Environmental risk evaluation report: Trideca-1,1,1,2,2,3,3,4,4,5,5,6,6-fluorohexane [1H-PFHx] (CAS no. 355-37-3)

Chief Scientist's Group report

April 2023

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Email: research@environment-agency.gov.uk

Author(s):
Chemicals Assessment Unit, Environment Agency

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Environment Agency's Project Executive:
Steve Dungey

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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 trideca-1,1,1,2,2,3,3,4,4,5,5,6,6-fluorohexane, also known as 1H-perfluorohexane or 1H-PFHx (CAS number 355-37-3).

1H-Perfluorohexane is a PFAS that belongs to the group of hydrofluorocarbons. It is imported to the UK and used as an industrial non-reactive processing aid at a single site.

The Environment Agency has identified publicly available information on the regulatory status, uses, physico-chemical properties, environmental fate and (eco)toxicity of 1H-perfluorohexane and has reviewed this information for reliability. Further information has also been sought from the UK importer. 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.

1H-Perfluorohexane is not readily biodegradable, does not hydrolyse and has a long atmospheric half-life. In addition, there is no information on degradation rates or half-lives available from simulation studies. 1H-Perfluorohexane is therefore considered to be potentially persistent or very persistent (P/vP). An experimental fish bioconcentration study and predictions using quantitative structure-activity relationships indicate that 1H-perfluorohexane is not bioaccumulative (B) in aquatic organisms. Bioaccumulation in air-breathing organisms is unlikely to be high, but there is some uncertainty in this conclusion. 1H-Perfluorohexane does not meet the criteria to be considered toxic (T). 1H-perfluorohexane is therefore not considered to be PBT or vPvB.

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). 1H-perfluorohexane does not meet the draft PMT/vPvM criteria.

An exposure assessment based on information provided by the UK importer has not identified risks for fresh and marine surface waters. However, 1H-perfluorohexane has an atmospheric half-life of 31 years and it could make a contribution to global warming based on analogy with other hydrofluorocarbons.

A number of recommendations are made to the UK importer of 1H-perfluorohexane to improve the data package to allow a more robust assessment of the environmental hazards and risks posed by 1H-perfluorohexane.

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 international concern about the emissions of per- and polyfluoroalkyl substances (PFAS) to the environment. This is principally due to their extreme persistence, which could lead to long-term irreversible 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 production facilities in the UK, namely AGC Chemicals Europe Ltd of Thornton Cleveleys, Lancashire and F2 Chemicals Ltd of Preston, Lancashire. Based on information provided by these companies, a provisional list of PFAS for further consideration was drawn up. This was narrowed down to 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 perfluoroctanesulfonic acid (PFOS, which is a known POP) was included that had been identified from UK surface water monitoring. All of the substances chosen for further evaluation are listed below, initially using their EU-registered name:

- 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 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 - also known as ‘F-53B’ (CAS no. 73606-19-6)

This report summarises the evaluation of the substance highlighted above in **bold** (i.e. 1H-perfluorohexane), 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. Unless stated otherwise, the ECHA website and data provided by the UK importer are the main source of the information for this report.

This 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 in Section 9, and an exposure and risk assessment in Sections 10 and 11. The final section (Section 12) summarises our findings. Although the focus of this evaluation is on environmental hazards and risks, there is a brief summary of mammalian toxicology information, where available and relevant to the environmental assessment. However, this report is not intended to provide a full consideration of hazards, exposure and risks to human health. This is not a formal UK REACH Evaluation.

1 Substance identity

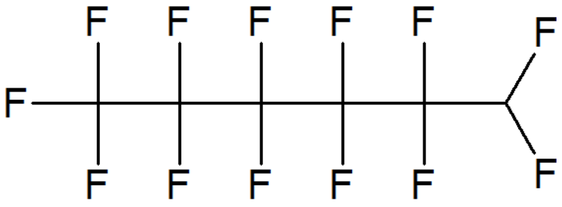
1.1 Name and other identifiers

Table 1.1 Substance identifiers

Public name	Trideca-1,1,1,2,2,3,3,4,4,5,5,6,6-fluorohexane or 1H-PFHx
IUPAC name	1,1,1,2,2,3,3,4,4,5,5,6,6-Tridecafluorohexane
CAS name	1H-Perfluorohexane
EC number	206-581-9
CAS number	355-37-3
Index number in Annex VI of the CLP Regulation	Not applicable
Molecular formula	C_6HF_{13}
Molecular weight	320.05
SMILES code	C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F
Synonyms	1H-Perfluorohexane; 1H-Tridecafluorohexane; 1,1,1,2,2,3,3,4,4,5,5,6,6-Tridecafluorohexane; Hexane, tridecafluoro-; Trideca-1,1,1,2,2,3,3,4,4,5,5,6,6-fluorohexane; Hexane, 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-; tridecafluorohexane; Asahiklin^{TM} AC-2000)
Type of substance	Mono-constituent

SMILES - Simplified Molecular Input Line Entry System

Figure 1.1 Structural formula of 1H-perfluorohexane representing the atoms and how they are bonded to each other



The substance is called 1H-PFHx throughout this report.

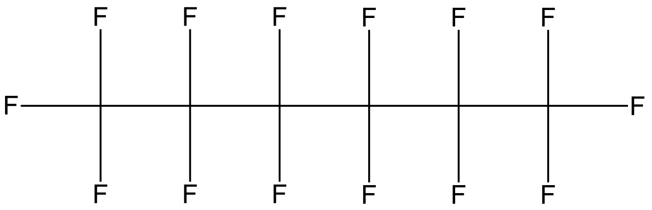
1.2 Structurally related substances

1H-PFHx is a hydrofluorocarbon (HFC), containing carbon, fluorine and one hydrogen atom. It is highly fluorinated and lacks functional groups such as acids, ethers or alcohols that characterize other PFAS categories (OECD, 2018).

The carbon-fluorine bond is very strong (up to 546 kJ/mol in tetrafluoromethane) and so highly fluorinated substances are much less reactive than their hydrocarbon analogues.

Potential structural analogues of 1H-PFHx include perfluoroalkanes (perfluorocarbons or PFCs) such as perfluorohexane (CAS no. 355-42-0), which is summarised in Table 1.2, and perfluoroisohexane (CAS no. 355-04-4). Since this latter substance is branched, the Environment Agency has not selected it for inclusion. Due to the limited data available for these substances, they have not been considered in detail for this report.

Table 1.2 Substance identifiers for selected analogues of 1H-PFHx

Name	Tetradecafluorohexane
CAS number	355-42-0
EC number	206-585-0
Structural formula	
Molecular formula	C_6F_{14}
Molecular weight	338 g/mol
SMILES code	FC(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)F
Synonyms	Perfluorohexane
Comment	This substance has a fluorine atom in place of the hydrogen atom that is present in 1H-PFHx, giving it a slightly higher molecular weight.

1.3 Transformation products

Although the carbon-fluorine bond is very strong, a slow reaction occurred in both the photolysis and ready biodegradation tests (see Section 6). The transformation products were not identified in either study but are likely to include perfluorohexan-1-ol, which might in turn slowly oxidise further to perfluorohexanoic acid. The properties of these substances have not been considered for the purposes of this evaluation, although they are likely to be persistent.

2 Analytical chemistry

2.1 Regulatory and academic methods

The EU REACH registration does not provide any analytical details (ECHA, 2020a).

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.

A validated analytical method was supplied to the Environment Agency by the UK importer. The method was developed as part of a GLP study (Unpublished, 2017a), and validated in accordance with EU guidance (EC, 2000). It uses gas chromatography with mass spectrometric detection (GC-MS) for the quantitative analysis of the substance in aqueous solution.

Method development included (though was not limited to) solvent selection, suitability of detector and chromatographic separation column. Optimisation was performed throughout the development to improve retention time stability, assess carry-over and improve peak shape. Only the conditions of the final method are reported in Unpublished (2017a). Full details are not presented in this evaluation as they are not in the public domain. Validation was performed for specificity, calibration curve ($R^2 \geq 0.995$, in the range 0.008 to 6.0 mg/L), accuracy (99 and 114 or 81% at 0.01 and 5 mg/L, respectively) and repeatability (2.4 and 4.8 or 5.3% at 0.01 and 5 mg/L, respectively), limit of quantification (LOQ) (0.01 mg/L), analytical system stability, stock solution stability and storage stability of samples. The Environment Agency assessed the method as valid as it meets is requirements set out in EC (2000).

In addition, the Environment Agency searched the academic literature for analytical methods for the detection of 1H-PFHx in environmental matrices (water, fresh and marine; soil, sediment, sludge and air). Numerous methods relating to short chain perfluorocarbons were found, although no specific methods for 1H-PFHx were identified.

Analytical monitoring of 1H-PFHx in environmental matrices is not documented as part of national or international monitoring programmes. It is, however, present in databases operated by the Swedish Chemicals Agency, OECD Global Database, EPA ToxCast/Tox21 and several others. No validated associated analytical methods were presented alongside. The US EPA states that methods for measurement of volatile PFAS in air are under development and undergoing validation (US EPA 2021).

The website of the contract laboratory Eurofins Test America (www.EurofinsUS.com/PFAS) indicates they have a validated method for the quantification of volatile perfluoroalkyl carboxylic acids in air. This method may be adaptable to allow measurement of 1H-PFHx .

3 Import, manufacture and uses

Although the UK left the European Union (EU) at the end of January 2020, European legislation in place by December 2020 has been retained and transposed into UK law, and ECHA, who administer EU REACH, is still the most relevant source of information about industrial chemicals on the UK market at the time of writing.

1H-PFHx is registered under the EU REACH Regulation at a supply level of 10 to 100 tonnes/year. There is one Registrant under both EU and UK REACH, AGC Chemicals Europe Ltd (www.agcce.com). The substance is imported into the UK for use at AGC Chemicals Europe Ltd's manufacturing site at Thornton Cleveleys near Blackpool, Lancashire. 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 ECHA website, 1H-PFHx is used at industrial sites as a non-reactive processing aid (no inclusion into or onto articles). AGC Chemicals Europe Ltd has confirmed that 1H-PFHx is only used in the production of ETFE.

An overview of uses provided in the EU REACH registration information on the ECHA website is presented in Table 3.1.

Table 3.1 Overview of uses

Life cycle stage	Use(s)
Formulation	ERC2: Formulation into mixture PROC 1: Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions PROC 2: Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment conditions PROC 3: Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions PROC 4: Chemical production where opportunity for exposure arises PROC 8a: Transfer of substance or mixture (charging and discharging)

Life cycle stage	Use(s)
	at non-dedicated facilities PROC 8b: Transfer of substance or mixture (charging and discharging) at dedicated facilities PROC 9: Transfer of substance or mixture into small containers (dedicated filling line, including weighing) PROC 15: Use as laboratory reagent PROC28: Manual maintenance (cleaning and repair) of machinery
Uses at industrial sites	**Use as a non-reactive processing aid** ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article) PROC 1: Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions PROC 2: Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment conditions PROC 3: Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions PROC 4: Chemical production where opportunity for exposure arises PROC 8a: Transfer of substance or mixture (charging and discharging) at non-dedicated facilities PROC 8b: Transfer of substance or mixture (charging and discharging) at dedicated facilities PROC 9: Transfer of substance or mixture into small containers (dedicated filling line, including weighing) PROC 15: Use as laboratory reagent
	Recovery of a non-reactive processing aid ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article) PROC 4: Chemical production where opportunity for exposure arises PROC 8a: Transfer of substance or mixture (charging and discharging) at non-dedicated facilities

Life cycle stage	Use(s)
Uses by professional workers	None identified in registration dossier
Consumer Uses	None identified in registration dossier
Article service life	None identified in registration dossier

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 EU REACH and CLP Regulations. No substance-specific activities have been identified for 1H-PFHx on PACT.

1H-PFHx is included under the EU REACH PFHxA restriction proposal, as it is considered a PFHxA related substance.

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 EU REACH restriction proposal. The current scope of the work is wide and includes all substances that contain at least one aliphatic -CF2- or -CF3 element (see ECHA Registry of Restriction Intentions: https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e18663449b, accessed October 2021). 1H-PFHx 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.

A search of the EFSA website (http://www.efsa.europa.eu/) did not identify 1H-PFHx as being evaluated or noted in any published scientific opinions.

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

The Oslo and Paris Convention for the Protection of the Marine Environment of the North-East Atlantic (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.

1H-PFHx 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). 1H-PFHx 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

1H-PFHx 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, 2020).

4.2.2 Canada

A search did not identify 1H-PFHx 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, accessed July 2020).

4.2.3 Australia

A search did not identify 1H-PFHx 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 1H-PFHx 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 (https://www.nite.go.jp/chem/jcheck/list3.action?category=141&request_locale=en, accessed July 2020). Under the Act there are 3 lists:

- Class I Specified Chemicals - 28 substances (persistent, bioaccumulative, toxic)
- Class II Specified Chemicals - 23 substances (toxic and high risk)
- Priority Assessment Chemical Substance (PACS), currently 226 substances

1H-PFHx 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)

1H-PFHx 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

Fluorinated gases (‘F-gases’) may contribute to climate change due to their global warming potential and they are often used as substitutes for ozone-depleting substances, because they do not damage the atmospheric ozone layer (EC, n.d.). F-gases are regulated under the Ozone-Depleting Substances and Fluorinated Greenhouse Gases (Amendment etc.) (EU Exit) Regulations (2019) which aims to reduce the emission of these gases into the environment. Annex I and II list the F-gases subject to the Regulation and 1H-PFHx is not included (it is a volatile liquid rather than a gas).

5 Physico-chemical properties

This evaluation focusses on vapour pressure, water solubility and n-octanol/water partition coefficient, as they are the key physico-chemical 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, 2020a; accessed July 2021) unless otherwise indicated. The reliability scores provided in the full registration for individual studies are cited, these generally follow the Klimisch score criteria (Klimisch *et al*., 1997). The scores in the database have presumably been generated in accordance with the ECHA R.4. Guidance Document (ECHA, 2011).

The Environment Agency has evaluated original study reports where provided. Where an independent evaluation has not been possible for a study, or the EU REACH registration dossiers lack sufficient supporting information, this is noted in the text (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 EU REACH 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) and openly available *in silico* QSAR models. 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 is provided in Appendix B.

An overview of physico-chemical data provided in the EU REACH registration or generated by the Environment Agency is presented in Table 5.1.

Table 5.1 Summary of physico-chemical properties for 1H-PFHx

Property	Value(s)	Reliability	Source
Physical state at 20 °C and 101.3 kPa	Colourless liquid	Registrant: 1 (key study)	EU REACH Registration dossier
Melting / freezing point	<-80 °C at 101.3 kPa (GLP, OECD TG 102; EPA OPPTS830.7200)	Registrant: 1 (key study)	EU REACH Registration dossier
Boiling point	67 °C at 101.3 kPa (GLP, OECD TG 103, EPA OPPTS 830.7220)	Registrant: 1 (key study)	EU REACH Registration dossier
Relative density	1.68 g/cm^3 at 20 °C (GLP, OECD TG 109. EPA OPPTS 830.7300)	Registrant: 1 (key study)	EU REACH Registration dossier
Vapour pressure	15 kPa at 20 °C (110 mmHg), 19 kPa at 25 °C (140 mmHg) (GLP, OECD TG 104, EPA OPPTS 830.7950)	Registrant: 1 (key study)	EU REACH Registration dossier
Surface tension	73.2 mN/m at 20°C and 90% saturation solubility in water (GLP, OECD TG 115, EU method A.5)	Registrant: 1 (key study)	EU REACH Registration dossier
Water solubility	1.5 mg/L at 20 °C pH >7.2, <8.25 (GLP, OECD TG 105, EPA OPPTS 830.7840)	Registrant: 1 (key study)	EU REACH Registration dossier
n-Octanol/water partition coefficient (log K_{OW})	4.1 (GLP, OECD TG 117, EPA OPPTS 830.7570)	Registrant: 1 (key study)	EU REACH Registration dossier
n-Octanol/air partition coefficient (log K_{OA})	0.85 (calculated)	-	Environment Agency
Dissociation constant	Not applicable	-	-

5.1 Vapour pressure

5.1.1 Measured data

The key experimental study in the EU REACH registration dossier was performed according to OECD Test Guideline (TG) 104 (OECD, 2006a) and was compliant with the principles of Good Laboratory Practice (GLP) (Unpublished, 2017a). The Environment Agency has reviewed the full study report.

In brief, the vapour pressure of 1H-PFHx was determined by a static method using a vapour pressure testing manifold. The test item was certified as 100% pure. The method is considered suitable for measurements in the range of 10^3 and 10^6 Pa. Analytical grade diethyl ether was used as a reference substance to validate the method. The measured vapour pressure of the diethyl ether at 20 °C deviated by < 5% of the literature value and was acceptable. Measurements of the vapour pressure of the test substance were performed in duplicate at 7 temperatures between 20 and 50 °C. Based on linear regression, the experimentally derived vapour pressure of 1H-PFHx was 15 kPa at 20 °C (110 mmHg) (ECHA, 2020a) and 19 kPa at 25 °C (140 mm Hg). The EU REACH registration considers that the data are reliable without restrictions (Klimisch 1), and the Environment Agency agrees that the study was well performed.

5.1.2 Predicted data

No *in silico* predictive data were presented in the EU REACH registration for this endpoint as there is a valid experimental result.

For comparative purposes, the Environment Agency has considered readily available QSARs to test how they perform for this type of substance. The ChemSpider database and the US EPA CompTox dashboard contain predicted vapour pressures for 1H-PFHx generated from EPISuite^{TM}, T.E.S.T., ACD/Labs and OPERA software (RSC, 2020a; US EPA, 2020a). Median predicted values are presented in Table 5.2. The Environment Agency converted the values from mmHg to kPa.

Table 5.2 Predicted vapour pressures for 1H-PFHx

Source	Prediction method	Predicted vapour pressure (kPa/mmHg) at 25 °C
ACD/Labs	Not available	15.6 kPa 117 mmHg
EPISuite™ **Estimation programme** **MPBPWIN v 1.42**	Mean of Antoine and Grain methods BP = 46.15 °C MP = -98.86 °C	47.2 kPa 354 mmHg

T.E.S.T. (EPISuite™ v 4.00)	Not available	4.20 kPa 31.5 mmHg
OPERA	Not available	651 kPa 4.88 x 10^3 mmHg

In silico predicted values should always be treated with caution where substances in the training set and external test set are not visible. For the ACD/Labs and MPBPWIN models this information was not available. Therefore no assessment of applicability could be performed. The good agreement between predicted and measured value using the ACD/Labs model may be coincidental.

Structural analogues of 1H-PFHx were included in both the training set and external test sets for the T.E.S.T. and OPERA models. Predicted vapour pressure values are therefore within the applicability domain of both models. Despite this, there is a large difference between the predicted and experimental values, illustrating that the OPERA model in particular is not reliable in this case.

5.1.3 Data from structural analogues

Analogues have not been considered by the Environment Agency as the experimental study data are considered fully reliable.

5.1.4 Additional sources

No relevant references were identified in the literature search.

5.1.5 Recommended value

The Environment Agency considers that a vapour pressure of **15 kPa at 20 °C** is sufficiently reliable for use in further assessment. This indicates that the substance is moderately volatile.

5.2 Surface tension

5.2.1 Measured data

The key experimental study in the EU REACH registration dossier was carried out according to OECD TG 115 (OECD, 1995), and was GLP compliant (Unpublished, 2017a). The Environment Agency has reviewed the full study report and agrees that the data are reliable without restrictions (Klimisch 1).

The experimentally derived surface tension of 1H-PFHx at 90% of the saturation solubility in water and at 20 °C was 73.2 mN/m (ECHA, 2020a and Unpublished, 2017a). The results indicate that 1H-PFHx is not surface active (as the surface tension is > 60 mN/m). This is to be expected, as 1H-PFHx does not have any hydrophilic structural groups that can form hydrogen or Van der Waals bonds in water.

5.2.2 Predicted data

For comparative purposes, the Environment Agency has considered readily available QSARs to test how they perform for this type of substance. The ChemSpider database (RSC, 2020a) and US EPA CompTox dashboard (US EPA, 2020a) include predictions of surface tension presented in Table 5.3.

Table 5.3 Predicted Surface tension for 1H-PFHx

Source	Surface tension (mN/m)
T.E.S.T. (EPISuite^{TM} v 4.00)	8.84
ACD/Labs	11.6
Chemspider	11.6

These values are clearly different from the reported surface tension of an aqueous solution, and are likely to be for the liquid substance itself. They are not relevant for this evaluation.

5.2.3 Data from structural analogues

Chernyshev and Skliar (2014) reported a small decrease in the surface tension of deionised water in the presence of perfluorocarbon vapours in an experiment using perfluoropentane and perfluorohexane at 20 °C. The surface tension of the water reduced from 72 mN/M to 64.6 mN/M in the presence of perfluoropentane and 66.7 mN/M in the presence of perfluorohexane. It was suggested that a separate perfluorocarbon layer may form at the water-air interface in aqueous solution.

5.2.4 Recommended value

Surface tension in water is important because it can affect the measurement and interpretation of other physico-chemical properties such as water solubility and n-octanol/water partition coefficients. The Environment Agency considers that 1H-PFHx will **not be surface active** in aqueous solution.

5.3 Water solubility

5.3.1 Measured data

The key experimental study for water solubility in the EU REACH registration dossier was carried out according to OECD TG 105 (OECD, 1995a) (slow-stirring flask method) and was GLP compliant (Unpublished, 2017a). The Environment Agency has reviewed the full study report.

The main study used containers filled with 116 mL (by weight) of double distilled water, sealed with a septum lidded cap to prevent evaporation of the test substance (one of which was used as a blank control). Aliquots of 10 µL of 1H-PFHx were injected through the septum of three containers using a syringe to provide a nominal concentration of 145 mg/L. The vessels were placed on a magnetic stirring device and gently stirred at 100 revolutions per minute for 24, 48 or 72 hours. Blank vessels were stirred for 72 hours. Turbulent mixing of the two phases was actively avoided and the head space of the containers was minimised. The temperature was maintained at 19.7 ± 0.3 °C.

After the stirring period, three samples of 2 mL were aliquoted from each container to a 10 mL vial containing 40 µL of dimethylsulfoxide (DMSO) and analysed. With the exception of the blank test vessels the pH of the solution in each dosed container was also measured. Analysis was performed using the validated GLP method presented in Section 3.1. Seven concentrations (analysed in duplicate) were used to construct the calibration curve. Responses were excluded from the curves if the back calculated accuracy was > 15% from the nominal concentration. The coefficient of correlation was > 0.99 for each curve.

The results from the main study met the validity criteria of OECD TG 105 (OECD, 1995a) and EC (2000), i.e. the maximum difference in the measured concentration between the 24, 48 and 72 hour stirred samples was below 15%, and the stability of the analytical system met the criterion that the coefficient of variation should be below 20%. No test substance was detected in samples from the control containers.

The reported water solubility after 72 hours was 1.5 mg/L at 19.7 ± 0.3 °C (pH 7.2 to 8.5). The authors of the study report consider that it is highly unlikely that a more accurate value could be measured due to the high volatility of 1H-PFHx.

The EU REACH registration assessed the data to be reliable without restrictions (Klimisch 1) (ECHA, 2020a).

5.3.2 Predicted data

No *in silico* predictive data were presented by the EU REACH registration for this endpoint as there is a valid experimental result.

For comparative purposes, the Environment Agency has considered readily available QSAR software to test how they perform for this type of substance. The ChemSpider database and US EPA CompTox dashboard contained predicted water solubility endpoint values generated from EPISuite™, T.E.S.T. and OPERA software (RSC, 2020a; US EPA, 2020a). These values are presented in Table 5.4. Values were converted by the Environment Agency from mol/L to mg/L using a molecular weight of 338.04 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.

- Guidance provided with the WSKOWWIN model indicates that the relationship between the experimental and predicted values for a training set of 1 450 compounds was good, with an R^2 of 0.97, standard deviation of 0.409 and an average deviation of 0.313. The validation set contained several perfluorocarbons (PFCs) (see Appendix B) and it is likely that the predicted value for 1H-PFHx falls within the applicability domain of the model.

Table 5.4 Predicted water solubility values for 1H-PFHx

Model	Details	Water solubility
EPISuite™ water solubility estimate from log K_{OW} (WSKOW v1.41)	Log K_{OW} used: 5.41 (estimated)	0.040 mg/L at 25 °C
EPISuite™ water solubility estimate from fragments (WATERNT v1.01 est.)	-	0.0082 mg/L
T.E.S.T. **(EPISuite™ v 4.00)**	Predicted value: 7.23×10^{-6} mol/L Low confidence, no structural analogues in training sets.	2.3 mg/L
ACD/Labs	7.00 mol/L Low confidence, no structural analogues in training sets.	2 240 000 mg/L
OPERA	Predicted value: 3.04×10^{-5} mol/L Global applicability domain: outside Local Applicability domain index: 0.341 Confidence Interval 0.498	9.7 mg/L

- Guidance provided with the WATERNT model indicates that the relationship between the experimental and predicted values for a training set of 4 636 compounds was good, with an R^2 of 0.85, standard deviation of 1.045 and an average deviation of 0.796. The validation set contained several perfluorocarbons (PFCs) (see Appendix B) and it is likely that the predicted value for 1H-PFHx falls within the applicability domain of the model.

- The Environment Agency considers the value predicted using ACD/Labs to be an error as such a high value is inconsistent with the observation of clear phase separation in the water solubility study. It will not be considered further.
- No close structural analogues of 1H-PFHx were included in either the training set or external test sets of the T.E.S.T. model. Therefore, predicted values from T.E.S.T. are considered to be outside the applicability domain of the model.
- For the OPERA model, structural analogues of 1H-PFHx were included in the external test set (including perfluoropropane), but not the training set. Perfluoropropane is considered to be outside the global applicability domain but has a high local applicability domain index (> 0.6). The predicted value of 9.7 mg/L for 1H-PFHx therefore has low to moderate confidence.

The *in silico* predictions therefore suggest that the water solubility of 1H-PFHx may lie in the range 0.008 to 10 mg/L. The model which predicts the closest value to the measured water solubility is T.E.S.T., which may just be coincidence.

5.3.3 Data from structural analogues

Analogues have not been considered in detail as a suitable experimental study is available. However, it is notable that the measured water solubility of perfluorohexane reported in the EU REACH registration of that substance is ≤0.1 mg/L at 20 °C (ECHA, 2020c). The Environment Agency has not evaluated the reliability of this value.

5.3.4 Additional sources

Chernyshev and Skliar (2014) reported that PFCs such as perfluorohexane form colloids in water, which may involve liquid droplets, vapour bubbles or a combination of both phases simultaneously.

5.3.5 Recommended value

A modern experimental study is available for 1H-PFHx, which the EU REACH registration considers to be fully reliable. The Environment Agency recognises that the substance is likely to partition significantly from water to air (see Section 6.2.2), and reasonable efforts to minimise losses were made in this instance (in accordance with the recommendations of OECD, 2019). Whilst pH dependence of water solubility appears unlikely for this substance based on the structure (i.e. there are no obvious acidic or basic functional groups), the study report does not include any discussion of the pH variation observed. In addition, the high hydrophobicity of the carbon-fluorine bond may result in colloid formation as observed for similar substances (Chernyshev and Skliar, 2014), and this was not considered in the study. The reported water solubility also appears to be at least an order of magnitude higher than that for the close structural analogue perfluorohexane. Therefore, the Environment suggests that the study may be reliable with restrictions (Klimisch 2).

Predicted values of water solubility ranged from 0.0082 to 9.7 mg/L.

In the absence of a further study to re-visit the pH variability and potential for colloid formation, the Environment considers that the water solubility of **1.5 mg/L at 20 °C** is a suitable estimate for the purposes of this evaluation.

5.4 Partition co-efficient (n-octanol/water; log K_{OW})

5.4.1 Measured data

The key experimental study for n-octanol/water dissociation constant in the EU REACH registration dossier was carried out according to OECD TG 117 (OECD, 2004) (high performance liquid chromatography (HPLC) method) and was GLP compliant (Unpublished, 2017a). The Environment Agency has reviewed the full study report.

This method was selected based on a QSAR prediction (see Section 5.4.2), and used a reverse phase ultra-high performance liquid chromatography (UPLC) at 35 °C coupled to a refractive index detector, in conjunction with an isocratic mobile phase. 1H-PFHx does not contain functional groups that will dissociate and therefore the mobile phase was not buffered. Test and reference substances were analysed in duplicate. A single analysis was performed on the blank. It was verified that only one peak was observed in the chromatograms of the 1H-PFHx solutions. The log K_{OW} values of the reference substances ranged from 2.7 to 5.7, and these were used to generate a calibration curve using column capacity factors calculated from the substances' retention times. A log K_{OW} of 4.1 was estimated for 1H-PFHx using this curve. The EU REACH registration considers the data to be reliable without restrictions (Klimisch 1), and the Environment Agency agrees that the study was well performed.

In addition, the Chemspider database (RSC, 2020a) reports an experimental log K_{OW} of 6.07, but no further details are available. Therefore the reliability of this value is unknown (Klimisch 4).

5.4.2 Predicted data

Unpublished (2017a) contains a preliminary calculation that was performed using the Rekker method (PrologP 6.0 module in Pallas 3.0, CompuDrug International, USA). This is a fragment based method and is recommended in the OECD test guideline. The log K_{OW} of 1H-PFHx was calculated to be 4.61. However, the study report does not provide any information about whether the training set and external test set contained similar substances, so its reliability cannot be established.

For comparative purposes, the Environment Agency has considered readily available QSAR software to test how they perform for this type of substance. The US EPA CompTox dashboard and ChemSpider database contained estimated log K_{OW} values for 1H-PFHx from ACD/Labs, EPISuite™ and OPERA (RSC, 2020a; US EPA, 2020a) (Table 5.5).

Table 5.5 Predicted log K_{OW} values for 1H-PFHx

Model	Details	log K_{OW}
ACD/Labs	ACD/LogP ACD/LogD (pH 5.5) ACD/LogD (pH 7.4)	4.62 4.37 4.37
EPISuite™	KOWWIN v 1.67 estimate	5.41
OPERA	Predicted value: 3.60 Global applicability domain: Inside Local Applicability domain index: 0.564 Confidence Interval 0.503	3.60

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 ACD/labs model, so no assessment of the applicability can be performed.
- Guidance provided with the KOWWIN model indicates that the relationship between the experimental and predicted values for a validation set of 10 331 compounds was good, with an R^2 of 0.94 and standard deviation of 0.47. The training set contained several PFCs (see Appendix B) and it is likely that the predicted value for 1H-PFHx falls within the applicability domain of the model.
- For the OPERA model, structural analogues of 1H-PFHx were included in both the training set and external test sets (e.g. perfluoroethane). 1H-PFHx is considered inside the global applicability domain and has a local applicability domain index of 0.564. The predicted value therefore has moderate confidence.

The *in silico* predictions therefore suggest that the log K_{OW} of 1H-PFHx may lie in the range 3.6 to 5.41. The model which predicts the closest value to the measured log K_{OW} is ACD/Labs, but the reliability of this model for this type of substance is unknown and so it may just be coincidence.

5.4.3 Data from structural analogues

Analogues have not been considered in detail as a suitable experimental study is available. A log K_{OW} of ≥4.5 has been estimated for perfluorohexane based on the ratio of its measured solubility in n-octanol (≥ 3.0 g/L) and water (≤0.1 mg/L) (ECHA, 2020c). The Environment Agency has not evaluated the reliability of this value, but it suggests that this type of substance may have a high affinity for organic phases such as lipids.

5.4.4 Additional sources

As noted in Section 5.3.4, PFCs such as perfluorohexane can form colloids in water. It is possible that the same may occur in organic liquids like n-octanol.

5.4.5 Recommended value

A modern experimental study is available for 1H-PFHx, which the EU REACH registration considers to be fully reliable. The Environment Agency notes that the method is indirect, in that it uses the retention time on a HPLC column in comparison to a series of reference standards to provide an estimate of K_{OW}. However, highly fluorinated substances may have the potential to form separate phases from water and n-octanol, and this was not investigated as part of the study.

The Environment Agency notes that a high solubility in n-octanol (≥3.0 g/L) was reported for perfluorohexane. Assuming that this is a reliable measurement of true solubility (which might not be the case, due to colloid formation), and that 1H-PFHx has a similar level of solubility in n-octanol, a log K_{OW} of ≥3.3 can be estimated for 1H-PFHx using its measured water solubility (1.5 mg/L). Further investigation of n-octanol solubility might be useful to provide an unbounded value.

The experimentally determined log K_{OW} value of **4.1** will be used for the purpose of this evaluation.

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

The octanol-air partition coefficient 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 1H-PFHx by the EU REACH registration (ECHA, 2020a).

5.5.2 Predicted data

The Environment Agency has estimated a K_{OA} value using the dimensionless Henry's Law constant (log K_{AW}) of 3.25 (see Section 6.2.2) and the recommended log K_{OW} value of 4.1 (Section 5.4) ($K_{OA} = K_{OW}/K_{AW}$). The resulting log K_{OA} is 0.85. As there is uncertainty in the K_{AW}, the reliability of these derived K_{OA} values is unknown

The US EPA CompTox dashboard and ChemSpider database contained predicted K_{OA} values for 1H-PFHx generated from KOAWIN v1.10 and OPERA software (RSC, 2020a, US EPA, 2020a). These values are presented in Table 5.6.

Table 5.6 Predicted log K_{OA} for 1H-PFHx

Source	Details	log K_{OA}
EPISuite™ **Estimation programme KOAWIN v1.1** **ChemSpider (RSC, 2020a)**	Log K_{OA} (log K_{OW} used: 5.41 and K_{AW} used: 4.977 estimated) Log K_{OA} (experimental database): None	0.433
OPERA	Global applicability domain: Inside Local Applicability domain index: 0.979 Confidence Interval: 0.803	1.57
Calculation	Calculated from log K_{AW} of 3.25 and a log K_{OW} value of 4.1 ($K_{OA} = K_{OW}/K_{AW}$)	0.85

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

- For the KOAWIN model, the values are estimated from either predicted or experimental K_{AW} and K_{OW} values sourced from HENRYWIN and KOWWIN respectively. The training sets for KOWWIN and HENRYWIN contain several PFCs (see Appendix B) and it is likely the respective predicted value for 1H-PFHx falls within the applicability domains of the two models. Therefore, the predicted K_{OA} for 1H-PFHx can be considered to be predicted with high confidence.
- Structural analogues of 1H-PFHx were included in the training and external test sets of the OPERA model. 1H-PFHx is considered inside the global applicability domain and has a high local applicability domain index (> 0.6), so the prediction has high confidence.

Additionally the US EPA CompTox dashboard also contained log K_{AW} for 1H-PFHx from OPERA (US EPA, 2020a). The reliability of this estimate is unknown.

5.5.3 Data from structural analogues

There are no measured data for structural analogues.

5.5.4 Additional sources

No relevant references were identified in the literature search.

5.5.5 Recommended value

No log K_{OA} values were presented in the EU REACH registration dossier (ECHA, 2020a).

In silico predictions for the log K_{OA} of 1H-PFHx were between 0.433 (RSC, 2020a) and 1.57 (US EPA, 2020a). The Environment Agency's estimated value of **0.85** lies within this range, and so is selected for the purposes of this evaluation, although there are uncertainties.

5.6 Dissociation constant

The Environment Agency notes that a dissociation constant is irrelevant for 1H-PFHx as it has no ionisable functional groups. It will remain as a neutral compound at environmentally relevant pH.

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

No studies on the hydrolysis of 1H-PFHx are available from the EU REACH registration dossier, as the information requirement was waived. However, the UK importer has provided a full study report to the Environment Agency as part of this evaluation. This has been reviewed, and limited details are presented below as the data contained in the report are not yet publicly available.

A preliminary study was performed in accordance with OECD TG 111 (OECD, 2004) (hydrolysis as a function of pH) (Unpublished, 2020), where 1H-PFHx was dosed with a co-solvent into buffer solutions at pH 4, 7 and 9. The nominal concentration of 1H-PFHx in the buffers was below the water solubility limit (See Section 5.3). These solutions were maintained at 50 ± 0.5 °C for 120 hours. Sampling was performed in duplicate at 0 h, 24 h and 120 h. The pH of the sample solutions was also recorded at these sampling intervals. The concentration of 1H-PFHx was measured using gas chromatography with flame ionisation.

Significant decreases in concentration were observed at all three pH values at 50 °C (i.e. down to below 2% of the nominal starting concentration). As this was consistent across for all buffers, the pH was not considered to be a contributing factor. The study authors noted that due to the chemical structure of 1H-PFHx hydrolysis should not occur. However, 1H-PFHx is volatile and even with precautions taken to minimise losses during the study, it appears that the test item volatilised out of solution.

The report authors concluded that the main test could not be performed reliably due to the volatility of the test item, and hydrolysis at an environmentally pH and temperature is likely to be negligible.

The Environment Agency agrees that based on structural considerations, further investigation into hydrolysis is unnecessary.

6.1.1.2 Phototransformation in air

The EU REACH registration presents non-GLP academically published data for this endpoint. The study (Chen, 2003) involved measurement of rate constants for the gas-phase reaction of 1H-PFHx with hydroxyl (OH) radicals. The methodology is equivalent to that presented for flash photolysis methods for absolute and relative rate determination in the OECD Guidance (OECD, 1992).

The absolute rate method involved kinetic measurements of hydroxyl radical concentrations in the presence of 1H-PFHx using both flash photolysis-laser induced fluorescence (FP-LIF) and laser photolysis-laser induced fluorescence (LP-LIF) at 25 °C. The absolute rate constant for the reaction of 1H-PFHx with hydroxyl radicals was determined to be 1.71 (±0.09) × 10^{-15} cm^3/molecule/s. Absolute methods can be subject to interference from hydroxyl radicals reacting with impurities or secondary reaction products. Approximately 80 repetitions of the experiments were performed to reduce variability and systematic error.

The relative rate method measured the disappearance of 1H-PFHx and a reference compound (chlorodifluoromethane or 1,1-difluoroethane) in the presence of hydroxyl radicals at 25 °C. Relative rate constants were calculated to be 1.87 (±0.11) × 10^{-15} cm^3/molecule/s or 2.12 (±0.11) × 10^{-15} cm^3/molecule/s, depending on the reference compound.

Using these data, the rate constant for the reaction of 1H-PFHx with hydroxyl radicals over the temperature range -23 to 157 °C can be **calculated** from the following equation (scaled against data for 1,1,1-trichloroethane at -1 °C):

Rate constant = $(4.71 \pm 0.94) \times 10^{-13} \exp[-(1630 \pm 80)/T]$ cm^3/molecule/s

The tropospheric lifetime of 1H-PFHx through reaction with hydroxyl radicals was estimated to be **31 years**. The abstraction of the hydrogen atom by reaction with hydroxyl radicals is clearly very slow. For comparison, the carbon-fluorine chain is expected to be stable to direct photolysis for more than 1 000 years (Environment Canada, 2012). Although transformation products were not investigated, it is likely that a perfluoroalcohol (perfluorohexan-1-ol) could be formed over a long period of time.

The EU REACH registration assessed this study to be reliable with restrictions (Klimisch 2) as it was well documented and followed generally accepted scientific principles, and the Environment Agency agrees with this rating.

For comparative purposes, the Environment Agency has considered readily available QSAR software to test how they perform for this type of substance. The US EPA CompTox dashboard contains a predicted atmospheric hydroxylation rate for 1H-PFHx generated from the OPERA software (US EPA, 2020a). The predicted value is 3.94 x 10^{-15} cm^3/molecule/sec, which is slightly higher than the measured value. Structural analogues of 1H-PFHx are included in the training set and so the substance is considered to be within the applicability domain of the model by CompTox. Following the method given in ECHA (2016), the Environment Agency calculates a rate constant for degradation in air of 0.00017 d^{-1}, which equates to a half-life of 4 070 days (11 years), which is shorter than that derived from the measured value.

The RSC Chemspider portal contains a predicted atmospheric hydroxylation rate for 1H-PFHx generated from the AOPWIN software (RSC, 2020a). The predicted value is 3×10^{-16} cm^3/molecule/sec. Gomis *et al*. (2015) note that the predictive power of AOPWIN for PFAS is limited despite the inclusion of some fluorinated substances in the training set, and that based on comparisons of predicted and measured photodegradation rates for 7 fluorinated substances they expect that AOPWIN may underestimate the true half-life in air. However, the Environment Agency notes that this predicted reaction rate is lower (more conservative) than the measured value.

6.1.1.3 Phototransformation in water

No studies are available from the EU REACH registration dossier or from published data sources.

6.1.1.4 Phototransformation in soil

No studies on are available from the EU REACH registration dossier or from published data sources.

6.1.2 Biodegradation in water

6.1.2.1 Measured data

Table 6.1 Summary of screening biodegradation studies

Method	Results	Reliability	Reference
OECD TG 301C (Ready Biodegradability: Modified MITI Test (I)) GLP	Not readily biodegradable Approximately 6% degradation after 28 days based on BOD; Approximately 4% degradation after 28 days based on GC	Registrant: 1 (key study)	Unpublished (1994a) cited in ECHA (2020a)

The biodegradation screening study in the EU REACH registration dossier is an OECD TG 301C (modified MITI) study carried out to GLP (Unpublished, 1994a; ECHA, 2020a). The inoculum used in the study was a mixture from a municipal sewage treatment plant, industrial sewage, surface waters and soil as specified in the test guideline. The sludge was not pre-adapted to the test material. Six test vessels were used: an abiotic control, a blank control, a positive control and three vessels with test substance and inoculum. Aniline was used as the positive reference substance. The test was carried out at a concentration of 100 mg/L of substance with 30 mg/L suspended solids over 28 days. As the test substance is volatile the test vessels were filled to minimise the amount of headspace. Degradation was monitored by measuring the Biological Oxygen Demand (BOD) and by direct measurement of the test substance concentration by GC analysis.

Degradation of the test substance was found to be 6% based on BOD and 4% based on GC analysis, showing that the substance did not meet the criteria to be considered readily biodegradable. The degradation of aniline was found to reach 41% after 7 days and 95% after 14 days, which met the criteria to demonstrate that the sludge was sufficiently active for the test to be valid. The EU REACH registration assessed this study to be reliable without restriction (Klimisch 1).

The Environment Agency found that the validity criteria were met and that this study followed the standards in OECD TG 301C. This guideline is considered suitable for testing substances which are volatile or poorly water soluble. The concentration of 1H-PFHx used in this study was above the water solubility of 1.5 mg/L (Section 5.3). Following the test guideline, no solvent or emulsifying agent was used. However, no information is given on whether any other method was used to disperse the test material. The Environment Agency considers that the study is reliable and demonstrates that the substance did not meet the criteria to be considered readily biodegradable.

6.1.2.2 Predicted data

The US EPA CompTox dashboard contains a predicted biodegradation half-life of 4.08 days generated from the OPERA software (US EPA, 2020a), but notes that 1H-PFHx is outside of the applicability domain of this model, so the prediction is not reliable.

The RSC Chemspider portal contains a prediction for the probability of rapid biodegradation for 1H-PFHx generated from the BIOWIN software (RSC, 2020a). All seven BIOWIN models predict that 1H-PFHx will not be readily biodegrade. The BIOWIN model predictions are based on the molecular fragments “carbons with four bonds that are not attached to hydrogens” and “trifluoromethyl group”. The Environment Agency considers that these fragments describe 1H-PFHx adequately and therefore that this substance is within the domain of these models.

6.1.2.3 Data from structural analogues

Analogues have not been considered as a suitable experimental study is available.

6.1.2.4 Discussion

The experimental data indicate that 1H-PFHx is not readily biodegradable, as only low levels of removal (4 to 6%) were observed in a standard test designed to minimise volatile losses. Dissolution kinetics may have had some impact on the results as the study was performed well in excess of water solubility. The small amount of oxygen consumption and apparent loss of parent substance suggests slow transformation occurred. This is surprising, as carbon-fluorine bonds are expected to be very stable. Transformation products were not investigated. However, the hydrogen-bearing terminal carbon atom may have been partially oxidised to form a perfluoroalcohol (perfluorohexan-1-ol). This substance may well be stable, or it could potentially be slowly oxidised further to perfluorohexanoic acid.

6.1.3 Biodegradation in sediment

No studies are available from the EU REACH registration dossier or from published data sources.

6.1.4 Biodegradation in soil

No studies are available from the EU REACH registration dossier or from published data sources.

6.1.5 Summary and discussion on degradation

1H-PFHx is not expected to hydrolyse. Experimental information on its phototransformation potential in air, together with a QSAR prediction, indicates that it has a very long atmospheric half-life, estimated to be 31 years based on rate constant measurements.

A fully valid biodegradation screening study is available, indicating that the substance achieved a low level of removal (up to 6%) over 28 days. 1H-PFHx is therefore not readily biodegradable. Highly fluorinated substances generally do not undergo significant mineralisation under relevant environmental conditions. The screening biodegradation result is consistent with this. There are no environmental simulation data so a realistic half-life in aquatic or terrestrial media cannot be established.

Although the carbon-fluorine bond is very strong, a slow reaction occurred in both the photolysis and ready biodegradation tests. The transformation product(s) were not identified but are likely to include perfluorohexan-1-ol, which might in turn slowly oxidise further to perfluorohexanoic acid. The properties of these substances have not been considered for the purposes of this evaluation, although they are likely to be persistent.

6.2 Environmental distribution

6.2.1 Adsorption/desorption

6.2.1.1 Measured data

Adsorption/desorption of a chemical to solid phases is assessed using the organic carbon/water partition coefficient (K_{OC}). The key experimental study in the EU REACH registration dossier was carried out according to OECD TG 121 (HPLC method) (OECD, 2001) and was GLP compliant (Unpublished, 2017a). The Environment Agency has reviewed the full study report.

This method was selected based on a QSAR prediction (see below) and used reverse phase UPLC at 35 °C coupled to a refractive index detector, in conjunction with an isocratic mobile phase. 1H-PFHx does not contain functional groups that will dissociate and therefore the mobile phase was not buffered. Test and reference substances were analysed in duplicate. A single analysis was performed on the blank. It was verified that only one peak was observed in the chromatograms of the 1H-PFHx solutions. The log K_{OC} values of the reference substances ranged from 1.26 to 5.63, and these were used to generate a calibration curve using column capacity factors calculated from the substances' retention times. A log K_{OC} of 3.7 was estimated for 1H-PFHx using this curve. Further experimental details provided in the study report are not presented in this evaluation as limited details are in the public domain.

The EU REACH registration considers the data to be reliable without restrictions (Klimisch 1), and the Environment Agency agrees that the study was well performed.

6.2.1.2 Predicted data

A preliminary calculation was performed using the Perrin calculation method (pKalc 5.0, module in Pallas 3.0, USA) as part of the HPLC study (Unpublished, 2017a). This is a fragment based method and is recommended in the OECD test guideline. The log K_{OC} of 1H-PFHx was calculated to be 4.61. However, the study report does not provide any information about whether the training set and external test set contained similar substances, so its reliability cannot be established.

For comparative purposes, the Environment Agency has considered readily available QSAR software to test how they perform for this type of substance. The US EPA CompTox dashboard contains a predicted log K_{OC} of 3.65 generated from the OPERA software (US EPA, 2020a), but notes that 1H-PFHx is outside of the applicability domain of this model, so the prediction is not reliable.

The RSC Chemspider portal contains a predicted log K_{OC} of 4.85 for 1H-PFHx generated from the PCKOCWIN software (RSC, 2020). It is unclear whether this prediction is based on the Molecular Connectivity Index (MCI) method or on the log K_{OW} method. If the latter, this value is unreliable, as it would have been based on a predicted log K_{OW} value of 5.41. No information is available on substances in the training set and external test set, so no assessment of the applicability can be performed.

A log K_{OC} of 3.42 can also be calculated based on the measured log K_{OW} of 4.1 and the 'predominantly hydrophobics' equation used in EUSES (v2.03). The Environment Agency notes that the applicability domain of this equation is unknown.

6.2.1.3 Data from structural analogues

Analogues have not been considered as a suitable experimental study is available.

6.2.1.4 Recommended value

A modern experimental study is available for 1H-PFHx, which the EU REACH registration considers to be fully reliable. OECD TG 121 is a suitable method for testing volatile substances or those that are poorly water soluble, so was appropriate for 1H-PFHx. However, the Environment Agency notes that the method is indirect, in that it uses the retention time on a HPLC column in comparison to a series of reference standards to provide an estimate of K_{OC}. Highly fluorinated substances may have the potential to form separate phases from water and organic media, and this was not investigated as part of the study.

In the absence of a direct measurement, the experimentally determined log K_{OC} value of **3.7** will be used for the purpose of this evaluation. This value suggests that the substance is likely to bind to soil and sediment to a moderate extent.

6.2.2 Volatilisation

Measured data

There is no relevant information in the EU REACH registration dossier. A measured value of 33 atm.m³/mol (3.34 x 10^6 Pa.m³/mol) is reported in the experimental database of the HENRYWIN v3.1 module of the EPISuite™ estimation programme. No further details are provided, so the reliability of this information is unknown.

Predicted data

There is no relevant information is available in the EU REACH registration dossier.

The Environment Agency has calculated a Henry's Law constant (HLC) using EUSES (v2.03). The US EPA CompTox dashboard and ChemSpider database also contained predicted HLC values for 1H-PFHx generated from OPERA software (RSC, 2020a, US EPA, 2020a). These values are presented in Table 6.2. The Environment Agency has converted the values from atm.m³/mol to Pa.m³/mol.

Table 6.2 Predicted Henry's Law constant for 1H-PFHx

Source	Details	HLC (Pa.m³/mol)
EPISuite™ Estimation programme **HENRYWIN v3.1**	Bond Method: 1.27 x 10^2 atm.m³/mol Group Method: 2.45 x 10^1 atm.m³/mol	1.29 x 10^7 2.48 x 10^6
	Vapour pressure/water solubility estimate using EPISuite™ derived values: 9.554 atm.m³/mol	9.68 x 10^5
OPERA	Predicted value: 6.8 x 10^{-2} atm.m³/mol Global applicability domain: outside Local Applicability domain index: 0.278 Confidence Interval: 0.357	6.89 x 10^3
EUSES v2.03	Calculated from the measured water solubility of 1.5 mg/L at 20 °C and vapour pressure of 15 kPa at 20 °C	4.22 x 10^6

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

- For the HENRYWIN model, the training and validation sets contained several PFCs (see Appendix B) and it is likely that the predicted value for 1H-PFHx falls within the applicability domain of the model. However, the prediction relies on predicted values for vapour pressure and water solubility, so the output should be treated with additional caution.
- No close structural analogues of 1H-PFHx were included in either the training set or external test sets of the OPERA model. 1H-PFHx is considered to be outside the global applicability domain and has a low local applicability domain index (< 0.4), so the prediction is not considered reliable based on the OPERA model applicability domain criteria.
- The equation in EUSES is a simple relationship between a substance's vapour pressure and water solubility, and is a suitable estimate although it does not necessarily reflect actual partitioning behaviour in a steady state system.

Data from structural analogues

There is no information for relevant analogues.

Recommended value

The Environment Agency recommends a HLC of **4.22×10^6 Pa.m^3/mol** for modelling purposes calculated from the preferred water solubility value and vapour pressure. This is similar to a reported measured value of unknown reliability (3.34×10^6 Pa.m^3/mol). This value suggests that the substance will readily volatilise from water to air.

This value has been used to derive a dimensionless HLC or air-water partition coefficient (log K_{AW}) of 3.25, which is used in the prediction of long-range transport (see Section 6.3).

6.2.3 Distribution modelling

The Environment Agency has used the SIMPLETREAT model in EUSES (v2.03) to predict the partitioning of 1H-PFHx in a wastewater treatment plant based on its lack of ready biodegradability, reported K_{OC} and vapour pressure, as follows:

Air: 68.6%

Water: 4.01%

Sludge: 27.4%

This model predicts that a significant fraction will partition to the atmosphere. The reliability of this model for this type of substance is unknown, and the uncertainties in the physico-chemical input parameters also mean that this distribution might not be fully reliable.

6.3 Long-range transport potential

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}).

To estimate the LRTP of 1H-PFHx, the Environment Agency has performed calculations using the input parameters indicated in Table 6.3.

Table 6.3 Estimated long-range transport potential of 1H-PFHx

Input Parameter	Value
Molecular mass	320.05 g/mol
Log K_{aw} [a]	3.25
Log K_{OW}	4.1
Half-life in air (hours)[b]	271 560
Half-life in water (hours)[c]	2.1 x 10^{41}
Half-life in soil (hours)[c]	2.1 x 10^{41}
LRTP output parameter	
Characteristic Travel Distance (km)	1 089 330
Transfer Efficiency (%)	679
P_{OV} (days)	17 044

Note: a - This is the log of the dimensionless HLC calculated using Equation R.16-5 of ECHA R16.

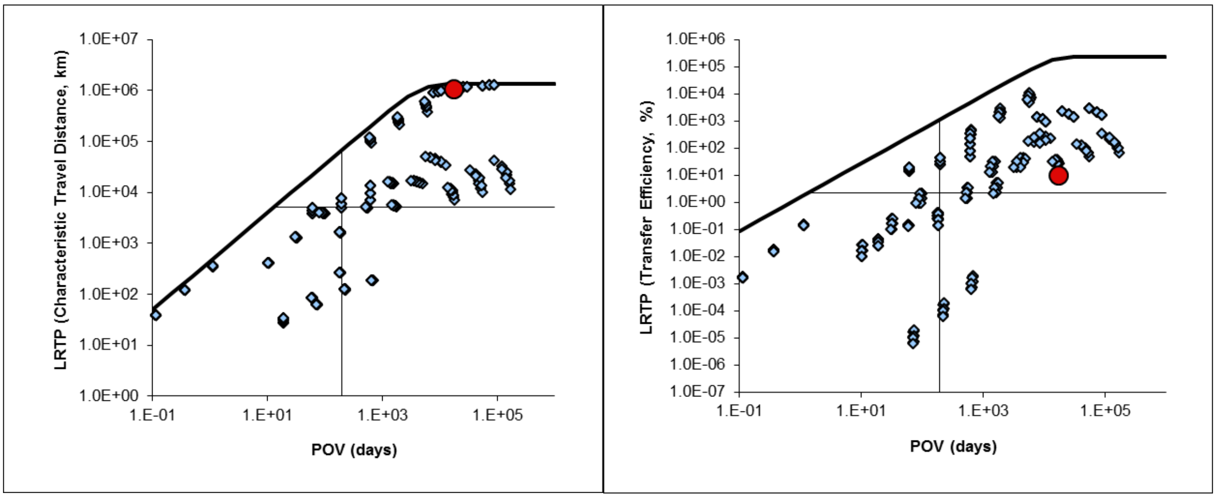
b -This is a measured half-life.

c -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.

Based on this screening tool, it appears that 1H-PFHx may be capable of long-range transport. Evidence of occurrence (or not) of 1H-PFHx 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 beyond the scope of this evaluation.

Figure 6.1 Long-range transport potential of 1H-PFHx



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 (%).

6.4 Bioaccumulation

6.4.1 Bioaccumulation in aquatic organisms

Measured data

Table 6.4 Summary of bioaccumulation studies

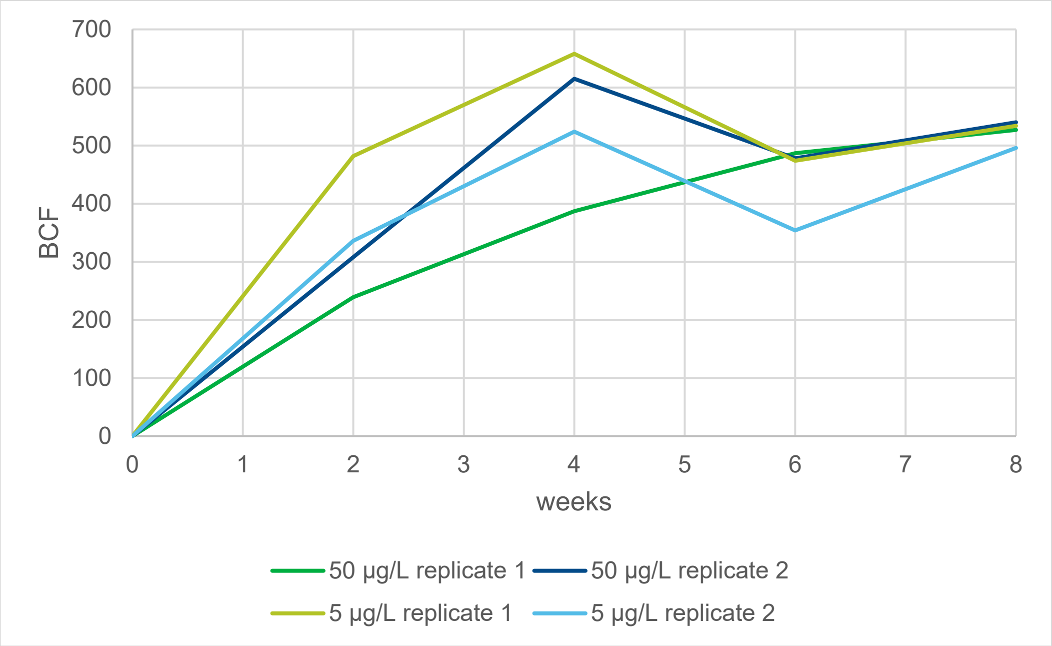
Method	Results	Reliability	Reference
OECD TG 305C **GLP**	*Cyprinus carpio* BCF 293 to 615 after exposure to 50 µg/L *Cyprinus carpio* BCF 336 to 658 after exposure to 5 µg/L	Registrant: 1 (key study)	Unpublished (1994b) cited in ECHA (2020)

The bioaccumulation study in the EU REACH registration dossier is an OECD TG 305C (OECD, 1981) study carried out to GLP using Common Carp (*Cyprinus carpio*) (Unpublished, 1994b; ECHA, 2020a). The test material was not radiolabelled. Test solutions were prepared by preparing a 10:1 solution of the test substance with the solvent MEGAFAC F-142D, before this was diluted with ion-exchanged water to produce stock solutions with nominal concentrations of 20 mg/L and 2 mg/L. The final test solutions had a nominal exposure concentration of 50 and 5 µg/L and the study was conducted using a flow-through exposure for 8 weeks. There was no depuration phase. The concentration of the solvent in the final test solution is not stated. Twelve fish (age not stated) were exposed to each exposure concentration, and five fish were used as a control. Test substance concentrations in the exposure media were analysed by GC/FID twice a week. Two fish were sampled in weeks 2, 4, 6 and 8. Sampled fish were weighed and measured before the concentration of test compound was determined by GC/FID. Lipid content of the fish was not measured. Control fish were only sampled at the beginning and end of the 8 week period.

Other than the flow through exposure system, no further information is given on measures taken to limit losses due to volatilisation. However, mean measured exposure concentrations ranged from 48.4 to 50.5 µg/L at the higher exposure level, and 4.37 to 4.56 µg/L at the lower exposure level, and it is stated that each average concentration was maintained at >90% nominal.

This study was conducted to a guideline that has since been superseded, so no depuration phase was included although the uptake phase of 8 weeks is longer than required by the current test guideline (OECD, 2012). The fish bioconcentration factors (BCF) were calculated for each two-week sampling period, and it is unclear whether steady state was reached during this study (Figure 6.2). For both exposure concentrations, BCF initially increased with the highest BCF observed during the fourth week of exposure. In three of the replicates, BCF decreased in week 6, before increasing in week 8 but not to the levels reported in week 4 (see Figure 6.2). The BCF was reported to range from around 300 to 660 at both exposure concentrations throughout the test, and from 496 to 540 at the final sampling point. The EU REACH registration gave the study a Klimisch score of 1 (reliable without restriction).

Figure 6.2 BCF over time (weeks) for each replicate



The Environment Agency considers that this study is of unknown reliability (Klimisch 2). The study was conducted to a guideline that was current at the time, but which has since been updated considerably. The number of fish used in this study is lower than that of the updated OECD TG 305, and the lack of information on growth and lipid content of the fish over the 8-week study period adds to the uncertainty. The variation in fish concentration during the test makes it questionable whether steady state was actually reached, even though it appears that a plateau was being approached. BCF reported on the last 3 sampling occasions (weeks 4, 6 and 8) were within ±20% of each other for all treatments except for replicate 2 at 5 µg/L (77% of average BCF at week 6), compared to the most recent TG requiring concentrations in fish to be within ±20% of each other over three successive samples for steady state to have been reached. There is no depuration period so it is not possible to calculate a kinetic BCF.

Predicted data

The US EPA CompTox dashboard contains predicted fish BCF values for 1H-PFHx generated from both the T.E.S.T. and OPERA software (US EPA, 2020a). The OPERA model predicts a BCF of 300, but notes that 1H-PFHx is outside of the applicability domain of this model, so the prediction is not valid. The T.E.S.T. model predicts a BCF of 483, and structural analogues of 1H-PFHx are included in the training set so this value might be more reliable.

The RSC Chemspider portal contains a predicted BCF of 2 930 for 1H-PFHx generated from the BCFWIN software (RSC, 2020a). However, this value is based on a predicted log K_{OW} of 5.41, so is not considered reliable for use in this assessment.

A BCF can also be calculated based on the log K_{OW} and the equation in ECHA (2017c). The Environment Agency has used the experimental log K_{OW} of 4.1 to calculate a BCF of 610. This is in good agreement with the highest reported measured BCF.

Data from structural analogues

Analogues have not been considered given the apparent agreement between measured and predicted BCF.

Recommended value

The experimental data provided in the EU REACH registration indicates a maximum fish **BCF of 658**. This is consistent with predicted BCF from two QSARs. Although neither the experimental study nor predicted values are fully reliable, together they indicate that the potential for aquatic bioaccumulation may be moderate. The highest BCF from the experimental study will be used for the purposes of this assessment.

6.4.2 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 highly fluorinated substances suggests that terrestrial bioaccumulation may be more relevant for this type of substance than aquatic bioaccumulation, although this is mainly related to the ability of some PFAS (particularly perfluorocarboxylic acids) to bind to proteins.

In terms of bioaccumulation in air breathing organisms, the screening criteria are log K_{OW} > 2 and log K_{OA} > 5 (ECHA, 2017c). Although the log K_{OW} (4.1) exceeds the threshold the log K_{OA} (3.7) does not, so this criterion is not met.

No information on bioaccumulation is available from the available mammalian toxicity studies.

6.4.3 Summary and discussion of bioaccumulation

Taken together, the results from the OECD TG 305 study (BCF 658) and the predicted values from two QSAR models that are considered valid (BCF 483 to 610) indicate that the substance can be considered to be moderately bioaccumulative in aquatic gill-breathing organisms as the BCF exceeds 500. The substance does not meet the screening criteria for terrestrial bioaccumulation.

7 Ecotoxicology

7.1 Aquatic compartment

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

7.1.1 Fish

Short-term (acute) toxicity

Table 7.1 Summary of acute toxicity to fish

Method	Species	Analytical method	Results	Reliability	Reference
JIS K 0102-1986-71 **(semi-static)** **GLP**	Japanese Medaka *Oryzias latipes*	None	Limit test 48-h LC_{50} >125 mg/L (nominal)	Registrant: 2 (key study)	Unpublished (1994b) cited in ECHA (2020)

The acute fish toxicity study in the EU REACH registration dossier is a Japanese Industrial Standard JIS K 0102-1986-71 guideline study carried out to GLP using Japanese Medaka (*Oryzias latipes*) (Unpublished, 1994b; ECHA, 2020). This study was conducted as a semi-static limit test. Test solutions were prepared by preparing a 10:1 solution of the test substance with the solvent MEGAFAC F-142D, which was then diluted with ion-exchanged water to produce a stock solution with a nominal concentration of 1 000 mg/L. The final test solution had a nominal concentration of 125 mg/L and renewal was conducted every 8 to 16 hours. The concentration of the solvent in the final test solution is not stated. Ten fish were exposed to the test substance and a control. As no mortality was observed in this limit test, the 48-h LC50 was reported to be >125 mg/L based on nominal concentrations. The EU REACH registration gave the study a Klimisch score of 2 (reliable with restriction).

The validity criteria were not stated in the study report or registration dossier. In addition, it is not stated whether the control is a blank control or a vehicle control. However, the Environment Agency considers that as no mortality was observed in the control or exposure vessels this suggests that the conditions of the test were appropriate.

The water solubility of this substance is 1.5 mg/L (Section 5.3). A solvent was used to produce a test solution far in excess of the water solubility, but no chemical analysis was undertaken to confirm the exposure concentration and the concentration of solvent is not stated. It is therefore unclear what concentration of the test substance and solvent the fish were exposed to. As the test substance is volatile it is likely that the actual concentrations of the test substance to which the fish were exposed were lower than the nominal value despite regular test medium renewal.

Overall, this study suggests that the substance has a low acute toxicity to fish over 48 hours, with no effects up to the limit of solubility in the test medium, although the exposure concentration was not confirmed by analysis. However, as this exposure duration is shorter than the standard 96 hours, this result should be treated with caution and only used if supported by other data (e.g. read across, QSAR, etc.) (ECHA, 2017b).

The Environment Agency has generated a predicted acute fish 96-hour LC50 using ECOSAR v1.11 (US EPA, 2012) and inputting a water solubility of 1.5 mg/L and a log K_{OW} of 4.1. This model predicts that acute toxicity will not be observed at the limit of solubility. It is recommended that the UK supplier uses ECHA's Read-Across Assessment Framework (RAAF) (ECHA, 2017d) to provide additional supporting information for this endpoint.

Long-term (chronic toxicity)

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

7.1.2 Aquatic invertebrates

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*	GC-MS	48-h EC_{50} >1.1 mg/L (measured initial); mobility end point	Registrant: 1 (key study)	Unpublished (2017b) cited in ECHA (2020)

The acute aquatic invertebrate toxicity study in the EU REACH registration dossier is an OECD TG 202 study carried out to GLP using the water flea *Daphnia magna* (Unpublished, 2017b; ECHA, 2020). Test solutions were prepared by slow stirring a 100 mg/L loading of test substance in M7 test medium in a closed vessel for one day by magnetic stirrer. The resulting mixture was allowed to settle for one hour before the clear and colourless saturated solution was siphoned out of the vessel and used as the highest (100%) test concentration. Lower test concentrations of 10%, 1% and 0.1% were prepared by dilution of the saturated solution. The test was conducted in sealed glass vessels that were filled so that there was no headspace. Chemical analysis of the 10% and 100% exposure concentrations showed that the initial measured exposure concentrations were 0.089 mg/L and 1.1 mg/L respectively and that these remained within ±20% for the duration of the test. Analysis of the lower exposure concentrations and blank control found that the concentrations were below the limit of detection (0.008 mg/L) at all times. Twenty daphnids were exposed to the control and 100% saturated solution, with ten daphnids being exposed to the remaining test concentrations. Only a single daphnid became immobilised in this test, at the highest exposure concentration. Therefore, the 48-h EC_{50} based on immobilisation was reported to be >1.1 mg/L expressed as the initial measured concentration. The EU REACH registration gave the study a Klimisch score of 1 (reliable without restriction).

The validity criteria for <10% immobility in the controls and ≥3 mg/L dissolved oxygen (DO) were met. Actual concentrations of the test substance were verified to be within 80 and 120% of the initial measured concentration at the highest two test concentrations, and the maximum exposure concentration achieved is similar to the water solubility of the test substance (1.5 mg/L, Section 5.3). All other test parameters followed the standards in OECD TG 202, and measures were taken to minimise volatile losses. Therefore, the Environment Agency considers that the study is reliable for the purposes of this assessment.

Overall, the data indicate that the substance has a low acute toxicity to aquatic invertebrates as effects were not observed when using a saturated solution.

The Environment Agency has generated a predicted acute invertebrate 48 hour EC50 using ECOSAR v1.11 (US EPA, 2012) and inputting a water solubility of 1.5 mg/L and a log K_{OW} of 4.1. This model predicts that acute toxicity will not be observed at the limit of solubility. It is recommended that the UK supplier uses ECHA’s Read-Across Assessment Framework (RAAF) (ECHA, 2017d) to provide additional supporting information for this endpoint.

Long-term (chronic) toxicity

Long-term toxicity tests on aquatic invertebrates 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*	GC-MS	72-h E_rC_{50} >0.098 mg/L (measured TWA) 72-h E_yC_{50} >0.098 mg/L (measured TWA) 72-h NOE_rC 0.098 mg/L (measured TWA) 72-h NOE_yC 0.098 mg/L (measured TWA)	Registrant: 1 (key study)	Unpublished (2017c) cited in ECHA (2020)

The algal growth inhibition study in the EU REACH registration dossier is an OECD TG 201 study carried out to GLP using *Pseudokirchneriella subcapitata* (Unpublished, 2017c; ECHA, 2020). Test solutions were prepared by slow stirring a 100 mg/L loading of test substance in adjusted M2 test medium for one day in a closed vessel by magnetic stirrer. The resulting mixture was allowed to settle for one hour before the clear and colourless saturated solution was siphoned out of the vessel and used as the highest (100%) test concentration. Lower test concentrations of 10%, 1% and 0.1% were prepared by dilution of the saturated solution. The test was conducted in sealed glass vessels that were filled so that there was no headspace. Chemical analysis of the 10% and 100% exposure concentrations showed that the initial measured exposure concentrations were 0.047 mg/L and 0.72 mg/L respectively. Analysis showed that exposure concentrations reduced over the exposure period, such that at 24 hours the 10% exposure concentration was below the limit of detection and the 100% exposure concentration had reduced to 13% of the initial measured concentration. At 72 hours, the 100% exposure concentration was below the limit of detection. Analysis of the lower exposure concentrations and blank control found that the concentrations were below the limit of detection (0.008 mg/L) at all times.

The study authors report that no statistical analysis of the data was performed as results were similar in the control and highest test concentration. The 72-h EC_{50} based on growth rate and yield were reported to be >0.098 mg/L expressed as a measured time weighted average (TWA) concentration (in accordance with OECD TG 201). The 72-h NOEC based on growth rate and yield were reported be 0.098 mg/L expressed as a measured TWA concentration. The EU REACH registration gave the study a Klimisch score of 1 (reliable without restriction).

All the validity criteria were met. The results were not statistically analysed by the report authors to determine the NOEC. However, as the highest exposure concentration resulted in a 0.6% increase in growth rate and a 2.2% increase to yield the Environment Agency agrees that no adverse effects were observed in this study.

Although measures were taken to minimise volatile losses, actual concentrations of the test substance could not be maintained within ±20% of the initial concentration. A similar decrease in exposure concentration was observed in duplicate test vessels without algae, indicating that the loss of test substance was independent of the presence of algal cells. In correspondence between AGC and the testing laboratory it is suggested that the sampling of the test solution through the exposure period resulted in an increasing headspace in the test vials, which could account for the decrease in exposure concentration as the test substance volatilised.

All other test parameters followed the standards in OECD TG 201 and the study took steps to achieve the maximum possible exposure concentration. The Environment Agency considers the use of a TWA to derive the NOEC is precautionary in this case.

Overall, the data suggest that the substance has a low toxicity to algae for both short- and long-term endpoints as effects were not observed when using a saturated solution, although the significant decline in test concentration confounds the interpretation of this study.

The Environment Agency has generated a predicted acute algal 96-hour EC50 and a chronic effect value using ECOSAR v1.11 (US EPA, 2012) and inputting a water solubility of 1.5 mg/L and a log K_{OW} of 4.1. This model predicts that acute and chronic toxicity will not be observed at the limit of solubility. It is recommended that the UK supplier uses ECHA's Read-Across Assessment Framework (RAAF) (ECHA, 2017d) to provide additional supporting information for this endpoint.

No toxicity data are available for higher aquatic plants, although this is not a standard REACH information requirement at the current level of supply.

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.

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.

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**	None	Combined limit/range finding test 3-h ELR_{50} >1 000 mg/L (nominal) 3-h NOELR not determined	Registrant: 1 (key study)	Unpublished (2017d) cited in ECHA (2020)

The key study in the EU REACH registration dossier is an OECD TG 209 study carried out to GLP (Unpublished, 2017d; ECHA, 2020). The test was conducted using activated sludge from a sewage treatment plant receiving predominantly domestic sewage. Due to the volatility and low solubility of the test substance, a stock solution was not prepared, and instead the test substance was added directly to the test vessels at three nominal loading rates (10, 100 and 1 000 mg/L) with single replicates at the lower two concentrations and three replicates at the highest loading rate. The test is described as a combined limit/range-finding test, and there was no analytical measurement of the exposure concentration as this is not required by the guideline when the test substance is added directly to the test vessels. Blank, reference compound, abiotic and nitrification controls were also included. At the end of the study the 10, 100 and 1 000 mg/L loading rates inhibited the respiration rate by 10, 6 and 14% respectively. The 3-h ELR_{50} could not be calculated as there were no effects above 50%. The highest loading rate was found to have a significant effect on respiration rate, but a NOELR could not be determined with confidence (it would lie in the range 100 to 1 000 mg/L (nominal)). The 3-h EC_{50} based on sludge respiration in the positive control with 3,5-dichlorophenol fell within the expected range and all other validity criteria were met. The EU REACH registration gave the study a Klimisch score of 1 (reliable without restriction).

The Environment Agency also considers that all test parameters followed the standards in OECD TG 209 and that this study is sufficient to demonstrate that the 3-h ELR_{50} is above the highest tested nominal loading rate of 1 000 mg/L. A NOELR could not be defined but was below the maximum nominal loading rate of 1 000 mg/L.

Overall, the available test indicates that the substance is not acutely toxic to sewage microbes at loading rates up to 1 000 mg/L.

7.4 Atmospheric effects

The Henry’s Law constant indicates that 1H-PFHx is likely to significantly partition to air (see Section 6.2.2). No data about biotic effects (e.g. to plants) from aerial exposure are available in the EU REACH registration (ECHA, 2020), but this is not a standard information requirement.

The available data in the EU REACH registration dossier suggest that 1H-PFHx is unreactive to ozone, and therefore is unlikely to be an ozone depleting substance.

PFCs are known to be potent greenhouse gases, and this is considered further in Section 9.5.

8 Mammalian toxicology

The following information is taken directly from the ECHA public dissemination website entry for 1H-PFHx (ECHA, 2020a). The focus is on those mammalian 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 poising assessment (see Section 9.5). No human health hazard assessment has 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.

8.1 Toxicokinetics

No information is available in the EU REACH registration dossier.

8.2 Repeated dose toxicity

Table 8.1 Summary of mammalian repeated dose toxicity endpoints

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
Repeated dose oral toxicity, OECD TG 421 + EPA OPPTS 870.3550 **GLP**	Rat	Administered via oral gavage at nominal 0, 100, 300 and 1 000 mg/kg bw/day test article for 29 days in males, 50 to 64 days in females that delivered and 43 to 53 days in females that failed to deliver healthy offspring.	NOAEL ≥1 000 mg/kg/day (nominal); systemic toxicity. No adverse treatment-related effects on mortality, clinical appearance, body weight and body weight gain, food consumption were observed.	Registrant: 1 (key study)	Unpublished (2017e) cited in ECHA (2020a)
Repeated dose oral toxicity,	Rat	Administered via oral gavage at nominal 0, 40, 200 and 1	NOEL 200 mg/kg bw/day (nominal); organ weights and	Registrant: 1 (key study)	Unpublished (1994c) cited in

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
OECD TG 407, 28-day **GLP**		000 mg/kg bw/day test article for 28 days followed by a 14-day recovery period.	organ / body weight ratios. Increased liver weights were observed in male rats exposed to the test material at 1 000 mg/kg/day. No histopathological changes were observed in the liver.		ECHA (2020a)

8.3 Mutagenicity

Three *in-vitro* genetic toxicity studies are included in the EU REACH registration dossier.

Table 8.2 Summary of mammalian mutagenicity endpoints

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
Bacterial reverse mutation assay, **JAPAN: Guidelines for Screening Mutagenicity Testing Of Chemicals** **GLP**	*Salmonella typhimurium* and *Escherichia coli*	Exposure at 0, 313, 625, 1 250, 2 500, or 5 000 µg/plate (nominal)	Negative (no adverse effects reported at these concentrations) The substance has no reverse mutagenic potential under the study conditions.	Registrant: 1 (key study)	Unpublished (1994d) cited in ECHA (2020a)

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
Mammalian cell micronucleus test, JAPAN: Guidelines for Screening Mutagenicity Testing Of Chemicals **GLP**	Chinese hamster lung fibroblast cells	Exposure of cell plates at nominal concentrations of 0, 12.5, 25, and 50 µg/mL for 24 hours, 0, 25, 50, and 100 µg/mL for 48 hours and 0, 1 250, 2 500, and 5 000 µg/mL for the metabolic activation method.	The substance did not induce chromosome aberrations in the absence or presence of metabolic activation.	Registrant: 2 (key study)	Unpublished (1994e) cited in ECHA (2020a)
Mammalian cell gene mutation test using the thymidine kinase gene, OECD TG 490 **GLP**	Mouse lymphoma L5178Y cells	Exposure of cell plates at 0.05, 0.17, 0.54, 1.7, 5.4, 17, 52, 164 µg/mL (nominal)	No significant increase in the mutation frequency was observed in the presence or absence of metabolic activation The substance is not mutagenic in the TK mutation test system.	Registrant: 1 (key study)	Unpublished (2016) cited in ECHA (2020a)

8.4 Carcinogenicity

No information is available in the EU REACH registration dossier.

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

Table 8.3 Summary of mammalian reproductive toxicity endpoints

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
Reproduction / developmental toxicity screening test, OECD TG 421 + EPA OPPTS 870.3550 **GLP**	Rat	Administered via oral gavage at 0, 100, 300 and 1 000 mg/kg bw/day (nominal) for 29 days in males, 50 to 64 days in females that delivered and 43 to 53 days in females that failed to deliver.	NOAEL: ≥1 000 mg/kg bw/day; systemic toxicity in the first parental generation and reproductive and developmental toxicity in the F1 generation. No adverse treatment-related effects on mortality, clinical appearance, body weight and body weight gain, food consumption were observed.	Registrant: 1 (key study)	Unpublished (2017f) cited in ECHA (2020a)

8.6 Summary of mammalian toxicology

Based on the available mammalian toxicology data, the EU REACH registration concludes that no effects were demonstrated in studies conducted at maximally attainable vapour concentrations, limit doses, or other limits imposed by safety considerations.

9 Environmental hazard assessment

9.1 Classification and labelling

9.1.1 Harmonised classification

1H-PFHx does not have a harmonised classification under the EU Classification, Labelling and Packaging (CLP) legislation ((EC) No 1272/2008), nor a mandatory classification under UK CLP.

9.1.2 Self-classification

The EU REACH registration dossier proposes that the substance is Not Classified.

ECHA’s Classification and Labelling (C&L) Inventory of aggregated self-classifications includes the hazard classes listed below (ECHA, 2020b):

- Skin Irrit. 2 (H315)

- Eye Irrit. 2 (H319)

- STOT SE 3 (H335)

9.1.3 Conclusions for classification and labelling

1H-PFHx is not readily biodegradable and there is no evidence that it degrades significantly via abiotic mechanisms in aquatic media (see Section 7.1). It is therefore considered to be “not rapidly degradable” for the purposes of hazard classification.

The highest reported experimental fish BCF value is 658, which is consistent with predicted values (see Section 7.3). Despite the limited reliability of the fish bioconcentration study, 1H-PFHx meets the bioaccumulation criterion for the purposes of hazard classification, since both experimental and predicted BCF values exceed 500 L/kg (the log K_{OW} also exceeds 4).

Acute ecotoxicity endpoints are available for fish, invertebrates and algae (see Section 8). No toxic effects were observed in acute studies for invertebrates and algae at the practical limit of solubility in the test media, although measured concentrations declined inexplicably in the algal test, resulting in a 72-h E_rC_{50} > 0.098 mg/L based on TWA. A 48-h LC_{50} of > 125 mg/L (nominal) was obtained for fish, which can be interpreted as showing no effects at the practical limit of solubility in the test medium, although the test duration was shorter than normal, and losses of test substance due to volatilisation cannot be ruled out. A conservative approach would be to use the algal E_rC_{50} at face value. However, since no acute toxic effects were reported in any test and predicted ecotoxicity values also indicate that acute effects would not be anticipated up to the limit of solubility, the Environment Agency considers that this would be overly precautionary, and so **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 invertebrates. No adverse chronic effects were observed in the algal toxicity test, resulting in a 72-h NOE_rC of ≥0.098 mg/L based on TWA, and chronic effects on algae were not predicted up to the limit of solubility. As the substance is not rapidly degradable, a NOEC in the range 0.01 to 0.1 mg/L would lead to classification as Aquatic Chronic 1 (with a multiplication (M-)factor of 1). This would be a conservative conclusion given the lack of effects, but could be warranted by the rapid decline in test concentration. The Environment Agency notes that in the absence of further long-term toxicity information for fish and invertebrates, classification as **Aquatic Chronic 4** is a minimum requirement because the substance is poorly water soluble, not rapidly degradable and BCF values are ≥500. The Environment Agency recommends that the UK importer updates their self-classification to reflect these findings.

The human health hazard classification has not been considered.

9.2 Assessment of endocrine disrupting (ED) properties

The ecotoxicity dataset does not include any studies that assess ED potential and no additional information was identified during the literature search (Appendix A).

9.3 PBT and vPvB assessment

<u>Persistence</u>: No environmental half-life data are available for comparison with the definitive criteria in REACH Annex 13. 1H-PFHx is not readily biodegradable and there is no evidence that it degrades significantly via abiotic mechanisms in aquatic media (see Section 6.1). It therefore meets the screening criterion for being potentially persistent (P) or very persistent (vP). The EU REACH registration dossier concludes that the substance is vP (and P) based on the ready biodegradability study.

<u>Bioaccumulation</u>: 1H-Perfluorohexane has a reported log K_{OW} of 4.1 (see Section 5.4), which does not meet the screening criterion for bioaccumulation ('B') (as it is <4.5). Although there are some uncertainties in the reported fish BCF (see Section 6.4), the maximum value (658) is also significantly below the definitive bioaccumulation ('B') criterion in REACH Annex 13 (>2 000 L/kg).

In terms of bioaccumulation in air-breathing organisms, the log K_{OW} meets the screening criteria (>2) but the log K_{OA} of 0.85 does not (as it is <5).

The EU REACH registration dossier considers that 1H-PFHx does not fulfil the criteria for 'B' based on the fish BCF values.

Toxicity: In terms of aquatic toxicity, a 72-h NOErC of ≥ 0.098 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 the acute EC_{50} values are higher than 0.1 mg/L. 1H-PFHx therefore does not meet the screening criterion for being potentially T based on toxicity to aquatic organisms.

1H-PFHx does not meet the T criterion based on mammalian toxicity as indicated by the self-classifications for human health presented in the EU REACH registration dossier and C&L Inventory (see Section 9.1). The EU REACH registration dossier has the same conclusion.

No information is available on ED potential.

Overall conclusion: 1H-PFHx screens as potentially P/vP, but it does not screen as potentially B or T.

The EU REACH registration concludes that the substance is not PBT or vPvB.

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 ED potential.

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

Persistence: 1H-PFHx meets the screening criterion for being potentially P or vP (see section 9.3).

Mobility: The experimental log K_{OC} value of 3.7 (see Section 6.2.1) meets the draft criterion as being mobile (M) (log K_{OC} ≤4).

Toxicity: 1H-PFHx does not meet the T criterion based on mammalian toxicity (see Section 9.1). Additional considerations under the PMT criteria for Carc. 2, Muta. 2 and effects via lactation are not fulfilled. The EU REACH registration has not derived an oral long-term derived no-effect level (DNEL) for the general population because they considered that no effects were demonstrated in the available toxicity studies. No information is available on ED potential.

1H-PFHx does not meet the T criterion based on aquatic toxicity (see Section 9.1).

Overall conclusion: 1H-PFHx screens as potentially P/vP and M, but not T. Further testing could be done to confirm the level of toxicity in chronic studies for fish and invertebrates. However, 1H-PFHx is a relatively volatile liquid, and the influence of volatility is not considered under the criteria.

9.5 Greenhouse gas hazard

1H-PFHx is a volatile liquid, and a significant proportion of emissions are expected to end up in the atmosphere (see Section 6.2.3). 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, 2020f).

The GWP is defined by the Intergovernmental Panel on Climate Change (IPCC, 2014) as *"an index measuring the radiative forcing following an emission of a unit mass of a given substance, accumulated over a chosen time horizon, relative to that of the reference substance, carbon dioxide (CO_2). The GWP thus represents the combined effect of the differing times these substances remain in the atmosphere and their effectiveness in causing radiative forcing."*

In 2010, fluorinated gases covered under the Kyoto Protocol (F-gases) accounted for 2% of total anthropogenic greenhouse gas emissions (IPCC, 2014) and PFCs contribute to this.

Greenhouse gas emissions for PFCs are quantified as CO_2-equivalent emissions (in gigatonnes) ($GtCO_2$-eq) using weightings based on the energy absorbed by a gas over 100 years (the 100-year GWP). PFCs that are close structural analogues of 1H-PFHx are listed in Table 9.1, along with values sourced from IPCC (2013).

Table 9.1 Global warming potential of PFCs

Perfluoroalkane	Trade name	Atmospheric lifetime (years)	GWP (100 years) as CO_2 equivalent
Perfluoropentane	PFC-41-12	4 100	8 550
Perfluorohexane	PFC-51-14	3 100	7 910
Perfluoroheptane	PFC-61-16	3 000	7 820

1H-PFHx is not listed in IPCC (2013) as it is not a gas. However, several other HFCs are listed. For example, 1,1,1,2,3,3,3-heptafluoropropane (also called HFC-227ea or HFC-227; CAS no. 431-89-0) has an atmospheric lifetime of 38.9 years and its GWP (100 years) is reported to be 3 350 $GtCO_2$-eq (IPCC, 2013).

The GWP of 1H-PFHx is stated to be 2 000 on the website of AGCCE (https://www.agcce.com/pure-solvents/).

As indicated in Section 6.1.1, 1H-PFHx has a predicted atmospheric half-life of 31 years. Although its atmospheric lifetime is expected to be significantly shorter than PFCs, it could still make a contribution to global warming based on analogy with HFCs. The Environment Agency recommends that this should be considered as part of any emission controls.

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 toxicity studies. Available hazard data are discussed in Sections 7 and 8. The PNECs in the EU REACH registration are presented in Table 9.2. PNECs have also been derived by the Environment Agency following REACH guidance (ECHA, 2008) and are shown in Table 9.3. Due to the lack of effects observed in the acute ecotoxicity studies, a reliable aquatic PNEC cannot be estimated. ECHA (2008) states that a long-term test (on invertebrates, preferably *Daphnia*) has to be carried out for substances showing no toxicity in short-term tests if the log K_{OW} > 3 (or BCF > 100) and if the Predicted Environmental Concentration (PEC) local or regional is greater than 1/100th of the water solubility (>0.015 mg/L in this case). This is effectively a screening PNEC and so has been used here to give an indication of whether additional chronic ecotoxicity testing may be required. Due to the lack of a reliable aquatic PNEC, soil and sediment PNEC have not been calculated based on the Equilibrium Partitioning Method (EPM) at this time.

Table 9.2 PNECs derived for 1H-PFHx in the EU REACH registration (ECHA, 2020a)

Protection goal	PNEC	Notes
Fresh surface water	0.001 mg/L	
Freshwater sediment	0.554 mg/kg sediment dw	Equilibrium partitioning method (EPM)
Sewage treatment micro-organisms	10 mg/L	
Marine surface water	0.001 mg/L	
Marine sediment	0.055 mg/kg sediment dw	EPM
Soil	0.109 mg/kg soil dw	EPM
Secondary poisoning	-	No potential for bioaccumulation

Table 9.3 PNECs derived for 1H-PFHx by the Environment Agency

Protection goal	Most sensitive toxicity descriptor	Assessment factor	PNEC	Justification/ remarks
Fresh surface water			0.015 mg/L	A reliable PNEC cannot be estimated based on the currently available ecotoxicity data set. A screening PNEC of 1/100th water solubility is used to indicate whether chronic ecotoxicity data are required.
Freshwater sediment				Not calculated
Sewage treatment micro-organisms	3-h ELR_{50} >1 000 mg/L	100	>10 mg/L	No sludge respiration EC_{10} or NOEC available.
Marine surface water			0.0015 mg/L	In the absence of reliable data, an additional assessment factor of 10 has been applied to the fresh water PNEC.
Marine sediment				Not calculated
Soil				Not calculated
Secondary poisoning	NOAEL: ≥1 000 mg/kg bw/day	Conversion factor 20 Assessment factor 300	≥66.67 mg/kg food	Rats were >6 weeks old at test initiation and the duration of the test was >28 but <90 days.

9.6.2 Qualitative/semi-quantitative descriptors for other critical hazards

As noted in Section 9.5, the substance may contribute to global warming, which could be considered a qualitative hazard.

10 Exposure assessment

10.1 Environment

10.1.1 Environmental releases

The information in this section is based on the Chemical Safety Report (CSR) submitted by AGC Chemicals Europe Ltd to ECHA when the UK was still a member of the EU, supplemented with other information from further dialogue with the company. Most of the available information is confidential, so only a summary is presented here.

1H-PFHx is used as a solvent in the polymerisation process to produce ethylene-tetrafluoroethylene copolymer (ETFE), which is subsequently sold to manufacturers of articles in pellet form. Releases of 1H-PFHx occur to air and waste water during the manufacture of fluoropolymers.

ETFE has a wide variety of uses both in industrial processes (e.g. in the semi-conductor industry, in cable coating, in the automotive industry and architecture). 1H-PFHx 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 ETFE.

10.1.2 Exposure scenarios and measures for reducing emissions to the environment

10.1.2.1 Polymer manufacture

1H-PFHx is manufactured in Japan and imported to a single site in the UK (AGC Chemicals Europe Ltd, Fleetwood Road North, Thornton Cleveleys, Lancashire FY5 4QD). An EU REACH registration existed in 2020, but the Environment Agency understands that there was no direct supply to any European companies, so the UK site is the only source considered as part of this evaluation.

1H-PFHx is used exclusively at this site as a solvent in the polymerisation process to make fluorinated copolymer resins. This process involves two production lines. 1H-PFHx is received in 1 tonne intermediate bulk containers and pumped into storage tanks and then transferred as necessary to the reactors. Sampling for quality control is not undertaken on the site.

The company has an environmental permit (ref: EPR/BU5453IY) under the Environmental Permitting (England and Wales) Regulations 2016. According to the permit, the ETFE production capacity is 2 000 tonnes/year. The permit does not require any monitoring for 1H-PFHx or require any specific control measures.

When the batch reaction in the reactor is complete, the ETFE slurry is processed so the water/1H-PFHx mixture is driven off in a number of heating steps to recover and distil the 1H-PFHx for reuse. ETFE resin is dried at the end of this recovery. The remaining water from this heating process is released as waste water

Routes of emission to surface water

The waste water from the recovery processes, along with waste water from other processes on site, drains to the waste effluent pit, where solids are removed, prior to discharge to the River Wyre. This process was not designed to capture 1H-PFHx. The solid residue is disposed of at landfill.

Routes of emission to land

There is no direct emission to land from the site, and since the wastewater is not treated in a municipal sewage treatment plant (STP), it is not present in sewage sludge that can be spread on agricultural land.

Routes of emission to air

The main release point to air is from the exhaust from an activated carbon gas/vapour abatement scrubber which captures gaseous 1H-PFHx and recovers it back to recycled solvent tanks.

10.1.2.2 Polymer use

The quantity of 1H-PFHx in the fluoropolymer products supplied to customers is below 0.1 tonnes/year, based on the mass balance.

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.

Routes of emission to land

The Environment Agency assumes that unused or waste ETFE (and articles containing it) may be disposed of to landfill. The migration rate of any residual 1H-PFHx from the ETFE is unknown.

Routes of emission to air

Releases of 1H-PFHx to air are possible from ETFE during thermal processing at downstream user sites. The worst-case assumption is that these sites do not have any abatement on their heating processes and therefore all the 1H-PFHx is released to the atmosphere. The mass balance undertaken by AGC Chemicals Europe Ltd shows a release of <0.1 tonnes/year.

10.1.3 Release assumptions made by the Environment Agency

The CSR does not contain an exposure assessment, because there is no requirement for the company to do so under EU REACH.

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

- the volume released in 2019 and the associated monitoring data supplied; and
- changes in environmental temperature and river flows based on climate change projections (“future scenario”).

10.1.3.1 Current scenario

ES 1: Industrial use - polymer manufacture

- Volume released: confidential (based on 2019 data as this was the highest value over the last 3 years).
- Number of emission days: 330 days/year (CSR).
- Releases to surface water: The Environment Agency has calculated a theoretical maximum release of approximately 40 kg/year using 2019 data based on the water solubility of 1H-PFHx and the amount of waste water discharged from the relevant processes.
    - 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 Ltd 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.
    - Marine dilution factor: For sites that discharge direct to the marine environment, a marine dilution factor can be used. The default is 100.
- Releases to land: As explained in Section 10.1.2.1, 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: The releases to air are 30.9 tonnes/year over a number of release points in the waste water process, based on the mass balance produced by the company.

ES 2: Industrial use - polymer processing

The Environment Agency considers that, as a worst case, all residual 1H-PFHx can be assumed to be completely released during the polymer processing stage to air for all the grades. The Environment Agency has assumed that there is no abatement to remove the 1H-PFHx from these downstream users' sites. 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).

10.1.4 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.

Table 10.1 Substance-specific input parameters for the EUSES model

Parameter	Values assumed by the Environment Agency
Molecular weight	320.05 g/mol
Vapour pressure	15 kPa at 25 °C
Water solubility at 20 °C	1.5 mg/L
Octanol-water partition coefficient (log K_{OW})	4.1
Octanol-carbon partition coefficient (K_{OC})	3.7

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

Table 10.2 Scenarios used for the polymer manufacture exposure assessment

Parameter	Reasonable worse case
Annual use at site	confidential
Emission days	330 days/year
Daily use at site	confidential
Regional release to surface water	40 kg/year
Regional release to air	30.9 tonnes/year
Percentage of tonnage used at regional scale	100%
Release factor to water	confidential
Receiving surface water flow rate	52 704 m^3/day

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
Polymer manufacture	Fresh surface water	1.7×10^{-3}	mg/L
	Freshwater sediment	0.206	mg/kg ww
	Marine surface water	1.02×10^{-3}	mg/L
	Marine sediment	0.123	mg/kg ww
	Air	0.234	mg/m^3
	Soil	5.81×10^{-5}	mg/kg ww
	Groundwater*	1.95×10^{-7}	mg/L
Polymer processing (dispersion)	Fresh surface water	1.26×10^{-6}	mg/L
	Freshwater sediment	1.79×10^{-3}	mg/kg ww
	Marine surface water	3.57×10^{-7}	mg/L
	Marine sediment	2.04×10^{-4}	mg/kg ww
	Air	0.21	mg/m^3
	Soil	6.54×10^{-5}	mg/kg ww
	Groundwater*	1.67×10^{-7}	mg/L

Note: ww – wet 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
Fresh surface water	3.89×10^{-7}	mg/L
Freshwater sediment	7.54×10^{-5}	mg/kg ww
Marine surface water	2.7×10^{-7}	mg/L
Marine sediment	4.61×10^{-5}	mg/kg ww
Air	0.21	mg/m^3
Groundwater*	2.91×10^{-7}	mg/L

Note: ww – wet weight

* The porewater concentration for agricultural soil is used to represent groundwater.

10.1.5 Monitoring data

The company does not have any reliable monitoring data for releases of 1H-PFHx to either waste water or the atmosphere, but is undertaking a project to develop an analytical method and monitoring programme.

11 Risk characterisation

The Environment Agency has estimated PECs arising from the use of 1H-PFHx in the manufacture of ETFE and the worst case downstream user scenario for processing of polymers that contain it in residual amounts (see Section 10.1.2). These can be compared to the PNECs derived in Section 9 to calculate deterministic risk characterisation ratios (RCRs). The RCRs derived by the Environment Agency are shown in Table 11.1. An RCR above 1 indicates a potential risk.

Table 11.1 Risk characterisation ratios derived by the Environment Agency

Life cycle stage	Fresh water	Marine water	Secondary poisoning fish
Polymer manufacture	0.125	0.751	8.38×10^{-3}
Polymer processing	1.09×10^{-3}	1.24×10^{-3}	8.11×10^{-6}
Regional	2.57×10^{-5}	1.8×10^{-4}	

The releases to atmosphere are significant, at 30.9 tonnes in 2019. Exposure of soil organisms may occur if 1H-PFHx is transferred from the air to land via deposition. An RCR has not been calculated by EUSES for soil organisms due to the lack of a reliable PNEC. 1H-PFHx has a predicted atmospheric half-life of 31 years and although its atmospheric lifetime is expected to be significantly shorter than PFCs, it could still make a contribution to global warming based on analogy with HFCs.

The modelling indicates RCRs below 1 for the fresh water and marine compartments arising from the polymer manufacturing site. There is significant uncertainty about the releases to the River Wyre. The quantity used by the Environment Agency for modelling purposes was estimated based on the water solubility of 1H-PFHx at 20 °C. This does not take into account any losses during the heating and distillation stages of the aqueous waste prior to discharge to the main site waste water system. The Environment Agency recommends that AGC Chemicals Europe Ltd continues their project to refine the mass balance, with particular emphasis on environmental releases.

The aquatic PNEC used here are screening values based on the solubility of 1H-PFHx as effects were not observed in the acute ecotoxicity studies. The RCR indicate that additional chronic ecotoxicity testing is not required to refine the assessment.

The UK importer has undertaken to develop an analytical method to monitor 1H-PFHx at levels expected in the aqueous effluent and to significantly improve the mass balance to refine the atmospheric emissions. Once this is done, they have committed to implement additional measures to reduce these emissions.

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 is assumed to be extremely persistent over a range of ambient temperatures and also has a high vapour pressure, so its general environmental behaviour is likely to be unaffected 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 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 current PECs for discharge to the river are very uncertain and therefore it is not possible to model the impact of reduced dilution until more reliable information has been gathered.

12 Conclusions and recommendations

12.1 Conclusion

1H-PFHx is a PFAS that belongs to the group of hydrofluorocarbons. It is imported to the UK and used as a non-reactive processing aid at a single site. A large level of release occurs to air during the manufacture of fluoropolymers at this site, and there is also likely to be release of smaller quantities to the River Wyre. Small releases may also occur at polymer processing sites.

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

- 1H-PFHx meets the criteria to be classified as Aquatic Chronic 4 for aquatic environmental hazard under the CLP Regulation.
- 1H-PFHx is not readily biodegradable, and is not expected to degrade abiotically. 1H-PFHx therefore screens as potentially persistent or very persistent.
- An experimental bioconcentration study and the log K_{OW} and log K_{OA} indicate that bioconcentration in fish and bioaccumulation in air-breathing organisms are unlikely to be high.
- 1H-PFHx does not meet the toxicity criterion of REACH Annex 13.
- In summary, 1H-PFHx screens as potentially P/vP, but is unlikely to be B or T.
- 1H-PFHx is likely to be P/vP and M but there is insufficient information to conclude whether it meets the T criterion. It might pose a concern regarding the contamination of groundwaters, although the influence of volatility is not considered in this assessment.
- 1H-PFHx is volatile and is expected to partition significantly to the atmosphere. It has a long atmospheric half-life and has the potential to be transported to remote regions. It is also likely to be a source of perfluorohexan-1-ol (and potentially other transformation products) for a very long time. Transformation products are likely to be more water soluble than the parent substance, and could therefore be removed from the atmosphere by wet deposition in precipitation and/or more mobile in water. The hazards and risks of these substances need further consideration.

The exposure assessment produced by the Environment Agency has identified RCRs below 1 for fresh and marine surface waters based on a screening PNEC, suggesting the risk is low. However, 1H-PFHx has an atmospheric half-life of 31 years and although its atmospheric lifetime is expected to be significantly shorter than PFCs, it could still make a contribution to global warming based on analogy with HFCs. In addition, no data about biotic effects (e.g. to plants) from aerial exposure are available.

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 1H-PFHx, including:

- A further consideration of the pH variability and potential for colloid formation on the water solubility.
- Provision of further details for the experimental OECD TG 111 hydrolysis study.
- Additional predicted aquatic ecotoxicity values, to support the conclusions for these endpoints.
- A self-classification of Aquatic Chronic 4 for aquatic environmental hazard under the CLP Regulation.
- An evaluation of the properties of possible transformation products as part of the risk assessment.

AGC Chemicals Europe Ltd has undertaken to develop an analytical method to monitor 1H-PFHx at levels expected in the aqueous effluent and to significantly improve the mass balance to identify the atmospheric emissions. Once this is done, the exposure assessment could be updated, and if necessary further refined to demonstrate that the RCR is below 1 for all relevant compartments.

1H-PFHx has an atmospheric half-life of 31 years. Although its atmospheric lifetime is expected to be significantly shorter than PFCs, it could still make a contribution to global warming based on analogy with HFCs. The UK supplier is invited to consider this as part of any voluntary action it may take to improve emission controls.

12.2.2 General regulatory recommendations for consideration by relevant UK authorities

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

%	Percentage
B	Bioaccumulative
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BMF	Biomagnification factor
CAS	Chemical Abstracts Service
CLP	Classification, labelling and packaging (of substances and mixtures)
cm	Centimetre
CoRAP	Community Rolling Action Plan
CSR	Chemical Safety Report
d	Day
$DegT_{50}$	Degradation half-life or transformation half-life (days)
DMEL	Derived Minimal Effect Level
DNEL	Derived No Effect Level
DSD	Dangerous Substances Directive
DT_{50}	Dissipation half-life (days)
dw	Dry weight
EC_{10}	10% effect concentration
EC_{50}	50% effect concentration
ELR50	50% effect loading rate
ECETOC TRA	European Centre for Ecotoxicology and Toxicology of Chemicals Targeted Risk Assessment
ECHA	European Chemicals Agency
EPA	Environmental Protection Agency

EPM	Equilibrium Partitioning Method
EQS	Environmental Quality Standard
ERC	Environmental release category
ES	Exposure Scenario
EU	European Union
EUSES	European Union System for the Evaluation of Substances
FSDT	Fish Sexual Development Test
g	Gramme
GC	Gas chromatography
GC/FID	Gas chromatography – Flame Ionisation Detection
GC/MS	Gas chromatography – mass spectrometry
GLP	Good laboratory practice
H	Hours
HLC	Henry's Law Constant
hPa	Hectopascal
HPLC	High performance liquid chromatography
HSE	Health and Safety Executive
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database
IUPAC	International Union of Pure and Applied Chemistry
kg	Kilogram
kJ	Kilojoule
km	Kilometre
K_{AW}	Air-water partition coefficient
K_{OA}	Octanol-air partition coefficient

K_{OC}	Organic carbon-water partition coefficient
K_{OW}	Octanol-water partition coefficient
kPa	Kilopascal
$K_{SUSP–WATER}$	Suspended matter–water partitioning coefficient
k_{X}	Rate constants (days-1)
L	Litre
LC_{50}	50% lethal effect concentration
LEV	Local Exhaust Ventilation
LOD	Limit of detection
Log	Logarithmic value
LOQ	Limit of quantitation
M	Molar
m/z	Mass to charge ratio
mg	Milligram
min	Minute
mL	Millilitre
mol	Mole
MS	Mass spectrometry
nm	Nanometre
NOAEL	No observed adverse effect level
NOEC	No-observed effect concentration
NOEL	No observed effect level
NONS	Notification of New Substances Regulations 1993
OC	Operational condition
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
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
p	Statistical probability
Pa	Pascal
PACT	Public Activities Co-ordination Tool
PBT	Persistent, Bioaccumulative and Toxic
PC	Product category
PEC	Predicted environmental concentration
pg	Picogramme
PFAS	Per- and polyfluorinated alkyl substances
PFOS	Perfluorooctanesulfonate
PFOA	Perfluorooctanoic acid
pKa	Acid dissociation constant
PNEC	Predicted no effect concentration
POP	Persistent organic pollutant
ppb	Parts per billion
PPE	Personal Protective Equipment
ppm	Parts per million
PROC	Process Category
QSAR	Quantitative structure-activity relationship
OPERA	OPEn structure–activity/property Relationship App
r^2	Correlation coefficient
RCR	Risk characterisation ratio
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals (EU Regulation No. 1907/2006)

RMM	Risk Management Measures
RPE	Respiratory protective equipment
rpm	Revolutions per minute
SMILES	Simplified Molecular Input Line Entry System
SVHC	Substance of Very High Concern
t	Tonne
T.E.S.T	Toxicity Estimation Software Tool
TG	Test Guideline
TMF	Trophic Magnification Factor
TSCA	Toxic Substances Control Act
UNEP	United Nations Environment Programme
UK	United Kingdom
US EPA	United Stated Environmental Protection Agency
UV	Ultraviolet
vB	Very bioaccumulative
vP	Very persistent
VP	Vapour pressure
vPvB	Very persistent and very bioaccumulative
WAF	Water Accommodated Fraction
WSF	Water Soluble Fraction
wt	Weight
ww	Wet weight
WWTP	Wastewater Treatment Plant
µg	Microgram

Appendix A: Literature search

A literature search was undertaken by the Environment Agency on the 20th April 2020 to identify published information relevant to the assessment of 1H-PFHx. 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
355-37-3	0	4
Trideca-1,1,1,2,2,3,3,4,4,5,5,6,6-fluorohexane	0	0
1H-Perfluorohexane	3	3
1H-Tridecafluorohexane	0	1
Tridecafluorohexane	0	22
Total unique records	3	28

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: 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 b.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 B.1 QSAR model outline

Name	Brief description
ACD/Labs	Predicts physicochemical properties via the Percepta Platform[2].
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.

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

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).

EPISuite™

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

Table B.2 EPISuite™ 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 (WATERNT 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 solubilities 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.

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