F-53B’ (CAS no. 73606-19-6)

This report summarises the evaluation of the substance highlighted above in **bold** (i.e. EEA-NH_4), to address the following questions:

- What data are currently available, and are they sufficiently reliable to assess the environmental hazards and risks from this substance?
- Can we establish numerical exposure limits for assessing environmental impacts (e.g. for use under permitting regimes)?
- Is this substance potentially able to reach remote environments and what is its groundwater contamination potential?
- Is this substance a potential candidate for future risk management?
- What information gaps remain, relative to the registered tonnage of this substance and, if required, what is the most appropriate way of obtaining this information?

The Environment Agency has performed a literature review (Appendix A). Information on the substance’s properties and uses is also provided on the European Chemicals Agency (ECHA) public dissemination website. EEA-NH_4 was subject to a formal Substance Evaluation by Germany in 2017 under the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation (EC) No. 1907/2006. Unless stated otherwise, the ECHA website and draft REACH Substance Evaluation report (BAUA, 2018) and final evaluation conclusion document (BAUA, 2021) are the main sources of regulatory information used in this report. Further information was also provided by the UK supplier.

The report describes the substance and its structural analogues, its analytical chemistry, manufacture and use, regulatory status and then various environmentally relevant properties. This is followed by an environmental hazard assessment, then an exposure and risk assessment. The final section summarises the findings of this review. Although the focus of this report is on environmental hazards and risks, there is a brief summary of the available mammalian toxicology data that are relevant to the environmental assessment. An assessment of risks to people is not included. This is not a formal UK REACH evaluation.

1 Substance identity

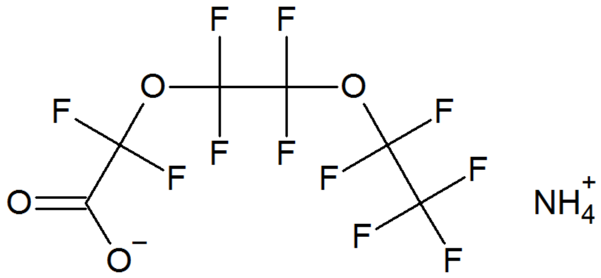
1.1 Name and other identifiers

Table 1.1 Substance identifiers

Public name	Ammonium difluoro[1,1,2,2-tetrafluoro-2-(pentafluoroethoxy)-ethoxy]acetate
IUPAC name	Ammonium difluoro[1,1,2,2-tetrafluoro-2-(pentafluoroethoxy)-ethoxy]acetate
EC number	700-323-3
Alternative name and acronym	Perfluoro(2-ethoxy-2-fluoroethoxy)acetic acid ammonium salt or EEA-NH_4*
CAS number	908020-52-0
Index number in Annex VI of the CLP Regulation	-
Molecular formula	$C_6H_4F_{11}NO_4$
Molecular weight	363.08 g/mol
SMILES code(s)	N.OC(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(F)(F)F (ECHA, 2021b) [NH4+].[O-]C(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(F)(F)F (US EPA, 2021a) C(=O)(C(OC(C(OC(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-].[NH4+] (PubChem, 2021a)
Synonyms	Acetic acid, 2,2-difluoro-2-[1,1,2,2-tetrafluoro-2-(1,1,2,2,2-pentafluoroethoxy)ethoxy]-, ammonium salt (1:1) Ammonium perfluoro-3,6-dioxaoctanoate Perfluoro[(2-ethyloxy-ethoxy)acetic acid], ammonium salt*
Type of substance	Mono-constituent

Note: * The substance is referred to using its abbreviated form [EEA-NH4] for the purposes of this report.
SMILES - Simplified Molecular Input Line Entry System

Figure 1.1Structural formula of EEA-NH_4



Further details of the composition (e.g. purity, impurities, etc.) of EEA-NH_4 are confidential.

1.2 Structurally related substances

EEA-NH_4 is a perfluoroether carboxylic acid (PFECA) (OECD, 2018). The presence of two lone pairs of electrons on each oxygen atom makes hydrogen bonding with water molecules possible. The ether group could potentially act as a point for chemical attack within the molecule, although ethers are generally of low reactivity. In addition, fluorine atoms are highly electronegative and so will withdraw charge away from the lone pairs, which may increase stability compared with other alkyl ethers.

Structurally related substances to EEA-NH_4 were identified through the US Environmental Protection Agency (US EPA) CompTox Dashboard (US EPA, 2021a) and the PubChem Dashboard (PubChem, 2021a). The dashboards identify related substances in their records using connectivity (first layer 'InChI'), mixture components and isotopic isomers, and the Tanamito coefficient (>0.8). InChI is the IUPAC international identifier, and uses a software model to assign an identifier to a molecule which describes structure. The dashboards suggested 22 structural analogues, tabulated in Appendix B. However, since none of these substances has been subject to regulatory review or registration under EU REACH, there are insufficient data for comparison with EEA-NH_4. The Environment Agency has therefore chosen to consider fairly well studied carboxylic acids that have a highly fluorinated alkyl chain for use in weight-of-evidence judgments for the purposes of this evaluation. The selected analogues are listed in Table 1.2 and their relationship to EEA-NH_4 is summarized as follows:

- The parent acid of EEA-NH_4 is perfluoro-3,6-dioxaoctanoic acid (EEA), which is expected to behave in an identical way to the ammonium salt in the environment as it will dissociate to the same anion. Any conclusions for EEA-NH_4 will therefore be applicable to the acid form.
- ADONA/DONA is a fluoroether carboxylic acid with one extra carbon atom in the alkyl chain than EEA-NH_4, although this atom is not fully (per-) fluorinated. It has the same number of oxygen atoms as EEA-NH_4 but they are in different positions along the alkyl chain relative to the carboxylic acid group. ADONA/DONA is therefore a longer

molecule with a higher molecular mass. The carbon-hydrogen bond is potentially a point of chemical attack, so it might be somewhat more reactive than EEA-NH_4.

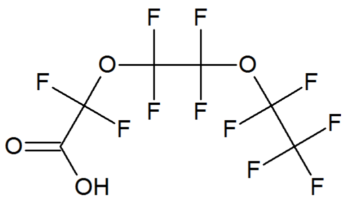
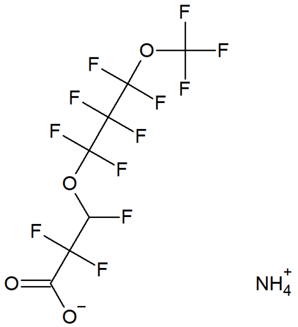
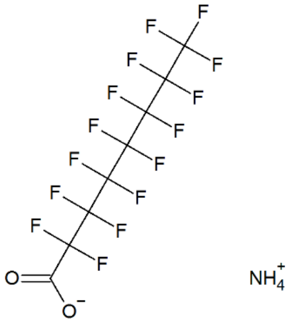
- APFO/PFOA is a perfluoralkyl carboxylic acid (PFCA). It has the same acidic functional group as EEA-NH_4 but has CF_2 groups instead of the 2 ether groups in the alkyl chain. This confers a higher molecular weight and different conformational and electronic properties, and also means that it is less polar. It is therefore not a close analogue, but since it has been studied in some detail, it has been considered in the context of general trends in properties for highly fluorinated substances.

Another PFECA that has attracted regulatory attention is 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoic acid (CAS no. 13252−13−6) (HFPO-DA, also known by its trade name GenX). Compared to EEA-NH_4 it has one less oxygen atom, branching (2 terminal CF_3 groups rather than 1) and 1 less CF_2 group. Due to the branching and lower molecular weight, the Environment Agency has decided not to include this as a relevant analogue.

1.3 Transformation products

As discussed in Section 6.1, EEA-NH_4 is not readily biodegradable but achieved up to 12% degradation after 28 days in one study. The Environment Agency notes that this degree of mineralisation is surprising for such a highly fluorinated substance. No further information is available about the identity or rate of formation of transformation products.

Table 1.2 Substance identifiers for selected analogues of EEA-NH_4

Name	**Perfluoro-3,6-dioxaoctanoic acid (EEA)**	**Ammonium 4,8-dioxa-3H-perfluoro-nonanoate (ADONA)**	**Ammonium perfluorooctanoate (APFO)**
IUPAC name	2,2-Difluoro-2-[1,1,2,2-tetrafluoro-2-(1,1,2,2,2-pentafluoroethoxy)ethoxy]acetic acid	ammonium 2,2,3-trifluoro-3-(1,1,2,2,3,3-hexafluoro-3-trifluoromethoxypropoxy)propionate	Ammonium pentadecafluorooctanoate
CAS number	80153-82-8	958445-44-8	3825-26-1
EC number	820-258-5	480-310-4	223-320-4
Structural formula			
Molecular formula	$C_6HF_{11}O_4$	$C_7H_5F_{12}NO_4$	$C_8H_4F_{15}NO_2$
Molecular weight	346.05 g/mol	395.10 g/mol	431.1 g/mol
SMILES code	C(=O)(C(OC(C(OC(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)O	C(C(C(=O)[O-])(F)F)(OC(C(C(OC(F)(F)F)(F)F)(F)F)(F)F)F.$[NH_4+]$	C(=O)(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)[O-].$[NH_4+]$

Name	**Perfluoro-3,6-dioxaoctanoic acid (EEA)**	**Ammonium 4,8-dioxa-3H-perfluoro-nonanoate (ADONA)**	**Ammonium perfluorooctanoate (APFO)**
Synonyms	Acetic acid, 2,2-difluoro-2-(1,1,2,2-tetrafluoro-2-(1,1,2,2,2-pentafluoroethoxy)ethoxy)- Acetic acid, difluoro(1,1,2,2-tetrafluoro-2-(pentafluoroethoxy)ethoxy)- Difluoro[1,1,2,2-tetrafluoro-2-(pentafluoroethoxy)ethoxy]acetic acid 2,2,4,4,5,5,7,7,8,8,8-Undecafluoro-3,6-dioxaoctanoic acid	3H-Perfluoro-3-[(3-methoxy-propoxy)propanoic acid], ammonium salt Propanoic acid, 2,2,3-trifluoro-3-[1,1,2,2,3,3-hexafluoro-3-(trifluoromethoxy)propoxy]-, ammonium salt (1:1)	Ammonium pentadecafluorooctanoate Ammonium perfluorocaprylate Fluorad FC 143 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-Pentadeca-fluorooctanoic acid, ammonium salt (1:1) Perfluorooctanoic acid, monoammonium salt
Data sources	Gomis *et al*. (2015) US EPA (2021b) PubChem (2021b)	There is an EU REACH registration (ECHA, 2021c). US EPA (2021c) PubChem (2021c)	A detailed regulatory review of properties is available (ECHA, 2013a). US EPA (2021d) PubChem (2021d)
Comment	Parent acid of EEA-NH_4.	The parent acid is 4,8-dioxa-3H-perfluorononanoic acid (DONA), CAS no. 919005-14-4.(ECHA, 2021f)	The parent acid is perfluorooctanoic acid (PFOA), CAS no. 335-67-1.

2 Analytical chemistry

2.1 Regulatory and academic methods

An analytical method is not available in the public EU REACH registration dossier for EEA-NH_4 (ECHA, 2021a). However, the Chemical Safety Report (CSR) contains a reference to a high performance liquid chromatography electrospray ionisation tandem mass spectrometry technique (HPLC-ESI-MS), where detection was performed in a negative ion mode. This was performed for the hydrolysis study presented in the dossier. No further details were given.

The Environment Agency searched the academic literature for analytical methods for the detection of EEA-NH_4 in the following environmental matrices: water, fresh and marine; soil; sediment; sludge; and air. Only the anionic form of EEA-NH_4 is expected in water and other media due to dissociation of the molecule.

The Environment Agency considers that the description of a robust analytical method will typically include the following details:

- Instruments and consumables, including chromatographic column, temperature, mobile phase composition, flow rates, gradient or isocratic separation and the detector optimisation and configuration.
- Certified reference standards, calibration range and sensitivity, limit of detection, limit of quantification, column recoveries, stability and reproducibility.
- Sample preparation including clean-up consumables, concentration techniques and use of internal standards (plus justification for choice) for validation and recoveries, etc.
- Identification and discussion of technical limitations.

Analytical monitoring of EEA-NH_4 in environmental matrices has not been widely performed as part of national or international programmes. It is present in databases operated by the Swedish Chemicals Agency, Organisation for Economic Co-operation and Development (OECD) Global Database and EFSA OpenFoodTox, but no associated analytical methods are presented alongside these.

Internationally validated methods for the analysis of related fluorinated carboxylic acids (such as ADONA) include:

- US EPA Method 533: Determination of per- and polyfluoroalkyl substances in drinking water by isotope dilution anion exchange solid phase extraction and liquid chromatography/tandem mass spectrometry (US EPA, 2019a). Quantitation is performed using isotope dilution. The lowest concentration minimum reporting level (LCMRL) ranges from 1.4 to 13 ng/L depending on the analyte.

- US EPA Method 537.1: Determination of selected per- and polyfluorinated alkyl substances in drinking water by solid phase extraction (SPE) and liquid chromatography/tandem mass spectrometry (LC/MS/MS) (US EPA, 2020b). Quantitation is performed using internal standards. The LCMRL ranges from 0.53 ng/L to 6.3 ng/L depending on the analyte.
- US EPA SW-846 Validated Method 8327: Determination of Selected Per- and polyfluorinated alkyl substances using external standard calibration and liquid chromatography/tandem mass spectrometry (LC/MS/MS); (US EPA, 2019b). This method is published under the Hazardous Waste Test Methods and was developed to measure a group of 24 PFAS in groundwater, surface water, and waste water samples. Quantitation is performed using external standards. The suggested lower limit of quantification (LLOQ) ranges from 10 to 50 ng/L and is analyte dependant. The calibration range for all analytes is 10 to 400 ng/L.

US EPA Method 537.1 (US EPA, 2018) was released in 2018 and updated in 2020 to version 2.0; the only updates were editorial and did not include any technical revisions. This method can be used to quantify 18 PFAS in drinking water, including HFPO-DA.

The US EPA's website notes that these methods were developed and validated for the analyses of finished drinking water (i.e. potable water) from both groundwater and surface water sources. Test samples evaluated during method development for each of the two US EPA PFAS methods included groundwater samples from challenging water matrices. The groundwater sample matrices had very high total dissolved solids (TDS)/hardness (up to 300 mg/L). The evaluation of the groundwater matrices generated acceptable method performance data that met stringent, method-defined quality control criteria. The Environment Agency considers that these methods are likely to be effective for analysing EEA-NH_4, assuming that an appropriate reference standard is available.

It is possible that the following internationally validated methods could also be suitable for the analysis of EEA-NH_4 in other environmental matrices:

- US FDA CAM Method C-010.01 (2019 version) is a single laboratory validated method for food (bread, lettuce, milk and fish). Reporting limits are available on purchase of the method.
- ISO 251010:2009 had no validation details presented. Quantitation is performed using isotope dilution. The reporting limit is 10 ng/L for PFOA.
- ISO 251675:2019 is a multi-laboratory validated method for unfiltered drinking water, ground water, and surface water. Quantitation is performed using external and internal standards. Reporting limits are available on purchase of the method.
- ASTM D7979-20 is a multi-laboratory validated method for water, sludge, influent, effluent and wastewater. Quantitation is performed using direct injection. Reporting limits are available on purchase of the method.

- ASTM D7979-17a is a single laboratory validated method for soil. Quantitation is performed using solvent extraction. Reporting limits range from 25 to 20 000 ng/kg depending on the analyte.

Three academic papers (and references therein) cover the analysis of PFECAs in water (drinking, natural, influent and effluent), soils, sediments, waste water sludge and biota:

- McCord, Newton and Strynar (2018) presented a general quantitative determination of PFECAs by LC–/MS/MS in a single laboratory validated method. The method was developed on spike-recovery samples in surface, drinking, and wastewater for a variety of standards. Relative error measurements for spike-recovery samples in each matrix ranged from 0.36% to 25.9%, with an average error of 10% overall. Coefficient of variation (CV) for each compound ranged from 10 to 28% with an average of 17%. Semi-quantitative concentration estimates for emerging PFECA compounds lacking analytical standards was also carried out using surrogate calibration curves and mass labelled HFPO-DA as an internal standard. The limit of detection was 16 ng/L. Estimates of the emerging compounds were possible using matched standards, but such estimates may differ from actual concentrations by up to an order of magnitude (or more).
- Munoz, Liu, Duy and Sauve (2019) discusses the analysis of fluoroalkylether compounds in environmental and biomonitoring samples. They stated that extensive monitoring activities were conducted from 2015 to 2019 for various substances including ADONA. Information on the methods employed for quantitative and semi-quantitative analysis were provided as part of the Supporting Information, including sample preparation and mass spectrometry analysis, analytical performance, and limitations. In particular, the compiled database of MS/MS fragment ions (n = 111) can be useful in spectrum interpretation of novel ether-PFAS.
- Zheng, Liu, Yin, Shen, Wang and Wu (2020) established a comprehensive method to analyse 17 classes of 58 PFAS in surface water by ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) after automated solid phase extraction (SPE). The method showed acceptable recoveries and precision with recoveries of 60 to 130% and RSD less than 30% with a few exceptions, and method detection limits (MDLs) of 0.004 to 2.0 ng/L.

2.2 Company-specific monitoring method

AGC Chemicals Europe Limited is required by their Environment Agency permit (EPR/BU5453IY) issued under the Environmental Permitting (England and Wales) Regulations 2016 to monitor for EEA-NH_4 (called 'SAA-1000' by AGC) in aqueous effluent from their production site. An LC/MS quantification method is used by an external un-named laboratory using sample standards of EEA-NH_4 to produce a calibration curve. Gradient separation was performed on an Agilent Poroshell EC-C18 column (3.0 mm x 50 mm, 2.7 µm internal diameter) using mobile phases of methanol and ammonium acetate (40 mM) at a flow rate of 0.3 mL/min. Electrospray ionisation was performed in conjunction with the mass spectrometer in negative polarity. The Environment Agency considers that this method is appropriate.

3 Import, manufacture and uses

Although the UK left the European Union (EU) at the end of January 2020, European chemicals legislation in place by December 2020 has been retained and transposed in to UK law. ECHA, who administer EU REACH as well as the EU Classification, Labelling and Packaging (CLP) Regulation ((EC) No. 1272/2008), is therefore still a relevant source of information about industrial chemicals on the UK market at the time of writing.

A single UK supplier, AGC Chemicals Europe Ltd (www.agcce.com), which has a manufacturing site at Thornton Cleveleys, near Blackpool, Lancashire has registrations under both EU and UK REACH. EEA-NH_4 is registered under both regimes at a supply level of 10 to 100 tonnes/year. It is imported into the UK from Japan.

AGC Chemicals Europe Ltd has an environmental permit (ref: EPR/BU5453IY) under the Environmental Permitting (England and Wales) Regulations 2016. It produces two main product streams:

- polytetrafluoroethylene (PTFE) with a capacity up to 4 000 tonnes/year
- ethylene-tetrafluoroethylene (ETFE) with a capacity up to 2 000 tonnes/year

According to the European Food Safety Agency (EFSA) application for use as a processing aid in the production of food contact materials, EEA-NH_4 is used as a surfactant during production of PTFE in amounts up to 0.83% weight by weight (w/w) polymer, with no function in the final article (EFSA, 2011). The Environment Agency understands that EEA-NH_4 was developed as a direct replacement for PFOA in the polymer production process and it is not used to make derivatives.

An overview of uses of EEA-NH_4 is also provided in the EU REACH registration information on the ECHA website. This is presented in Table 3.1.

Table 3.1 Overview of uses

Life cycle stage	Use(s)
Manufacture	None identified in registration dossier
Formulation	None identified in registration dossier
Uses at industrial sites	PROC 1: Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 15: Use as laboratory reagent
Uses by professional workers	None identified in registration dossier
Consumer uses	None identified in registration dossier
Article service life	None identified in registration dossier

Note: PROC codes are Process C, descriptors for the process types

4 Summary of relevant regulatory activities

4.1 Europe

4.1.1 European Chemicals Agency (ECHA)

The Public Activities Co-ordination Tool (PACT) (https://echa.europa.eu/pact) provides an overview of the substance-specific activities that EU regulatory authorities are working on under the REACH and CLP Regulations. EEA-NH_4 has been identified on PACT for both Dossier Evaluation and Substance Evaluation.

The Dossier Evaluation was concluded in October 2018 (ECHA, n.d.). EEA-NH_4 was subject to a Substance Evaluation by Germany in 2017 under the EU REACH Regulation (EC) No. 1907/2006 (https://echa.europa.eu/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table/-/dislist/details/0b0236e1807eddbb). This was based on concerns about suspected persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) properties and environmental exposure. An additional concern identified during the evaluation was its potential for high mobility in water and soil and a possible impact on drinking water sources. The German Competent Authority has subsequently terminated the decision-making process, the conclusion document has now been published (BAUA, 2021).

Between May and July 2020, the national authorities of Germany, the Netherlands, Norway, Sweden and Denmark invited interested parties to send in evidence and information on the use of PFAS in preparation for a joint REACH restriction proposal. The current scope of the work is wide, and includes all substances that contain at least one aliphatic -CF_2- or -CF_3 element (https://www.rivm.nl/en/pfas/pfas-restriction-proposal). EEA-NH_4 is therefore within scope of this initiative.

4.1.2 European Food Safety Agency (EFSA)

EFSA provides scientific advice on safety of food additives, enzymes, flavourings, processing aids and other substances intentionally added to food; safety of food packing and other food contact materials.

AGC Chemicals Europe Ltd submitted an application for approval of EEA-NH_4 for use in food contact materials via the UK Food Standards Agency in 2010 (EFSA, 2011). The EFSA Panel on food contact materials, enzymes, flavourings and processing aids (CEF) concluded that there is no safety concern for the consumer if the substance is only used in the polymerisation of fluoropolymers that are processed at temperatures higher than 300 °C for at least 10 minutes (EFSA, 2011) and the approval was granted on 19th May 2011.

4.1.3 Oslo and Paris Convention for the Protection of the Marine Environment of the North-East Atlantic (OSPAR)

OSPAR is a mechanism by which 15 national governments and the EU co-operate to protect marine resources. Much of OSPAR's work on chemicals is now being addressed by REACH activities.

EEA-NH_4 is not on the OSPAR List of Substances of Possible Concern (https://www.ospar.org/work-areas/hasec/hazardous-substances/possible-concern, accessed July 2020). EEA-NH_4 is also not on the list of Chemicals for Priority Action adopted in 2002 (https://www.ospar.org/work-areas/hasec/hazardous-substances/priority-action, accessed July 2020).

4.2 Regulatory activity outside Europe

4.2.1 United States

The US EPA is planning to carry out tiered toxicity and toxicokinetic testing for a range of PFAS in the near future (Patlewicz *et al.*, 2019). EEA-NH_4 is not listed in the Patlewicz *et al.* study. The US EPA also have a PFAS Strategic Roadmap which sets out their commitments to action for the period 2021-2024 (https://www.epa.gov/pfas/pfas-strategic-roadmap-epas-commitments-action-2021-2024 accessed October 2021).

EEA-NH_4 is not listed as one of the substances undergoing risk evaluation as part of US EPA's existing chemical initiative under the Toxic Substances Control Act (TSCA) to determine whether they present an unreasonable risk to public health or the environment under the conditions of use (US EPA, n.d. a; US EPA, n.d. b).

4.2.2 Canada

A search did not identify EEA-NH_4 as being under assessment under the Prohibition of Certain Toxic Substances Regulations, 2012 (https://www.canada.ca/en/environment-climate-change/services/canadian-environmental-protection-act-registry/substances-list/toxic.html).

4.2.3 Australia

A search did not identify EEA-NH_4 as being under assessment under the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessments, accessed July 2020).

4.2.4 New Zealand

A search did not identify EEA-NH$_4$ as being under assessment under the Hazardous Substances and New Organisms Act 1996 (https://www.epa.govt.nz/industry-areas/hazardous-substances/, accessed July 2020; https://www.epa.govt.nz/industry-areas/hazardous-substances/chemical-reassessment-programme/screened-chemicals-list/, accessed July 2020).

4.2.5 Japan

Industrial chemicals are managed under the Chemical Substances Control Law (CSCL), most recently amended in 2009. Under the Act there are 3 lists:

- Class I Specified Chemicals - 28 substances (persistent, bioaccumulative, toxic) (https://www.nite.go.jp/chem/jcheck/list6.action?category=211&request_locale=en)
- Class II Specified Chemicals - 23 substances (toxic and high risk) (https://www.nite.go.jp/chem/jcheck/list6.action?category=212&request_locale=en)
- Priority Assessment Chemical Substance (PACS), currently 226 substances (https://www.nite.go.jp/chem/jcheck/list7.action?category=230&request_locale=en)

EEA-NH$_4$ is not on any of the above lists.

4.3 Other international agreements

4.3.1 United Nations Stockholm Convention on Persistent Organic Pollutants (POPs)

EEA-NH$_4$ is not identified as a POP, and is not currently under evaluation (http://chm.pops.int/TheConvention/ThePOPs/AllPOPs/tabid/2509/Default.aspx, accessed July 2020).

4.3.2 Greenhouse gases

EEA-NH$_4$ is not a gas at normal temperatures and pressures, so is not subject to the EU F-Gas Regulation (EU) No. 517/2014 (https://ec.europa.eu/clima/policies/f-gas/legislation_en#).

5 Physicochemical properties

This evaluation focusses on vapour pressure, water solubility and n-octanol-water partition coefficient, because they are the key physicochemical end points for the environmental assessment of most organic chemicals. Surface tension and dissociation constant are also considered. The available information is discussed in this section, and a conclusion drawn about which value the Environment Agency considers most suitable for the further evaluation of this substance.

The source of this information is the publicly available EU REACH registration database (ECHA, 2021a; ECHA, 2021b; accessed March 2021) unless otherwise indicated. The reliability scores provided in the full registration for individual studies are cited. These scores have presumably been generated in accordance with the ECHA R.4. Guidance Document (ECHA, 2011) and generally follow the Klimisch score criteria (Klimisch *et al*., 1997). An independent evaluation has not been possible since original study reports were not available (and have not been requested at this stage) and the EU REACH public registration dossiers generally lack sufficient detail and supporting information. The Environment Agency is therefore not currently in a position to assign its own reliability scores (except in the case of data presented in academic journals or obtained using quantitative structure-activity relationship (QSAR) models).

Where an endpoint value is missing from the registration dossier, or an initial review raised questions around the validity of an experimentally derived value, the assessment has been supplemented with information from analogues (see Section 1.2) and publicly available *in silico* QSAR models. EU REACH registration data for the analogues are taken at face value, although preference is given to regulatory reviews (if available). QSAR models are generally considered to be a screening-level tool and measured values are preferable provided that they are sufficiently reliable. Further information on the models used in this assessment is provided in Appendix C.

Where a value for an endpoint was not presented in the registration dossier, or where questions arose around the validity of an experimentally derived endpoint, openly available QSAR model data were referenced. *In silico* models are screening-level tools and were not used if acceptable measured values were available in the registration dossier. One main database was used to source *in silico* data for this evaluation when required. This was the United States Environmental Protection Agency (US EPA) CompTox Dashboard (https://comptox.epa.gov/dashboard). This database integrates diverse types of relevant domain data through a cheminformatics platform, and is built upon a database of curated substances properties linked to chemical structures (Williams *et al*., 2017). The US EPA CompTox Dashboard allows access to data produced from the QSAR models, these data have been used to supplement information where limited data were presented in the EU REACH registration (data from other open access models are available from the dashboard). In addition, where the EU REACH registration had generated QSAR values for endpoints that were not considered to be feasible the Environment Agency has used

EPISuite™v4.1 to perform further predictions. Additional restraint in judgement of reliability should be applied to the values generated using *in silico* tools because this substance is a salt conjugate. EPISuite™v4.1 inputs rely on SMILES codes that cannot be input as charged substances or fragments.

An overview of physico-chemical data provided in the EU REACH registration or generated by the Environment Agency is presented in Table 5.1. Key data selected for the exposure assessment are presented in Table 10.1.

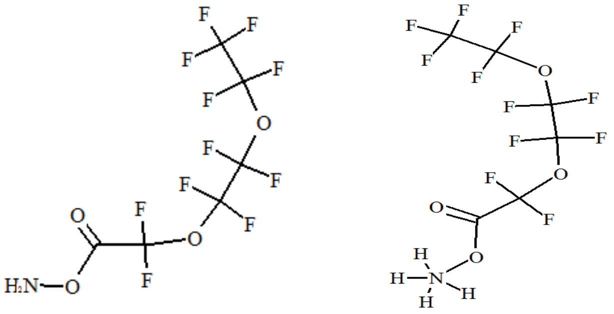
Table 5.1 Summary of physico-chemical properties

Property	Value(s)	Reliability Klimisch score	Reference
Physical state at 20 °C and 101.3 kPa	Solid	Registrant: 2	Unpublished (2008a), from ECHA (2021a)
Melting / freezing point	95.8 °C	Registrant: 1 (key study)	Registration dossier
Boiling point	181 °C	Registrant: 1 (key study)	Registration dossier
Relative density	1 355 kg/m^3 at 20 °C (1.355 g/cm^3; Converted by EA)	Registrant: 1 (key study)	Registration dossier
Vapour pressure	0.002 Pa at 25 °C (predicted)	Registrant: 2 (key study)	Registration dossier
Surface tension	59.1 mN/m 21 °C (90% solution)	Registrant: 1 (key study)	Registration dossier
Water solubility	516 mg/L at 25 °C (predicted)	Registrant: 2 (key study)	Registration dossier
n-Octanol/water partition coefficient (log K_{OW})	1.18 (predicted)	Registrant: 2 (key study)	Registration dossier
Particle size distribution	10% of the material is <236.8 µm 50% of the material is <716.5 µm 90% of the material is <1416.2 µm	Registrant: 1 (key study)	Registration dossier

	0.47% by volume of sample was seen to be <10 µm		
Stability in organic solvents and identity of relevant degradation products	Data waiver	-	Registration dossier
Dissociation constant	Data waiver	-	Registration dossier

The Environment Agency notes that the SMILES code used in the EU REACH registration to supplement some endpoints appears to relate to either a covalently bound NH_2 group, or a structure containing a covalently bound pentavalent nitrogen atom. The structures are provided below. These are not realistic so the Environment Agency has adjusted the SMILES code to represent the neutral form of the molecule (i.e. the parent acid EEA; see Section 1.2) as well as the parent acids of the two chosen structural analogues.

Figure 5.1 Chemical structures used in the EU REACH registration for predictive modelling



5.1 Vapour pressure

5.1.1 Measure data

The EU REACH registration dossier indicates that an attempt was made to measure the vapour pressure of EEA-NH_4 using the static method (EU Method A.4; EC, 2009) (Unpublished, 2008c). This method is equivalent to OECD Test Guideline (TG) 104. The study was terminated due to sample sublimation at 100 °C. Below this temperature the sample was in a solid state and the vapour pressure proved too low to be measured. No further details are provided (ECHA, 2021a).

The Environment Agency notes that the recommended measurement range for the static method according to OECD TG 104 is 0.01 Pa to 105 Pa (10-5 to 102 kPa). The Environment Agency considers that an attempt could have been made to measure the vapour pressure using a method more suited to lower vapour pressure ranges (such as an effusion method).

5.1.2 Predicted data

The key vapour pressure data presented in the registration dossier are derived from an *in silico* prediction using the MPBPWIN (v 1.42) model of EPISuite™. The predicted vapour pressure of EEA-NH_4 was 2.17 x 10^{-6} kPa (1.63 x 10^{-5} mmHg) at 25 °C (ECHA, 2021a). The EU REACH registration assessed the reliability of this value as Klimisch 2 (reliable with restrictions), citing that a validated software estimation method was used. However, there is no description of input parameters, applicability domain, presence of similar substances in the training set, etc.

The Environment Agency was unable to reproduce the EU REACH registration's value using MPBPWIN (v 1.42): the predicted values obtained were 2.57 x 10^{-2} kPa using just the SMILES code[2] or 2.30 x 10^{-2} kPa when refining the output using the measured boiling and melting points presented in the registration dossier (both at 25 °C).

The US EPA CompTox Dashboard contains predicted vapour pressures for EEA-NH_4 from 2 different models (US EPA, 2020a): 5.99 x 10^{-3} kPa (ACD/Labs) or 5.16 x 10^{-4} kPa (OPERA) at 25 °C.

In silico predicted values should always be treated with caution where substances in the training set and external test set are not visible:

- This information was not available for the MPBPWIN model. Therefore no assessment of the applicability can be performed. Guidance provided with the MPBPWIN model indicates that the relationship between the experimental and predicted vapour pressure values for a test set of 1 642 compounds was good, with an R^2 of 0.949, standard deviation of 0.59 and an average deviation of 0.32. It is not known whether the training set contained structurally similar substances of EEA-NH_4.
- This information was not available for the ACD/Labs model. Therefore no assessment of the applicability can be performed.

The OPERA prediction is inside the global applicability domain, with a local applicability domain index of 0.280 and confidence interval of 0.359. Structural analogues of EEA-NH_4 were included in both the training set and external test sets for the OPERA model, and so vapour pressure values for EEA-NH_4 predicted using this model are considered to fall within its applicability domain.

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[2] C(F)(F)(F)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(=O)O

5.1.3 Data from structural analogues

The Environment Agency has sought data for the analogues ADONA and APFO (the ammonium salts of DONA and PFOA respectively). In comparison with these substances, EEA-NH_4 has a lower molecular weight and so is likely to have a slightly higher vapour pressure.

The REACH registration dossier for ADONA (ECHA, 2021c) states that the measured vapour pressure was 1.9 kPa at 20 °C in the key study conducted in accordance with OECD TG 104 and compliant with Good Laboratory Practice (GLP). It is considered to be reliable without restrictions in the EU REACH registration, although the test substance was a 30% w/w solution in water. A similar value of 2.2 kPa at 20 °C was obtained in a supporting study using a 25% w/w solution in water. The Environment Agency notes that the vapour pressure of water is 2.3 kPa at 20 °C (Ambrose and Lawrenson, 1972) and so these results provide no useful information about the vapour pressure of ADONA itself.

Consequently, the Environment Agency interrogated the US EPA CompTox Dashboard for predicted vapour pressures for ADONA. (US EPA, 2021c). A vapour pressure of 3.52×10^{-3} kPa (ACD/Labs) or 9.12×10^{-7} kPa (OPERA) is generated at 25 °C (the OPERA prediction is inside the global applicability domain, with a local applicability domain index of 0.283 and confidence interval of 0.335). The same caveats about reliability apply as for EEA-NH_4.

ECHA (2013a) reports a vapour pressure for APFO of 0.0081 Pa at 20 °C (calculated from measured data; Washburn *et al*., 2005) and 0.0028 Pa at 25 °C (Kaiser *et al*., 2010). The Environment Agency expects the vapour pressure of EEA-NH_4 to be around the same order of magnitude to that of APFO.

5.1.4 Additional sources

Due to the expected relatively low vapour pressure, no further values were sought from the general literature.

5.1.5 Recommended value

In the absence of a measured value, the EU REACH registration relies on a predicted value (2.17×10^{-6} kPa at 25 °C) calculated by a single modelling platform. The robust study summary in the registration dossier does not provide enough information to justify the validity of this prediction and the Environment Agency was unable to replicate this value. As this is the key study, the Environment Agency recommends that the UK supplier provides relevant information in the form of a QSAR Prediction Reporting Format (QPRF), and also considers alternative models.

The reliability of QSARs for this type of substance is highly uncertain, but vapour pressures sourced from the US EPA CompTox Dashboard were in the range 2.17 x 10^{-6} kPa to 5.99 x 10^{-3} kPa at 25 °C.

The information from the analogues ADONA and APFO suggest that the vapour pressure will be below 3 x 10^{-3} kPa at room temperature.

The Environment Agency notes that EEA-NH_4 is expected to have a low vapour pressure since it is an ionic solid. The predicted value of **2.17 x 10^{-6} kPa at 25 °C** presented in the EU REACH registration will be used in further assessment as an approximation.

5.2 Surface tension

5.2.1 Measured data

A surface tension of 59.1 mN/m at 21 °C for an aqueous solution (concentration 90% by volume) is cited in the registration dossier of EEA-NH_4 (Unpublished, 2008d; ECHA 2021a). The study was performed using the ring method set out in EU Method A.5 (equivalent to OECD TG 115) and was considered GLP compliant. The EU REACH registration gave the study a Klimisch score of 1 (reliable without restrictions). The Environment Agency considers this value is valid for the purposes of this evaluation.

5.2.2 Predicted data

For information, the US EPA CompTox Dashboard contains a predicted value of 19.9 mN/m for the parent acid EEA using ACD/Labs software (US EPA, 2021b). Based on the measured value for both the substance itself and its analogue ADONA (see Section 5.2.3), the model is inappropriate for EEA-NH_4.

5.2.3 Data from structural analogues

As reliable measured data for EEA-NH_4 are available, there is no need to present information on analogues. However, it is illustrative to note that the EU REACH registration dossier for ADONA (ECHA, 2021c) states that the measured surface tension test of an aqueous solution at 1 g/L is 61.4 mN/m at 20 °C. The study was conducted in accordance with OECD TG 115 (harmonised ring method) and is compliant with GLP. It is considered to be reliable without restrictions in the EU REACH registration. For comparison, the US EPA CompTox Dashboard contained a predicted surface tension of 19.8 mN/m for ADONA, generated from ACD/Labs (US EPA, 2021c).

5.2.4 Additional sources

Not considered as valid data for the endpoint are available for the substance under evaluation.

5.2.5 Recommended value

The surface tension of EEA-NH_4 is **59.1 mN/m at 21 °C**. Substances showing surface tension lower than 60 mN/m under the conditions of OECD TG 115 should be regarded as being surface active materials. EEA-NH_4 is therefore surface active, and this needs to be taken into account in the measurement and interpretation of other physico-chemical properties such as water solubility and partition coefficients.

Following an informal request for further information, the UK supplier has agreed to carry out further studies of micelle formation for EEA-NH_4, which may affect the conclusion drawn for surface tension.

5.3 Water solubility

5.3.1 Measured data

The EU REACH registration dossier states that a water solubility measurement was attempted using EU Method A.6 (EC, 2008; equivalent to the OECD TG 105) (Unpublished, 2008e; ECHA, 2021a). Initial results were inconsistent with preliminary experimental data and software predictions. The EU REACH registration states that EEA-NH_4 was observed to undergo rapid hydrolysis in water as denoted by changing spectral readings on the same solution. The test was repeated using alternative mobile phases and with multiple buffer solutions (pH between 2 and 7) in an attempt to improve reproducibility. These adjustments were unsuccessful as inconsistent results were still observed (i.e. variation in peak area, peak fronting, multiple peaks, etc.). The dossier does not explicitly state which method was used (e.g. column elution or shake flask).

The EU REACH registration concluded that it is not possible to experimentally determine the water solubility under the conditions of the test because of rapid hydrolysis. The experimental study was therefore terminated (ECHA, 2021a).

The Environment Agency notes that the definitive hydrolysis study presented in the EU REACH registration (see Section 6.1.1) concluded that EEA-NH_4 is hydrolytically stable at environmentally relevant pH values. The Environment Agency notes that some form of reaction also appears to have been reported during the log K_{OW} test (see Section 5.4), but there is no evidence of reaction in other studies that involved water, such as the aquatic toxicity tests (see Section 7.1), nor for the related substance ADONA (see Section 5.3.3 and 5.4.3). The EU REACH registration does not explain this contradiction. EEA-NH_4 is also surface active (see Section 5.2.5) and so care must be taken in the measurement of water solubility because of the potential formation of micelles. This does not appear to have been considered in the EU REACH registration either in the choice of test method. The UK supplier has, following an informal request, committed to carrying out further testing to determine the water solubility of EEA-NH_4.

5.3.2 Predicted data

The key data presented in the EU REACH registration were generated using the WSKOW (v 1.41) and HENRYWIN (v 3.10) models of EPISuite™. The water solubility of EEA-NH_4 was predicted to be 516 mg/L at 25 °C (ECHA, 2021a). The EU REACH registration assessed the data reliability as Klimisch 2 (reliable with restrictions), citing that a validated software estimation method was used. However, there is no description of input parameters, applicability domain, presence of similar substances in the training set, etc.

The Environment Agency was unable to reproduce this value using WSKOW (v 1.42): the predicted values obtained were 5.61 mg/L using just the SMILES code[3] or 17.89 mg/L if the measured melting point is included as the input, both at 25 °C. Using the fragment-based method (Wat Sol v 1.01), the Environment Agency predicted a water solubility of 322.77 mg/L.

The US EPA CompTox Dashboard contained predicted water solubility values for EEA-NH_4 from 2 different models (US EPA, 2021a): 2.32 mol/L [0.84 mg/L] (ACD/Labs) or 1.1×10^{-3} mol/L [3.99×10^{-4} mg/L] (OPERA). Values were converted by the Environment Agency from mol/L to mg/L using a molecular weight of 363.08 g/mol.

In silico predicted values should always be treated with caution where substances in the training set and external test set are not visible:

- This information was not available for the EPISuite™ or ACD/Labs models, so no assessment of the applicability can be performed.
- The OPERA prediction is outside the global applicability domain, with a local applicability domain index of 0.323 and confidence interval of 0.426, so it cannot be considered reliable.

Given the available information for ADONA (see Section 5.3.3), none of these models appear appropriate for this type of substance.

5.3.3 Data from structural analogues

The Environment Agency has sought data for the analogues ADONA and APFO. In comparison with these substances, EEA-NH_4 has a lower molecular weight and will be similarly ionised at environmental pH (see Section 5.6) and so is likely to have a water solubility in the same order of magnitude. Due to the presence of lone pairs of electrons in

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[3] C(F)(F)(F)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(=O)O

its structure that should facilitate hydrogen bonding in water, ADONA is expected to be a better analogue than PFOA.

The EU REACH registration of ADONA states that the test substance is supplied as a 30% aqueous solution and so the solubility is ≥300 000 mg/L by visual inspection. The EU REACH registration considers this value to be reliable with restriction, since it meets “generally accepted principles”. For comparison, the US EPA CompTox Dashboard (Values were converted by the Environment Agency from mol/L to mg/L using a molecular weight of 395.10 g/mol) contained a predicted water solubility of 2.6 mol/L [1.03 mg/L] (ACD/Labs) or 1.43 x 10^{-3} mol/L [5.65 x 10^{-4} mg/L] (OPERA) (the OPERA prediction is outside the global applicability domain, with a local applicability domain index of 0.322 and confidence interval of 0.423) (US EPA, 2021c). Given the reported measured value, these models are clearly not appropriate for this type of substance.

ECHA (2013a) reports a water solubility for APFO of >500 g/L or 14.2 g/L at 2.5 °C. ECHA (2013b) reports a water solubility for PFOA of 9.5 g/L (25 °C) and 4.14 g/L (22 °C).

5.3.4 Additional sources

No relevant references were identified in the literature search.

An aqueous stock solution prepared for the fish bioconcentration test (see Section 6.3.1) reportedly achieved a nominal concentration of 1 000 mg/L.

5.3.5 Recommended value

The EU REACH registration did not report a measured water solubility value due to apparent hydrolysis, although this is not supported by other evidence. Instead the EU REACH registration relies on a predicted value (516 mg/L at 25 °C) calculated by a single modelling platform. The robust study summary in the registration dossier does not provide enough information to justify the validity of this prediction and the Environment Agency was unable to replicate this value. As this is the key study, the Environment Agency recommends that the UK supplier provides relevant information in the form of a QPRF, and also considers alternative models. Further explanation for the reasons behind the apparent degradation observed in the standard test would also be useful, along with a discussion about why this was not seen in other aqueous tests.

However, evidence from the structural analogue ADONA suggests that QSARs are currently unreliable for this type of substance. Information from the analogues ADONA and APFO/PFOA suggest that the water solubility of EEA-NH_4 should be in the order of >300 000 mg/L at room temperature. A nominal EEA-NH_4 concentration of 1 000 mg/L was apparently achieved in the fish bioconcentration study.

The Environment Agency notes that EEA-NH_4 is ionic and has lone pairs of electrons in its structure that should facilitate hydrogen bonding in water. It is therefore expected to have a similar water solubility to ADONA, although the fact that it is surface active may mean that there is a critical micelle concentration. There is significant uncertainty in the actual value. In the absence of better information, the predicted water solubility of **516 mg/L at 25 °C** presented in the EU REACH registration will be used in further assessment as an approximation. This is likely to be an underestimate, and so sensitivity analysis assuming a solubility of **10 000 mg/L is also recommended**.

Following an informal request for further information, the UK supplier has agreed to carry out further studies of micelle formation and water solubility for EEA-NH_4. These may affect the conclusion drawn for this end point.

5.4 Partition coefficient (n-octanol/water; log K_{ow})

5.4.1 Measured data

The EU REACH registration dossier states that a log K_{OW} measurement was attempted using EU Method A.8 (EC, 2008; equivalent to OECD TG 107) (Unpublished, 2008f; ECHA 2021a). The EU REACH registration noted that after the test substance was shaken in n-octanol and water and left to equilibrate the solutions solidified into a gel. The EU REACH registration stated that it is not possible to experimentally determine the log K_{OW} under the conditions of the test. The explanation given was that the substance undergoes a reaction with water.

The Environment Agency notes that although some form of reaction also appears to have been reported during the water solubility test (see Section 5.3.1), there is no evidence of reaction in other studies that involved water such as the hydrolysis study (see Section 6.1.1) or aquatic toxicity tests (see Section 7.1), nor for the related substance ADONA (see Sections 5.3.3 and 5.4.3). This inconsistency has not been explained in the EU REACH registration. EEA-NH_4 is also surface active (see Section 5.2.5) and so care must be taken in the measurement of log K_{OW} because of the potential formation of micelles. The UK supplier has, following an informal request, committed to carrying out further testing to determine the water solubility of EEA-NH_4. Some PFAS are also known to form a third phase between water and n-octanol which prevents the direct measurement of a log K_{OW} value.

5.4.2 Predicted data

The key data presented in the registration was generated using the KOWWIN (v1.67), KOAWIN (v1.10) and BCFWIN (v2.17) models of EPISuite™. The predicted log K_{OW} was 1.18 (ECHA, 2021a). The EU REACH registration assessed the data reliability as Klimisch 2 (reliable with restrictions), citing that a validated software estimation method was used. However, there is no description of input parameters, applicability domain, presence of similar substances in the training set, etc.

The Environment Agency was unable to reproduce this value using KOWWIN (v1.68): the predicted value obtained was a log K_{OW} of 4.05 using the SMILES code[4].

The US EPA CompTox Dashboard contained predicted log K_{OW} values for EEA-NH_4 from 2 different models (US EPA, 2021a): a log K_{OW} of 8.97 (5.30 consensus value) (ACD/Labs) or 2.22 (OPERA).

In silico predicted values should always be treated with caution where substances in the training set and external test set are not visible:

- This information was not available for the EPISuite™ or ACD/Labs models. Therefore no assessment of the applicability can be performed.
- The OPERA prediction is inside the global applicability domain, with a local applicability domain index of 0.288 and confidence interval of 0.332.

Given the available information for ADONA, none of these models appear appropriate for this type of substance.

5.4.3 Data from structural analogues

The Environment Agency has sought data for the analogues ADONA and APFO. In comparison with these substances, EEA-NH_4 has a lower molecular weight and will be similarly ionised at environmental pH (see Section 5.6) and so is considered likely to have broadly similar partitioning properties. Due to the presence of lone pairs of electrons in its structure that should facilitate hydrogen bonding in water, it is expected to have a similar solubility in water and n-octanol as ADONA in particular.

The EU REACH registration of ADONA reports a log K_{OW} of 1.3 at 25 °C and pH 7, measured using OECD TG 117 (HPLC method) in compliance with GLP. The EU REACH registration considers this value to be reliable without restriction. For comparison, the US EPA CompTox Dashboard contained a predicted log K_{OW} of 8.65 (5.78 consensus value) (ACD/Labs) or 2.21 (OPERA) (the OPERA prediction is inside the global applicability domain, with a local applicability domain index of 0.287 and confidence interval of 0.332) (US EPA, 2021c). Given the reported measured value, these models are clearly not appropriate for this type of substance.

ECHA (2013a) has no predicted or measured log K_{OW} for APFO. The US EPA CompTox Dashboard listed 3 log K_{OW} values: 3.89 (OPERA), 5.58 (Concensus; ACD/Labs) and 7.75 (ACD/Labs). ECHA (2013b) includes predicted values of 2.69 or 6.3 for PFOA, but notes

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[4] C(F)(F)(F)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(=O)O

that since it has combined properties of oleophobicity, hydrophobicity and hydrophilicity, the assumption that ‘traditional’ hydrophobic and lipophilic interactions between compound and substrate are the main mechanisms governing partitioning may not be applicable.

5.4.4 Additional sources

No relevant references were identified in the literature search.

Based on the discussion of the organic carbon-water partition coefficient (see Section 6.2.1), a log K_{OC} of 1 is assumed as an approximation based on evidence from analogues. Using the ‘predominately hydrophobic” QSAR in the EUSES model, this would be equivalent to a log K_{OW} of 1.1.

5.4.5 Recommended value

The EU REACH registration did not report a measured log K_{OW} value due to an apparent reaction with water and/or n-octanol, although this reaction has not been observed in most other aqueous studies. Instead the EU REACH registration relies on a predicted value (1.18) calculated by a single modelling platform. The robust study summary in the public REACH registration dossier does not provide enough information to justify the validity of this prediction and the Environment Agency was unable to replicate this value. As this is the key study, the Environment Agency recommends that the UK supplier provides relevant information in the form of a QPRF, and also considers alternative models. Further explanation for the reasons behind gel formation in the standard test would also be useful, along with a discussion about why this was not seen in other aqueous tests. However, evidence from the structural analogue ADONA suggests that QSARs are currently unreliable for this type of substance.

The log K_{OW} value is used in environmental hazard and risk assessment to provide an indication of partitioning behaviour (including bioaccumulation potential) and ecotoxicity. Given the uncertainties in the available information, the Environment Agency considers that direct measurements of bioaccumulation, partitioning to solid phases and ecotoxicity are necessary for this type of substance. For those models for which a K_{OW} value is necessary, the Environment Agency considers that even though it has significant uncertainty, the log K_{OW} of **1.18** presented in the EU REACH registration is suitable for use in further assessment as an approximation.

Following an informal request for further information, the UK supplier has agreed to carry out further studies of micelle formation and log K_{OW} for EEA-NH_4. These may affect the conclusion drawn for log K_{OW}.

5.5 n-Octanol/air partition coefficient (log K_{OA})

Log K_{OA} is non-standard endpoint for hazard assessment under REACH. It is used to predict the partitioning behaviour of organic compounds between air and environmental matrices such as soil, vegetation, and aerosol particles (Meylan and Howard, 2005). Methods for measurement and calculation of the value are discussed in Environment Agency (2009).

5.5.1 Measured data

No experimental log K_{OA} values were presented for EEA-NH_4 in the EU REACH registration (ECHA, 2021a).

5.5.2 Predicted data

The Environment Agency used the KOAWIN v1.10 model of EPISuite™ to predict log K_{OA} values of 8.18 and 6.83. This model uses the log K_{OW} derived within the same modelling platform (4.05). As noted in Section 5.4.2, this value is unreliable, so these log K_{OA} values are also unreliable.

The K_{OA} can be predicted as the ratio between the K_{OW} and the air-water partitioning coefficient (K_{AW}). Using the preferred K_{OW} of 15.1 and K_{AW} of 4.22×10^{-7} (see Section 6.2.2) gives a log K_{OA} of 7.6.

The US EPA CompTox Dashboard has an estimated log K_{OA} of 3.95 for EEA-NH_4 using OPERA software (US EPA, 2021a). This value was deemed to be within the global applicability domain, with a local applicability domain index of 0.979 and confidence interval of 0.897.

5.5.3 Data from structural analogues

The US EPA CompTox Dashboard has an estimated log K_{OA} of 4.25 for ADONA using OPERA software (US EPA, 2021c). This value was deemed to be within the global applicability domain, with a local applicability domain index of 0.95 and confidence interval of 0.813.

The US EPA CompTox Dashboard has a predicted log K_{OA} of 4.16 for APFO using OPERA (CompTox, 2021) software. This value was deemed to be within the global applicability domain, with a local applicability domain index of 0.963 and confidence level 0.827.

5.5.4 Additional sources

No relevant references were identified in the literature search.

5.5.5 Recommended value

The EU REACH registration did not provide a value for the log K_{OA} endpoint. The Environment Agency generated a predicted log K_{OA} of 7.6, based on the ratio of the preferred K_{OW} and K_{AW}, although the reliability of this value is unknown.

The US EPA CompTox Dashboard has log K_{OA} values for EEA-NH_4, ADONA and APFO generated using OPERA software. The OPERA model calculates log K_{OA} directly from the linear free energy relationship (LFER) descriptor: MLFER_Molecular linear free energy relation: Solute gas-hexadecane partition coefficient (US EPA, 2021a). The internal training set of 202 chemicals ranges from log K_{AW} values of around -1 to -12. The external validation set of 68 chemicals ranges from log K_{AW} values of around -1.5 to -11. Both the internal training set of chemicals and the external validation set of chemicals contain structurally related substances to EEA-NH_4. On this basis, the log K_{OA} of 3.95 for EEA-NH_4 appears to be within the applicability domain of the software.

For the purposes of this evaluation the log K_{OA} is considered to be around 7.6.

5.6 Dissociation constant

5.6.1 Measure data

No experimental acid dissociation constant (pKa) data were presented for EEA-NH_4 in the EU REACH registration (ECHA, 2021a).

5.6.2 Predicted data

No predicted pKa data were presented for EEA-NH_4 in the EU REACH registration (ECHA, 2021a). No pKa was available for EEA-NH_4 or EEA from either EPISuite^{TM} or the US EPA CompTox Dashboard (US EPA, 2021a).

5.6.3 Data from structural analogues

No pKa was available for ADONA. The parent acid DONA has a reported pKa of 1 in a 1:1 water-acetonitrile mixture or 2.43 in a 8:2 DMSO-water mixture (ECHA, 2021c). These values are from a 2012 study report and were assigned a Klimish score of 3 (unreliable) in the EU REACH registration. No values are included in the US EPA CompTox Dashboard for comparison.

ECHA (2013a) reports a pKa for APFO of 2.80 in 50% aqueous ethanol and 2.5 in water. The parent acid PFOA has 2 experimentally derived pKa values in the US EPA CompTox Dashboard: 2.50 and 3.80. The experimental details were not available to allow an evaluation of the methodology. ECHA (2013b) includes these and an additional pKa of 1.5 to 2.8.

5.6.4 Additional sources

Vierke *et al.* (2013) noted that the determination of pKa of PFCAs is challenging due to their surfactant properties. These properties lead to enrichment at aqueous surfaces, and self-aggregation in solution below their water solubility limit. At relatively high solute concentrations (around 1 mg/L) substances like PFOA form dimeric clusters, which have higher pKa values compared to individual molecules. A wide range of pKa values have been measured for PFOA (pKa <1.0 to 3.8) and this is a reflection of these difficulties. Theoretical estimations and model calculations are similarly variable with predicted pKa values between −0.2 and 2.9 reported for PFOA.

Vierke *et al*. (2013) verified that dissociated anionic forms of PFCAs have negligible vapour pressures, are soluble in water, and have very low air–water partition coefficients. In contrast, neutral acids were shown to have relatively higher vapour pressures and transfer from water to air. The extent of volatilisation of PFCAs is therefore dependent on the pH of the aqueous phase and their pKa. Vierke *et al*. (2013) used this relationship to derive an experimental pKa of 0.5 for PFOA by determining its volatilisation from water at 1 µg/L in the pH range 0.3 to 6.9. Using this same methodology, the pKa of PFCAs with C_4 to C_{11} chain lengths was reported to be below 1.6. Fractions of the neutral form were < 0.1% at pH 5 and 7 for all of the substances considered. The Environment Agency rates this study as Klimisch 2 (reliable with restrictions).

5.6.5 Recommended value

The Environment Agency expects that EEA-NH_4 will have a similar pKa to PFOA (i.e. around 1.6). Consequently, under environmentally relevant pH conditions, EEA-NH_4 will be present in the form of its anionic conjugate base.

6 Environmental fate properties

The same comments about sources of data, reliability scoring and use of supplemental information apply as for Section 5.

6.1 Degradation

6.1.1 Abiotic degradation

6.1.1.1 Hydrolysis

Table 6.1 Summary of hydrolysis studies

Method	Results	Remarks	Reference
OECD TG 111 (Hydrolysis as a Function of pH) GLP	Preliminary test at 50 °C Recoveries after 5 days: pH 4: 103.8% pH 7: 90.7% pH 9: 94.7% Transformation products were not measured	Registrant: 1 (key study)	Unpublished (2008g) cited in ECHA (2021a)
Non-guideline study Not to GLP	Test at 80 °C Recovery after 6 hours: 98.5%	Non-standard test, not included in the registration dossier	Hori *et al.* (2008a)

The EU REACH registration dossier includes an OECD TG 111 study carried out to GLP (Unpublished, 2008g; ECHA 2021a). The EEA-NH_4 had an analytical purity of 99.4%. The study was performed in the absence of light at 50 °C and at three pH levels (pH 4, 7 and 9). Test vials were sealed to minimise volatile loss of the test substance. After the test systems were dosed, the concentration of the EEA ion was measured on day 0 and day 5. Analysis of the EEA ion was by HPLC-MS/MS with Electrospray Ionisation in the negative mode, so that only the negatively charged EEA ion was measured. The pH was not found to alter the hydrolysis rate, with less than 10% degradation observed at all three pH levels. The EU REACH registration gives the study a reliability rating of Klimisch 1 (reliable without restriction).

The Environment Agency notes that the data indicate that if the substance remains in water the EEA ion is hydrolytically stable under environmentally relevant conditions.

A second study was identified by the Environment Agency during the literature search. Hori *et al*. (2008a) investigated the decomposition of EEA in hot water in the presence or absence of persulfate. An aqueous solution of EEA was maintained at 80 °C for 6 hours and the concentration of EEA at the start and end determined by HPLC analysis with conductometric detection. In the absence of persulfate, 98.5% of the initially added EEA was still present after 6 hours, indicating that the substance did not hydrolyse even at high temperature. The Environment Agency considers that this study is suitable for use as supporting information and that it confirms the findings of the available guideline study.

In contrast to the findings of these studies, some form of degradation appears to have occurred during the water solubility study (see Section 5.3.1). The EU REACH registration does not offer any explanation for this apparent discrepancy.

6.1.1.2 Phototransformation in air

No studies on the phototransformation of EEA-NH_4 in air are available from the EU REACH registration dossier. This is not an information requirement at the current level of supply, so was not discussed further by BAUA in their provisional REACH Substance Evaluation of EEA-NH_4 (2018).

Hori *et al*. (2008b) report that EEA has no UV absorption above 230 nm. This indicates that EEA will not undergo direct photolysis in air (based on OPPTS 835.2310).

Direct photolysis of a carbon-fluorine chain is expected to be very slow, with stability expected to be sustained for more than 1 000 years (Environment Canada, 2012). The effect that the presence of oxygen atoms in the chain has on photolysis rates is not known.

Gomis *et al*. (2015) estimated the degradation half-lives of EEA-NH_4 using the AOPWIN model in EPISuite^{TM} v4.11, which estimates the half-life in air based on molecular structures and an assumed concentration of 5×10^5 hydroxyl molecules/cm^3. A half-life of 31 days was estimated for the neutral form of EEA. The authors note that the predictive power of AOPWIN for PFAS is limited, although some fluorinated substances are included in the training set. Based on comparisons of predicted and measured photodegradation rates for 3 fluorinated substances and 4 legacy PFAS they expect that AOPWIN may underestimate the true half-life in air.

The US EPA CompTox Dashboard contains a predicted atmospheric hydroxylation rate for EEA-NH_4 generated from the OPERA software (US EPA, 2021a): 8.59×10^{-13} cm^3 molecule/sec. However, EEA-NH_4 is not considered to be within the applicability domain of the model, so this value is not reliable.

6.1.1.3 Phototransformation in water

No studies on the phototransformation of EEA-NH_4 in water are available from the EU REACH registration dossier. This is not an information requirement at the current level of supply, so was not discussed further by BAUA (2018).

A single study on phototransformation in water was identified by the Environment Agency during the literature search. Hori *et al*. (2008b) investigated the photochemical decomposition of EEA in water with various catalysts. EEA has no UV absorption above 230 nm, which indicates that it will not undergo direct photolysis in water (OECD TG 316). EEA photodegradation was also investigated in the presence of hydrogen peroxide (H_2O_2) and UV-visible irradiation (>290 nm), to generate hydroxyl radicals. After 12 hours under these conditions, 4.27% EEA was degraded and only low concentrations of fluoride ions and carbon dioxide were formed. EEA photodegradation was also investigated with the addition of Fenton’s reagent (Fe^{2+} and H_2O_2) and UV-visible irradiation as the hydroxyl radical source. After 12 hours, 1.9% of the initially added EEA was degraded. The authors conclude that EEA is not very reactive with hydroxyl radicals.

6.1.1.4 Phototransformation in soil

No studies on the phototransformation of EEA-NH_4 in soil are available from the EU REACH registration dossier or from published data sources. This is not an information requirement at the current level of supply, so was not discussed further by BAUA (2018). The Environment Agency has not located any additional data.

6.1.2 Biodegradation in water

6.1.2.1 Measured data

Table 6.2 Summary of screening biodegradation studies

Method	Results	Reliability	Reference
OECD TG 301 C (Ready Biodegradability: Modified MITI Test (I)) GLP	Not readily biodegradable 8% degradation after 28 days (DOC removal) 12% degradation after 28 days (BOD)	Registrant: 1 (key study) BAUA (2018): 3 (“*no data on validity criteria for the reference substance*”)	Unpublished (2005) cited in ECHA (2021a)

The biodegradation screening study in the EU REACH registration dossier is an OECD TG 301C (modified MITI) guideline study carried out to GLP (Unpublished, 2005; ECHA 2021a). The test was conducted using EEA-NH_4 with an analytical purity of 99.5%. The inoculum used in the study was from a mixture of sewage treatment plant treating municipal sewage, industrial sewage, surface waters and soil as specified in the OECD TG. Whether or not the sludge was pre-adapted to the test material is not specified. Six test vessels were used: an abiotic control, a blank control, a positive control and three vessels with test compound and inoculum. Aniline was used as the positive reference substance. The test was carried out at a concentration of 100 mg/L EEA-NH_4 or aniline with 30 mg/L suspended solids activated sludge over 28 days. Degradation was monitored by measuring the Biological Oxygen Demand (BOD) and the Dissolved Organic Carbon (DOC). Degradation of the test substance was found to be 12% based on BOD and 8% based on DOC removal, showing that the substance did not meet the criteria to be considered readily biodegradable. The degradation of aniline was found to reach 77% after 28 days, but the values at 7 and 14 days were not reported. The EU REACH registration gives the study a reliability rating of Klimisch 1 (reliable without restriction). In their review, BAUA (2018) considered the study to be unreliable because there were "*no data on validity criteria for the reference substance*". The Environment Agency notes that it was not possible to confirm whether the validity criteria were met based on the information provided in ECHA's public registration dossier. In addition, no information is provided on whether the inoculum was pre-adapted to the test material.

6.1.2.2 Predicted data

Gomis *et al*. (2015) estimated the degradation half-lives for the neutral form of EEA using EPISuite^{TM}. Outputs from the BIOWIN3 model, which estimates the biodegradation rate based on molecular structures, were converted into half-lives using the conversion scheme proposed by Aronson, Boethling, Howard and Stiteler (2006). Half-lives of 240 days were estimated for both water and soil. However, the authors note that the predictive power of BIOWIN3 for PFAS is limited due to a lack of data for these substances in the training set and that there is insufficient empirical data to determine the effect of ionisation on degradation rate.

For comparison, the US EPA CompTox Dashboard contains a predicted biodegradation half-life of 3.68 days generated from the OPERA software (US EPA, 2021a), but notes that EEA-NH_4 is outside of the applicability domain of this model, so the prediction is not reliable.

6.1.2.3 Data from structural analogues

Analogues have not been considered by the Environment Agency as the substance is considered to be not readily biodegradable based on an experimental study that the EU REACH registration considers fully reliable. Stability is a feature of highly fluorinated substances.

6.1.2.4 Discussion

The only experimental study available indicates that EEA-NH_4 is not readily biodegradable. Whilst the EU REACH registration rates the study as fully reliable, there is insufficient detail in ECHA's public registration database to confirm whether the validity criteria were met. However, as the EU REACH registration has concluded that the substance is not readily biodegradable, the Environment Agency does not consider that further information is required. As a worst case, the Environment Agency assumes that the substance is not readily biodegradable. The Environment Agency notes that the reported degree of mineralisation (up to 12% over 28 days) is surprising for such a highly fluorinated substance.

6.1.3 Biodegradation in sediment

No relevant information is available in the EU REACH registration dossier or from published data sources. This is not an information requirement at the current level of supply, so was not discussed further by BAUA (2018).

6.1.4 Biodegradation in soil

No relevant information is available in the EU REACH registration dossier or from published data sources. This is not an information requirement at the current level of supply, so was not discussed further by BAUA (2018).

6.1.5 Summary and discussion on degradation

EEA-NH_4 is hydrolytically stable at pH 4, 7, and 9. Based on its UV absorption, EEA will not undergo direct photolysis. EEA has also been found to have low rates of indirect photodegradation in the presence of hydroxyl radicals in water.

A 28-day biodegradation screening study is available which indicates that the substance achieved a low level of mineralisation (up to 12%) over 28 days. The EU REACH registration therefore concludes that EEA-NH_4 is not readily biodegradable, which the Environment Agency agrees with.

There are no environmental simulation data so a realistic half-life in relevant media cannot be established. Highly fluorinated substances generally do not undergo significant abiotic or biotic degradation under relevant environmental conditions. The screening biodegradation result is consistent with this and the EU REACH registration concludes that EEA-NH_4 is potentially persistent in their submitted PBT assessment. The Environment Agency notes that the analogue PFOA is assumed to have a half-life significantly longer than 60 days in water and 180 days in sediments and soils (ECHA, 2013b).

6.2 Environmental distribution

6.2.1 Adsorption/desorption

6.2.1.1 Measured data

The EU REACH registration dossier includes an adsorption/desorption screening study according to OECD TG 121 using the HPLC method (Unpublished, 2008h; ECHA 2021a). The organic carbon-water partition coefficient (K_{OC}) could not be determined because the negatively charged EEA ion exhibited a peak in the chromatogram with a retention time lower than that of urea, which is used as a compound that is not retained by the HPLC column to define t_0. The Environment Agency notes that this implies that EEA-NH_4 could therefore be assumed to have a lower K_{OC} than urea. According to the REACH registration of urea, the log K_{OC} is in the range -1.4 to -1.2 (ECHA, 2021e).

6.2.1.2 Predicted data

Table 6.3 Summary of predicted adsorption/desorption

Method	Results	Reliability	Reference
EUSES calculation for 'predominantly hydrophobics'	log K_{OC} 1.06 Based on a log K_{OW} of 1.18 and the relationship: log K_{OC} = 0.81 log K_{OW} + 0.10	Registrant: not scored	ECHA (2021a)
Bespoke calculation	log K_{OC} 1.41 for anionic EEA	Non-standard calculation, not included in the registration dossier	Gomis *et al.* (2015)
OPERA	log K_{OC} 2.83	QSAR, not included in the registration dossier	US EPA (2021a)

As an experimental log K_{OC} could not be determined, the EU REACH registration dossier (ECHA, 2021a) includes a calculated value based on the predicted log K_{OW} and the equation used in EUSES. As noted in Section 5.4, the log K_{OW} value is likely to be unreliable and consequently the calculated log K_{OC} will be too, regardless of whether the equation is appropriate for this type of substance or not. As a result, BAUA (2018) suggested that a soil column leaching test (OECD TG 312) could be performed but decided not to follow this up with a formal request.

Gomis *et al*. (2015) estimated the log K_{OC} of the anionic form of EEA as 1.41 using a method proposed by Tülp *et al*. (2009). Initially, a log K_{OC} for the neutral form was calculated based on a predicted log K_{OW} from COSMOtherm. This was then adjusted to a log K_{OC} for the anionic form based on the ratio of measured log K_{OC} for the neutral and anionic forms of PFOA and PFOS. As above, the Environment Agency considers that the predicted log K_{OW} value is likely to be unreliable and consequently the calculated log K_{OC} will be too.

The US EPA CompTox Dashboard contains a predicted K_{OC} of 670 (log K_{OC} 2.83) generated from the OPERA software (US EPA, 2021a), but notes that EEA-NH_4 is outside of the applicability domain of this model, so the prediction is not reliable.

6.2.1.3 Data from structural analogues

The Environment Agency has sought data for the analogues ADONA and PFOA. In comparison with these substances, EEA-NH_4 has a lower molecular weight and will be similarly ionised at environmental pH (see Section 5.6) and so is likely to be somewhat more mobile in the environment.

The REACH registration of ADONA (ECHA, 2021c) reports a log $K_{OC} \leq 1.3$ for the DONA anion, measured by HPLC (OECD TG 121) at pH 7.1. The DONA anion eluted before the least-retained reference compound (acetanilide, log K_{OC} 1.25) and was assigned an upper limit. The Environment Agency notes that the log K_{OC} should in fact be <1.25. For comparison, the US EPA CompTox Dashboard contained a predicted log K_{OC} of 2.98 for ADONA, generated from the OPERA software, although the prediction is outside the global applicability domain (US EPA, 2021c). Given the reported measured value, this model is clearly not appropriate for this type of substance.

ECHA (2015) reports several K_{OC} values for the ammonium salt of PFOA in soil (48.9 to 229), activated sludge (20.5 to 59.6) and soil (14), i.e. the log K_{OC} ranges from 1.15 to 2.36. PFOA has a low to moderate potential to adsorb on soil and sludge. Sorption onto sludge is stronger than onto soil and a high mobility of PFOA in soils can be assumed.

6.2.1.4 Recommended value

The information provided in the REACH registration suggests that the log K_{OC} is below -1.2, whilst data for the analogues ADONA and PFOA suggest that the log K_{OC} could be below 1.25 or in the range 1.15 to 2.36 (depending on the medium). The Environment Agency suggests that a **log K_{OC} of 1** can be used as an approximation, although this might be an overestimate. This is broadly equivalent to the recommended log K_{OW} value of 1.18 (see Section 5.4).

6.2.2 Volatilisation

6.2.2.1 Measured data

No relevant information is available in the EU REACH registration dossier or from published data sources.

6.2.2.2 Predicted data

The Environment Agency has calculated a Henry's Law constant for EEA-NH_4 using a number of available QSAR.

Table 6.4 Summary of predicted Henry's Law constant

Method	Results	Reference
Calculated based on vapour pressure, water solubility and molecular weight	0.001 Pa m^3/mole	ECHA (2016a)
HENRYWIN v.3.20	0.18 Pa m^3/mole (bond estimate) (could not be estimated based on group estimate)	US EPA (2012)
OPERA	9.69×10^{-6} Pa m^3/mole	US EPA (2021a)

The vapour pressure of EEA-NH_4 is assumed to be 0.002 Pa at 25°C (Section 5.1) and the water solubility is approximately 516 mg/L at 25°C (Section 5.3), although it could be significantly higher. Based on these values and the molecular weight of EEA-NH_4 the Henry's Law constant can be calculated using Equation R.16-4 of ECHA (2016a) as 0.001 Pa m^3/mol. A higher water solubility would lead to a lower value.

The Environment Agency also used the HENRYWIN (v3.20) model in EPISuite™ to predict a Henry's Law constant based on the SMILES code[5] using two different methods, a bond estimate approach and a group estimate approach. Only a bond estimate could be made for EEA-NH_4. There is no defined applicability domain for the bond estimate in HENRYWIN. However, the molecular weight and predicted Henry's Law constant are within the range of the training set compounds, and all the functional groups present in EEA-NH_4 are included within the bond estimate method.

The US EPA CompTox Dashboard contains a predicted Henry's Law constant of 9.56×10^{-11} atm m^3/mole (9.69×10^{-6} Pa m^3/mole) generated from the OPERA software (US EPA, 2021a). EEA-NH_4 is stated to be outside the applicability domain of the model by CompTox, so this prediction is not reliable.

6.2.2.3 Data from structural analogues

The Environment Agency has sought data for the analogues ADONA and PFOA. Although a measured or experimental Henry's Law constant is not included in the EU REACH registration dossier for ADONA the EU REACH registration states that "as an ionic salt

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[5] C(F)(F)(F)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(=O)O

volatility is not expected” (ECHA, 2021c). ECHA (2015) concludes that under environmental conditions, PFOA is present as conjugate base which is not volatile.

6.2.2.4 Recommended value

Despite the uncertainties in the QSAR, the Environment Agency considers that EEA-NH_4 is unlikely to be volatile in water.

6.2.3 Distribution modelling

To estimate the distribution of EEA-NH_4 in the environment, the Environment Agency has run the EQC v3.0 Mackay Level III fugacity model using the input parameters indicated in Table 6.5. The model was run twice. In scenario 1 all emissions were assumed to be released to water. In scenario 2 emissions were split equally between air, water and soil.

Table 6.5 Estimated distribution of EEA-NH_4

Input Parameter	Value	
Molecular mass	363.08 g/mol	
Melting point	95.8 °C	
Water solubility	516 mg/L	
Vapour pressure	0.002 Pa	
Henry’s Law constant	0.001 Pa m^3/mol	
Log K_{OW}	1.18	
Half-life in air (hours)[a]	2.1×10^{41}	
Half-life in water (hours)[a]	2.1×10^{41}	
Half-life in soil (hours)[a]	2.1×10^{41}	
Half-life in sediment (hours)[a]	2.1×10^{41}	
Model output	Scenario 1	Scenario 2
Air %	0	0.08
Water %	99.8	56.9
Soil %	0.01	42.9
Sediment %	0.2	0.11

Note: a - The upper bound value for biodegradation of a non-readily biodegradable substance in EUSES is 1×10^{40} days to represent infinity (equivalent to 2.1×10^{41} hours).

On the basis of these input parameters and the assumption that EEA-NH_4 does not degrade in the environment, the model predicts that if released to water then nearly all the substance would remain in the water compartment. If released to air, water and soil equally then EEA-NH_4 would be expected to partition to the water and soil compartments.

6.2.4 Long-range transport

The OECD has produced a decision support tool for estimating the long-range transport potential (LRTP) of organic chemicals at a screening level (Wegmann *et al*., 2009). It is a steady state non-equilibrium model in a standardised evaluative environment, and predicts three characteristics that can be used to provide an indication of the LRTP of a substance: Characteristic Travel Distance, Transfer Efficiency and overall persistence (P_{OV}).

Gomis *et al*. (2015) used the OECD LRTP screening tool to estimate the potential distribution of EEA. The input parameters needed to run the model are log K_{OW}, log K_{AW}, and the half-lives in air, water and soil. Gomis *et al*. (2015) estimated the physico-chemical parameters for the neutral form of EEA using the SPARC or COSMOtherm models, which were adjusted to account for the proportion expected to be ionised. The degradation half-lives were those predicted for the neutral form of EEA, as there was too little empirical data to justify any adjustment. Three emission scenarios were modelled, with emissions to air, water or soil only. Gomis *et al*. (2015) predicted that the highest overall persistence was 346 days, with a characteristic travel distance of 592 km and transfer efficiency of 0.015%. Given the uncertainty in the input parameters, the Environment Agency considers this information to be highly uncertain.

To estimate the LRTP of EEA-NH_4, the Environment Agency has performed calculations using the input parameters indicated in Table 6.6.

Table 6.6 Estimated distribution of EEA-NH_4

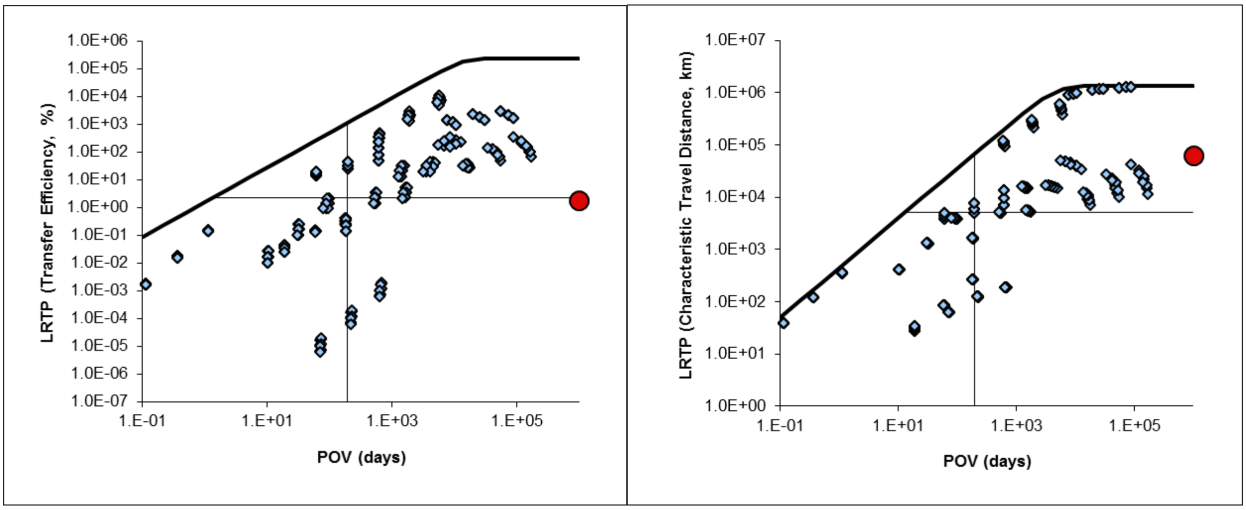
Input Parameter	Value
Molecular mass	363.08 g/mol
Log K_{AW} [a]	-6.4
Log K_{OW}	1.18
Half-life in air (hours)[b]	2.1×10^{41}
Half-life in water (hours)[b]	2.1×10^{41}
Half-life in soil (hours)[b]	2.1×10^{41}
LRTP output parameter	
Characteristic Travel Distance (km)	63016
Transfer Efficiency (%)	1.76
P_{OV} (days)	1.26×10^{40}

Note: a - This is the log of the dimensionless HLC calculated using Equation R.16-5 of ECHA (2016a).

b -The upper bound value for biodegradation of a non-readily biodegradable substance in EUSES is 1 x 10^{40} days to represent infinity (equivalent to 2.1 x 10^{41} hours).

The OECD LRTP screening tool allows comparisons of these three characteristics for a range of substances, provided in Figure 6.1.

Figure 6.1 Long-range transport potential of EEA-NH_4 for predictive modelling



Note: In the left hand graph the x axis is overall persistence in days (Pov) and the y axis is the Characteristic Travel Distance (km). In the right hand graph the x axis is overall persistence in days (Pov) and the y axis is the Transfer Efficiency (%).

Based on this screening tool and the assumption that EEA-NH_4 does not degrade in the environment, it appears that EEA-NH_4 may be capable of long-range transport as it falls into or near the top right quadrant of Figure 6.1. However, evidence of occurrence (or not) of EEA-NH_4 in the Arctic and other remote regions also needs to be taken into account (noting the proximity of industrial activity and population centres). This is outside scope of this evaluation.

6.3 Bioaccumulation

6.3.1 Bioaccumulation in aquatic organisms

6.3.1.1 Measured data

Table 6.7 Summary of bioaccumulation studies

Method	Results	Reliabilty	Reference
OECD TG 305	*Cyprinus carpio* kinetic BCF ≤ 0.59 at 20 µg/L after 28 d kinetic BCF ≤ 5.8 at 2 µg/L after 28 d	Registrant: 1 (key study)	Unpublished (2006) cited in ECHA (2021a)

GLP	(dimensionless, whole body wet weight (ww)) The concentration in fish was below the detection limit. Lipid content: 2.43% (start of exposure) 2.48% (end of exposure)		

The bioaccumulation study in the EU REACH registration dossier was performed in accordance with OECD TG 305 and carried out to GLP using Common Carp (*Cyprinus carpio*) (Unpublished, 2006, cited in ECHA, 2021a). The study design included an uptake phase of 28 days, but no depuration phase. The test was conducted using EEA-NH_4 with an analytical purity of 99.5%. The test material was not radiolabelled. Test solutions were prepared by dissolving EEA-NH_4 in ion-exchanged water to produce a stock solution with a nominal concentration of 1 000 mg/L. The final test solutions had a nominal exposure concentration of 20 and 2 µg/L, and the study was conducted using a flow through exposure for 28 days. Twenty-nine fish were exposed to each exposure concentration, and twelve fish were used as a control. The concentrations of test compound in the exposure media were analysed on the same days as fish were sampled. The analysis method is not stated. Four fish were sampled on days 4, 7, 12, 21 and 28. Sampled fish were weighed and measured before the concentration of test compound was determined. Lipid content of the fish was also measured. Control fish were only sampled at the beginning and end of the experiment.

Average measured exposure concentrations were 1.94 µg/L at the lower exposure rate and 19.0 µg/L at the higher exposure rate, and it is stated that each average concentration was maintained at >91% nominal. At all sampling times the concentration of EEA-NH_4 in fish was below the detection limit (estimated by the Environment Agency to be 11 µg/kg ww). Bioconcentration factors (BCFs) were calculated in the EU REACH registration as ‘less than’ values. The EU REACH registration gave the study a Klimisch score of 1 (reliable without restriction).

It is stated in the REACH registration dossier that the reported BCF are kinetic BCF. However, as no depuration phase was included, the kinetic BCF cannot have been derived. The calculation performed in the EU REACH registration gives the upper bound to the steady state BCF, as the concentration of EEA-NH_4 in fish was below the detection limit after 28 days exposure.

6.3.1.2 Predicted data

The assumption that hydrophobic and lipophilic interactions between compound and substrate (as modelled by the log K_{OW}) are the main mechanisms governing bioaccumulation behaviour may not be applicable for this type of substance due to the oleophobic repellency of the perfluorinated alkyl chain as well as binding to proteins. QSARs have therefore not been considered.

6.3.1.3 Data from structural analogues

For information, the REACH registration of ADONA reports a fish BCF of <0.1, measured in *Cyprinus carpio* using OECD TG 305 with flow through exposure over 34 days, in compliance with GLP (ECHA, 2021c). The EU REACH registration considers this value to be reliable without restriction. PFOA shows a similarly low bioaccumulation potential in aquatic organisms, with a BCF in the range 1.8 to 8.0 (ECHA, 2013b).

6.3.1.4 Recommended value

The Environment Agency has not been able to independently assess the reliability of the experimental study. However, based on the available information in the registration, the study appears to have followed the OECD TG available at the time and the validity criteria are said to have been met. For both exposure concentrations and at all sampling points, EEA-NH_4 was not detected in the fish during the uptake phase, so no depuration period was required. The updated OECD TG 305 (2012) recommends that BCFs are normalised for lipid content and corrected for growth. In this study, the reported average lipid values are fairly constant over the 28 days. Based on the mean of the lipid values (2.46%), the BCFs normalised to a fish lipid content of 5% would be <1.2 and <11.8 for the low and high exposure levels, respectively (assuming that bioaccumulation is directly related to lipid content, which may not be the case for some PFAS). As a kinetic BCF could not be calculated from this study, because no uptake was measured and no depuration phase was included, a correction for growth rate cannot be made. Despite this, the Environment Agency considers that the study is likely to be reliable.

The information provided in the REACH registration indicates that the fish steady state **BCF is ≤ 11.8**. This is consistent with data for similar substances and indicates that bioaccumulation in fish is unlikely to be significant.

6.3.2 Terrestrial bioaccumulation

The EU REACH registration has not assessed the potential for terrestrial bioaccumulation as this is not an information requirement at the current level of supply.

Evidence from other PFAS suggests that terrestrial bioaccumulation may be more relevant than aquatic bioaccumulation for this type of substance. For example, PFOA has a low bioaccumulation potential in aquatic organisms (BCF 1.8 to 8.0) but field studies show that it biomagnifies in air-breathing organisms; together with elevated levels of PFOA in human blood and a half-life in humans of 2 to 4 years, this leads to the conclusion that PFOA is bioaccumulative (ECHA, 2013b).

In terms of bioaccumulation in air breathing organisms, the screening criteria are a log K_{OW} > 2 and log K_{OA} > 5. Based on the values discussed in Section 5, although the log K_{OA} exceeds the threshold, the log K_{OW} does not, so this criterion is not met.

There are two relevant mammalian studies in the EU REACH registration dossier (see section 8). Both studies administered the substance via a single intravenous dose at 10 mg/kg bw. In a study with rats, the half-life for EEA in serum was 9.4 hours in females and 5.4 hours in males (Unpublished, 2007a; ECHA, 2021a). In a study with monkeys, no differences were observed between the sexes, and a half-life of 29 hours was reported for urinary elimination (Unpublished 2007b; ECHA 2021a).

No half-life thresholds are available for defining whether a substance should be considered bioaccumulative in mammals. The clearance time of EEA-NH_4 in rats and monkeys is an order of magnitude lower than PFOA (which has a clearance time of up to 60 days in the same species) (ECHA, 2013b). EEA-NH_4 therefore appears to be less bioaccumulative than PFOA in mammals. However, the human clearance time for PFOA is an order of magnitude higher (2 to 4 years) than that of all tested mammalian species. It is therefore possible that the human half-life of EEA-NH_4 could also be high. No human biomonitoring data are available for EEA-NH_4 according to Uhl *et al*. (2017).

Ng and Hungerbühler (2014) compared a protein (albumin) binding model that they had developed with the Arnot and Gobas (2004) model of absorption of PFCAs in phospholipids. This is based on absorption to liver fatty acid binding proteins and organic anion transporters (Ng and Hungerbühler, 2013). Ng and Hungerbühler (2014) concluded that neither model is preferred over the other. This paper goes on to draw general observations of the pattern of protein binding of PFCAs, including the role of organic anion transporters in renal excretion and reabsorption, but did not consider PFECAs like EEA-NH_4. According to BAUA (2018), EEA-NH_4 has a high affinity to bind to proteins, based on an unpublished and confidential masters thesis at the ETH Zürich (https://ethz.ch/en.html) the Environment Agency has not been able to review this thesis.

The Environment Agency considers that it is not possible to draw a conclusion on the bioaccumulation potential of EEA-NH_4 in air-breathing organisms in the absence of data on the human clearance time or better predictive methods.

6.3.3 Summary and discussion of bioaccumulation

EEA-NH_4 appears unlikely to bioaccumulate significantly in aquatic gill-breathing organisms, based on a measured fish BCF well below 100 L/kg (≤ 11.8). This is consistent with the bioaccumulation behaviour demonstrated by the analogues ADONA and PFOA.

Bioaccumulation in air-breathing organisms is a possibility, but there are no definitive data on the substance itself to support this hypothesis. A conclusion on the bioaccumulation potential of EEA-NH_4 would require further data on the human clearance time or better predictive methods.

7 Ecotoxicology

The same comments about sources of data, reliability scoring and use of supplemental information apply as for Section 5.

7.1 Aquatic compartment (including sediment)

7.1.1 Fish

7.1.1.1 Short-term (acute) toxicity

Table 7.1 Summary of acute toxicity to fish

Method	Species	Analytical method	Results	Reliability	Reference
OECD TG 203 (semi-static) GLP	Japanese Medaka *Oryzias latipes*	HPLC	Limit test 96-h LC_{50} >100 mg/L (nominal)	Registrant: 1 (key study)	Unpublished (2006) cited in ECHA (2021a)

One acute fish toxicity study is included in the REACH registration dossier as the key study (Unpublished, 2006, cited in ECHA, 2021a). This study was carried out according to OECD TG 203 and GLP using *Oryzias latipes* (Japanese Medaka). The test was conducted using EEA-NH_4 with an analytical purity of 99.5% (w/w). Test solutions were prepared by dilution of the test substance with dechlorinated, aerated tap water to a nominal concentration of 100 mg/L and renewal was conducted after 48 hours. Analytical verification of the test concentrations was conducted at the start and end of the exposure, as well as before and after renewal using HPLC. Ten fish were exposed to the test substance and the control. As no mortality was observed in this limit test, the 96-h LC_{50} (half maximal lethal concentration) was reported to be >100 mg/L based on nominal concentrations. The EU REACH registration gave the study a Klimisch score of 1 (reliable without restriction).

The validity criteria for <10% mortality in the control and >60% dissolved oxygen (DO) saturation were met. Most other test parameters were closely related to the standards recommended in OECD TG 203. However, information on the frequency of feeding before the test and the intervals for the measurement of pH, DO and temperature were not available in the registration dossier. In addition, total fish length at study initiation was 2.3 ± 1.2 cm which slightly exceeds the maximum recommended fish length and variability for the test species (2.0 ± 1 cm). Given that no abnormal effects or mortality were observed in either the control or at a test substance concentration of 100 mg/L, the Environment Agency considers that these deviations did not affect the validity of the study.

Although measured concentrations averaged 102% of the nominal concentration throughout the test, information was not available in the registration dossier to determine whether all measured concentrations were within ±20% of the nominal concentrations. The Environment Agency recommends that the robust study summary is updated to include information on the initial and end measured concentrations.

Overall, the Environment Agency considers that the study is reliable for the purposes of this assessment because there were no significant deviations from the study guideline and the study validity criteria were met.

7.1.1.2 Long-term (chronic toxicity)

Long-term toxicity tests are not available. This is not a standard REACH information requirement at the current level of supply.

7.1.2 Aquatic invertebrates

7.1.2.1 Short-term (acute) toxicity

Table 7.2 Summary of acute toxicity to aquatic invertebrates

Method	Species	Analytical method	Results	Reliability	Reference
OECD TG 202 (static) GLP	*Daphnia magna*	HPLC	Limit test 48-h EC_{50} >100 mg/L (nominal) mobility endpoint	Registrant: 1 (key study)	Unpublished (2006) cited in ECHA (2021a)

One acute invertebrate toxicity study is included in the REACH registration dossier as the key study (Unpublished, 2006, cited in ECHA, 2021a). This study was an OECD TG 202 study carried out to GLP using *Daphnia magna*. The substance tested was EEA-NH_4 with an analytical purity of 99.5% (w/w). Test solutions were prepared by dilution of the test substance with dechlorinated, aerated tap water to a nominal concentration of 100 mg/L. Available information on the measured concentrations of the test item at the start and end of the test indicated that these were maintained within ±20% of the nominal concentration (at 99% and 99.3% of the nominal, respectively), although it is not clear whether this represented mean values or the full range of measured test concentrations for replicate samples. Twenty daphnids were exposed to the test substance and the control. No immobilisation was observed in this limit test and therefore the 48-h EC_{50} (half maximal effective concentration) based on immobilisation was reported to be >100 mg/L expressed as the nominal concentration. The EU REACH registration gave the study a reliability score of 1 (reliable without restriction).

The validity criteria for <10% immobility in the controls and ≥3 mg/L DO were met. Actual concentrations of the test substance were verified to be within 80 and 120% of the nominal. All other test parameters were closely related to the standards recommended in OECD TG 202, except for the low water hardness. The concentration of $CaCO_3$ in the study was 41.7 mg/L in comparison to the recommended levels of $CaCO_3$ between 140 and 250 mg/L. Since no abnormal effects or immobility were observed in the control or the test concentration, it is considered that the low water hardness did not impact the reliability of the study.

The Environment Agency recommends that the robust study summary is updated to clarify whether the test concentration maintenance information represents mean values or the full range of measured test concentrations for replicate samples.

Overall, the Environment Agency considers that the study is reliable for the purposes of this assessment because all study parameters were comparable to the OECD TG 202 standards, except for the low water hardness which was not considered to affect the reliability of the study as explained above.

7.1.2.2 Long-term (chronic toxicity)

Long-term toxicity tests are not available. This is not a standard REACH information requirement at the current level of supply.

7.1.3 Algae and aquatic plants

Table 7.3 Summary of toxicity to algae

Method	Species	Analytical method	Results	Reliability	Reference
OECD TG 201 (static) GLP	*Pseudo-kirchneriella subspicata*	HPLC	Limit test 72-h E_rC_{50} >100 mg/L 72-h E_rC_{10} >100 mg/L 72-h NOE_rC <100 mg/L (nominal)	Registrant: 1 (key study)	Unpublished, (2006) cited in ECHA (2021a)

One algal growth inhibition study is included in the REACH registration dossier as the key study (Unpublished, 2006, cited in ECHA, 2021a). No toxicity data are available for aquatic macrophytes, although this is not a standard REACH information requirement.

The algal toxicity study is an OECD TG 201 study carried out to GLP using *Psuedokirchneriella subcapitata*. The test substance was EEA-NH_4 with an analytical purity of 99.5% (w/w). Test solutions were prepared by dilution of the test substance with dechlorinated, aerated tap water to a nominal concentration of 100 mg/L. Available information on the measured concentrations of the test item at the start and end of the test indicated that test concentrations were maintained within ±20% of the nominal concentration (at 96.4% and 98.6% of the nominal, respectively), although it is not clear whether this represented mean values or the full range of measured test concentrations for replicate samples. The 72-h E_rC_{50} was reported to be >100 mg/L expressed as a nominal concentration. Due to slight but statistically significant mean reductions in growth rate by 1.78% and area under the growth curve by 7.24% at 100 mg/L, the 72-h no observed effect concentration (NOEC) values were reported to be less than (but close to) 100 mg/L. The EU REACH registration considered that the study was reliable without restriction (Klimisch 1).

The Environment Agency notes that the preferred observational endpoint for algal studies is growth rate as recommended in the REACH Guidance (ECHA, 2017a). Raw cell data and details on the statistical method are not available to verify if the low percent inhibition of growth rate was statistically significant. In addition, there is a regulatory preference for EC_{10} statistical endpoints as opposed to NOEC values to describe chronic toxicity to algae (OECD, 1998; 2006; 2011; ECHA, 2008; 2017a; 2017b). In this instance, the E_rC_{10} is above 100 mg/L.

Cell densities in the control cultures increased by a factor of 132 within the 72 hour test period which meets the validity criterion of ≥16 for this parameter. Based on confidential information, the Environment Agency considers that the coefficients of variation for section-by-section specific growth rates and for the average specific growth rates during the whole test period in the control cultures met the other OECD TG 201 validity criteria. The Environment Agency recommends that the robust study summary in the registration dossier is updated to include information on the coefficients of variation of control growth and a statement about whether all of the validity criteria for control growth were met.

The Environment Agency also recommends that information on all the initial and end measured concentrations is clarified in the robust study summary.

All other test parameters were closely related to the standards recommended in OECD TG 201.

The Environment Agency considers that the study is reliable for the purposes of this assessment because the study validity criteria were met and all study parameters were closely related to the standards recommended in OECD TG 201. The E_rC_{10} will be used in preference to the NOE_rC for reasons discussed above.

7.1.4 Sediment organisms

No relevant information is available in the EU REACH registration dossier. This is not a standard REACH information requirement at the current level of supply of 10 to 100 tonnes/year, so it was not discussed further by BAUA (2018). The approximate log

K_{OW} of 1.18 (see Section 5.4) and log Koc of 1 (see Section 6.2.1) are below the trigger value of ≥3 for sediment effects assessment under REACH (ECHA, 2017b). Therefore, the Environment Agency does not currently consider that information on sediment-dwelling organisms is required.

7.1.5 Other aquatic organisms

No other relevant information is available.

7.2 Terrestrial compartment

No relevant information is available in the EU REACH registration dossier. This is not a standard REACH information requirement at the current level of supply, so was not discussed further by BAUA (2018). Long-term exposure of terrestrial organisms is possible due to the high persistence of the substance (see Section 6.1) (ECHA, 2017c). However, the Environment Agency does not currently consider that information on soil or other terrestrial organisms is required given the low soil sorption potential indicated by the approximate log K_{oc} of 1 and lack of any signs of toxicity in the aquatic tests (see Section 6.2.1).

7.3 Microbiological activity in sewage treatment systems

Table 7.4 Summary of toxicity to sewage microorganisms

Method	Analytical method	Results	Reliability	Reference
OECD TG 209 (static) GLP	N/A	Limit test 3-h EC_{50} >100 mg/L (nominal concentration) respiration rate inhibition endpoint	Registrant: 1 (key study)	Unpublished (2008) cited in ECHA (2021a)

Note: N/A – not applicable.

One Activated Sludge Respiration Inhibition Test (ASRIT) is included in the EU REACH registration dossier as the key study (Unpublished, 2008, cited in ECHA, 2021a). This study followed OECD TG 209 and was carried out to GLP. The test was conducted using EEA-NH_4 with an analytical purity of 99.4% (w/w) and activated sludge from a sewage treatment plant receiving predominantly domestic sewage.

The test substance was diluted with water purified by reverse osmosis and the sludge was coarsely sieved, washed and diluted with ISO-medium. Test media with a concentration of 100 mg/L of EEA-NH_4, 0.4 g/L of sludge and 32 mL/L of synthetic sewage feed were prepared by adding the corresponding volumes of inoculum and sewage feed to the EEA-NH_4 stock solution. Analytical measurement of the test concentration was not required according to OECD TG 209 because the substance has a high water solubility above the nominal test concentration and it is not considered to be volatile or rapidly degradable (see Sections 5.1 and 6.1).

The EU REACH registration stated that there was no effect on respiration rate, and consequently, the 3-h EC_{50} for sludge respiration rate was reported to be >100 mg/L based on the nominal concentration. The EU REACH registration considered the study reliable without restriction (Klimisch 1).

The Environment Agency notes that the raw data on the percentage respiration inhibition rate was not included in the registration dossier to verify the EC_{50}. Methods of statistical analysis were not detailed and a NOEC was not derived. Although the EC_{50} based on sludge respiration in the positive control with 3,5-dichlorophenol fell within the expected range, no information was available in the registration dossier to assess whether the other validity criteria for oxygen uptake in the blank controls were met. Information was also missing on the DO concentration and the amount of aeration during the contact time. The Environment Agency recommends that the UK supplier revises the robust study summary to include these additional details.

The Environment Agency also notes that the pH of the test mixtures at 8.2 – 8.3 was higher than the recommended range of pH 7.5 ± 0.5 and the concentration of activated sludge in the controls and the test vessels (0.4 g/L) was lower than the recommended concentration of 1.5 g/L. In addition, only two replicates for the control and the test concentration were conducted instead of the recommended 3 replicates for the test concentration and 6 replicates for the control.

Based on these deviations to the study guideline outlined above, the Environment Agency considers that the study is not fully reliable, especially because information on the oxygen uptake in the blank controls is not currently available to assess the relevant validity criteria. However, as the EC_{50} for the reference substance met the validity criterion and no other information on the toxicity of EEA-NH_4 to activated sludge are available, the Environment Agency will use the study for the purposes of this assessment.

7.4 Atmospheric effects

These have not been considered in the EU REACH registration nor BAUA (2018). The substance is not volatile, and so is not expected to partition significantly to the atmosphere (see Section 6.2.2).

8 Mammalian toxicology

BAUA (2018) did not address human health endpoints. With the exception of the reproductive toxicity data, the following information is taken directly from the ECHA public dissemination website entry for EEA-NH_4 (ECHA, 2021a). The focus is on those longer term endpoints which are potentially relevant for determination of the substance as Toxic ('T') according to the REACH Annex 13 criteria (see Section 9.3) or for a wildlife secondary poisoning assessment (see Section 9.6). No acute data are included here and no human health hazard assessment has currently been undertaken. The study details and their reliability (Klimisch) scores are as presented in the EU REACH registration and the Environment Agency has not evaluated this information.

Human health toxicologists at the Health and Safety Executive (HSE) have provided a view on the reproductive toxicity information and the same comments about sources of data, reliability scoring and use of supplemental information apply as for Section 5.

8.1 Toxicokinetics

Two supporting basic toxicokinetc studies are available using the parent acid, EEA (see Section 1.2).

Table 8.1 Summary of toxicokinetic endpoints

Method and test substance	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
No guideline Conducted using EEA GLP	Rat	Administered via a single intravenous dose at 10 mg/kg bw.	Systemic exposure (area under the curve from zero to infinity ($(AUC)0-\infty$)) to EEA for male rats was almost 7-fold higher than for female rats. EEA remained mostly in the circulation in male rats (approximate volume of distribution of 0.2 L/kg), whereas extensive tissue distribution occurred in female rats (volume of	Registrant: 2 (supporting study)	Unpublished (2007) cited in ECHA (2021a)

Method and test substance	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
			distribution of >2.5 L/kg). Terminal elimination phase half-life for EEA in serum: 9.4 hours in female rats and 5.4 hours in male rats. Half-life for EEA in urine: 1.8 hours for female rats and 3.2 hours for male rats. Percent of EEA dose eliminated over 24 hours post-dosing in urine: approximately 65% for male rats and female rats.		
No guideline Conducted using EEA GLP	Monkey	Administered via a single intravenous dose at 10 mg/kg bw.	Pharmacokinetic parameters for EEA in serum were generally similar between the sexes. Half-life for urinary elimination: 29 hours, no sex differences On average, 60-65% of the administered dose of EEA was recovered in the urine during the 7 days post-dosing. One male was observed with tremors (intermittent or continuous), intermittent shivering, depressed attitude,	Registrant: 2 (supporting study)	Unpublished (2007) cited in ECHA (2021a)

Method and test substance	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
			slightly distended abdomen and weak appearance.		

8.2 Repeated dose toxicity

Table 8.2 Summary of mammalian repeated dose toxicity endpoints

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
Repeated dose oral toxicity, OECD TG 407 + other International. TG, 28-day GLP	Rat	Administered via oral gavage at nominal concentrations of 0, 5, 25 and 100 mg/kg bw/day test article for 28 days followed by 14-day recovery period.	NOAEL 5 mg/kg bw/day (nominal); based on increased absolute and relative kidney weights in males of the 25 mg/kg bw/day group and higher	Registrant: 1 (key study)	Unpublished (2006) cited in ECHA (2021a)

8.3 Mutagenicity

Three *in-vitro* genetic toxicity studies and one *in-vivo* genetic toxicity study are available.

Table 8.3 Summary of mutagenicity endpoints

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
Bacterial Reverse Mutation Assay, OECD TG 471 GLP	*Salmonella typhimurium* and *Escherichia coli* strains	Exposure at 156, 313, 625, 1250, 2500, 5000 µg/plate, both in absence and presence of metabolic activation.	Negative (no adverse effects reported at these concentrations). The test article is not mutagenic with or without metabolic activation under the test conditions.	Registrant: 1 (key study)	Unpublished (2005) cited in ECHA (2021a)
Mammalian Chromosome Aberration	Chinese hamster lung	Exposure of cell plates at 723, 868,	Positive (IC50 for structural aberration: 1400	Registrant: 1 (key study)	Unpublished (2006) cited

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
Test, OECD TG 473 GLP	fibroblasts (V79)	1040, 1250, 1500, 1800 µg/ml in the absence of metabolic activation and 603, 723, 868, 1040, 1250, 1500, 1800 µg/ml in the presence of metabolic activation.	µg/ml without metabolic activation and 1100 µg/ml with metabolic activation). The test item does not induce numerical aberrations but it induces structural aberrations under the test conditions.		in ECHA (2021a)
Mammalian Cell Gene Mutation Test, OECD TG 476 GLP	Mouse lymphoma L5178Y cells	Exposure of cell plates at 0, 0.10, 0.19, 0.39, 0.55, 0.79, 1.1, 1.3, 1.6 and 1.8 mmol/L in the absence of metabolic activation and 0, 0.05, 0.10, 0.20, 0.40, 0.58, 0.82, 1.2, 1.7 and 2.4 mmol/L in the presence of metabolic activation.	Negative (no adverse effects reported at these concentrations). Under the study conditions, the test substance is not mutagenic at the TK-locus of mouse lymphoma L5178Y cells.	Registrant: 1 (key study)	Unpublished (2010) cited in ECHA (2021a)
Mammalian Erythrocyte Micronucleus Test, OECD TG 474	Rat	Administered via oral gavage at 0, 125, 250 and 500 mg/kg bw/day for	Negative (no adverse effects at these concentrations).	Registrant: 1 (key study)	Unpublished (2010) cited in ECHA (2021a)

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
GLP		two days followed by a 24 hour recovery period.			

8.4 Carcinogenicity

No information on carcinogenicity is available in the EU REACH registration dossier.

8.5 Toxicity to reproduction (effects on fertility and developmental toxicity)

Table 8.4 Summary of mammalian reproductive toxicity endpoints

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
Reproduction / Developmental Toxicity Screening Test, OECD TG 421 + US EPA OPPTS 870.3550 GLP	Rat	Administered via oral gavage at 0, 5, 25 and 100 mg/kg bw/day for a total of 28 doses for males and 40-52 doses for females.	NOAEL: 5 mg/kg bw/day; general toxicity in the first parental generation based on lower mean body weights, body weight gains and food consumption (significantly affected) during lactation days 1 to 4 in the 100 mg/kg bw/day group females, as well as higher absolute and relative liver weights in the 25 and 100 mg/kg bw/day group males.	Registrant: 1 (key study)	Unpublished (2011) cited in ECHA (2021a)

			NOAEL: 100 mg/kg bw/day; effects on fertility in the first parental generation NOAEL: 5 mg/kg bw/day; developmental toxicity in the F1 generation based on clinical findings of a body that was cool to the touch and of small stature at 100 mg/kg bw/day, as well as reduced post-natal survival and lower mean male and female pup body weights in the 25 and 100 mg/kg bw/day groups		

One reproductive toxicity study is included in the REACH registration dossier as the key study (Unpublished, 2011, cited in ECHA, 2021a). This study was carried out according to OECD TG 421 (pre-2016 version) and GLP using EEA-NH_4 with an analytical purity of 30%. The test substance was administered orally by gavage to groups of rats (Sprague-Dawley 12/sex/dose) at 0, 5, 25, and 100 mg/kg bw/day. Males received at least 14 daily doses prior to mating and were dosed throughout the mating period. Females received 14 daily doses prior to pairing and were dosed through to lactation day 3. All F0 females were allowed to deliver and rear their pups until lactation day 4. Males were sacrificed 1-day after the final dose.

There were no treatment-related effects on male and female mating and fertility indices, male copulation index, or female conception index. The mean number of days between pairing and coitus and mean gestation lengths in the 5, 25, and 100 mg/kg bw/day groups were comparable to controls. The mean numbers of corpora lutea and implantation sites were comparable to controls, indicating no pre-implantation loss.

A lower mean live litter size was reported at 100 mg/kg bw/day only. The effect was not statistically significant but was reported to be below the mean historical control value for the strain of rat in the testing laboratory. No treatment-related effects on gestation length were reported, suggesting that the decrease in live litter size was not a consequence of prolonged parturition. No gross structural external changes were reported for pups from any dose group.

Reduced mean postnatal survival from birth to post-natal day (PND) 4 was reported in the 25 and 100 mg/kg bw/day groups, which included 2 dams with total litter loss at the top dose of 100 mg/kg bw/day. The reduction in pup survival occurred at doses which also caused a decrease in mean pup body weights (up to 10.8% and 27.7% at 25 and 100 mg/kg bw/day, respectively) from birth to PND 4. These changes in top dose pups occurred against a background of slight maternal toxicity (decreased body weight, body weight gain and food consumption) during the lactation period only.

Mean body weights, body weight gains, and food consumption were comparable to controls during the pre-mating and gestation periods for females and over the entire treatment period for males. There were no treatment-related gross changes reported at necropsy in males or females. Absolute and relative liver weights were reported to have increased at 25 and 100 mg/kg bw/day males. Adverse histopathological changes in males were confined to vacuolation/ hypertrophy of basophilic cells in the anterior pituitary gland (minimal to mild severity) in groups (including the control group) but did not show a dose-response. No adverse histopathological changes were reported in dams from any dose group.

On the basis of this study alone, HSE considers that there is no evidence to indicate that EEA-NH_4 has any potential to adversely affect sexual function and fertility. However, the screening test is limited when compared to standard higher tier (Annex IX and X) protocols for investigation of sexual function and fertility (OECD TG 443 or TG 416). Therefore, it is currently not possible to reliably conclude on the potential of EEA-NH_4 to adversely affect sexual function and fertility. This does not constitute an information gap under REACH given the registered tonnage of this substance.

The reduction in postnatal survival at 25 mg/kg bw/day and above appears to be treatment-related and accompanied by large decreases in pup weight at 25 mg/kg bw/day and above. HSE considered this information provides clear evidence that EEA-NH_4 can adversely affect post-natal pup survival.

It is unclear whether these effects on pups were a result of an effect on lactation (nursing behaviour, quantity, or quality of milk production) or secondary to developmental toxicity. Furthermore, as no skeletal or visceral investigations of foetuses/pups or investigation of key postnatal developmental landmarks are part of the study protocol, HSE considered it is currently not possible to reliably conclude on the potential of EEA-NH_4 to adversely affect development in animals. There is no information available from humans to inform on the potential of EEA-NH_4 to adversely affect development.

Overall, the Environment Agency considers this study is reliable for the purpose of this assessment based on the review by HSE.

8.6 Data from structural analogues

The Environment Agency notes that ADONA currently lacks data to classify for specific target organ toxicity (STOT) (single dose), reproductive toxicity and carcinogenicity, but is not classifiable for germ cell mutagenicity or STOT (repeat dose), according to the EU REACH registration dossier (ECHA, 2021c).

The EU REACH registration dossier for DONA (ECHA, 2021f) states that data is lacking to classify DONA for STOT (single and repeat dose), reproductive toxicity, carcinogenicity and germ cell mutagenicity.

ECHA (2013b) concludes that PFOA meets the criteria for classification as toxic for reproduction (Repr. 1B), and causes specific target organ toxicity after repeated dosing, category 1 (STOT RE 1).

8.7 Summary of mammalian toxicology

The EU REACH registration proposes an inhalation Derived No Effect Level (DNEL) for workers of 0.49 mg/m^3 air, based on the most sensitive repeated dose toxicity endpoint with an overall assessment factor (AF) of 9. A dermal DNEL for workers of 0.14 mg/kg bw/day is also proposed, based on the most sensitive repeated dose toxicity endpoint with an overall assessment factor of 36.

The EU REACH registration includes a self-classification as Repr. 2 (H361d), based on the post-natal developmental toxicity observed in the oral reproduction/developmental toxicity screening study; no classifications for mutagenicity or carcinogenicity are proposed (see Section 9.1).

9 Environmental hazard assessment

9.1 Classification and labelling

9.1.1 Harmonised classification

EEA-NH_4 does not have a harmonised classification under the EU Classification, Labelling and Packaging (CLP) Regulation ((EC) No. 1272/2008), nor a mandatory classification under UK CLP.

9.1.2 Self-classification

The EU REACH registration dossier (ECHA 2021a) includes the following hazard warnings*:*

- Acute Tox. 4 (H302)

- Eye Dam. 1 (H318)

- Repr. 2 (H361)

No additional hazard classes are notified in the aggregated self-classifications in the Classification and Labelling (C&L) Inventory (ECHA, 2021d).

9.1.3 Conclusions for classification and labelling

EEA-NH_4 is not readily biodegradable and there is no evidence that it degrades significantly via abiotic mechanisms (see Section 6.1). It is therefore considered to be "not rapidly degradable" for the purposes of hazard classification.

Lipid normalised experimental fish BCF values are ≤ 11.8 (see Section 6.3). As the BCF is < 500 L/kg, EEA-NH_4 does not meet the bioaccumulation criterion for the purposes of hazard classification.

Acute ecotoxicity endpoints are available for fish, invertebrates and algae (see Section 7). The Environment Agency has not been able to independently assess the studies for reliability, but they are considered reliable in the EU REACH registration. All acute L/EC_{50} values exceed 100 mg/L. Since these are higher than 1 mg/L, **Aquatic Acute classification is not required**. This is consistent with the UK supplier's view.

Chronic aquatic toxicity data are not available for fish or aquatic invertebrates. A 72-h E_rC_{10} of >100 mg/L is available for algae, which does not meet the criteria for an Aquatic Chronic classification because it is >1 mg/L. The surrogate approach for this non-rapidly degradable substance using the acute toxicity endpoints for fish and invertebrates also results in no Aquatic Chronic classification because these are all >100 mg/L. An Aquatic

Chronic 4 classification is not applicable because the substance is water soluble and the data indicate that the bioaccumulation potential in aquatic organisms is low. In conclusion, **Aquatic Chronic classification is not required**. This is consistent with the UK supplier's view.

The human health hazard classification has not been considered, except for reproductive toxicity.

In the reproductive toxicity screening study, a lower mean live litter size was reported at 100 mg/kg bw/day only. A reduction in postnatal pup survival (PND 0-4) was reported at doses of 25 mg/kg bw/day and above, which included 2 dams with total litter loss at the top dose of 100 mg/kg bw/day. The reduction in pup survival occurred at doses which also caused a decrease in mean pup body weights (up to 10.8% and 27.7% at 25 and 100 mg/kg bw/day, respectively) from birth to PND 4. These changes in top dose pups occurred against a background of slight maternal toxicity (decreased body weight, body weight gain and food consumption) during the lactation period only.

Based on this information, HSE considers there is a serious, treatment-related effect on postnatal pup survival; the available information does not allow a clear conclusion on whether this is an effect on development or on/via lactation. The UK supplier self-classifies for **reproductive toxicity in Category 2 (Repr. 2, H361d)**.

Given the findings in the available study, on the basis of which the UK supplier self-classifies as Repr. 2, there is a requirement to seek harmonised classification and labelling under the EU CLP Regulation (or a mandatory classification under UK CLP). The Environment Agency recommends that the UK supplier discusses this with HSE at the earliest opportunity.

9.2 Assessment of environmental endocrine disrupting (ED) properties

The ecotoxicity data set does not include any studies that assess ED potential and no additional information was identified during the literature search.

9.3 PBT and vPvB assessment

Persistence: No environmental half-life data are available for comparison with the definitive criteria in REACH Annex 13. EEA-NH_4 is not readily biodegradable and there is no evidence that it degrades significantly via abiotic mechanisms (see Section 6.1). It therefore meets the screening criterion for being potentially persistent (P) or very persistent (vP). Based on evidence from related substances (like PFOA), it is likely to be extremely persistent. It is therefore precautionary to treat it as meeting the vP criterion.

Bioaccumulation: Lipid normalised experimental fish BCF values are <11.8 (see Section 6.3). This is below the definitive bioaccumulation ('B') criterion of 2 000 L/kg in REACH Annex 13.

In terms of bioaccumulation in air breathing organisms, the screening criteria are log K_{ow} > 2 and log K_{OA} > 5. The log K_{OW} is around 1.18 as an approximation, and so this criterion is not met (see Section 5.4).

Evidence from other highly fluorinated substances, such as PFOA, suggests that terrestrial bioaccumulation may be relevant. The Environment Agency considers that it is not possible to draw a conclusion on the bioaccumulation potential of EEA-NH_4 in air-breathing organisms in the absence of data on the human clearance time or better predictive methods.

Toxicity: In terms of aquatic toxicity, a 72-h E_rC_{10} of >100 mg/L is available for algae, which does not meet the REACH Annex 13 criterion for toxicity (T) of <0.01 mg/L (see Section 7). There are no chronic aquatic toxicity data for fish or aquatic invertebrates, but these are not a standard requirement under Annex 8 at the current level of supply. All acute L/EC_{50} values exceed 100 mg/L. Since these are higher than 0.1 mg/L, EEA-NH_4 does not meet the screening criterion for being potentially T based on toxicity to aquatic organisms.

EEA-NH_4 meets the definitive T criterion based on mammalian toxicity as indicated by the self-classification as Repr. 2 presented in the REACH registration dossier and C&L Inventory.

No avian toxicity data are available.

Overall conclusion: EEA-NH_4 is likely to be extremely persistent and is therefore considered to be vP. Based on the current self-classification, it is T. Whether it also screens as potentially B is unclear and further information is needed to evaluate bioaccumulation in air-breathing organisms.

9.4 Groundwater hazard

Draft persistence, mobility and toxicity (PMT) criteria have been developed by the German Federal Environment Agency as intrinsic hazard criteria to identify substances that are difficult to remove during normal wastewater treatment practices and may be a threat to remote aquatic environments and drinking water sources, including groundwater (Arp and Hale, 2019). The criteria for P and vP are consistent with those in REACH Annex 13, whereas the mobile criterion is unique to PMT assessments. The T criteria include those in REACH Annex 13, in addition to considerations for carcinogenicity, effects via lactation, long-term toxicity to the general human population and endocrine disruption potential.

There is no legal basis for these criteria under the REACH Regulation, but for completeness, a brief evaluation is included here.

Persistence: EEA-NH_4 is likely to be extremely persistent and is therefore considered to be vP (see section 9.3).

Mobility: An experimental log K_{OC} value is not available but the information provided in the REACH registration suggests that the log K_{OC} is below -1.4. The Environment Agency suggests that a log K_{OC} of 1 can be used as an approximation, although this might be an overestimate. EEA-NH_4 would therefore meet the draft criterion as being mobile (M) (log K_{OC} ≤4) or very mobile (vM) (log K_{OC} ≤3). Since a definitive log K_{OC} value is not available from a relevant soil study, there is some uncertainty in this assessment, but the Environment Agency considers it likely that the substance will be (highly) mobile in the environment.

Toxicity: EEA-NH_4 meets the definitive T criterion based on mammalian toxicity as indicated by the self-classification as Repr. 2 presented in the REACH registration dossier and C&L Inventory (see Section 9.3).

Overall conclusion: EEA-NH_4 likely to be extremely persistent and is therefore considered to be vP. It is likely to be vM and, based on the current self-classification, it is also T. It therefore meets the draft criteria as a PMT and vPvM substance.

9.5 Greenhouse gas hazard

Many fluorinated gases have very high global warming potentials (GWPs) relative to other greenhouse gases, so small atmospheric concentrations can have disproportionately large effects on global temperatures (US EPA, 2020c).

EEA-NH_4 is not volatile, and so is not expected to partition significantly to the atmosphere (see Section 6.2.2). PFECAs are not covered under the Kyoto Protocol and related EU and UK Regulations for F-gases (EC, 2014; Coffey, 2019). Therefore, the Environment Agency considers there are no concerns for greenhouse gas effects from this substance.

9.6 Limit values

9.6.1 Predicted No Effect Concentration (PNEC) derivation

A PNEC is an indication of an acceptable environmental concentration based on evidence from (eco)toxicity studies. Available hazard data are discussed in Sections 7 and 8. No adverse effects ≥10% have been observed in the available aquatic ecotoxicity studies up to a limit of 100 mg/L. Long-term data for fish and invertebrates are not available.

The EU REACH registration's PNECs are presented in Table 9.1. PNECs have also been derived by the Environment Agency following REACH guidance (ECHA, 2008) and the EUSES model (ECHA, 2019). The values are presented in Table 9.2 and are based on the endpoints that are considered reliable in the EU REACH registration. Although PNECs have been derived, they are "greater than" values.

Table 9.1 PNECs derived for EEA-NH_4 in the EU REACH registration (ECHA, 2021a)

Protection goal	PNEC	Notes
Fresh surface water	>0.1 mg/L	
Freshwater sediment	>0.474 mg/kg sediment dry weight (dw)	EPM
Sewage treatment micro-organisms	>1 mg/L	
Marine surface water	>0.01 mg/L	
Marine sediment	>0.047 mg/kg sediment dw	EPM
Soil	>0.036 mg/kg soil dw	EPM
Secondary poisoning	No data	

Note: EPM – equilibrium partitioning method.

Table 9.2 PNECs derived for EEA-NH_4 by the Environment Agency

Protection goal	Most sensitive toxicity descriptor	Assessment factor	PNEC	Justification/ remarks
Fresh surface water	All acute $L(E)C_{50}$ >100 mg/L	1 000	>0.1 mg/L	No chronic toxicity endpoints available for fish or invertebrates.
Freshwater sediment			>0.172 mg/kg wet weight	EUSES calculation (EPM)
Sewage treatment micro-organisms	3-h EC_{50} >100 mg/L	100	>1 mg/L	Sludge respiration EC_{50} available. No sludge respiration EC_{10} or NOEC available.
Marine surface water	All acute $L(E)C_{50}$ >100 mg/L	10 000	>0.01 mg/L	No chronic toxicity endpoints available for fish or invertebrates and no data for additional taxonomic groups.
Marine sediment			>0.0172 mg/kg wet weight	EUSES calculation (EPM)

Soil			>0.0876 mg/kg wet weight	EUSES calculation (EPM)
Secondary poisoning	NOAEL 5 mg/kg bw/day	Conversion factor 20 Assessment factor 300	0.33 mg/kg food	

9.6.2 Qualitative/semi-quantitative descriptors for other critical hazards

EEA-NH_4 is potentially a PBT and/or PMT/vPvM substance.

Risk management for PBT substances focusses on minimizing environmental releases. If PBT properties are confirmed (or accepted by the UK supplier), risk assessment should be based on an assumption of no safe level of exposure rather than the PNECs derived in Section 9.6. However, it may be appropriate to set a recommended maximum acceptable concentration under legislation such as the Water Framework Directive (Elis-Thomas and Morley, 2003). This would require further policy discussion.

The policy approach for PMT/vPvM substances has not yet been decided.

10 Exposure assessment

10.1 Environment

10.1.1 Environmental releases

The information in this section is based on the CSR submitted by AGC Chemicals Europe Ltd to ECHA, supplemented with other information from further dialogue with the company. Most of the available information is confidential, so only a summary is presented here.

EEA-NH_4 is used as a surfactant in the aqueous polymerization process to produce polytetrafluoroethylene (PTFE), which is subsequently sold to manufacturers of articles as a dispersion or in a powdered form. Releases occur to air and waste water during the manufacture of fluoropolymers.

PTFE has a wide variety of uses both in industrial processes (e.g. in the semi-conductor industry, in cable insulation, in the automotive industry and architecture) and in consumer products (non-stick coatings for cookware, and breathable, water-repellent outdoor garments). EEA-NH_4 can be present as an impurity in the final consumer or industrial product. Environmental releases may therefore occur to waste water and air during the processing and use of PTFE.

10.1.2 Exposure scenarios and measures for reducing emissions to the environment

10.1.2.1 Polymer manufacture

EEA-NH_4 is manufactured in Japan and imported as a 30% dispersion in water to a single site in the UK (AGC Chemicals Europe Ltd, Fleetwood Road North, Thornton-Cleveleys, Lancashire FY5 4QD). There are no other REACH Registrants in the EU or UK, so this is the only source considered as part of this evaluation.

EEA-NH_4 is used exclusively at this site as a surfactant in the aqueous polymerisation process to make fluorinated copolymer resins. This manufacture involves two production lines at the site, one producing aqueous dispersions and the other solids (powders). The EU REACH registration describes the use as taking place in closed systems, with occasional controlled exposure, such as sampling for laboratory analysis for quality control. The lab analysis is done very rarely as the site relies on the testing undertaken at the manufacturing site in Japan. The dispersion is supplied to the AGC Chemicals Europe Ltd site in 1 tonne intermediate bulk containers (IBCs), one of which is used at a time. It is connected to the pipework directly to the dosing system.

The company has an environmental permit (ref: EPR/BU5453IY) under the Environmental Permitting (England and Wales) Regulations 2016. According to the permit, the fluoropolymer production capacity is 6 000 tonnes/year. The permit stipulates a requirement to monitor for EEA-NH_4 in effluent entering the receiving environment, but does not set a numerical limit or require any specific control measures.

EEA-NH_4 is removed following the polymerisation step by a method which depends on the polymer form, as follows:

- Aqueous dispersion: The polymer suspension is mixed with non-fluorinated anionic surfactant and then pumped into the ion exchange resin to remove the EEA-NH_4. Once the ion exchange resin is saturated it is dewatered and packed into drums for disposal via high temperature incineration. The remaining polymer suspension undergoes a concentration step where more of the water is removed, which is then transferred to the west effluent pit.
- Coagulated dispersion: The resulting mixture from the polymerisation process is agitated to coagulate the solid polymer, this turns the polymer into a solid with associated water. The mixture is then filtered to remove the water, which is passed through an ion exchange resin to remove the EEA-NH_4. The water is then pumped to the west effluent pit prior to discharge to the River Wyre. The solids, which contain trace EEA-NH_4, are then heated to dry the polymer, the gaseous emissions of which are passed through an aqueous scrubber to remove most of the residual EEA-NH_4.

Routes of emission to surface water

Waste water from the PTFE process (along with waste water from the ETFE manufacturing process, raw material storage and surface water drainage) drains to the west effluent pit prior to discharge to the River Wyre.

Routes of emission to air

In the production of the coagulated dispersion the gases emitted from the drying oven are passed through the aqueous scrubber to remove the EEA-NH_4.

10.1.2.2 Polymer use

The PTFE product containing non-functional residual amounts of EEA-NH_4 is sold to downstream users. Examples of final uses of the PTFE include as coatings for non-stick frying pans, as an insulator in cables and connector assemblies, as a material for printed circuit boards used at microwave frequencies, for plain bearings or as magnetic stirrer coatings in laboratories.

EFSA (2011) discusses use of the PTFE in food contact materials, including coated cookware (such as coatings on frying pans and articles for oven baking) and moulded articles for industrial use (such as tubings, gaskets, seals, pipes, conveyor belts, etc.). Food contact applications are normally repeated use articles for all types of foods and at all temperatures (single use applications may occur in rare cases). Contact conditions can be up to 2 hours at 230 °C and in rare applications up to 15 minutes at up to 380 °C.

According to EFSA (2011), EEA-NH_4 is completely evaporated (and in a very small part decomposed into volatiles) at temperatures above 250 °C. The PTFE used in food contact applications is processed at high temperatures, typically 380 °C for one hour or more. In the case of coatings or thin articles, this can be up to 430 °C for 10 minutes. It can therefore be expected that any post-polymerization residual content of the substance is efficiently removed during thermal processing (high temperature extrusion, baking or sintering) into a final article. This was supported by an analytical screening experiment on a finished food contact PTFE polymer. Migration of the substance was tested on 5 different commercial test samples including thick PTFE homopolymer tape material as well as thin coated foil sheets. Migration was performed according to repeated use test scheme (3 repeated tests on the same specimen) using 3% acetic acid, 10% ethanol and 95% ethanol as food simulants, where each test was done under contact conditions of 4 hours at reflux temperature. Migration of the substance was analysed after the first experiment and after the third experiment. In these tests a very conservative surface-to-volume ratio of 30 dm^2/kg food simulant was applied. In all cases, migration of the substance was in not detectable at detection limits of 2 ppb in the aqueous food simulants and 6.5 ppb in 95% ethanol. EFSA (2011) concluded that there is no safety concern for the consumer if the substance is only used in the polymerisation of fluoropolymers that are processed at temperatures higher than 300 °C for at least 10 minutes.

The Environment Agency does not know what proportion of the PTFE sold by AGC Chemicals Europe Ltd is used in food contact applications, or whether the high temperature processing described for this application is also used for the other applications.

Routes of emission to surface water

From the limited information available, it is possible that there may be some losses to drain following condensation of any volatilised substance during thermal processing. The Environment Agency does not know whether different processing techniques are used for dispersions. As these are aqueous, there is some potential for losses to drain during handling.

Routes of emission to land

The Environment Agency assumes that unused or waste PTFE (and articles containing it) may be disposed of to landfill. The migration rate of any residual EEA-NH_4 from the PTFE is unknown.

Routes of emission to air

Releases of EEA-NH_4 to air are possible from PTFE during thermal processing. The material from the reactor is dried in an oven to drive off the water, all the gaseous emissions from the oven pass through an aqueous scrubber. The efficiency of the removal is between 41.1 and 99.97%, the mass balance undertaken by the company shows a release of <0.1 tonnes/year.

10.1.3 Release assumptions made by the Environment Agency

AGC Chemicals Europe Ltd supplied a range of information to the Environment Agency, including monitoring data and effluent volumes released to the River Wyre. The following exposure scenarios (ES) were modelled based on:

- the volume used in 2019 and the associated monitoring data supplied ("current scenario"),
- an assumption of a 50% increase in the 2019 volume used in a year ("realistic worst case scenario"), and
- changes in environmental temperature and river flows based on climate change projections ("future scenario").

10.1.3.1 Current scenario

<u>ES 1: Industrial use - polymer manufacture</u>

- Volume used: confidential (based on 2019 data).
- Number of emission days: 330 days/year (CSR).
- Releases to surface water: The Environment Agency has assumed that the 2019 release rate of 0.783 tonnes/year is representative of current operations. This is based on the average effluent concentration and the effluent flow rate.
    - Effluent flow: The average daily volume of effluent discharged to the River Wyre was 803 m^3/day in 2018 and 893 m^3/day in 2019 (company data). The Environment Agency has assumed that the 2019 average daily flow of 893 m^3/day is representative of current operations.
    - River flow: River flows are measured/calculated at an Environment Agency gauging station which lies roughly 16 km upstream of the AGC Chemicals Europe site (St Michael's flow monitoring station at national grid reference SD4633041131). The long-term daily mean flow was 6.67 m^3/s, which equates to 576 288 m^3/day. The 95th percentile low flow was 0.61 m^3/s, which equates to 52 704 m^3/day, and this is the figure that is used in this evaluation. This results in an effluent dilution factor of 60. For comparison, the EU REACH registration assumed a default dilution factor of 10 in their CSR.
    - Marine dilution factor: For sites that discharge direct to the marine environment, a marine dilution factor can be used. The default is 100. In this case, the site discharges to a river which is under tidal influence, and the estuary is nearby. It could be argued that the marine dilution factor might be more relevant. The Environment Agency has no information about the level of dilution in the estuary of the River Wyre. Therefore both the river dilution factor and the marine dilution factor will be applied separately.
- Releases to land: As explained in Section 2.1, there is no release to agricultural land (e.g. via spreading of sewage sludge) from this site. There may be some local deposition from atmospheric releases.

- Releases to air: Releases from the wet scrubber are significantly less than 1 tonne per year.

ES 2: Industrial use - polymer processing

The releases of EEA-NH_4 from the PTFE products supplied to customers is confidential.

The Environment Agency considers that, as a worst case, all residual EEA-NH_4 can be assumed to be completely released during the polymer processing stage to air for all the grades. The entire tonnage can also be assumed to be released within the UK (which is also a worst case scenario as the products are supplied outside of the UK too). The fraction of main local source is set to the EUSES default of 0.5, in the absence of any additional information to refine this figure. The number of release days is 20 days/year, as defined in the by ECHA R.16 Guidance Document (ECHA, 2016a).

10.1.3.2 Realistic worst case scenario

To account for potentially higher use volumes, the Environment Agency has assumed a use of 50% higher than 2019 as a 'realistic worse case' scenario.

- Volume used: confidential.
- Number of emission days: 330 days/year (CSR).
- Releases to surface water: The release has been increased by 50% of the value in the current scenario.
    - Effluent flow: Same as "current" scenario.
    - River flow: Same as "current" scenario.
    - Marine dilution factor: Same as "current" scenario.
- Releases to land: Same as "current" scenario.
- Releases to air: The release from the wet scrubber are still significantly less than 1 tonne per year.

ES 2: Industrial use - polymer processing

Assuming that there is a linear correlation between use volume and residual amounts in PTFE products, the levels would be increased proportionately to the "current" scenario.

10.1.4 Predicted Environmental Concentrations (PECs)

Based on confidential information PECs were estimated in various types of environmental media using the EUSES model (version 2.0.3) for the various life cycle stages. The tonnage, release rates and physico-chemical properties are input parameters, and the relevant information for polymer manufacture is summarized in Table 10.1 and Table 10.2. The concentration in the current scenario is described in more detail in section 10.1.5. A risk characterisation cannot be performed for predatory organisms due to the significant uncertainties in the bioaccumulation behaviour of this type of substance.

Table 10.1 Substance-specific input parameters for the EUSES model

Parameter	Values assumed by the Environment Agency
Molecular weight	363.08 g/mol
Vapour pressure	0.002 Pa at 25 °C
Water solubility at 20 °C	516 mg/L (software estimation)
Octanol-water partition coefficient (log K_{ow})	1.18 (software estimation)
Octanol-carbon partition coefficient (K_{oc})	11.4 L/kg (software estimation)

Note: See Sections 2, 5 and 6 of the main report for the origins of these values.

Table 10.2 Scenarios used for the exposure assessments

Parameter	Scenario	
	Current	Reasonable worst case
Annual use at site	confidential	confidential
Emission days	330 days/year	330 days/year
Daily use at site	confidential	confidential
Regional release to surface water	0.783 tonnes/year	1.16 tonnes/year
Percentage of tonnage used at regional scale	100%	100%
Release factor to water	confidential	confidential
Receiving surface water flow rate	52 704 m^3/day	52 704 m^3/day

Note: This information is the same as that used in the CSR, with the exception of the tonnage (confidential), daily use (due to the higher tonnage), release factors to water and air and the dilution factor (10).

The PECs calculated by the Environment Agency are presented in Table 10.3 and Table 10.4.

Table 10.3 Local PECs calculated by the Environment Agency

Life cycle stage	Compartment	PEC		Unit
		Current scenario	RWC scenario	
Polymer manufacture	Fresh surface water	0.0442	0.0656	mg/L
	Freshwater sediment	0.0442	0.0656	mg/kg ww
	Marine surface water	0.0265	0.0394	mg/L
	Marine sediment	0.0265	0.0394	mg/kg ww

Life cycle stage	Compartment	PEC		Unit
		Current scenario	RWC scenario	
	Air	5.33 x 10^{-5}	7.85 x 10^{-5}	mg/m^3
	Soil	6.59 x 10^{-5}	9.7 x 10^{-5}	mg/kg ww
	Groundwater*	2.24 x 10^{-4}	3.3 x 10^{-4}	mg/L
Polymer processing (dispersion)	Fresh surface water	2.79 x 10^{-5}	4.16 x 10^{-5}	mg/L
	Freshwater sediment	2.79 x 10^{-5}	4.16 x 10^{-5}	mg/kg ww
	Marine surface water	2.73 x 10^{-6}	4.05 x 10^{-6}	mg/L
	Marine sediment	2.73 x 10^{-6}	4.05 x 10^{-6}	mg/kg ww
	Air	3.81 x 10^{-5}	5.71 x 10^{-5}	mg/m^3
	Soil	4.79 x 10^{-5}	7.18 x 10^{-5}	mg/kg ww
	Groundwater*	1.63 x 10^{-4}	2.44 x 10^{-4}	mg/L

Note: RWC – reasonable worst case
dw – dry weight
* The porewater concentration for agricultural soil is used to represent groundwater.

Table 10.4 Regional PECs calculated by the Environment Agency

Compartment	PEC		Unit
	Current scenario	RWC scenario	
Fresh surface water	2.79 x 10^{-5}	4.16 x 10^{-5}	mg/L
Freshwater sediment	2.5 x 10^{-5}	3.74 x 10^{-5}	mg/kg ww
Marine surface water	2.793 x 10^{-6}	4.05 x 10^{-6}	mg/L
Marine sediment	2.48 x 10^{-6}	3.67 x 10^{-6}	mg/kg ww
Air	1.45 x 10^{-9}	2.15 x 10^{-9}	mg/m^3
Groundwater*	9.88 x 10^{-6}	1.48 x 10^{-5}	mg/L

Note: RWC – reasonable worst case
dw – dry weight
* The porewater concentration for agricultural soil is used to represent groundwater.

By way of comparison, using the 95th percentile concentration of 3.2 mg/L in the wastewater discharge to the River Wyre, a daily discharge volume of 893 m^3/day and the 95th percentile low flow of 52 704 m^3/day, the surface water concentration downstream of the outflow at the edge of the mixing zone would be 0.054 mg/L in the EUSES modelling undertaken by the Environment Agency.

As the initial PECs were above the PNECs for the marine compartment, AGC Chemicals Europe Ltd undertook additional modelling of the releases to the Wyre estuary (Ecospan 2021). The model used the average EEA-NH_4 concentration in the site's wastewater discharge of 2.24 mg/L and a maximum concentration of 6.4 mg/L. The maximum concentration used for this modelling was from August 2017 which was outside the date range used by the Environment Agency. The modelling report was reviewed by the Environment Agency, and the parameters and output were considered to be appropriate. The model predicted EEA-NH_4 concentrations for both the average discharge and maximum discharge loads for the spring (where high tides are a little higher and low tides are a little lower than average) and neap (where high tides are a little lower and low tides are a little higher than average) tides (https://oceanservice.noaa.gov/facts/springtide.html). Spring tides give the best case dilution, while neap tide the worst case dilution. The site discharges to the River Wyre estuary which contains a number of ecologically important areas and the concentrations were modelled at these sites as well as a mixing zone of 100 m upstream and 100 m downstream of the discharge point.

Table 10.5 Concentrations from the UK supplier's marine modelling

	Average concentration of 2.24 mg/L		Maximum concentration of 6.4 mg/L	
	Spring tide concentration, mg/L	Neap tide concentration, mg/L	Spring tide concentration, mg/L	Neap tide concentration, mg/L
Outside mixing zone 100 m downstream from the outfall	**0.14**	**0.14**	**0.53**	**0.53**
Outside mixing zone (100 m upstream from the outfall)	**0.092**	**0.072**	**0.35**	**0.27**
Peak concentration exiting the estuary	**<0.0044**	**<0.0052**	**<0.0165**	**<0.0196**
Peak concentration at Shard bridge	**<0.00059**	**<0.00049**	**<0.0022**	**<0.00184**

10.1.5 Monitoring data

Monitoring data for EEA-NH_4 were provided by the UK supplier to the Environment Agency during this evaluation. These were collected as part of the requirements under the environmental permit. Samples of effluent discharged to the River Wyre from the site are collected daily and chemically analysed using an in-house method. The flow rates are continuously monitored. These data are used to calculate a monthly flow-weighted composite result, and these are provided for 2018 to 2020 in Appendix D. The average concentration over this period of time was 2.24 mg/L and the 95%ile concentration was 3.2 mg/L. This was the value used in the EUSES evaluation.

The UK supplier and a neighbouring company (which also uses fluorine based substances in its manufacturing process) take a number of sediment samples downstream of the sites' discharge points every 2 years, which are analysed for EEA-NH_4 (Ecospan 2018). In the latest survey undertaken in 2018, triplicate samples of the sediment in 6 locations were taken and no detectable levels were found in any of the samples, the limit of detection for the analytical method use is 10 µg/kg. The Environment Agency notes that the low adsorption potential of the substance to organic matter (see Section 6.2.1) means that sediment is unlikely to be a major sink.

11 Risk characterisation

The Environment Agency has estimated PECs arising from the use of EEA-NH_4 in the manufacture of PTFE and the worst case downstream user scenario for PTFE that contain it in residual amounts (see Section 10.1.2). These can be compared to the PNECs derived in Section 10 to calculate deterministic risk characterisation ratios (RCRs). The RCRs derived by the Environment Agency and UK supplier are shown in Table 11.1 and Table 11.2, respectively. An RCR above 1 indicates a potential risk. The surface water and sediment risks are the same because the equilibrium partitioning method has been used to derive both sediment PECs and PNECs.

Note: The figures from the CSR shown in Table 11.2 are only provided for completeness since the Environment Agency was unable to replicate the output of the UK supplier's CSR.

Table 11.1 Risk characterisation ratios derived by the Environment Agency

Life cycle stage	Fresh water		Fresh water sediment		Marine water		Marine sediment	
	Current	RWC	Current	RWC	Current	RWC	Current	RWC
Production of fluoropolymer	<0.442	<0.656	<0.442	<0.656	**<2.65**	**<3.94**	**<2.65**	**<3.94**
Downstream user	$<2.79 \times 10^{-4}$	$<4.16 \times 10^{-4}$	$<2.79 \times 10^{-4}$	$<4.16 \times 10^{-4}$	$<2.73 \times 10^{-4}$	$<4.05 \times 10^{-4}$	$<2.51 \times 10^{-4}$	$<4.05 \times 10^{-4}$
Regional	$<2.79 \times 10^{-4}$	$<4.16 \times 10^{-4}$	$< 2.5 \times 10^{-4}$	$<3.74 \times 10^{-4}$	$<2.73 \times 10^{-4}$	$<4.05 \times 10^{-4}$	$<2.48 \times 10^{-4}$	$<3.67 \times 10^{-4}$

Table 11.2 Risk characterisation ratios derived by the UK supplier in the original CSR

Life cycle stage	Fresh water	Fresh water sediment	Marine water	Marine sediment	Agricultural soil	Sewage treatment plant
Production of PTFE	0.174	0.174	0.174	0.174	0.002	0.174

No risks are implied by the undisturbed sediment concentrations measured at 6 locations downstream from the manufacturing site in 2018 (not detected up to 10 µg/kg). The UK supplier has conducted some additional modelling in response to the findings of the Environment Agency modelling which suggested RCRs above 1 in marine surface waters (and sediment through equilibrium partitioning). The conclusion was that for the average

EEA-NH_4 concentration of 2.24 mg/L in the site's wastewater discharge (based on the overall 2016 - 2020 monthly average concentration), the area of the estuary that exceeds the PNEC was 9.1 to 9.9 hectares. When the maximum EEA-NH_4 concentration of 6.4 mg/L in the site's wastewater discharge (also based on the overall 2016 - 2020 monthly average concentration) was used, the area of the estuary that exceeds the PNEC was 151 to 153 hectares.

Uncertainty in the PNECs arises because they are "greater than" values and a high assessment factor is required in the absence of ecotoxicity data for marine species and/or longer-term toxicity studies. The high RCRs for the marine compartment may therefore be misleading. On the other hand, it should be noted that the PNECs do not account for potential mixture effects.

The UK supplier and a neighbouring company undertake an ecological survey every 2 years to assess the potential environmental impacts of their sites on the Wyre estuary. Samples of plants were taken from 5 locations to assess the overall condition of the saltmarsh. The conclusion of this survey was that the discharge from the site is not having a significant effect on the ecologically important areas of the estuary. The Environment Agency notes that since the relative sensitivity of different species to EEA-NH_4 is unknown, this conclusion may be premature.

Further refinement of the exposure assessment is recommended, with particular emphasis on the dilution factor and/or measurement of concentrations in the receiving waters for the manufacturing site. Alternatively, additional ecotoxicity studies could be performed to reduce the assessment factor and therefore lower the PNECs. Vertebrate testing should be a last resort.

A conclusion about the PBT properties of EEA-NH_4 cannot currently be drawn, and so a qualitative risk cannot be excluded. The Environment Agency notes that the substance is likely to meet the draft PMT/vPvM criteria, suggesting that it might be hazardous for groundwaters (see Section 9.4), and may be transported long distances via water. There appears to be limited potential for the substance to reach groundwaters in the UK as it is used at a single site discharging to an estuary and there is no land spreading of waste (e.g. sludges) arising from that site. The effluent is temporarily stored in a pit prior to discharge, and there is also some disposal to landfill, either of which could be a source of local groundwater contamination. The highest worst case PEC estimated using simplistic EUSES modelling is 0.33 µg/L, and this could be refined by either monitoring data or more sophisticated modelling. Other sources of exposure are likely to give rise to lower groundwater concentrations.

11.1.1 Future climate scenario

The default temperature of the environmental compartments modelled by EUSES is 12 °C. The sensitivity of the modelled PECs to potential changes under future climate change scenarios has therefore been considered, to highlight whether controls may be necessary to avoid future risks. An increase of 4 °C in annual mean air temperatures is the maximum change considered in climate change projections published by the Met Office (2020).

Increasing the environmental compartment temperature to 16 °C had no effect on the PEC values. This is because the substance has a low volatility and is assumed to be extremely persistent over a range of ambient temperatures, so its general environmental behaviour is unlikely to be affected by a change in temperature of 4 °C.

Climate change is also expected to have an impact on the amount and distribution of rainfall, and consequently the dilution of sewage treatment plant (STP) effluent in rivers during prolonged periods of dry weather. The default dilution factor for STP effluent is 10 for generic modelled scenarios, although the Environment Agency (2013) reported that this value is insufficiently protective of a large proportion of surface watercourses in England (a dilution factor of 2 was recommended).

As the discharge of effluent from the manufacturing site is tidal it is difficult to predict what changes there will be to the river flow. The 95th percentile low flow of the River Wyre would need to be 34 200 m^3/day to reach an RCR of 1 under the realistic worse case release scenario, which is a reduction of around 35% of the current assumed low flow (52 704 m^3/day).

The PECs and RCRs derived for the downstream uses are both very low and a reduction of the default dilution factor from 10 to 2 would not increase the RCRs sufficiently to demonstrate a risk.

12 Conclusion and recommendations

12.1 Conclusion

EEA-NH_4 is a PFAS that belongs to the group of perfluoroether carboxylic acids. It is imported to the UK and used as a surfactant in the aqueous polymerization process to produce polytetrafluoroethylene at a single site. Releases occur to air and waste water during the manufacture of fluoropolymers at this site. Smaller releases may occur at polymer processing sites and from articles in use.

Based on the available hazard data the following conclusions can be reached:

- EEA-NH_4 does not meet the criteria to be classified for aquatic environmental hazard under the CLP Regulation.
- EEA-NH_4 is self-classified for reproductive toxicity in mammals by the UK supplier, and this meets the toxicity ‘T’ criterion of REACH Annex 13.
- EEA-NH_4 is not readily biodegradable and there is no evidence that it degrades significantly via abiotic mechanisms. In addition, there is no information on environmental degradation rates or half-lives available from simulation studies. EEA-NH_4 therefore screens as potentially persistent or very persistent, although based on evidence from related substances (like PFOA), it is likely to be extremely persistent.
- Although experimental data are available to indicate that bioconcentration in fish is likely to be low, it is not possible to draw a conclusion on the bioaccumulation potential of EEA-NH_4 in air-breathing organisms in the absence of data on the human clearance time or better predictive methods.
- In summary, EEA-NH_4 is likely to be extremely persistent and is therefore considered to be vP. Based on the current self-classification, it is T for mammalian effects. Whether it also screens as potentially B is unclear and further information is needed to evaluate bioaccumulation in air-breathing organisms before a PBT assessment can be concluded. A qualitative risk cannot be excluded until this is resolved.
- EEA-NH_4 meets the draft PMT/vPvM criteria, suggesting that it might be hazardous for groundwaters and has the potential for long distance transport via water. The Environment Agency notes that there appears to be limited potential for the substance to reach groundwaters in the UK as it is used at a single site discharging to an estuary and there is no land spreading of waste (e.g. sludges) arising from that site. The effluent is temporarily stored in a pit prior to discharge, and there is also some disposal to landfill, either of which could be a source of local groundwater contamination.

The exposure assessment produced by the Environment Agency has identified RCRs above 1 for marine surface waters (and sediments) due to emissions from the production of fluoropolymers at a single site. This suggests that there potentially may be an unacceptable level of risk to the marine environment. However, the Environment Agency notes that the PNEC is an unbounded value based on ecotoxicity studies which show no acute toxic effects at the highest concentrations tested. The RCRs are therefore "less than" values, which means they could be below 1 (no risk). No risks have been identified for other environmental compartments or life cycle stages based on RCRs. However, until data are available to demonstrate that the PBT/vPvB criteria are *not* met, it would be appropriate for the company to seek to minimise emissions as a precautionary measure.

12.2 Recommendations

12.2.1 Recommendations to the UK supplier

Although this evaluation is not a formal assessment under UK REACH, the Environment Agency proposes several ways to improve the data package to allow a more robust assessment of the hazards and risks posed by EEA-NH_4, including:

- A QPRF for the predicted vapour pressure key study, and also considers alternative models.
- The results of further studies that the UK supplier has planned on micelle formation, water solubility and the log K_{OW} of EEA-NH_4 and takes account of the findings for hazard and risk characterisation.
- A QPRF for the predicted water solubility and also considers alternative models if the new water solubility test does not provide a reliable experimental value. Further explanation for the reasons behind the apparent degradation observed in the original standard test would also be useful, along with a discussion about why this was not seen in other aqueous tests.
- A QPRF for the predicted log K_{OW} and also considers alternative models if the new log K_{OW} test does not provide an experimental value. Further explanation for the reasons behind gel formation in the original standard test would also be useful, along with a discussion about why this was not seen in other aqueous tests.
- Updates the robust study summaries for the available aquatic toxicity studies in the REACH registration dossier to include information on the initial and end measured concentrations.
- Additional information in the robust study summary for algal toxicity on the coefficients of variation of control growth and a statement about whether all of the validity criteria for control growth were met.
- A revised robust study summary for the ASRIT to include the raw data on the percentage respiration inhibition rate to verify the EC_{50}, the methods of statistical analysis and derivation of a NOEC, information on the oxygen uptake in the blank controls, a statement about whether all the validity criteria for control oxygen uptake were met, information on the dissolved oxygen concentration and the amount of aeration during the contact time.
- Additional data on environmental degradation rates and evidence of the potential for EEA-NH_4 to bioaccumulate in air-breathing organisms to allow a firm conclusion to be

reached on its persistence and bioaccumulation potential for the PBT/vPvB assessment.

- The additional modelling that has been carried out for the marine exposure assessment in the CSR, and further refines the risk assessment to demonstrate that the RCR is below 1 for all relevant compartments. This could include further refinement of the exposure assessment (e.g. monitoring of concentrations in estuarine waters), or additional ecotoxicity studies to reduce the assessment factor and therefore lower the PNECs. Vertebrate testing should be a last resort. Alternatively, additional risk management measures could be considered, in line with the last bullet point (i.e. attempts should be made to further minimise the emissions of EEA-NH_4 from the site).

The Environment Agency also recommends that AGC Chemicals Europe Ltd discusses the requirement for mandatory classification and labelling for reproductive toxicity under the UK CLP Regulation with HSE at the earliest opportunity.

12.2.2 General regulatory recommendations for consideration by relevant UK authorities

The proposed EU PMT/vPvM criteria are not an official hazard category under UK REACH. Development of Government policy on PMT/vPvM criteria and the risk management implications for substances of this type could provide benefits to reduce potential risks posed to the environment and human health.

The Environment Agency's National Permitting Service may also need to review how it sets discharge limits for PBT/vPvB and PMT/vPvM substances in future. Any review of this type could include consideration of whether a recommended maximum acceptable concentration should be set for monitoring purposes.

The potential for local groundwater contamination arising from the site effluent pit and associated underground drainage pipes could be investigated further (by confirming the containment, monitoring data or more sophisticated modelling). Leachate monitoring could also be considered at the landfill site that accepts solid waste from AGC Chemicals Europe Ltd.

The Environment Agency along with HSE have been undertaking a Regulatory Management Options Analysis (RMOA) for PFAS, and the information summarised in this evaluation has fed into that analysis to identify the most appropriate risk management measures for PFAS in a UK context.

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14 List of abbreviations

6:2 Cl-PFESA	6:2 chlorinated polyfluorinated ether sulfonate
ADONA	ammonium 2,2,3-trifluoro-3-(1,1,2,2,3,3-hexafluoro-3-trifluoromethoxy-propoxy) propionate
BCF	bioconcentration factor
CAS	Chemical Abstracts Service
C&L	Classification and Labelling [Inventory]
CLP	Classification, Labelling and Packaging [Regulation]
CSR	Chemical Safety Report
dw	dry weight
ECHA	European Chemicals Agency
EC_{50}	half maximal effective concentration
EPM	equilibrium partitioning method
ETFE	ethylene-tetrafluoroethylene
HFPO-DA	propanoic acid, 2,3,3,3-tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy)-, ammonium salt (1:1)
LC_{50}	half maximal lethal concentration
NOEC	no observed effect concentration
OECD	Organisation for Economic Co-operation and Development
OSPAR	Oslo and Paris Convention for the Protection of the Marine Environment of the North-East Atlantic
PACT	Public Activities Co-ordination Tool
PBT	persistent, bioaccumulative and toxic
PFAS	per- and polyfluorinated alkyl substances
PFCAs	perfluoroalkyl carboxylic acids
PFOA	perfluorooctanoic acid

PFOS	perfluorooctane sulfonic acid
PMT	persistent, mobile and toxic
PND	post-natal day
POP	persistent organic pollutant
PTFE	polytetrafluoroethylene
QPRF	QSAR Prediction Reporting Format
QSAR	Quantitative Structure Activity Relationship
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals [Regulation]
RMOA	Risk Management Option Analysis [REACH]
SMILES	Simplified Molecular Input Line Entry System
SVHC	Substance of Very High Concern
US EPA	US Environmental Protection Agency
vPvB	very persistent, very bioaccumulative
vPvM	very persistent, very mobile
ww	wet weight
w/w	weight by weight

Appendix A: Literature search

A literature search was undertaken by the Environment Agency on the 8th April 2020 to identify published information relevant to the assessment of EEA-NH_4. The keywords listed in Table A.1 were searched for in PubMed (https://pubmed.ncbi.nlm.nih.gov/) and Science Direct (https://www.sciencedirect.com/). In order to maximise the number of records identified keywords were based on the substance name only and not on the endpoints of interest or year of publication.

Table A.1 Literature search terms and number of hits

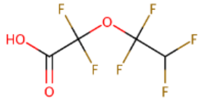
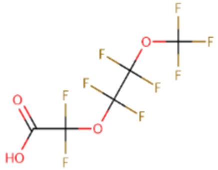
Search terms	PubMed	Science Direct
908020-52-0	0	5
Ammonium difluoro[1,1,2,2-tetrafluoro-2-(pentafluoroethoxy)ethoxy]acetate	0	0
Perfluoro(2-ethoxy-2-fluoroethoxy)acetic acid ammonium salt	0	0
Ammonium perfluoro-3,6-dioxaoctanoate	0	4
Total unique records	0	9

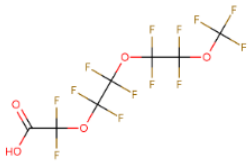
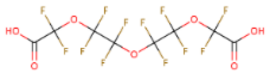
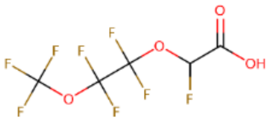
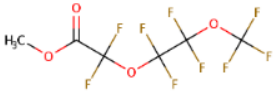
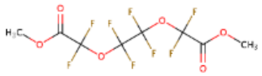
The identified records were screened manually for relevance to this assessment based on the title and abstract. Articles identified as of potential interest were obtained and reviewed for relevance. Those that were found to be relevant are discussed in the appropriate sections of this report.

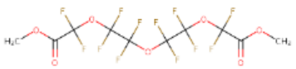
Appendix B: Additional analogues of EEA-NH_4

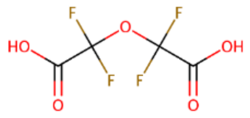
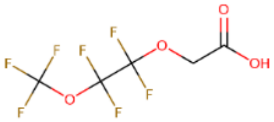
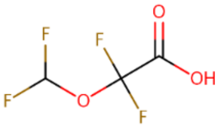
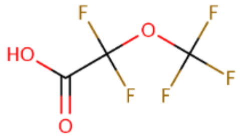
The US EPA CompTox Chemicals database (US EPA, 2021a; accessed March 2021) and PubChem database (RSC, 2021a; accessed March 2021) were used to identify structures with Tanamito similarity coefficient >0.8 (Excluding parent acid EEA). No experimental data were available for any of those included.

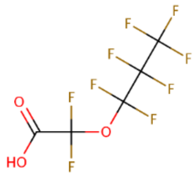
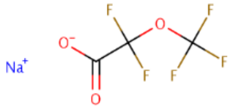
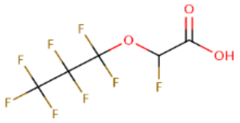
Table B.1 Structural identifiers for additional analogues of EEA-NH_4

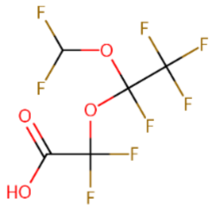
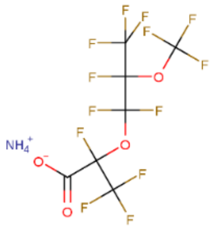
IUPAC name	CAS number	EC number	Structural formula	Molecular formula	Molecular weight (g/mol)	SMILES code	Source
Difluoro(1,1,2,2-tetrafluoroethoxy)acetic acid	81233-13-8	-		$C_4H_2F_6O_3$	212.047	OC(=O)C(F)(F)OC(F)(F)C(F)F	US EPA (2021b)
Perfluoro-3,6-dioxaheptanoic acid	151772-58-6	671-204-0		$C_5HF_9O_4$	296.045	OC(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)F	US EPA (2021c)
Perfluoro-3,6-dioxaoctane-1,8-dioic acid	55621-21-1	671-206-1		$C_6H_2F_8O_6$	322.063	OC(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(O)=O	US EPA (2021d)

IUPAC name	CAS number	EC number	Structural formula	Molecular formula	Molecular weight (g/mol)	SMILES code	Source
Perfluoro-3,6,9-trioxadecanoic acid	151772-59-7	671-215-0		$C_7HF_{13}O_5$	412.059	OC(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)F	US EPA (2021e)
Perfluoro-3,6,9-trioxaundecane-1,11-dioic acid	55621-18-6	671-193-2		$C_8H_2F_{12}O_7$	438.078	OC(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(O)=O	US EPA (2021f)
Fluoro[1,1,2,2-tetrafluoro-2-(trifluoromethoxy)ethoxy]acetic acid	919005-05-3	-		$C_5H_2F_8O_4$	278.054	OC(=O)C(F)OC(F)(F)C(F)(F)OC(F)(F)F	US EPA (2021g)
Methyl perfluoro-3,6-dioxaheptanoate	39187-41-2	-		$C_6H_3F_9O_4$	310.072	COC(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)F	US EPA (2021h)
Dimethyl 2,2'-[(1,1,2,2-tetrafluoroethane-1,2-	24647-20-9	-		$C_8H_6F_8O_6$	350.117	COC(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(=O)OC	US EPA (2021i)

IUPAC name	CAS number	EC number	Structural formula	Molecular formula	Molecular weight (g/mol)	SMILES code	Source
diyl)bis(oxy)]bis(difluoroacetate)							
Methyl difluoro{1,1,2,2-tetrafluoro-2-[1,1,2,2-tetrafluoro-2-(trifluoromethoxy)ethoxy]ethoxy}acetate	169289-58-1	671-228-1		$C_8H_3F_{13}O_5$	426.086	COC(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)F	US EPA (2021j)
Methyl 4,4,6,6,7,7,9,9,10,10,12,12-dodecafluoro-3-oxo-2,5,8,11-tetraoxatridecan-13-oate	35910-59-9	671-117-8		$C_{10}H_6F_{12}O_7$	466.132	COC(=O)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(F)(F)OC(F)(F)C(=O)OC	US EPA (2021k)
Ethyl difluoro(1,1,2,2-tetrafluoroethoxy)acetate	88239-69-4	-		$C_6H_6F_6O_3$	240.101	CCOC(=O)C(F)(F)OC(F)(F)C(F)F	US EPA (2021l)

IUPAC name	CAS number	EC number	Structural formula	Molecular formula	Molecular weight (g/mol)	SMILES code	Source
2,2'-Oxybis(difluoroacetic acid)	6535-10-0	-		$C_4H_2F_4O_5$	206.049	OC(=O)C(F)(F)OC(F)(F)C(O)=O	US EPA (2021m)
[1,1,2-Trifluoro-2-(trifluoromethoxy)ethoxy]acetic acid	919005-31-5	-		$C_5H_4F_6O_4$	242.073	OC(=O)COC(F)(F)C(F)OC(F)(F)F	US EPA (2021n)
[1,1,2,2-Tetrafluoro-2-(trifluoromethoxy)ethoxy]acetic acid	919005-40-6	-		$C_5H_3F_7O_4$	260.064	OC(=O)COC(F)(F)C(F)(F)OC(F)(F)F	US EPA (2021o)
2-Difluoromethoxy-2,2-difluoroacetic acid	75780-06-2	-		$C_3H_2F_4O_3$	162.04	OC(=O)C(F)(F)OC(F)F	US EPA (2021p)
Difluoro(perfluoromethoxy)acetic acid	674-13-5	821-118-6		C_3HF_5O	180.03	OC(=O)C(F)(F)OC(F)(F)F	US EPA (2021q)

IUPAC name	CAS number	EC number	Structural formula	Molecular formula	Molecular weight (g/mol)	SMILES code	Source
Difluoro(perfluoropropoxy)acetic acid	919005-50-8	-		$C_5HF_9O_3$	280.046	OC(=O)C(F)(F)OC(F)(F)C(F)(F)C(F)(F)F	US EPA (2021r)
Ethyl difluoro(trifluoromethoxy)acetate	61206-59-5	-		$C_5H_5F_5O_3$	208.084	CCOC(=O)C(F)(F)OC(F)(F)F	US EPA (2021s)
2,2-Difluoro-2-(trifluoromethoxy)acetate sodium salt	21837-98-9	-		$C_3F_5NaO_3$	202.012	[Na+].[O-]C(=O)C(F)(F)OC(F)(F)F	US EPA (2021t)
Fluoro(heptafluoropropoxy)acetic acid	919005-00-8	-		$C_5H_2F_8O_3$	262.055	OC(=O)C(F)OC(F)(F)C(F)(F)C(F)(F)F	US EPA (2021u)

IUPAC name	**CAS number**	**EC number**	**Structural formula**	**Molecular formula**	**Molecular weight (g/mol)**	**SMILES code**	**Source**
[1-(Difluoromethoxy)-1,2,2,2-tetrafluoroethoxy](difluoro)acetic acid	267901-01-9	-		$C_5H_2F_8O_4$	278.054	OC(=O)C(F)(F)OC(F)(OC(F)F)C(F)(F)F	US EPA (2021v)
Ammonium 2,3,3,3-tetrafluoro-2-[1,1,2,3,3,3-hexafluoro-2-(trifluoromethoxy)propoxy]propanoate	510774-77-3	-		$C_7H_4F_{13}NO_4$	413.091	[NH4+].[O-]C(=O)C(F)(OC(F)(F)C(F)(OC(F)(F)F)C(F)(F)F)C(F)(F)F	US EPA (2021w)

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US EPA CompTox 2021c
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID30382063

US EPA CompTox 2021d
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID20375106

US EPA CompTox 2021e
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID80380837

US EPA CompTox 2021f
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=55621-18-6

US EPA CompTox 2021g
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=919005-05-3

US EPA CompTox 2021h
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=39187-41-2

US EPA CompTox 2021i
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=24647-20-9

US EPA CompTox 2021j
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=169289-58-1

US EPA CompTox 2021k
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=35910-59-9

US EPA CompTox 2021l
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID60521322

US EPA CompTox 2021m
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=6535-10-0

US EPA CompTox 2021n
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=919005-31-5

US EPA CompTox 2021o
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=919005-40-6

US EPA CompTox 2021p
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=75780-06-2

US EPA CompTox 2021q
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=674-13-5

US EPA CompTox 2021r
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=919005-50-8

US EPA CompTox 2021s
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=61206-59-5

US EPA CompTox 2021t
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=21837-98-9

US EPA CompTox 2021u
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=919005-00-8

US EPA CompTox 2021v
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=267901-01-9

US EPA CompTox 2021w
https://comptox.epa.gov/dashboard/dsstoxdb/results?search=510774-77-3

Appendix C: QSAR models

Two main databases were used to source in silico data for this evaluation when required. These were the United States Environmental Protection Agency (US EPA) CompTox Dashboard (US EPA, 2020a) and the Royal Society of Chemistry (RSC) ChemSpider portal (RSC, 2020a). Both integrate diverse types of relevant domain data through a cheminformatics platform, and are built upon a database of curated substance properties linked to chemical structures (Williams *et al*., 2017).

The QSAR models available from these two platforms are presented in Table C.1 (data from other open access models are available in the CompTox dashboard, but for the sake of brevity, these have not been used for the purposes of this evaluation).

Table C.1 QSAR model outline

Name	Brief description
ACD/Labs	Predicts physicochemical properties via the Percepta Platform[6].
EPISuite™ Estimation Programs Interface Suite™ for Microsoft® Windows	A Windows®-based suite of physical/chemical, environmental fate and ecotoxicity property estimation programs developed by the US EPA and Syracuse Research Corp. It uses a single input (typically a SMILES string) to run the following estimation programs: AOPWIN™, AEROWIN™, BCFBAF™, BioHCwin, BIOWIN™, ECOSAR™, HENRYWIN™, HYDROWIN™, KOAWIN™, KOCWIN™, KOWWIN™, LEV3EPI™, MPBPWIN™, STPWIN™, WATERNT™, WSKOWWIN™ and WVOLWIN™.
OPEn structure–activity/property Relationship App (OPERA)	Open source suite of QSAR models providing predictions and additional information including applicability domain and accuracy assessment, as described in Williams *et al*. (2017). All models were built on curated data and standardized chemical structures as described in Williams *et al*. (2016). All OPERA properties are predicted under ambient conditions of 760 mmHg (103 kPa) at 25 °C.
T.E.S.T. Toxicity Estimation Software Tool	US EPA software application for estimating the toxicity of chemicals using QSAR methods. EPISuite™ is the model used to generate some physico-chemical data, although T.E.S.T. does not report K_{OW} values and uses a different database for surface tension. (US EPA, 2016).

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[6] http://www.acdlabs.com/products/percepta/

EPISuite^{TM}

Table C.2 summarises the PFCs identified in the training / validation sets for EPISuite^{TM}. Applicability domain (US EPA, 2020c).

Table C.2 EPISuite^{TM} PFCs included in training and validation sets

EPISuite model	Training set	Validation set
MPBPVP v 1.42	tetrafluoromethane hexafluoroethane tetrafluoroethylene octafluoropropane hexafluoropropene decafluorobutane perfluorocyclobutane perfluoro-n-hexane perfluorocyclohexane perfluoroheptane perfluoromethylcyclohexane	Not available
WSKOWWIN v 1.41	None identified	octafluoropropane octafluorocyclobutane
Water solubility estimate from fragments (v 1.01 est)	trifluoromethane	tetrafluoromethane hexafluoroethane octafluoropropane perfluorocyclobutane tetrafluoroethylene
KOAWIN v 1.1	Uses KOWWIN and HENRYWIN databases	
KOCWIN v 1.66	None identified	None identified
KOWWIN v 1.67	tetrafluoromethane hexafluoroethane	perfluorocyclohexane
HENRYWIN v 3.1	tetrafluoromethane hexafluoroethane tetrafluoroethene	octafluoropropane perfluorocyclobutane

Open Structure-activity/property Relationship App (OPERA)

OPERA is a free and open-source/open-data suite of QSAR models providing predictions for physicochemical properties, environmental fate parameters, and toxicity endpoints.

Applicability domain (AD) (Williams *et al.,* 2017):

- If a chemical is considered outside the global AD and has a low local AD index (< 0.4), the prediction can be unreliable.
- If a chemical is considered outside the global AD but the local AD index is average (0.4–0.6), the query chemical is on the boundary of the training set but has quite similar neighbours (average reliability). If the local AD index is high (> 0.6), the prediction can be trusted.
- If a chemical is considered inside the global AD but the local AD index is average (0.4–0.6), the query chemical falls in a “gap” of the chemical space of the model but still falls within the boundaries of the training set and is surrounded with training chemicals. The prediction therefore should be considered with caution.
- If a chemical is considered inside the global AD and has a high local AD index (> 0.6), the prediction can be considered reliable.

T.E.S.T. (Toxicity Estimation Software Tool)

Data sets used in T.E.S.T. (US EPA, 2016) for parameters reported at 25 °C:

- Surface tension: Dataset for 1 416 chemicals obtained from the data compilation of Jasper 1972;
- Water solubility: Dataset of 5 020 chemicals was compiled from the database in EPI Suite^{TM}. Chemicals with water solubility’s exceeding 1,000,000 mg/L were omitted from the overall dataset;
- Vapour pressure: Dataset of 2 511 chemicals was compiled from the database in EPI Suite^{TM}.

T.E.S.T. displays structures for substances from the test and training sets that are closest to the substance where a predicted value is required. A comparison between the experimental and predicted value for the substances in the test and training sets provides a similarity coefficient. If the predicted values match the experimental values for similar chemicals in the test and training set (and the similar chemicals were predicted well), there is greater confidence in the predicted value for the substance under evaluation.

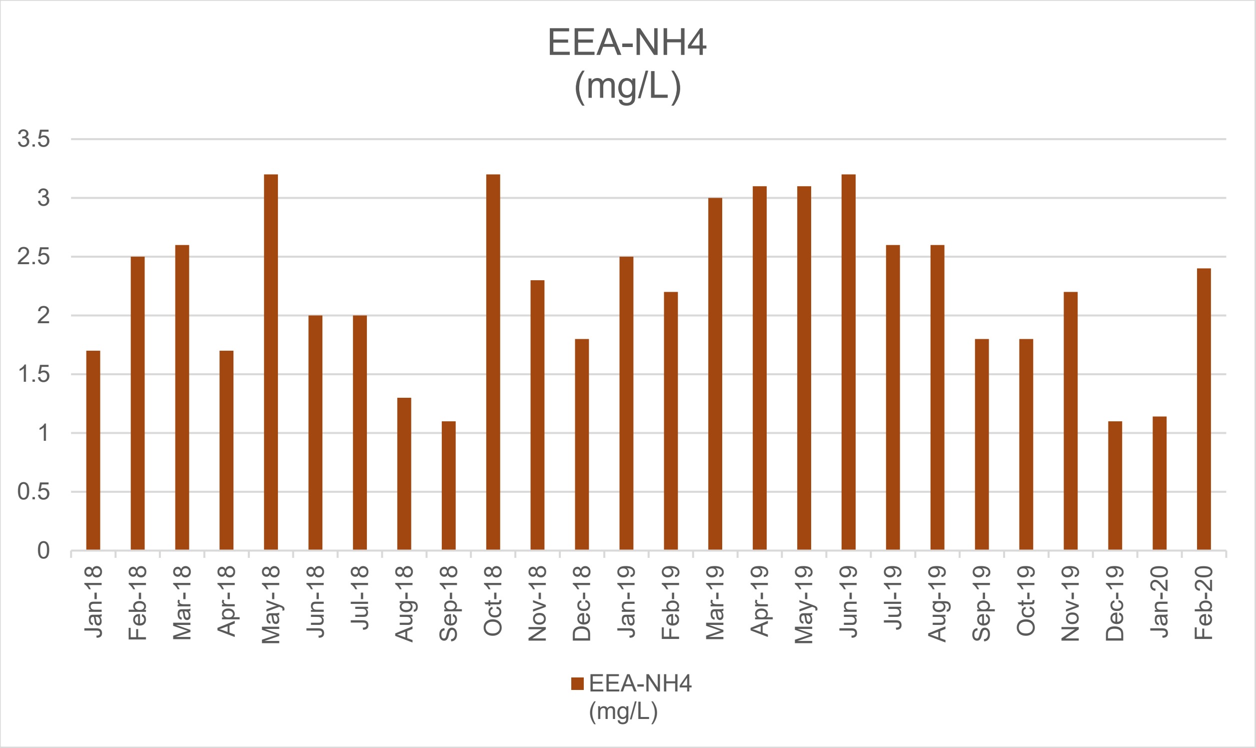
Appendix D: Monitoring data

Monitoring data undertaken for the permit.

Table D.1 EEA-NH_4 monitoring data for wastewater effluent discharged at the AGC Chemicals Europe Ltd site

Date	Total flow (m^3)	Flow-weighted mean concentration (mg/L)	Estimated monthly loading (kg)
January 2018	26,846	1.7	45.64
February 2018	20,950	2.5	52.38
March 2018	25,058	2.6	65.15
April 2018	26,565	1.7	45.16
May 2018	25,306	3.2	80.98
June 2018	28,311	2	56.62
July 2018	26,169	2	52.34
August 2018	27,454	1.3	35.69
September 2018	15,427	1.1	16.97
October 2018	17,024	3.2	54.48
November 2018	23,089	2.3	53.10
December 2018	31,014	1.8	55.83
January 2019	24,719	2.5	61.80
February 2019	25,326	2.2	55.72
March 2019	30,068	3	90.20
April 2019	23,919	3.1	74.15
May 2019	23,199	3.1	71.92
June 2019	25,591	3.2	81.89
July 2019	28,298	2.6	73.57
August 2019	31,274	2.6	81.31
September 2019	28,366	1.8	51.06
October 2019	30,652	1.8	55.17
November 2019	25,195	2.2	55.43
December 2019	28,822	1.1	31.70
January 2020	27,461	1.14	31.31
February 2020	30,780	2.4	73.87
Minimum	**15,427**	**1.1**	**16.97**
Maximum	**31,274**	**3.2**	**90.20**
Average	**26,034**	**2.24**	**57.82**
95th percentile	**30,956**	**3.2**	**81.75**

Figure D.1 EEA-NH_4 monitoring data for wastewater effluent discharged at the AGC Chemicals Europe Europe Ltd site



There is no obvious pattern in the data.

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