Environmental risk evaluation report: Perfluoropropane [PFP]

(CAS no. 76-19-7)

Chief Scientist's Group report

April 2023

We are the Environment Agency. We protect and improve the environment.

We help people and wildlife adapt to climate change and reduce its impacts, including flooding, drought, sea level rise and coastal erosion.

We improve the quality of our water, land and air by tackling pollution. We work with businesses to help them comply with environmental regulations. A healthy and diverse environment enhances people's lives and contributes to economic growth.

We can't do this alone. We work as part of the Defra group (Department for Environment, Food & Rural Affairs), with the rest of government, local councils, businesses, civil society groups and local communities to create a better place for people and wildlife.

Published by:

Environment Agency
Horizon House, Deanery Road,
Bristol BS1 5AH

www.gov.uk/environment-agency

Further copies of this report are available from our publications catalogue: www.gov.uk/government/publications or our National Customer Contact Centre: 03708 506 506

Email: research@environment-agency.gov.uk

Author(s):
Chemicals Assessment Unit, Environment Agency

Keywords:
Perfluorinated alkyl substances; PFAS; perfluorocarbons; PFC; perfluoropropane; octafluoropropane; PFP

Environment Agency's Project Executive:
Steve Dungey

Citation:
Environment Agency (2023) Environmental risk evaluation reports: Perfluoropropane [PFP] (CAS no. 76-19-7). Environment Agency, Bristol.

Contents

Research at the Environment Agency

Scientific research and analysis underpins everything the Environment Agency does. It helps us to understand and manage the environment effectively. Our own experts work with leading scientific organisations, universities and other parts of the Defra group to bring the best knowledge to bear on the environmental problems that we face now and in the future. Our scientific work is published as summaries and reports, freely available to all.

This report is the result of research commissioned by the Environment Agency's Chief Scientist's Group.

You can find out more about our current science programmes at https://www.gov.uk/government/organisations/environment-agency/about/research

If you have any comments or questions about this report or the Environment Agency's other scientific work, please contact research@environment-agency.gov.uk.

Dr Robert Bradburne
Chief Scientist

Acknowledgements

The co-operation and additional information provided by the sole UK manufacturer, F2 Chemicals Ltd, is acknowledged.

This report also benefitted from comments received from Defra's Hazardous Substances Advisory Committee (HSAC) who reviewed an initial draft version of the report.

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 have 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 made or used at two UK production facilities. The substance reviewed in this evaluation report is perfluoropropane or PFP (CAS no. 79-19-7).

PFP is a PFAS belonging to the group of perfluoroalkanes and it is a gas at standard environmental temperatures and pressures. It is produced for use in a wide range of applications including as a processing, etching and cleaning fluid, coolant and solvent in semi-conductor and electrical equipment manufacture (see Section 3 for further details).

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

PFP is not readily biodegradable and there is no evidence that it degrades significantly via abiotic mechanisms. PFP therefore screens as Persistent (P) or very Persistent (vP). There are no valid experimental aquatic bioconcentration data and also no log K_{OW} data for PFP itself. In the absence of better information and based on Quantitative Structure-Activity Relationship (QSAR) approaches, the likely log K_{OW} range of 2.5 to 3.1 for PFP (Section 5.4.5) indicates that it does not screen as potentially Bioaccumulative (B) in aquatic organisms. PFP is a gas and so this might not be a relevant trigger. There are some indications of retention in mammalian tissues (which is possibly non-lipid mediated) but also of elimination by exhalation of high vapour pressure perfluorocarbons in mammalian studies. Overall PFP is unlikely to bioaccumulate in aquatic or air-breathing organisms.

There are no ecotoxicity data on PFP itself to determine whether it meets the toxicity (T) criteria. However, as PFP is a gas, its high volatility could make testing difficult. Information from QSAR models and suggested analogues of PFP indicates that the acute and chronic aquatic toxicity for fully saturated perfluoroalkanes is expected to be low. The UK supplier has not proposed any aquatic hazard self-classification for PFP under Classification, Labelling and Packaging legislation and similarly they do not identify any classifications that would meet human health 'T' criteria. Whilst there are some

uncertainties with the assumptions made, the information considered in Sections 7 and 8 indicates overall that PFP is unlikely to exhibit significant toxic effects in aquatic and soil-dwelling organisms. Recommendations are made for the UK supplier to provide further scientific support and justification for their waiving of (eco)toxicological testing and to update their dossier accordingly.

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). PFP is considered to be vP and screens as M and so it might pose a concern relating to the contamination of groundwaters. However the influence of volatility is not currently considered under these criteria

The substance is expected to partition predominantly to air rather than soil or water. Available information suggests that PFP has the potential for long-range transport. PFP is a greenhouse gas identified in the Ozone-Depleting Substances (ODS) Substances and Fluorinated Greenhouse Gases (F-gas) regulations. It therefore presents a risk to the environment once emitted to the atmosphere and is expected to have a significant global warming potential (GWP), with a 100-year GWP in the order of 8 800 to 8 900 $GtCO_2$-eq (see Section 9.5). No data are available on effects on plants via aerial exposure.

The direct emission estimates and Predicted Environmental Concentrations (PEC) for the production site in Section 10 are based largely on default exposure modelling assumptions. Emissions from other downstream uses within the UK have not been considered due to a lack of information. However, given the physico-chemical properties of PFP, a significant proportion of the overall production volume could eventually end up in the atmosphere (unless specific measures are taken to recover or destroy this). Certain potential downstream user industries (e.g. the semi-conductor industry) have exemptions from some F-gas controls.

In the absence of more detailed information regarding emissions, use pattern and measured environmental concentrations, there remains significant uncertainty in this exposure assessment. Further refinement would be required to improve its reliability, such as specific information on UK tonnages, uses and releases, monitoring data and more reliable experimental data for physico-chemical properties.

Due to the expected lack of significant ecotoxicity from PFP, no environmental Predicted No-Effect Concentration (PNEC) values have been calculated to perform a risk characterisation using the derived PEC values (Section 11).

A number of recommendations are made to the UK supplier to improve the data package to allow a more robust assessment of the environmental hazards, exposure and risks posed by PFP. In particular this relates to supporting and improving the scientific justification for the grouping and read-across data waivers in the physico-chemical properties, ecotoxicity and mammalian toxicity sections of their dossier.

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 Regulations.

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 made or 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-NH4 (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)

---

[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)
- **Perfluoropropane - also known as octafluoropropane or PFP (CAS no. 76-19-7)**

The additional substance also being considered is:

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

This report summarises the evaluation of the substance highlighted above in **bold** (i.e. PFP), 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 on this substance (Appendix A: Literature search). As the substance was, at the time of writing, registered under EU REACH, information on the substance's properties and uses was obtained from the European Chemicals Agency (ECHA) public dissemination website (https://echa.europa.eu/information-on-chemicals/registered-substances accessed from July 2020) (ECHA, 2020a). Unless otherwise stated, this website is the main source of information used in this report. Full scientific study reports have generally not been reviewed by the Environment Agency, only the publicly available literature and EU REACH dossier information have been consulted at this stage. Some additional information was also provided directly by the UK manufacturer.

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, then an exposure and risk assessment. The final section summarises the findings of this review. 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. This report is however not intended to provide a consideration of hazards, exposure and risks to human health. This is not a formal UK REACH Evaluation.

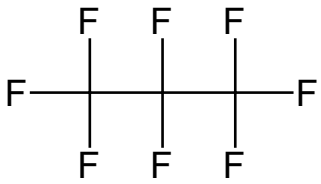
1 Substance Identity

1.1 Name and other identifiers

Public name	Octafluoropropane
IUPAC name	1,1,1,2,2,3,3,3-Octafluoropropane
CAS name	-
Alternative name	Perfluoropropane or PFP*
EC number	200-941-9
CAS number	76-19-7
Index number in Annex VI of the CLP Regulation	-
Molecular formula	C_3F_8
Molecular weight	188 g/mol
SMILES code	C(C(F)(F)F)(C(F)(F)F)(F)F
Synonyms	C_3F_8-gas, Freon 218, Perfluoropropane [PFP]*, Perflutren, PFC-218, Propane, octafluoro-
Type of substance	Mono-constituent

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

Figure 1.1 Structural formula of PFP



1.2 Structurally related substances

PFP is a branched perfluoroalkane. It is an example of a perfluorocarbon (PFC) which contains only carbon and fluorine atoms. Substances in this perfluoroalkane category have fully fluorinated (i.e. saturated) carbon atoms and lack functional groups such as the 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 (CF_4)) and so PFCs are much less reactive than their hydrocarbon analogues.

The US EPA CompTox Chemicals database (USEPA, 2020a; USEPA, 2020b) was used to identify three key structural analogues of PFP:

- Perfluoroethane;
- Heptafluoropropane; and
- Hexafluoropropene (HFP).

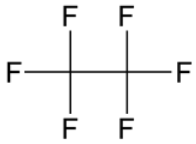
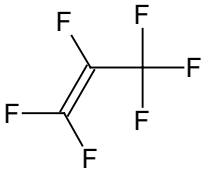
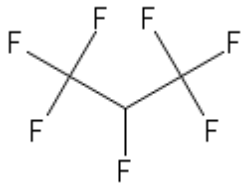
Further information on these is provided in Table 1.1.

Higher molecular weight perfluoroalkanes such as perfluoropentane (CAS no. 678-26-2) and perfluorohexane (CAS no. 355-42-0) are volatile liquids at standard temperature and pressure rather than gases and have not been considered in this report. Perfluorobutane (CAS no. 355-25-9) is a gas at standard temperature and pressure but is not registered under EU REACH and has not been considered in this report.

1.3 Transformation products

Information from Section 29 of this report indicates that PFP is very stable and unlikely to react or degrade further through biotic or abiotic means. Consideration of further transformation products is therefore not relevant for the purposes of this report.

Table 1.1 Substance identifiers for perfluoroethane

Public name	**Perfluoroethane**	**Hexafluoropropene**	**1,1,1,2,3,3,3-heptafluoropropane**
CAS number	76-16-4	116-15-4	431-89-0
EC number	200-939-8	204-129-5	207-079-2
Structural formula			
Molecular formula	C_2F_6	C_3F_6	C_3HF_7
Molecular weight	138.01 g/mol	150 g/mol	170 g/mol
SMILES code	C(C(F)(F)F)(F)(F)F	F\C(F)=C(/F)C(F)(F)F	C(F)(F)(F)C(F)C(F)(F)F
Synonyms	Ethane, hexafluoro- Hexafluorethane 1,1,1,2,2,2-Hexafluoroethane Freon 116 Perfluoroethane	Hexafluoropropylene HFP Perfluoropropene Perfluoropropylene	heptafluoropropane HFC 227ea HFC 227
Relationship to PFP	Belongs to the perfluoroalkane group but has one less carbon atom (along with two associated fluorine atoms) in its chain.	Both are perfluorocarbons, but HFP is unsaturated, which may affect its reactivity compared to PFP. PFP has a slightly higher molecular weight.	HFC 227ea is not a perfluorocarbon, as the second carbon is bonded to one not two fluorine atoms (the other bond is to a hydrogen atom).

2 Analytical chemistry

2.1 Regulatory and academic methods

No analytical details are included in the EU REACH registration dossier (ECHA, 2020a).

The Environment Agency searched the academic literature for analytical methods for the detection of PFP in the following environmental matrices: water, fresh and marine; soil; sediment; sludge; and air (Appendix A: Literature search). This identified one record of environmental monitoring for concentrations for PFP in air, a gas chromatography/mass spectrometry analysis method (Culbertson *et al.*, 2000). A chromatogram of the single ion CF_3^+ was used for the detection of different PFC gases in background air samples.

Analytical monitoring of PFP environmental matrices has not been widely performed as part of national or international programmes, in particular it is not present in the following PFAS databases accessed via the NORMAN network substance database (https://www.norman-network.com/nds/susdat/):

- PFASTRIER list;
- PFASNTREV19 list;

However, PFP was listed in these databases:

- KEMI PFAS Market List;
- OECD PFAS list (OECD 2018);
- Drugbank (https://go.drugbank.com/drugs/DB00556).

No associated analytical methods were presented.

Internationally validated LC/MS/MS methods for the analyses of specific PFAS in general include several methods used by the US EPA of which none were found to include PFP.

It is recommended that the UK supplier provides details of their analytical methodology for measuring atmospheric emissions of PFP (and related PFCs). 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.

- The use of procedural blanks and control samples in both sample preparation and analysis.
- 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.

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 in to UK law. The European Chemicals Agency (ECHA) public databases are however still a relevant source of information about industrial chemicals on the UK market at the time of writing.

According to the ECHA website (ECHA, 2020a), PFP is registered in the EU by Chementors Ltd, Raisio, Finland (a consultancy firm) at an aggregated supply level of 100 to 1,000 tonnes/year (ECHA, 2020a). The substance is manufactured by F2 Chemicals Ltd (www.f2chemicals.com), Preston, Lancashire. F2 Chemicals Ltd has an environmental permit (ref: EPR/BU3485IS) under the Environmental Permitting (England and Wales) Regulations 2016. It produces a range of liquid and gaseous PFC substances, with a total production capacity of around 400 tonnes per year.

An overview of uses according to the public REACH registration is presented in Table 3.1. The F2 Chemicals Ltd website (2020) provides some additional details. PFP's characteristics are said to include:

- Compatibility with most construction materials.
- No residue on evaporation.
- Non-flammability.
- Limited toxicity.

Applications include use in semiconductor manufacture, as a fluid for etching processes and chemical vapour deposition (CVD) chamber cleaning to remove dielectric film build up. In a plasma with oxygen, it generates a variety of reactive species that breakdown chemical deposits to make volatile products, which are readily removed under vacuum.

Industrial and professional uses of PFP in the EU REACH registration (ECHA, 2020a) include:

- Calibration of analysis equipment.
- Cleaning/etching agent.
- Coolant and detector fluid.
- Manufacture of computer, electronic and optical products, electrical equipment.
- Processing agent.
- Refrigerant.
- Solvent in polymerisation process.

Bartos *et al.* (2007) suggest that PFP is a thermal degradant of Novec™ 612 (1,1,1,2,2,4,5,5,5-Nonafluoro-4-(trifluoromethyl)-3-pentanone, CAS no. 756-13-8). This is EU REACH registered and used as a low global-warming potential (GWP) replacement for sulfur hexafluoride as a cover gas in magnesium die casting. There is an individual registration of the substance at a supply level of ≥ 1 000 tonnes/year, and a separate joint registration at a supply level of 100 to 1 000 tonnes/year.

Cai *et al.* (2018) report that the molten-fluoride electrolysis process used to produce rare-earth metals releases PFCs including PFP. They made measurements at 3 Chinese production sites and measured emissions ranging from 0.03 to 0.27 g/tonne of rare-earth metal for PFP. The authors indicate that rare-earth metal production is around 0.1% of the volume of aluminium production, and so releases of PFP from aluminium processing may need to be considered further.

Table 3.1 Overview of uses

Life cycle stage	Use(s)
Manufacture	**Manufacture of substance** ERC1: Manufacturing PROC 2: Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment conditions
Formulation	**Formulation, Transfer and (Re-)Filling** ERC2: Formulation into mixture PROC 1: Chemical production or refinery in closed process without likelihood of 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 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)
Uses at industrial sites	**Use as intermediate** ERC6a: Use of intermediate PROC 1: Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions

Life cycle stage	Use(s)
	Calibration of analysis equipment ERC4: Use of non-reactive processing aid at industrial site (no inclusion into or onto article) PROC 9: Transfer of substance or mixture into small containers (dedicated filling line, including weighing) PROC 15: Use as laboratory reagent **Industrial use as cleaning/etching reagent** ERC6b: Use of 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 **Solvent in polymerisation process** 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 8b: Transfer of substance or mixture (charging and discharging) at dedicated facilities **Use for electronic component manufacture** ERC5: Use at industrial site leading to inclusion into/onto article PROC 3: Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions PROC 8b: Transfer of substance or mixture (charging and discharging) at dedicated facilities **Refrigerant** ERC7: Use of functional fluid at industrial site PROC 2: Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment condition
Uses by professional workers	**Use gas to refill refrigeration equipment, refrigerant gas** ERC9b: Widespread use of functional fluid (outdoor) PROC 8a: Transfer of substance or mixture (charging and discharging) at non-dedicated facilities

Life cycle stage	Use(s)
Consumer uses	None identified in the registration dossier
Article service life	None identified in the registration dossier

Source: EU REACH registration dossier (ECHA, 2020a).

4 Summary of relevant regulatory activities

4.1 Europe

4.1.1 European Chemicals Agency (ECHA)

The Public Activities Co-ordination Tool (PACT) (ECHA, 2020g) provides an overview of the substance-specific activities that EU regulatory authorities are working on under the EU REACH and CLP Regulations. PFP is not currently included on PACT, and neither is it listed on the Community Rolling Action Plan (CoRAP) (https://echa.europa.eu/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table - accessed July 2020).

Between May and July 2020, the national authorities of Germany, the Netherlands, Norway, Sweden, and Denmark invited interested parties to send in evidence and information on the use of PFAS in preparation for a joint REACH restriction proposal. The current scope of the work is wide, and includes all substances that contain at least one aliphatic $-CF_2-$ or $-CF_3$ element (see https://www.rivm.nl/en/pfas/pfas-restriction-proposal last accessed July 2020 and ECHA Registry of Restriction Intentions: https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e18663449b, accessed October 2021). Therefore HFP is within scope of this initiative.

4.1.2 European Food Safety Authority (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 EFSA (http://www.efsa.europa.eu/ - accessed July 2020) did not identify PFP as being evaluated 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 EU REACH activities.

PFP 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), nor 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 of America

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

PFP 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 (https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/chemicals-undergoing-risk-evaluation-under-tsca accessed July 2020; https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/low-priority-substances-under-tsca accessed July 2020).

4.2.2 Canada

A search did not identify PFP 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 2021).

4.2.3 Australia

A search did not identify PFP as being under assessment under the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (https://www.industrialchemicals.gov.au/chemical-information/search-assessments accessed July 2020). It is understood that there was a NICNAS assessment from 1992 from the registration information although this assessment was not cited.

4.2.4 New Zealand

A search did not identify PFP as being under assessment under the Hazardous Substances and New Organisms Act 1996 (https://www.epa.govt.nz/industry-areas/hazardous-substances/chemical-reassessment-programme/ 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

PFP 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)

PFP is not identified as a POP, and is not currently under evaluation (http://chm.pops.int/%20TheConvention/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, 2015). F-gases are regulated under the Ozone-Depleting Substances and Fluorinated Greenhouse Gases (Amendment etc.) (EU Exit) Regulations (2019) (https://www.legislation.gov.uk/uksi/2019/583/contents/made accessed 12 February 2021) 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 PFP is included.

5 Physico-chemical properties

This evaluation focusses on vapour pressure, water solubility and n-octanol-water partition coefficient, because 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 2020) unless otherwise indicated. The reliability scores provided in the full registration for individual studies are cited. These scores have presumably been generated in accordance with the ECHA R.4. Guidance Document (ECHA, 2011). An independent evaluation has not been possible since original study reports were not available and the EU REACH registration dossiers generally lack sufficient supporting information. The Environment Agency is therefore not in a position to assign its own reliability scores (except in the case of data presented in academic journals or obtained using quantitative structure-activity relationship (QSAR) models).

Where an endpoint value is missing from the 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. EU REACH registration data for the analogues are taken at face value, although preference is given to regulatory reviews (if available). QSAR models are generally considered to be a screening-level tool and measured values are preferable provided that they are sufficiently reliable. Further information on QSARs is provided in Appendix B: QSAR models.

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

Property	Value(s)	Reliability	Reference
Physical state at 20 °C and 101.3 kPa	Colourless gas	Registrant: 2 (key study)	Registration dossier
Melting / freezing point	-183 °C (unknown method, unnamed reference)	Registrant: 2 (key study)	Registration dossier
Boiling point	-37 °C (unknown method, unnamed reference)	Registrant: 2 (key study)	Registration dossier
Relative density	1.36 g/m^3 at 25 °C (unknown method, unnamed reference)	Registrant: 2 (key study)	Registration dossier
Vapour pressure	767 kPa at 20 °C (static method, Crowder *et al., (*1967); Brown, (1963); and unnamed reference, 1992)	Registrant: 2 (key study)	Registration dossier
Surface tension	4.3 mN/m (unknown method, unnamed reference)	Registrant: 2 (key study)	Registration dossier
Water solubility	5.7 mg/L at 20 °C (EPIWIN V4.11 experimental database, Yalkowsky and Dannenfelser 1992)	Registrant: 2 (key study)	Registration dossier
n-Octanol/water partition coefficient (log K_{OW})	2.8 (software prediction using module KOWWIN v1.67)	Registrant: 2 (key study)	Registration dossier
Particle size distribution	Data waiver	-	Registration dossier
Stability in organic solvents and identity of relevant degradation products	Material is stable in all solvents	Registrant: 2 (key study)	Registration dossier
Dissociation constant	Data waiver	-	Registration dossier

5.1 Vapour pressure

5.1.1 Measured data

An experimentally derived vapour pressure value was presented in the EU REACH registration dossier of PFP. This key study data used the static method and is referenced to Brown (1963), Crowder *et al.,* (1967) and an unnamed secondary source (1992) (ECHA, 2020a) and was classed as not GLP compliant. The EU REACH registration assessed the data reliability as Klimisch score 2 (reliable with restrictions). The experimentally derived vapour pressure of PFP was 767 kPa at 20 °C (ECHA, 2020a). No further details of methodology or generation of data were provided.

According to EU REACH Guidance R7a (ECHA, 2017a), vapour pressure testing is not required for substances with a standard boiling point of < 30 °C, as these substances will have vapour pressures above the limit of laboratory measurement 1 x 10^5 Pa (100 kPa). The boiling point of PFP is -37 °C.

The ChemSpider database contained a measured vapour pressure for PFP of 793 kPa at 21 °C (5.9 x 10^3 mmHg at 21 °C). Value converted from psia to kPa by the Environment Agency. No details of methodology were provided for generation of data (RSC, 2020a).

5.1.2 Predicted data

No *in silico* predictive data were presented in the EU REACH registration for this endpoint.

The ChemSpider database and the US EPA CompTox dashboard contain predicted vapour pressures for PFP generated from EPISuite™, 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 PFP

Source	Details	Vapour pressure at 25 °C
ACD/Labs	N/A	840 kPa [6.25 x 10^3 mmHg]
EPISuite™ estimation programme **MPBPVP v1.42**	Mean of Antoine and Grain methods BP = 49.54°C MP = -88.87°C	712 kPa [5.34 x 10^3 mmHg]
	exp. database BP = -36.6°C MP = -147.6°C	884 kPa [6.63 x 10^3 mmHg]
T.E.S.T.	N/A	857 kPa [6.43 x 10^3 mmHg]

Source	Details	Vapour pressure at 25 °C
OPERA	Global applicability domain: Inside Local applicability domain index: 0.998 Confidence interval 0.750	895 kPa [6.71 x 10^3 mmHg]

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

- For the ACD/labs model this information was not available, therefore no assessment of the applicability could be performed.
- Guidance provided with the MPBPWIN v1.42 model indicated that the relationship between the experimental and predicted vapour pressure values for a test set of 1 642 compounds was good, with an R^2 of 0.949, standard deviation of 0.59 and an average deviation of 0.32. The training set contained several PFCs (see Appendix B: QSAR models) and it is likely that the predicted value for PFP falls within the applicability domain of the model.
- For the OPERA model, structural analogues of PFP were included in both the training set and external test sets (including PFP). PFP is considered inside the global applicability domain and has a high local applicability domain index (> 0.6), therefore the prediction is considered reliable based on the OPERA model applicability domain criteria.
- For the T.E.S.T. model, structural analogues of PFP were included in both the training set and external test sets (e.g. perfluoroethane). Therefore, predicted values from T.E.S.T. could be considered within the applicability domain of the model.

5.1.3 Data from structural analogues

Given the consistency in the reported experimental values, which are similar to the predicted values using a variety of methods, information from structural analogues was not sought.

5.1.4 Additional sources

No additional relevant information was reviewed as part of this evaluation.

5.1.5 Recommended value

For PFP a vapour pressure value of 767 kPa (at 20 °C) was measured (ECHA, 2020a). *In silico* predicted values range from 712 kPa to 895 kPa (both at 25°C; US EPA, 2020a and RSC, 2020a).

The robustness and reliability of the experimentally derived value presented in the EU REACH registration could not be assessed. This was due to the age of the studies and the lack of detail in supporting information. For example, the Environment Agency could not perform a review of methodology against OECD Test Guideline (TG) 104 (OECD, 2006). However, the weight of evidence from other sources (a second reported measured value and QSAR estimates) provides support to the value of **767 kPa (at 20°C)**, and this is taken forward to derive conclusions and as part of the exposure and risk assessment. The measurement by far exceeds the limits of laboratory measurement. However, there is no guidance about how to proceed with data in excess of 100 kPa.

The upper bound value for vapour pressure in the European Union System for Evaluation of Substances (EUSES) model (ECHA, 2020c) is 1 000 kPa. Given the value for PFP is close to this limit, it is unlikely to be a sensitive parameter for exposure modelling.

5.2 Surface tension

5.2.1 Measured data

No experimentally derived data for PFP were presented in the EU REACH registration (ECHA, 2020a).

Key data presented in the EU REACH registration dossier were sourced from other company data. A value of approximately 4.3 mN/m at 20 °C was estimated from the trend observed across similar substances using data derived from literature values and estimates. No further information was presented. The EU REACH registration gave the study a reliability rating of 2 (reliable with restrictions).

Based on evidence from other PFCs, the Environment Agency believes that this value is the surface tension of the pure liquid, not an aqueous solution, and this was confirmed by the UK supplier. It is therefore irrelevant for this evaluation.

5.2.2 Predicted data

No *in silico* predictive data were presented in the EU REACH registration for this endpoint.

The ChemSpider database (RSC, 2020a) and US EPA CompTox dashboard (US EPA, 2020a) include predictions of surface tension generated from T.E.S.T. and ACD/Labs software at 12.0 and 9.3 mN/m at 25 °C respectively (US EPA, 2020a). The Environment Agency believes that this represents the surface tension of the substance itself, rather than an aqueous solution. QSARs have therefore not been considered further.

5.2.3 Data from structural analogues

No information from structural analogues was considered necessary for surface activity given the above data measured and predicted data available for PFP.

5.2.4 Additional sources

Chernyshev and Skliar (2014) reported a small decrease in the surface tension of deionised water in the presence of PFC 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 presence of perfluoropentane and 66.7 mN/M in the presence of perfluorohexane.

As part of this evaluation, the Environment Agency reviewed data for perfluorophenanthrene (CAS no. 306-91-2). It is reported to have a minimal effect on the surface tension of water. Whilst not a close analogue of HFP, the lack of hydrophilic functional groups means that PFCs generally are unlikely to be surface active in water.

5.2.5 Recommended value

Surface tension in water is important because it affects the measurement and interpretation of other physico-chemical properties such as water solubility and partition coefficients. There is no legal requirement to provide a surface tension value for substances with a water solubility below 1 mg/L, but the water solubility proposed for PFP is 6.4 mg/L at 25 °C (see Section 5.3 below). Although the EU REACH registration reports a surface tension of 4.3 mN/m at 20 °C for PFP, the Environment Agency considers that this is the surface tension of the neat substance rather than that of an aqueous solution and so is not relevant for this evaluation.

The Environment Agency notes that PFP does not have any hydrophilic structural groups that can form hydrogen or Van der Waals bonds in water. This suggests that it is unlikely to be significantly surface active in aqueous solutions. The Environment Agency recommends that the robust study summary for this end point is updated.

5.3 Water solubility

5.3.1 Measured data

No experimentally derived water solubility value was presented in the EU REACH registration dossier (ECHA, 2020a).

The Environment Agency notes that an experimental water solubility value of 5.7 mg/L at 15 °C (Yalkowsky and Dannenfelser, 1992) is referenced in the WSKOW v1.42 model of the EPISuite™ platform. No detailed study methodology or analytical details are available.

The Environment Agency notes that the substance is a gas, so measurement using standard (e.g. OECD) methods is not possible.

5.3.2 Predicted data

The EU REACH registration cites a water solubility of 5.7 mg/L at 20 °C derived from EPISuite™ (v4.1) as the key data for this end point (ECHA, 2020a). The Environment Agency believes that this refers to an experimental result rather than a prediction (see above).

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 5.3. Values were converted by the Environment Agency from mol/L to mg/L using a molecular weight of 188.82 g/mol.

Table 5.3 Water solubility values for PFP

Model	Details	Water Solubility
EPISuite™ water solubility estimate from log K_{OW} (WSKOW v1.41)	log K_{OW} used: 3.12 (estimated) water sol (experimental data base match) = 5.7 mg/L (15 °C; Yalkowsky and Dannenfelser 1992)	19.68 mg/L at 25 °C
EPISuite™ water solubility estimate from fragments (v1.01 est.)	-	12.72 mg/L
T.E.S.T.	Predicted value: 2.23 x 10^{-4} mol/L	42.11 mg/L
OPERA	Predicted value: 3.04 x 10^{-5} mol/L Global applicability domain: Outside Local Applicability domain index: 0.998 Confidence Interval 0.784	6.40 mg/L

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

- Guidance provided with the WSKOWWIN v1.41 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 PFCs (see Appendix B: QSAR models) and it is likely that the predicted value for PFP falls within the applicability domain of the model but the value should be treated with caution.
- For the OPERA model, structural analogues of PFP were included in both the training set and external test sets (including PFP). PFP is considered to be outside the global applicability domain but has a high local applicability domain index (> 0.6). However, as the training and external training sets include PFP, the value is considered reliable.
- For the T.E.S.T. model, no close structural analogues of PFP were included in both the training set and external test sets. Therefore, predicted values from T.E.S.T. could be considered to be outside the applicability domain of the model.

5.3.3 Data from structural analogues

The Environment Agency evaluation of the analogue HFP recommends a water solubility of 82 mg/L at 28 °C (Environment Agency, 2023a). PFP has a higher molecular weight and does not have an unsaturated alkene group, and so it is likely to be less water soluble than HFP.

The Environment Agency has sought data for the analogue perfluoroethane. PFP has a higher molecular weight and so it is likely to be less water soluble than this substance.

A water solubility of 520 mg/L at 25 °C using the column elution method according to OECD TG 105 (OECD, 1995a) is cited in the EU REACH registration of perfluoroethane (ECHA, 2020b). The method was GLP compliant. The EU REACH registration gave the study a Klimisch score of 2 (reliable with restrictions). No analytical conditions were provided. As perfluoroethane is a gas, OECD TG 105 is not an appropriate method. From the tabulated information, it appears that the substance was introduced into a test cell containing water, and a mass balance was used. Its validity cannot be determined without more information.

For comparison, the ChemSpider database contained estimated water solubilities from EPISuite™ (RSC, 2020b). The US EPA CompTox dashboard contained predicted water solubility endpoint values generated from EPISuite™, T.E.S.T. and OPERA software (US EPA, 2020b). 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 138.01 g/mol.

Table 5.4 Predicted water solubility values for perfluoroethane

Model	Details	Water Solubility
EPISuite™ water solubility estimate from log K_{OW} (WSKOW v1.41)	log K_{OW} used: 2.00 (estimated) no melting point equation used water sol (experimental data base match) = 7.78 mg/L (25 °C; Yalkowsky and Dannenfelser, 1992)	302.8 mg/L at 25 °C
EPISuite™ water solubility estimate from fragments (v1.01 est.)	-	217.7 mg/L
T.E.S.T.	Predicted value: 9.12 x 10^{-4} mol/L	125.9 mg/L
OPERA	Predicted value: 5.64 x 10^{-5} mol/L Global applicability domain: Inside Local Applicability domain index: 0.998 Confidence Interval 0.808	7.8 mg/L

This suggests that the EPISuite™ models are more relevant than the other 2 for this end point and substance type.

The water solubility of 520 mg/L at 25 °C is significantly greater in value than the 7.78 mg/L at 25 °C reported in Yalkowsky and Dannenfelser (1992). No experimental or analytical conditions were provided for these two values.

5.3.4 Additional sources

Tsai *et al.* (2002) and Tsai (2009) roughly estimated the water solubility of several PFCs from measured water solubility of tetrafluoromethane. The estimation was performed using a regression equation derived from plotting water solubility against octanol-water partition co-efficient. These values are summarised in Table 5.5.

Table 5.5 Summary of estimated water solubility of PFC analogues

Substance	Molecular weight (g/mol)	Water Solubility (mol/L)	Water solubility (mg/L)	Measured/ Estimated	Reference
Perfluoromethane	88	1.7×10^{-4}	15.0	Not stated	Tsai *et al.* (2002)
Perfluoromethane	88	2.1×10^{-4}	18.5	Measured†	Tsai (2009)
Perfluoropentane	288	1.9×10^{-5}	5.5	Estimated	
Perfluorohexane	338	1.0×10^{-5}	3.4	Estimated	
Perfluoroheptane	388	5.7×10^{-6}	2.2	Estimated	
Perfluorooctane	438	3.1×10^{-6}	1.4	Estimated	
Perfluorononane	488	1.7×10^{-6}	0.8	Estimated	

†Measured at 25 °C

The Environment Agency does not consider this to be a reliable approach, given the uncertainties in the octanol-water partition coefficients used in this study (see Section 5.4.4).

5.3.5 Recommended value

The key water solubility value of PFP is 5.7 mg/L at 20 °C in the EU REACH registration (ECHA, 2020a), although the Environment Agency notes that this value was obtained at 15 °C according to the quoted source. Its reliability is unknown.

The Environment Agency notes that according to Chernyshev and Skliar (2014), PFCs such as perfluorohexane form colloids in water, which may involve "liquid droplets, vapour bubbles or a combination of both phases simultaneously". The substance is likely to partition from water to air (see Section 6.2.2), so controls to limit losses due to volatility may also be required during measurement. Both factors complicate the measurement of aqueous solubility.

In silico predictions for the water solubility of PFP were between 6 and 42 mg/L (RSC, 2020a; US EPA, 2020a). Given the issues around colloid formation and volatility for this type of substance, these predictions may not be fully reliable. The studies of Tsai *et al.* (2002 and 2009) suggest the water solubility of PFP could lie between 5.5 mg/L (perfluoropentane) and 18.5 mg/L (perfluoromethane), but the Environment Agency considers this study to be unreliable.

The Environment Agency considers that the water solubility of PFP is probably between 1 and 10 mg/L, although there is uncertainty in the actual value. Ideally the water solubility should be measured using an appropriate method. In the absence of better information, a

water solubility of **5.7 mg/L at 15 °C** will be used in the assessment, based on the experimentally derived value from Yalkowsky and Dannenfelser (1992). The Environment Agency has performed a temperature correction of this value using EUSES (v2.03), which results in a water solubility of **6.4 mg/L at 25 °C**. The Environment Agency recommends that further information is provided to support a reliable water solubility value for PFP and the robust study summary is updated accordingly.

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

5.4.1 Measured data

No experimentally derived log K_{OW} value was presented in the EU REACH registration dossier of PFP (ECHA, 2020a).

5.4.2 Predicted data

The supporting information in the registration refers to a log K_{OW} value of approximately 2.8 at 25 °C predicted in the EU REACH registration using the EPISuite™ platform (ECHA, 2020a). The EU REACH registration assessed the data reliability as Klimisch score 2 (not assignable). The Environment Agency also generated a predicted log K_{OW} value of 2.8 using KOWWIN v1.68.

The ChemSpider database and US EPA CompTox dashboard contained estimated log K_{OW} values from EPISuite™, ACD/Labs and OPERA software (RSC, 2020a; US EPA, 2020a). Values are presented in Table 6.6. The value for log K_{OW} derived via KOWWIN v1.67 as presented by ChemSpider differs to the value calculated by the Environment Agency using v1.68 and in the EU REACH registration and this is the preferred value derived via KOWWIN v1.68.

Table 5.6 Predicted log K_{OW} values for PFP

Model	Details	log K_{OW}
ACD/Labs	ACD/LogP ACD/LogD (pH 5.5)	2.65 2.9
EPISuite™	KOWWIN v1.67 estimate	3.12
EPISuite™	KOWWIN v1.68 estimate	2.8
OPERA	Global applicability domain: Inside Local applicability domain index: 0.453 Confidence interval 0.517	1.76

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

- For the ACD/labs model this information was not available, therefore no assessment of the applicability can be performed.

- Guidance provided with the KOWWIN v1.67 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: QSAR models) and it is likely that the predicted value for PFP falls within the applicability domain of the model but the value should be treated with caution.
- For the OPERA model, structural analogues of PFP were included in both the training set and external test sets (e.g. perfluoroethane). PFP is considered inside the global applicability domain and has a local applicability domain index of 0.4 to 0.6 and therefore the prediction should be considered with caution.

5.4.3 Data from structural analogues

No experimentally derived log K_{OW} value was presented in the EU REACH registration dossier of perfluoroethane (ECHA, 2020b) or Hexafluoropropene (ECHA, 2020c). The KOWWIN v1.41 model in the EPISuite™ platform reports an experimental value of log K_{OW} of 2.0 (referenced to Hansh et al., 1995). No further information has been sought about the reliability of this value. Given the issues around colloid formation and volatility for this type of substance, the measured result may not be fully reliable. However, it is very similar to values predicted using various QSARs as reported in the ChemSpider database and US EPA CompTox dashboard (RSC, 2020b; US EPA, 2020b). Values are presented in Table 5.7.

Table 5.7 Predicted log K_{OW} values for perfluoroethane

Model	Details	log K_{OW}
ACD/Labs	ACD/LogP ACD/LogD (pH 5.5)	2.0 2.2
EPISuite™	KOWWIN v1.67 estimate log K_{OW} (experimental database match; Hansch, *et al.,* 1995)	2.15 2.0
OPERA	Global applicability domain: Inside Local applicability domain index: 0.998 Confidence interval 0.844	2.0

The apparent consistency between models might be a consequence of the use of a measured value in the training sets.

5.4.4 Additional sources

Tsai (2009), estimated the log K_{OW} of several PFCs using a fragment constant approach as summarised below in Table 5.8.

Table 5.8 Summary of estimated log K_{OW} of perfluoroalkane analogues

Substance	Molecular weight (g/mol)	Log K_{OW}
Perfluoropentane	288	1.53
Perfluorohexane	338	1.79
Perfluoroheptane	388	2.05
Perfluorooctane	438	2.31
Perfluorononane	488	2.57

These values suggest a general trend of increasing hydrophobicity as the chain length gets longer, so the log K_{OW} of PFP could be expected to be below 1.53. However, the Environment Agency notes that the predicted value for each substance is much lower than those estimated using other models (Appendix B: QSAR models). The reliability of these values is therefore highly uncertain.

5.4.5 Recommended value

No experimental log K_{OW} values are available for PFP. The Environment Agency notes that according to Chernyshev and Skliar (2014), PFCs such as perfluorohexane form colloids in water, which may involve "liquid droplets, vapour bubbles or a combination of both phases simultaneously". PFP is likely to partition from water to air (see Section 6.2.2), so controls to limit losses due to volatility may also be required during measurement. Both factors complicate the measurement of log K_{OW}. Ideally a log K_{OW} value should be estimated using measured data (e.g. the ratio of solubility in water and in n-octanol).

In silico predictions for the log K_{OW} of PFP were in the range 1.76 to 3.12 (US EPA, 2020a and RSC, 2020a), although the reliability of these values is unknown.

A measured log K_{OW} of 2.0 at 25 °C has been reported for the analogue perfluoroethane (with QSAR predictions in the range 2.0 to 2.15).

There is significant uncertainty in the log K_{OW} of PFP. In the absence of better information, the Environment Agency recommends a log K_{OW} of 2.8 at 25 °C for modelling purposes (with a range of 2.5 to 3.1 for the purposes of sensitivity analysis). The Environment Agency recommends that further information is provided to support a reliable log K_{OW} value for PFP, ideally based on measured data, and the robust study summary updated accordingly. There would be technical challenges as this substance is a gas, but it may be possible to measure solubility in n-octanol and then derive a K_{OW} value using a reliable water solubility measurement.

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

The log K_{OA} is a non-standard endpoint under REACH 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).

5.5.1 Measured data

No relevant information is available in the EU REACH registration dossier of PFP (ECHA, 2020a).

5.5.2 Predicted data

The Environment Agency has estimated a K_{OA} value using the dimensionless Henry's Law constant (K_{AW}) of 3.98 (see Section 6.2.2) and the recommended log K_{OW} value of 2.8 (Section 5.4.5) ($K_{OA} = K_{OW}/K_{AW}$). The resulting log K_{OA} is -1.18.

As noted in Section 5.4.5, the Environment Agency recommends that the uncertainty in the K_{OW} value should be addressed using sensitivity analysis. If a log K_{OW} value of 2.5 is assumed, the log K_{OA} would be -1.48 and if a log K_{OW} value of 3.1 is assumed, the log K_{OA} would be -0.88.

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 PFP generated from KOAWIN v1.10 and OPERA software (RSC, 2020a, US EPA, 2020a). These values are presented in Table 5.6 Predicted log K_{OW} values for PFP.

Table 5.6 Predicted log K_{OA} for PFP

Source	Details	log K_{OA}
EPISuite™ Estimation programme KOAWIN v1.1	Log K_{OA} (log K_{OW} used: 3.12 and K_{AW} used: 3.13 estimated) Log K_{OA} (experimental database): None	-0.01
OPERA	Global applicability domain: Inside Local Applicability domain index: 0.877 Confidence Interval: 0.711	-1.33
Calculation	Calculated from log K_{AW} of 3.98 and a log K_{OW} value of 2.8 ($K_{OA} = K_{OW}/K_{AW}$)	-1.18

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

- For the KOAWIN v1.1 model, the values are estimated from either predicted or experimental K_{AW} and K_{OW} values sourced from HENRYWIN and KOWWIN respectively. Therefore, the reliability of the predicted K_{OA} for PFP is dependent on

the reliability of HENRYWIN and KOWWIN and the presence of structural analogues in their respective data sets.

- For the OPERA model, no close structural analogues of PFP were included in the training and external test sets. PFP is considered inside the global applicability domain and has a high local applicability domain index (> 0.6), therefore the prediction is considered reliable based on the OPERA model applicability domain criteria.

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).

Predicted values from the open literature and derived by the Environment Agency suggest a log K_{OA} in the range -1.33 to -0.01, although the reliability of these predictions is uncertain. The Environment Agency does not consider it appropriate to choose a single value from this estimated data range. This is considered further in the assessment of bioaccumulation in air-breathing organisms (Section 6.3.2).

5.6 Dissociation constant

No experimental dissociation constants were presented for PFP in the EU REACH registration (ECHA, 2020a). The EU REACH registration states PFP “does not dissociate”. The Environment Agency agrees a dissociation constant is irrelevant for PFP as it has no ionisable functional groups. It will remain as a neutral compound at environmentally relevant pH.

6 Environmental fate properties

6.1 Degradation

6.1.1 Abiotic degradation

6.1.1.1 Hydrolysis

There are no measured data in the EU REACH registration dossier, which states that "PFCs do not hydrolyse", with the additional justification of "saturated PFCs are extremely stable compounds, with strong carbon-fluorine and carbon-carbon bonds (no other bonds are present). They are resistant to a vast range of chemicals, including strong acids and bases. We can say with certainty that they do not hydrolyse." Further references are provided to support this assertion in the Chemical Safety Report (CSR).

The Environment Agency considers that the lack of hydrolysable groups in the chemical structure means that hydrolysis is unlikely to be a relevant degradation pathway for PFP.

6.1.1.2 Phototransformation in air

There is no relevant information in the public EU REACH registration dossier. However the CSR provides a discussion indicating an expectation that PFP will have a long atmospheric half-life. This is based on a paper by Mühle *et al.* (2010) which discusses PFP, perfluoroethane and tetrafluoromethane, with estimated "atmospheric lifetimes" of 2 600, 10 000 and 50 000 years, respectively. References are provided in the paper to support the timescale for tetrafluoromethane, but not PFP or perfluoroethane (so it is unclear whether these values are extrapolated from experimental data or estimated by modelling). The EU REACH registration provides a suggested degradation pathway for direct photolysis via cleavage of the carbon chain. The Environment Agency has not assessed the reliability of this information given that the substance has been evaluated by the International Panel on Climate Change (IPCC) (see below).

The CSR also references a NICNAS assessment (NICNAS, 1992) for the substance published in 1992. That report provides a qualitative discussion of the photodegradation, indicating an expectation of the half-life of similar to CF_3Cl (400 years) and C_2F_5Cl (380 years). Again, it is noted that the NICNAS report was prepared 15 years before the IPCC assessment, and so superseded by the IPCC conclusion.

6.1.1.2.1 Other information

Direct photolysis of a carbon-fluorine chain is expected to be very slow, with stability expected to be sustained for more than 1 000 years (Environment Canada, 2012).

The IPCC Fourth Assessment Report states that PFP has an atmospheric lifetime of 2 600 years (Forster *et al.*, 2007).

The US EPA CompTox dashboard and ChemSpider database contained predicted photodegradation half-life values for PFP generated from AOPWIN v1.92 and OPERA software (RSC, 2020a, US EPA, 2020a). These values are presented in Table 6.1 Predicted photodegradation half-life values for PFP.

Table 6.1 Predicted photodegradation half-life values for PFP

Source	Atmospheric hydroxylation rate constant	Half-life (days)
EPISuite™ Estimation programme AOPWIN v1.92	No indirect photodegradation as the chemical bonds that the QSAR uses are not present in PFP	-
OPERA	4.55 x 10^{-16} cm^3/molecule-sec Global applicability domain: Inside Local Applicability domain index: 0.423 Confidence Interval: 0.496	35 300[1]

[1] Calculated by the Environment Agency using EUSES (v2.03)

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 AOPWIN v1.92 model this information was not available, therefore no assessment of the applicability can be performed. It is not known whether the training set contained structurally similar substances of PFP.
- For the OPERA model, a close structural analogue of PFP (e.g. 2H-perfluoropropane) was included in the training and external test sets. PFP is considered inside the global applicability domain and has a local applicability domain index of 0.4 to 0.6 and therefore the prediction should be considered with caution.

6.1.1.3 Phototransformation in water

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

6.1.1.4 Phototransformation in soil

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

6.1.2 Biodegradation in water

6.1.2.1 Measured data

There is no ready biodegradation study for PFP itself in the EU REACH registration dossier.

The CSR notes the difficulty in performing biodegradation testing on a gas. It cites three ready biodegradation tests conducted on other PFAS: perfluoroperhydrophenanthrene

(CAS no. 306-91-2), perfluoroperhydrofluorene (CAS no. 307-08-4; also referred to as docosafluorododecahydrofluorene in the registration for this substance (ECHA, 2012)) and perfluoro-2-methylpentane (PFiHx), all of which showed no degradation. The EU REACH registration concluded that the substance was “not inherently biodegradable” (presumably in the absence of any biodegradation being observed), and that this is consistent with the “very high stability of the material, and it is reasonable to conclude that all PFCs do not appreciably biodegrade”.

The Environment Agency notes that the OECD methods to test biodegradation are not suitable for a gas. For the cited analogues, the first 2 substances are not considered by the Environment Agency to be close analogues of PFP as they have a cyclic structure and are of much higher molecular weight. PFiHx (CAS no. 355-04-4) is a closer analogue of PFP (with 6 carbon atoms in its structure compared to the 3 present in PFP), although it is a volatile liquid rather than a gas. The Environment Agency has assessed the study on PFiHx: it was a recent test performed to OECD TG 310 and GLP and showed no biodegradation over 28 days (OECD, 2014).

There are no simulation data available in the EU REACH registration dossier, the EU REACH registration waives the requirement with the justification that the test is “scientifically not necessary / other information available”. Although not specifically stated, the “other information available” appears to be the general conclusion about biodegradation detailed above.

6.1.2.2 Predicted data

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

The Environment Agency is not aware of a biodegradation QSAR for which PFP is within the applicability domain.

6.1.2.3 Data from structural analogues

The structural analogues in section 2.2 are also gases. Within the registration dossiers for these substances, an OECD 301D study was performed for HFC 227ea, which determined that no biodegradation had occurred after 28 days. A QSAR cited for hexafluoropropene was concluded to show no significant biodegradation for the substance. The endpoint was waived for perfluoroethane. Overall the data for HFC 227ea and hexafluoropropene are consistent with the conclusion of not readily biodegradable for PFP.

6.1.2.4 Recommended value

The Environment Agency considers that the read-across justification from other substances is weak since it relies on substances that are not particularly close analogues. However, PFP is a gas, and the EU REACH registration considers that it is not readily biodegradable. The Environment Agency agrees with this conclusion.

6.1.3 Biodegradation in sediment

There are no simulation data available in the EU REACH registration dossier. The EU REACH registration waives the requirement with the justification that the test is “scientifically not necessary / other information available”. Although not specifically stated, the “other information available” appears to be the general conclusion about biodegradation detailed in Section 6.1.2.1.

6.1.4 Biodegradation in soil

There are no simulation data available in the EU REACH registration dossier. The EU REACH registration waives the requirement with the justification that the test is “scientifically not necessary / other information available”. Although not specifically stated, the “other information available” appears to be the general conclusion about biodegradation detailed in Section 6.1.2.1.

6.1.5 Summary and discussion of degradation

The EU REACH registration expects very little abiotic degradation, providing mainly qualitative arguments to support the expected lack of hydrolysis and very limited photodegradation. Based on the structure, the Environment Agency agrees that hydrolysis will not be a relevant degradation pathway. The Environment Agency also notes that the IPCC Fourth Assessment Report states that PFP has an atmospheric lifetime of 2 600 years, indicating negligible photodegradation.

There are no measured biodegradation data for PFP in the EU REACH registration dossier. The EU REACH registration considers PFP to not be readily biodegradable based on 0% biodegradation read-across from PFiHx and two further ready biodegradation tests on other perfluorinated cycloalkyl substances. In the absence of better data and read-across justification, the Environment Agency agrees with the conclusion of not readily biodegradable as it is in line with the expectation that PFP will not be significantly biodegraded due to its perfluorinated structure. This conclusion is of limited relevance for a gas.

6.2 Environmental distribution

6.2.1 Adsorption/desorption

6.2.1.1 Measured data

The EU REACH registration dossier waives the endpoint as technically infeasible and justifies this in the CSR because the substance is a water-insoluble gas. The Environment Agency notes that measuring an organic carbon-water partition coefficient (K_{OC}) is unlikely to be practically possible for a gas.

6.2.1.2 Predicted data

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

The Environment Agency has predicted a log K_{OC} of 2.37 for PFP using the preferred log K_{OW} value of 2.8. This was done in EUSES (v2.03) using the 'Predominantly hydrophobics" chemical class (the equation is: log K_{OC} = 0.81 log K_{OW} + 0.10). There is uncertainty in the K_{OW} value, which is likely to lie in the log K_{OW} range of 2.5 to 3.1 (see Section 5.4); the log K_{OC} range could be 2.12 to 2.61 using the same equation.

According to the published paper for the QSAR (Sabljic *et al.*, 1995), it is suitable for chemicals containing fluorine (despite none of the 81 chemicals in the training set containing fluorine). The log K_{OW} value of PFP means that it is within the applicability domain.

The US EPA CompTox dashboard and ChemSpider database contained predicted log K_{OC} values for PFP generated from KOCWIN v1.66 and OPERA software (RSC, 2020a, US EPA, 2020a). The Environment Agency has generated predicted K_{OC} values for PFP using KOCWIN v2.0 as ChemSpider does not report whether this prediction is based on the Molecular Connectivity Index method or on the log K_{OW} method. These values are presented in Table 6.2.

Table 6.2 Predicted log K_{OC} for PFP

Source	Details	log K_{OC}
EPISuite™ Estimation programme KOCWIN v1.66	It is unclear whether this prediction is based on the Molecular Connectivity Index (MCI) method or on the log K_{OW} method	3.0
EPISuite™ Estimation programme KOCWIN v2.0	Molecular Connectivity Index method Koc = 882.4 L/kg Log K_{OW} method (estimated log K_{OW} = 2.82) K_{OC} = 279.9 L/kg	2.95 2.48
OPERA	Global applicability domain: Inside Local Applicability domain index: 0.469 Confidence Interval: 0.583	2.96
EUSES model calculation from Log K_{OW}	Log K_{OW} = 3.0 and 'predominantly hydrophobics" equation	2.37

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 KOCWIN v2.0 model, the training and validation sets contained no PFCs (see Appendix B: QSAR models) and it is likely that the predicted value for PFP does not fall within the applicability domain of the model, so the value may be unreliable.

- For the OPERA model, no close structural analogues of PFP were included in either the training set or external test sets. PFP is considered to be outside the global applicability domain and has a local applicability domain index of 0.4 to 0.6. The prediction may therefore be unreliable.

6.2.1.3 Data from structural analogues

There are no measured data available for relevant analogues.

6.2.1.4 Recommended value

There is significant uncertainty in the log K_{OC} of PFP. In the absence of better information, the Environment Agency recommends a **log K_{OC} of 2.53 at 25 °C** for modelling purposes (with a range of **2.12 to 2.93 for the purposes of sensitivity analysis**). This conclusion is of limited relevance for a gas. Only a small fraction will partition between water and organic carbon compared to the much larger fraction partitioned to air (see Section 6.2.3).

6.2.2 Volatilisation

6.2.2.1 Measured data

In the CSR, the endpoint is waived with the justification that the substance is gas. The Environment Agency disagrees that this is sufficient to disregard the endpoint as volatilisation provides a measure of partitioning between air and water.

6.2.2.2 Predicted data

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

A Henry's Law constant (HLC) at 25 ° C of 2.25 x 10^7 Pa m^3/mol) was calculated by the Environment Agency using EUSES (v2.03) with the recommended water solubility of 6.4 mg/L at 25 °C and vapour pressure of 767 kPa at 25 °C (see Sections 5.3.5 and 5.1.5).

The US EPA CompTox dashboard and ChemSpider database contained predicted HLC values for PFP generated from OPERA software (RSC, 2020a, US EPA, 2020a). These values are presented in Table 6.3. The Environment Agency has converted the values from atm m³/mol to Pa m³/mol.

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 v3.1 model, the training and validation sets contained several PFCs (see Appendix B: QSAR models) and it is likely that the predicted value for PFP 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.
- For the OPERA model, no close structural analogues of PFP were included in either the training set or external test sets. PFP 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.

Table 6.3 Predicted Henry's Law constant for PFP

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 Experimental database: 3.3 x 10^1 atm m³/mol	1.29 x 10^7 2.48 x 10^6 3.34 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	6.89x 10^3
EUSES	Calculated from water solubility of 6.4 mg/L at 25 °C and vapour pressure of 767 kPa at 25 °C	2.25 x 10^7

6.2.2.3 Data from structural analogues

There is no information for relevant analogues.

6.2.2.4 Recommended value

The Environment Agency recommends a HLC of **2.25 x 10^7 Pa m³/mol** for modelling purposes calculated from the preferred water solubility value (6.4 mg/L) and vapour pressure (767 kPa).

This value has been used to derive a dimensionless HLC or air-water partition coefficient (log K_{AW}) of 3.98, which is used in the prediction of long-range transport (see Section 6.2.4). The Environment Agency recommends that further information is provided to support a reliable HLC value for PFP and the robust study summary updated accordingly.

6.2.3 Distribution modelling

The CSR provides a general qualitative summary stating that as PFCs are neither hydrophilic nor lipophilic they are unlikely to be adsorbed to soil or sediment, nor dissolve in water. No data is provided to support these assertions, and the Environment Agency notes that a water solubility value has been reported for PFP (see Section 5.3).

The EU REACH registration concludes that as PFP is a gas, it will be almost exclusively distributed to air.

Fugacity modelling predicts how a substance may be distributed in the environment following a release to a specific compartment (i.e. air, water or soil). The potential environmental distribution of PFP has been assessed by the Environment Agency using EPI Suite (US EPA 2020c, version 4.11) and is summarised in Table 6.5 below. This program contains a Level III multimedia fugacity model and predicts partitioning of chemicals to air, soil, sediment and water under steady state conditions for a generic model "environment". A fixed temperature of 25 °C is assumed. Mass transport between the compartments via volatilization, diffusion, deposition and runoff are modelled.

The model was run four times with a nominal release rate of 1,000 kg/hour initially entering the air, soil or water compartments and the same release to all three compartments using substance properties as per Table 6.6 and Table 10.2.

Table 6.4 Results of generic level III fugacity model for PFP

Compartment (per cent distribution at steady state)	Emission rate (1,000 kg/h) to air	water	soil	air: water: soil equally
Amount in air (%)	100.0	19.6	98.0	48.8
Amount in water (%)	<0.1	78.6	<0.1	49.7
Amount in soil (%)	<0.1	<0.1	2.0	0.37
Amount in sediment (%)	<0.1	1.8	<0.1	1.14

The Environment Agency has used the SimpleTreat model in EUSES (v2.03) to predict the following partitioning of PFP in a wastewater treatment plant. The sensitivity of changing the log K_{OC} value is summarised in Table 6.5.

Table 6.5 Predicted partitioning of PFP in a wastewater treatment plant

Fraction of emission to compartment / degraded	Log K_{OC}		
	2.12	**2.53**	**2.93**
Air	93.9 %	92.2 %	88.3 %
Water	4.9 %	4.9 %	4.7 %
Sludge	1.2 %	3.0 %	7.0 %
Biodegradation	0.0 %	0.0 %	0.0 %

This model predicts that a significant fraction will partition to air, with a small fraction emitted to effluent and partitioned to sludge. The reliability of this prediction 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. It is expected that there are weak interactions with organic matter for a neutral non-polar substance and volatilisation to air is likely to be the dominant pathway.

6.2.4 Long-range transport potential

The REACH Guidance (Chapter R.7b, Section R.7.9.4.3, see ECHA 2017d) indicates that long-range transport can be considered on a case-by-case basis, but there is no guidance about how to use the information in the overall assessment.

The OECD has produced a decision support tool for estimating the long-range transport potential (LRTP) of organic chemicals at a screening level. 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 PFP, the Environment Agency has performed calculations using the input parameters indicated in Table 6.6. The OECD LRTP screening tool allows comparisons of these three characteristics for a range of substances, provided in Figure 6.1 Long-range transport potential of PFP (log K_{OW} of 2.8)

Table 6.6 Estimated long-range transport potential of PFP

Input Parameter	Value		
Molecular mass	188 g/mol		
Log K_{AW} [a]	3.98		
Log K_{OW}	2.8 (range of 2.5 to 3.1)		
Half-life in air (hours)	2.4×10^{41}		
Half-life in water (hours)[b]	2.4×10^{41}		
Half-life in soil (hours)	2.4×10^{41}		
LRTP output parameter	Log K_{OW}		
	2.5	2.8	3.1
Characteristic Travel Distance (km)	1 350 000	1 350 000	1 350 000
Transfer Efficiency (%)	1 042	1 042	1 042
Pov (days)	2.4×10^{40}	2.4×10^{40}	2.4×10^{40}

Note: a - This is the log of the dimensionless HLC calculated using Equation R.16-5 of ECHA R16 (ECHA, 2016) – see section 6.2.2.

b -The upper bound value for biodegradation of a non-readily biodegradable substance in EUSES is 1×10^{40} days to represent infinity (equivalent to 2.4×10^{41} hours).

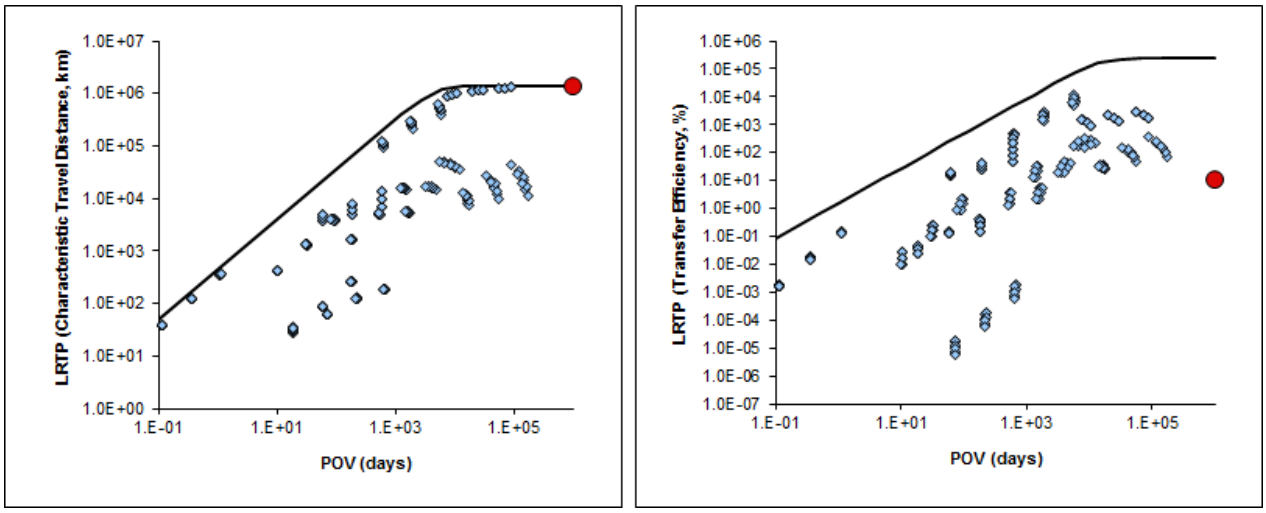
The OECD LRTP screening tool predicts the following outputs:

- Overall persistence (Pov).

- Characteristic Travel Distance (CTD): a transport-oriented LRTP indicator. It quantifies the distance from the point of release to the point at which the concentration has dropped to 1/e, or about 37% of its initial value; and
- Transfer Efficiency (TE): is a target-oriented LRTP indicator originally applied to quantify the deposition of chemicals transported from different regions to the North American Great Lakes.

The sensitivity of changing the log K_{OW} value was investigated but due to the very slow degradation rate used for the air, water and soil compartments, negligible change in the output was recorded over the log K_{OW} value range 2.5 to 3.1.

Figure 6.1 Long-range transport potential of PFP (log K_{OW} of 2.8)



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

Based on this screening tool, it appears that PFP may be capable of long-range transport.

Wet and dry deposition, which is important for the atmospheric fate of perfluorinated acids, are less relevant for PFP due to its different physico-chemical characteristics (PFP is considerably more volatile and less water soluble than PFAS such as PFOA). Due to its low water solubility, removal of PFP from the atmosphere through precipitation is not likely to be a significant process and rainwater concentrations are likely to be low.

Evidence of occurrence (or not) of PFP 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.

6.3 Bioaccumulation

6.3.1 Bioaccumulation in aquatic organisms

6.3.1.1 Screening data

The likely log K_{OW} of PFP of around 3 (range 2.5 to 3.1 – see Section 5.4.5) suggests that it screens as potentially bioaccumulative. For example, the REACH Guidance for environmental exposure assessment uses a threshold of log $K_{OW} \geq 3$ as a trigger for the secondary poisoning assessment (ECHA, 2016), although it is less than the REACH screening criterion (≤ 4.5) for being potentially bioaccumulative (B) in aquatic organisms (see Section 9.3). However, PFP is a gas so these might not be a relevant trigger.

The longer-chain analogue perfluorohexane has a relatively high solubility in n-octanol, which is a surrogate for lipid (≥ 3.0 g/L at 20 °C). The n-octanol solubility of PFP is unknown.

6.3.1.2 Measured data

There is no fish bioaccumulation study for PFP itself, and the end point is waived with the justification that the "study is scientifically not necessary / other information available."

The CSR states that the bioaccumulation of PFP is "very low". This assertion is based on three pieces of information:

- The first is the result of a fish bioaccumulation study performed with perfluoroperhydrophenanthrene (PFPh) which gave a "low result". This study has been evaluated by the Environment Agency as part of this review. The registration dossier records the fish bioconcentration factor (BCF) for that substance as up to 30. The EU REACH registration indicates that PFPh is a saturated PFC, but with a higher boiling point than PFP. No other read-across justification is provided.
- They also cite the findings of Yokoyama *et al*. (1975) who researched the use of PFCs as blood extenders. The EU REACH registration summarises that the chemicals were mainly expelled via expiration, with the rate being dependent on the vapour pressure. They suggest that as PFP has a much higher vapour pressure than PFPh it would be eliminated far quicker.

  These data (and related studies) are discussed in the Environment Agency evaluation of perfluoroisohexane (PFiHx) (Environment Agency, 2023b). In general, none of the substances tested was a close analogue of PFP. In the introduction of one of the papers (Okamoto *et al*., 1975), it is stated that "the long-term retention of the [PFC] in body tissues has been the main impediment for their use as the substitute of blood." Therefore, it appears that tissue retention cannot be ruled out as a possibility.
- The EU REACH registration supports this hypothesis of rapid expiration by reference to the use of the substance in ultrasound imaging. This is briefly

discussed in the human toxicokinetics section of the CSR, citing a review article by Platts and Fraser (2011; see also Section 8.1). The article discusses the use of microbubbles injected into a patient to enhance the contrast in echocardiography imaging. The microbubbles are produced prior to administration by agitation of a solution of the contrast agent. They have an outer shell made of lipid or albumin and a gaseous core. The bubbles lose their structure a short period of time after injection (3 to 5 minutes for a product called 'Definity', which has a PFP core). The PFP is not metabolised and is excreted unchanged via the lungs. The article indicates that the PFP in 'Definity' is eliminated very quickly, stating a mean half-life < 2 minutes in healthy people as well as those with airflow restrictions. The outer shell is metabolised by the body.

The Environment Agency notes that for the bioaccumulation study of PFPh, there is very limited information in either registration dossier about the study. One of the main issues is whether the two test concentrations in the study exceeded the water solubility of PFPh, as an exact water solubility value is not available. Without this, it is not possible verify the reliability of the study. Furthermore, the study was performed to an old methodology, which reduces the confidence that can be placed on the results.

The Environment Agency also notes that PFPh is a much larger substance than PFP with a cyclic structure, so is not a close analogue. The aquatic bioaccumulation assessment is also focussed on gill-breathing organisms. The relevance of these arguments for the aquatic bioaccumulation of PFP therefore appears to be low. However, the Environment Agency recognises that it would be technically difficult to maintain test concentrations in a standard test with PFP as although it appears to have some solubility in water, it exists predominantly as a gas.

6.3.2 Terrestrial bioaccumulation

The EU REACH registration has not assessed the potential for terrestrial bioaccumulation as this is not a standard REACH information requirement.

6.3.2.1 Screening data

In terms of bioaccumulation in air-breathing organisms, the screening criteria are log K_{OW} > 2 and log K_{OA} > 5. The likely log K_{OW} of PFP is in the range 2.5 to 3.1; the predicted log K_{OA} ranges from -1.48 to -0.88 (Section 5.5). These values are uncertain but suggest that PFP does not meet the screening criteria for bioaccumulation in air-breathing organisms.

The Environment Agency has predicted a BCF for PFP for earthworms using the preferred log K_{OW} value of 2.8 in EUSES v2.03 using the 'Predominantly hydrophobics" chemical class. The calculated BCF was 8.41 L/kg ww. Despite the uncertainty in the K_{OW} value (Section 5.4.5) the low value of the predicted BCF means that a sensitivity analysis has not been performed. It is unlikely that perfluoroalkanes are within the applicability domain of this QSAR which was derived on a small number of organochlorine compounds and this value remains uncertain.

6.3.2.2 Measured data

As described in Section 6.3.1.2, the EU REACH registration cites several medical studies providing some information on the elimination of perfluorinated substances from air-breathing organisms, including one study involving PFP. These are discussed in Section 9.1. These non-standard data indicate very rapid elimination of PFP from humans via exhalation when administered via direct injection to the blood.

The available information indicates that PFP is unlikely to bioaccumulate in air-breathing organisms.

6.3.3 Summary and discussion of bioaccumulation

PFP is estimated to have a log K_{OW} value around 3, and therefore may potentially be bioaccumulative. There are no measured fish bioaccumulation data for PFP, and an aqueous study is likely to be very challenging to perform (and may not be environmentally relevant for the substance). Fish bioaccumulation data cited in the EU REACH registration for PFPh suggests a low BCF for this type of substance, but the Environment Agency does not consider that this is a reasonable analogue for PFP and has concerns about the reliability of the cited study.

The assumption that hydrophobic and lipophilic interactions between compound and substrate (as modelled by the log K_{OW}) are the main mechanisms governing bioaccumulation behaviour may not be applicable for this type of substance due to the oleophobic repellency of the perfluorinated alkyl chain. However, the Environment Agency notes that the analogue perfluorohexane appears to have a high level of solubility in n-octanol, which is a surrogate for lipids. The n-octanol solubility of PFP is unknown.

Estimates of log K_{OA} are restricted by the limitations of the predicted input data but suggest elimination by exhalation is likely in air-breathing organisms, rather than bioaccumulation. This is supported by limited, non-standard information for humans regarding the use of the substance in medical applications (which is discussed in Section 8.1). An assessment of PHP against the REACH Annex 13 B/vB criteria is conducted at Section 9.3.

7 Ecotoxicology

The same comments about sources of data, reliability scoring and use of supplemental information apply as for Section 5. Performance of aquatic toxicity tests may be impractical as the substance is a poorly water-soluble gas. Measures would be needed to limit volatilisation, and analytical monitoring would be required to ensure that test concentrations are adequately maintained.

7.1 Aquatic compartment (including sediment)

For all aquatic toxicity endpoints, the EU REACH registration considers that testing is unnecessary because PFP is a gas and has a very low water solubility, therefore indicating that it will not be present in the aquatic environment. They consider that these properties would also make aquatic toxicity testing prohibitively expensive. They claim that there is evidence that PFCs as a class are not toxic, noting that several PFCs including PFP are routinely used in medical applications.

7.1.1 Fish

7.1.1.1 Short-term (acute) toxicity

No acute fish toxicity data are included in the EU REACH registration (ECHA, 2020a). This is a standard information requirement under REACH Annex 8 for substances registered at 10 tonnes/year or more. The EU REACH registration justifies the data waiving because PFP is “highly insoluble in water and is unlikely to cross biological membranes, indicating that aquatic toxicity is unlikely to occur”. They add that available testing of related substances indicates that PFP is non-toxic. Further details on the justification for the data waiving of aquatic toxicity tests as mentioned at the start of Section 7.1 apply.

7.1.1.1.1 Data from structural analogues

Table 7.1 Summary of acute toxicity of analogues to fish

Substance	Method	Species	Results	Reliability (Klimisch score)	Reference
Perfluoroper-hydrofluorene	OECD TG 203 (static) To GLP	Rainbow Trout *Oncorhynchus mykiss*	96-h LC_{50} >100 mg/L based on unverified nominal concentrations	Registrant: 1 (key study)	Unnamed (1998) cited in the CSR for PFP
Hexafluoro-propene (HFP)	ECOSAR™ v1.00 estimation using a log K_{OW} of 1.95	No information	96-h LC_{50} of 128.5 mg/L	Registrant: 2 (supporting study)	Unnamed (2009), cited in ECHA, (2020d)
Perfluoro-ethane	ECOSAR™ v1.00 estimation	Fathead Minnow *Pimephales promelas*	96-h LC_{50} of 82.3 mg/L	Registrant: 2 (key study)	Unnamed (2013), cited in ECHA, (2020b)

The CSR notes that the only report the Registrant has access to that they consider relevant for assessing the acute fish toxicity of PFP is a 96-hour toxicity study conducted in 1989 exposing Rainbow Trout *Oncorhynchus mykiss* to perfluoroperhydrofluorene. The EU REACH registration considers that perfluoroperhydrofluorene is a similar substance to PFP but does not provide any further explanation. Test solutions were prepared using Megaface F142-D as a dispersing agent. The test was carried out at a single nominal concentration of 100 mg/L which the EU REACH registration considers is the highest achievable concentration. The EU REACH registration for perfluoroperhydrofluorene reports a water solubility of <0.012 mg/L at 20°C for this substance (ECHA, 2012). No mortality or adverse effects were observed. There was no apparent measurement or reporting of actual dissolved concentrations in the test medium and no further information is available to assess the reliability of this study in either the CSR for PFP or the EU REACH registration for perfluoroperhydrofluorene (ECHA, 2012). Although a sufficient justification for the analogue approach has not been provided (as set out in ECHA, 2008a), the Environment Agency does not consider that perfluoroperhydrofluorene is a suitable analogue for the purposes of this evaluation because it has a very different carbon structure (involving cyclic rings) and much higher molecular weight.

Given the lack of information for PFP, the Environment Agency has sought data for more relevant analogue substances (see Section 1.2):

- No experimental acute fish toxicity data are included in the EU REACH registration for HFP (ECHA, 2020d). The EU REACH registration refers to data waiving for the acute fish toxicity endpoint, with the justification presented in their CSR that there is limited potential for aqueous exposure based on the high vapour pressure and use pattern of the substance and therefore, aquatic toxicity is unlikely.

  As supporting information, the EU REACH registration for HFP includes a 96-h LC_{50} of 128.5 mg/L for fish estimated using ECOSARTM v1.00 and a log K_{OW} of 1.95 (Unnamed, 2009, cited in ECHA, 2020d). The EU REACH registration rates this result as 'reliable with restrictions' (Klimisch 2) because they consider that it was derived from a valid QSAR model with adequate and reliable documentation and claim that HFP fits the applicability domain. The Environment Agency evaluation of HFP considers that there is significant uncertainty in the log K_{OW} and recommends a log K_{OW} of 2.0 at 25°C for modelling purposes with a range of 1.5 to 2.5 for the purposes of sensitivity analysis. The estimated ecotoxicity endpoint is above the water solubility of 82 mg/L at 28 °C recommended in the Environment Agency evaluation of HFP (Environment Agency, 2023a).

- No experimental acute fish toxicity data are included in the EU REACH registration for perfluoroethane (ECHA, 2020b). The key study is a 96-h LC_{50} of 82.3 mg/L for Fathead Minnow *Pimephales promelas* estimated using ECOSARTM v1.11 and a log K_{OW} of 2.15 (Unnamed, 2013, cited in ECHA, 2020b). The EU REACH registration rates this result as 'reliable with restrictions' (Klimisch 2) because they consider that it was derived from a valid QSAR model and claim that the information provided is sufficient for the purpose of classification and labelling and/or risk assessment. The EU REACH registration also considers that potential exposure to aquatic organisms is mitigated by the high vapour pressure of the substance and its log K_{OW} of < 3.0. The Environment Agency notes that the estimated toxicity endpoint is below the water solubility of 520 mg/L reported in the EU REACH registration (Unnamed, 2012, cited in ECHA, 2020b).

7.1.1.1.2 Predicted data

The Environment Agency calculated a 96-h fish LC_{50} of 29.5 mg/L for PFP in ECOSARTM v1.11 as part of the EPISuite™ platform (US EPA, 2012), using the log K_{OW} of 2.8 and water solubility of 6.4 mg/L recommended in this evaluation (see Sections 5.4 and 5.3). To account for the uncertainty associated with the log K_{OW} for PFP (see Section 5.4), this model input parameter was varied from 2.5 and 3.1, which led to 96-h LC_{50} values of 54.9 mg/L and 15.9 mg/L, respectively, for fish. However, no PFCs are included in the model training set (US EPA, 2012) and it is not clear therefore that PFP is within the applicability domain. Consequently these values should be treated with caution and may be unreliable.

Using the US EPA T.E.S.T. v4.2.1 software (which includes a number of different QSAR models as set out below) the Environment Agency also generated 96-h LC_{50} values for PFP (with prediction toxicity intervals) for Fathead Minnow of 14.1 mg/L (≥ 3.7, ≤ 53.4), 39.8 (≥ 9.4, ≤ 168), 27.1 mg/L (≥ 1.6, ≤ 454) and 931 mg/L using the hierarchical clustering

model, Food and Drug Administration (FDA) model, single model and nearest neighbour model methods, respectively. The nearest neighbour estimate is the average of experimental toxicity values for 1,1,1,3,3,3-hexafluor-2-propanol (CAS no. 920-66-1), ethyl trifluoroacetate (CAS no. 383-63-1) and 2,2,2-trifluoroethanol (CAS no. 75-89-8) which are the three chemicals in the training set that are most similar to PFP (although they have a variety of functional groups so are not close analogues). A disadvantage of the nearest neighbour method is that it does not use a QSAR model to correlate the differences between the test compound and the nearest neighbour. It was also shown to achieve the worst prediction results during external validation of the T.E.S.T. methods (Martin, 2016). The average of all of these predicted toxicity values is a 96-h LC_{50} of 61.3 mg/L calculated using the consensus method. The consensus method was shown to achieve the best prediction results during external validation of the T.E.S.T. methods (Martin, 2016). The group contribution method in the software was not able to predict a toxicity value. No PFCs are included in the training sets used for any of the T.E.S.T. models (US EPA, 2020d) and consequently, these values should be treated with caution and may be unreliable. In particular, the Environment Agency notes that all of the predicted LC_{50} values exceed the solubility of PFP in pure water of around 6.4 mg/L at 25 °C (see Section 5.3).

No further predicted data were available on ChemSpider (RSC, 2020a) or US EPA CompTox (US EPA, 2020a) for PFP.

7.1.1.1.3 Recommendations

Overall, the data indicate that the substance is likely to have a low acute toxicity to fish with all predicted LC_{50} values for PFP and analogue substances being above their limit of water solubility or above 1 mg/L. However, there is uncertainty regarding the suitability of the QSAR models to predict toxicity for PFCs. In addition, the Environment Agency recommends that the UK supplier reconsiders the analogues selected for this end point.

The HLC (see Section 6.2.2) and the distribution modelling (see Section 6.2.3) also suggest that PFP will mostly volatilise to air. Given the low water solubility of PFP (see Section 5.3.5), the Environment Agency therefore agrees that acute toxicity is unlikely to be expressed in fish, in accordance with the specific rules for adaptation of standard testing set out in Annex 8 of REACH.

The Environment Agency recommends that detailed information on the available test data for related substances is included to support the current data waiving. The appropriate format for use of the analogue and any QSAR approaches should be as set out in Chapter 6 of the Guidance on REACH information requirements relating to QSARs and grouping of chemicals (ECHA, 2008a) and the read-across assessment framework (ECHA, 2017b).

7.1.1.2 Long term (chronic) toxicity

Long-term fish toxicity tests are not available in the EU REACH registration (ECHA, 2020a). This is a standard information requirement under REACH Annex 9 for substances

registered at 100 tonnes/year or more. The EU REACH registration refers to data waiving because they consider that available testing of related substances indicates that PFP is non-toxic. Further details on the justification for the data waiving of aquatic toxicity tests as mentioned at the start of Section 7.1 apply. No further details relevant to long-term fish toxicity are included in the EU REACH registration, or in the CSR.

7.1.1.2.1 Data from structural analogues

Given the lack of information for PFP, the Environment Agency has sought data for more relevant analogue substances (see Section 1.2):

- No chronic fish toxicity data are included in the EU REACH registration for HFP (ECHA, 2020d). The EU REACH registration refers to data waiving for the chronic fish toxicity endpoint with the justification presented in the CSR that there is limited potential for aqueous exposure based on the high vapour pressure and use pattern of the substance and therefore, aquatic toxicity is unlikely.
- No chronic fish toxicity data are included in the EU REACH registration for perfluoroethane (ECHA, 2020b). The EU REACH registration for perfluoroethane also refers to data waiving because they consider that potential exposure to aquatic organisms is limited by the high vapour pressure of the substance and its log K_{OW} of < 3.0.

7.1.1.2.2 Predicted data

The Environment Agency calculated a fish Maximum Acceptable Toxicant Concentration (MATC) of 3.2 mg/L for PFP in ECOSAR™ v1.11 as part of the EPISuite™ platform (US EPA, 2012), using the log K_{OW} of 2.8 and water solubility of 6.4 mg/L recommended in this evaluation (see Sections 5.4 and 5.3). To account for the uncertainty associated with the log K_{OW} for PFP (see Section 5.4), this model input parameter was varied to 2.5 and 3.1, which led to MATC values of 5.7 mg/L and 1.8 mg/L, respectively. MATC values are the geometric mean of the NOEC and LOEC and therefore, the NOEC would be lower than these values. No PFCs are included in the model training set (US EPA, 2012) and it is therefore not clear that PFP is within the applicability domain. Consequently, these values should be treated with caution. No further predicted data were available on ChemSpider (RSC, 2020a) or US EPA CompTox (US EPA, 2020a) for PFP.

7.1.1.2.3 Recommendations

Despite the uncertainties with the model predictions, predicted MATC values were > 1 mg/L indicating that PFP is unlikely to be chronically toxic to fish at a level that would trigger a hazard classification (see Section 9.1). However, the HLC (see Section 6.2.2) and the distribution modelling (see Section 6.2.3) suggest that PFP will mostly volatilise to (and remain in) air and there is little potential for exposure to aquatic organisms (see Section 10.1). Therefore, aquatic toxicity is unlikely to occur. This information supports the data waiver for the chronic fish toxicity endpoint according to the general rules for adaptation of testing set out in Annex 11 of REACH. The Environment Agency

recommends that the additional information on the exposure assessment is added to the justification for the data waiving, noting the relevant Guidance on adaptation of long-term aquatic toxicity testing (ECHA, 2020f).

The Environment Agency also recommends that detailed information on the available test data for related substances is added to support the current data waiving. The appropriate format for use of the analogue and any QSAR approaches should be as set out in Chapter 6 of the Guidance on REACH information requirements relating to QSARs and grouping of chemicals (ECHA, 2008a) and the read-across assessment framework (ECHA, 2017b).

7.1.2 Aquatic invertebrates

7.1.2.1 Short-term (acute) toxicity

No acute aquatic invertebrate toxicity data are included in the EU REACH registration (ECHA, 2020a). This is a standard information requirement under REACH Annex 7 for substances registered at 1 tonne/year or more. The EU REACH registration justifies the data waiving for the same reasons as the acute fish toxicity test end point (see Section 7.1.2).

7.1.2.1.1 Data from structural analogues

Table 7.2 Summary of acute toxicity of analogues to invertebrates

Substance	Method	Species	Results	Reliability (Klimisch score)	Reference
Perfluoroper-hydrofluorene	OECD TG 202 (static) To GLP	*Daphnia magna*	48-h EC_{50} >0.1 mg/L based on unverified nominal concentrations; mobility end point	Registrant: 1 (key study)	Unnamed (1989) cited in the CSR for PFP
Hexafluoro-propene (HFP)	ECOSAR™ v1.00 estimation using a log K_{OW} of 1.13	*Daphnia* sp.	48-h LC_{50} of 71.9 mg/L	Registrant: 2 (supporting study)	Unnamed (2009) cited in ECHA (2020d)
Perfluoroethane	ECOSAR™ v1.11 using a log K_{OW} of 2.0	*Daphnia magna*	48-h LC_{50} of 47.4 mg/L	Registrant: 2 (key study)	Unnamed (2013) cited in ECHA (2020b)

The CSR notes that the only report the Registrant has access to that they consider relevant for assessing the acute toxicity of PFP to aquatic invertebrates is a 48-hour immobilisation test conducted in 1989 exposing *Daphnia* to perfluoroperhydrofluorene. The species of *Daphnia* was not specified in the CSR or the EU REACH registration for

perfluoroperhydrofluorene (ECHA, 2012). The test was carried out at a single nominal concentration of 0.1 mg/L and the EU REACH registration states that this concentration was chosen due to the toxicity of the dispersing agent towards *Daphnia*. From the total of 40 *Daphnia* exposed during the test, no immobilisation was observed. There was no apparent measurement or reporting of actual dissolved concentrations in the test medium and no further information is available to assess the reliability of this study in either the CSR for PFP or the EU REACH registration for perfluoroperhydrofluorene (ECHA, 2012). The identity and concentration of the dispersing agent was not reported in the CSR. The Environment Agency also notes that the acute fish study on the same substance (see Section 7.1.2) was carried out at a nominal concentration of 100 mg/L which the EU REACH registration noted was the highest achievable concentration (3 orders of magnitude higher than the concentration in this test). The EU REACH registration for perfluoroperhydrofluorene reports a water solubility of <0.012 mg/L at 20°C for this substance (ECHA, 2012). Although a sufficient justification for the analogue approach has not been provided (as set out in ECHA, 2008a), the Environment Agency does not consider that the data for perfluoroperhydrofluorene are suitable for the purposes of this evaluation because a) the solubility of PFP in pure water (6.4 mg/L at 25 °C) is likely to be an order of magnitude higher than the limit concentration selected, b) a much higher concentration was achieved in the acute fish test with the same substance (see Section 7.1.2), and c) it is not a suitable analogue for PFP as it has a very different carbon structure (involving cyclic rings) and much higher molecular weight.

Given the lack of information for PFP, the Environment Agency has sought data for more relevant analogue substances (see Section 1.2):

- No experimental acute aquatic invertebrate toxicity studies are included in the EU REACH registration for HFP (ECHA, 2020d). The EU REACH registration for HFP refers to data waiving for the acute aquatic invertebrate toxicity endpoint with the justification presented in the CSR that there is limited potential for aqueous exposure based on the high vapour pressure and use pattern of the substance and therefore, aquatic toxicity is unlikely.

  As supporting information, the registration for HFP includes a 48-h LC_{50} of 71.9 mg/L for daphnids estimated using ECOSAR™ v1.00 and a log K_{OW} of 1.13 (Unnamed, 2009, cited in ECHA, 2020d). The EU REACH registration rates this result reliable with restrictions (Klimisch 2) because they consider that it was derived from a valid QSAR model with adequate and reliable documentation and they claim that HFP fits the applicability domain. The Environment Agency notes that the log K_{OW} used for this ecotoxicity estimate is different to those used for the acute fish toxicity and algal toxicity endpoints for HFP and no explanation for this is included in the EU REACH registration. The Environment Agency of HFP evaluation considers that there is significant uncertainty in the log K_{OW} and recommends a log K_{OW} of 2.0 at 25°C for modelling purposes with a range of 1.5 to 2.5 for the purposes of sensitivity analysis (Environment Agency, 2023a). The

estimated ecotoxicity endpoint is below the water solubility of 82 mg/L at 28 °C recommended in the Environment Agency evaluation of HFP.

- No experimental acute aquatic invertebrate toxicity studies are included in the EU REACH registration for perfluoroethane (ECHA, 2020b). The EU REACH registration for perfluoroethane considers that potential exposure to aquatic organisms is mitigated by the high vapour pressure of the substance and its log K_{OW} of < 3.0.

  The registration for perfluoroethane includes a 48-h LC_{50} of 47.4 mg/L for *Daphnia magna* estimated using ECOSAR™ v1.11 and a log K_{OW} of 2.0 as the key study on the acute toxicity to aquatic invertebrates (Unnamed, 2013, cited in ECHA, 2020b). The EU REACH registration rates this result reliable with restrictions (Klimisch 2) because they consider that it was derived from a valid QSAR model and because they claim that the information provided is sufficient for the purpose of classification and labelling and/or risk assessment. The Environment Agency notes that the estimated toxicity endpoint is below the water solubility of 520 mg/L reported in the EU REACH registration (Unnamed, 2012, cited in ECHA, 2020b).

7.1.2.1.2 Predicted data

The Environment Agency calculated a 48-h daphnid LC_{50} of 18.1 mg/L for PFP in ECOSAR™ v1.11 as part of the EPISuite™ platform (US EPA, 2012), using the log K_{OW} of 2.8 and water solubility of 6.4 mg/L recommended in this evaluation (see Sections 5.4 and 5.3). To account for the uncertainty associated with the log K_{OW} for PFP (see Section 6.4), this model input parameter was varied to 2.5 and 3.1, which led to 48-h LC_{50} values of 32.7 mg/L and 10.0 mg/L, respectively, for daphnids. However, no PFCs are included in the model training set (US EPA, 2012) and it is not clear therefore that PFP is within the applicability domain, so these values should be treated with caution.

The Environment Agency also generated *Daphnia magna* 48-h LC_{50} values (and prediction toxicity intervals) of 46.7 mg/L (≥ 0.02, ≤ 140000), 253 (≥ 37.8, ≤ 1700) and 151 mg/L (≥ 3.9, ≤ 5900) with the hierarchical clustering model, FDA model and single model methods, respectively, using the US EPA T.E.S.T. v4.2.1 software. The average of these predicted toxicities is a 48-h LC_{50} of 121 mg/L for *Daphnia magna* calculated using the consensus method. The consensus method was shown to achieve the best prediction results during external validation of the T.E.S.T. methods (Martin, 2016). The nearest neighbour and group contribution methods in the software were not able to predict toxicity values. High uncertainty with the predicted toxicity values is indicated by the large prediction toxicity intervals for the hierarchical, FDA and single models. In addition, no PFCs are included in the training sets used for any of the T.E.S.T. models (US EPA, 2020d) and so these values should be treated with caution.

No further predicted data were available on ChemSpider (RSC, 2020a) or US EPA CompTox (US EPA, 2020a) for PFP.

7.1.2.1.3 Recommendations

Overall, the data indicate that the substance is likely to have a low acute toxicity to aquatic invertebrates with all predicted LC_{50} values for PFP and the analogue substances being either above their limit of water solubility or above 1 mg/L. However, there is uncertainty regarding the suitability of the QSAR models to predict toxicity for PFCs. The Environment Agency recommends that the analogues selected for this end point are reconsidered.

The HLC (see Section 6.2.2) and the distribution modelling (see Section 6.2.3) also suggest that PFP will mostly volatilise to (and remain in) air and therefore, aquatic toxicity is unlikely. Given the low water solubility of PFP (see Section 5.3.5), the Environment Agency therefore agrees that acute toxicity is unlikely to be expressed in aquatic invertebrates, in accordance with the specific rules for adaptation of standard testing set out in Annex 7 of REACH.

The Environment Agency recommends that detailed information on the available test data for related substances is included to support the current data waiving. The appropriate format for use of the analogue and any QSAR approaches should be as set out in Chapter 6 of the Guidance on REACH information requirements relating to QSARs and grouping of chemicals (ECHA, 2008a) and the read-across assessment framework (ECHA, 2017b).

7.1.2.2 Long term (chronic) toxicity

Long-term toxicity tests on aquatic invertebrates are not available in the EU REACH registration (ECHA, 2020a). This is a standard information requirement under REACH Annex 9 for substances registered at 100 tonnes/year or more. The EU REACH registration (ECHA, 2020a) refers to data waiving because they consider that available testing of related substances indicates that PFP is non-toxic. Further details on the justification for the data waiving of aquatic toxicity tests as mentioned at the start of Section 7.1 apply. No further details relevant to the chronic invertebrate toxicity are included in the EU REACH registration, or in the CSR.

7.1.2.2.1 Data from structural analogues

Given the lack of information for PFP, the Environment Agency has sought data for more relevant analogue substances (see Section 1.2):

- No chronic aquatic invertebrate toxicity data are included in the EU REACH registration for HFP (ECHA, 2020d). The EU REACH registration for HFP refers to data waiving for the chronic aquatic invertebrate toxicity endpoint with the justification presented in the CSR that there is limited potential for aqueous exposure based on the high vapour pressure and use pattern of the substance and therefore, aquatic toxicity is unlikely.
- No chronic aquatic invertebrate toxicity data are included in the EU REACH registration for perfluoroethane (ECHA, 2020b). The EU REACH registration for perfluoroethane also refers to data waiving because they consider that potential

exposure to aquatic organisms is mitigated by the high vapour pressure of the substance and its log K_{OW} of < 3.0.

7.1.2.2.2 Predicted data

The Environment Agency calculated a daphnid MATC of 2.2 mg/L for PFP in ECOSAR™ v1.11 as part of the EPISuite™ platform (US EPA, 2012), using the log K_{OW} of 2.8 and water solubility of 6.4 mg/L recommended in this evaluation (see Sections 5.4 and 5.3). To account for the uncertainty associated with the log K_{OW} for PFP (see Section 5.4), this model input parameter was varied to 2.5 and 3.1, which led to MATC values of 3.6 mg/L and 1.3 mg/L, respectively, for daphnids. MATC values are the geometric mean of the NOEC and LOEC and therefore, the NOEC would be lower than these values. No PFCs are included in the model training set (US EPA, 2012) and it is not clear therefore that PFP is within the applicability domain. Consequently, these values should be treated with caution. No further predicted data were available on ChemSpider (RSC, 2020a) or US EPA CompTox (US EPA, 2020a) for PFP.

7.1.2.2.3 Recommendations

Despite the uncertainties with the model predictions, predicted MATC values were >1 mg/L indicating that PFP is unlikely to be chronically toxic to aquatic invertebrates at a level that would trigger a hazard classification (see Section 9.1). However, the HLC (see Section 6.2.2) and the distribution modelling (see Section 6.2.3) suggest that PFP will mostly volatilise to (and remain in) air and there is little potential for exposure to aquatic organisms (see Section 10.1). Therefore, aquatic toxicity is unlikely to occur. This information supports the data waiver for the chronic aquatic invertebrate toxicity endpoint according to the general rules for adaptation of testing set out in Annex XI of REACH. The Environment Agency recommends that the additional information on the exposure assessment is added to the justification for the data waiving.

The Environment Agency also recommends that detailed information on the available test data for related substances is included to support the current data waiving. The appropriate format for the analogue and any QSAR approaches should be used as set out in Chapter 6 of the guidance on REACH information requirements relating to QSARs and grouping of chemicals (ECHA, 2008a) and the read-across assessment framework (ECHA, 2017b).

7.1.3 Algae and aquatic plants

No data on the toxicity to algae and aquatic plants are included in the EU REACH registration (ECHA, 2020a). This is a standard information requirement under REACH Annex 7 for substances registered at 1 tonne/year or more. The EU REACH registration justifies the data waiving for the same reasons as the acute fish toxicity test end point (see Section 7.1.2).

7.1.3.1 Data from structural analogues

Given the lack of information for PFP, the Environment Agency has sought data for more relevant analogue substances (see Section 1.2):

- No experimental data on toxicity to algae and aquatic plants are included in the EU REACH registration for HFP (ECHA, 2020d). The EU REACH registration for HFP refers to data waiving for the algae and aquatic plant endpoint with the justification presented in the CSR that there is limited potential for aqueous exposure based on the high vapour pressure and use pattern of the substance and therefore, aquatic toxicity is unlikely.

  As supporting information, the registration for HFP includes a 96-h EC_{50} of 33.4 mg/L for algae estimated using ECOSAR™ v1.00 and a log K_{OW} of 1.95 (Unnamed, 2009, cited in ECHA, 2020c). The EU REACH registration rates this result reliable with restrictions (Klimisch 2) because they consider that it was derived from a valid QSAR model with adequate and reliable documentation and they claim that HFP fits the applicability domain. The Environment Agency evaluation of HFP (Environment Agency, 2023a) considers that there is significant uncertainty in the log K_{OW} and recommends a log K_{OW} of 2.0 at 25°C for modelling purposes with a range of 1.5 to 2.5 for the purposes of sensitivity analysis. The estimated ecotoxicity endpoint is below the water solubility of 82 mg/L at 28 °C recommended in the Environment Agency evaluation of HFP.

- No experimental data on toxicity to algae and aquatic plants are included in the EU REACH registration for perfluoroethane (ECHA, 2020b). The EU REACH registration for perfluoroethane considers that potential exposure to aquatic organisms is mitigated by the high vapour pressure of the substance and its log K_{OW} of < 3.0.

  The registration for perfluoroethane includes a 96-h EC_{50} of 37.5 mg/L for green algae estimated using ECOSAR™ v1.11 and a log K_{OW} of 2.0 as the key study on the toxicity to algae and aquatic plants (Unnamed, 2013, cited in ECHA, 2020d). The EU REACH registration rates this result reliable with restrictions (Klimisch 2) because they consider that it was derived from a valid QSAR model and because they claim that the information provided is sufficient for the purpose of classification and labelling and/or risk assessment. The Environment Agency notes that the estimated toxicity endpoint is below the water solubility of 520 mg/L reported in the EU REACH registration (Unnamed, 2012, cited in ECHA, 2020b).

7.1.3.2 Predicted data

Algal endpoints predicted in ECOSAR™ are based on growth rate or biomass (Mayo-Bean *et al.*, 2012). The Environment Agency calculated a 96-h EC_{50} of 18.3 mg/L and a MATC of 5.6 mg/L for PFP in ECOSAR™ v1.11 as part of EPISuite™ platform (US EPA, 2012), using the log K_{OW} of 2.8 and water solubility of 6.4 mg/L recommended in this evaluation (see Sections 5.4 and 5.3). To account for the uncertainty associated with the log K_{OW} for

PFP (see Section 5.4), this model input parameter was varied to 2.5 and 3.1, which led to 96-h EC_{50} values of 29.4 mg/L and 11.3 mg/L, respectively, for green algae. MATC values were 8.5 mg/L based on the log K_{OW} of 2.5 and 3.7 mg/L based on the log K_{OW} of 3.1. MATC values are the geometric mean of the NOEC and LOEC and therefore, the NOEC would be lower than these values. No PFCs are included in the model training set (US EPA, 2012) and it is not clear therefore that PFP is within the applicability domain, so these values should be treated with caution. In particular, the Environment Agency notes that the predicted EC_{50} values exceed the solubility of PFP in pure water of around 6.4 mg/L at 25 °C (see Section 5.3).

No further predicted data were available on ChemSpider (RSC, 2020a) or US EPA CompTox (US EPA, 2020a) for PFP.

7.1.3.3 Recommendations

Despite the uncertainties with the model predictions, the data indicate that the substance is likely to have a low short-term and long-term toxicity to algae with all predicted EC_{50} and MATC values for PFP being either above the limit of water solubility or above 1 mg/L.

The HLC (see Section 6.2.2) and the distribution modelling (see Section 6.2.3) suggest that PFP will mostly volatilise to (and remain in) air and therefore, aquatic toxicity is unlikely. Given the low water solubility of PFP (see Section 5.3.5), the Environment Agency therefore agrees that growth inhibition of aquatic plants is unlikely, in accordance with the specific rules for adaptation of standard testing set out in Annex 7 of REACH.

The Environment Agency recommends that detailed information on the available test data for related substances is included to support the current data waiving. The appropriate format for the analogue and any QSAR approaches should be used as set out in Chapter 6 of the guidance on REACH information requirements relating to QSARs and grouping of chemicals (ECHA, 2008a) and the read-across assessment framework (ECHA, 2017b).

7.1.4 Sediment organisms

No relevant information is available in the online EU REACH registration dossier and no argument for the omission of this information is included. REACH Annex IX requirements note sediment toxicity testing may be required for substances with a high potential for adsorption to sediment at this level of supply. However, the CSR justifies the data waiving because the substance is a gas with a high vapour pressure and a low water solubility.

The Environment Agency notes that the range of possible log K_{OW} values is from 2.5 to 3.5 (see Section 5.4.5) and log K_{OC} of 2.12 to 2.93 (see Section 6.2.1). These are below the trigger value of ≥ 3 for sediment effects assessment under REACH (ECHA, 2017b). The substance is not readily biodegradable, but HLC (see Section 6.2.2) and the distribution modelling (see Section 6.2.3) also suggest that PFP will mostly volatilise to (and remain in) air and there is little potential for exposure to sediment organisms (see Section 10.1). Therefore, the Environment Agency considers that toxicity to sediment organisms is

unlikely and that testing for this endpoint is not required. The Environment Agency recommends that the additional information on the exposure assessment and the K_{OC} is added to the justification for the data waiving.

7.1.5 Other aquatic organisms

No relevant information is available.

7.2 Terrestrial compartment

No key studies on the toxicity to terrestrial organisms are available in the EU REACH registration (ECHA, 2020a). REACH Annex IX requirements note terrestrial toxicity testing may be required at this level of supply. The EU REACH registration refers to data waiving although no further details are available online.

The CSR does not refer to data waiving and instead includes information on the toxicity of various PFCs to soil macro-organisms, terrestrial plants and other terrestrial organisms. Reference is made to a study investigating the effects of PFCs on insect cells (Gotoh *et al.*, 2001, cited in ECHA 2020a) for soil macroorganisms and studies on cultivating plant cells in media containing PFCs (Wardrop *et al.*, 1998; Lowe *et al.*, 1999, both cited in ECHA 2020a) for terrestrial plants. The CSR states that these studies indicated no harmful effects from PFCs. For other terrestrial organisms, the CSR references Elibol (1996) and Rocha-Leao *et al.* (no date, both cited in ECHA 2020a) who they consider showed beneficial effects of PFCs in yeast cultures.

In the study by Lowe *et al.* (1999), protoplasts from a number of species were cultured for up to 35 days in a medium containing perfluorodecalin (CAS 306-94-5) which is a larger bicyclic $C_{10}F_{18}$ molecule than PFP. Miotic division measured as initial plating efficiency increased in the media containing perfluorodecalin and morphologically normal plants were regenerated from the cultures.

No further details on the studies referenced in the CSR have been accessed by the Environment Agency.

7.2.1 Data from structural analogues

Given the lack of information for PFP, the Environment Agency has sought data for more relevant analogue substances (see Section 1.2):

- No key studies on the toxicity to terrestrial organisms are included in the EU REACH registration for HFP (ECHA, 2020d). The EU REACH registration for HFP refers to data waiving because direct and indirect exposure to the soil compartment is unlikely. The CSR adds the high volatility of the substance to the justification for the data waiving.

As supporting information, the registration for HFP includes a predicted 14-d LC_{50} value of 264 ppm for earthworms generated using ECOSAR™ v1.00 and an estimated log K_{OW} of 1.95 (Unnamed, 2009, cited in ECHA, 2020c). The EU REACH registration rates this result reliable with restrictions (Klimisch 2) because they consider that it was derived from a valid QSAR model with adequate and reliable documentation and because they claim that HFP fits the applicability domain. The Environment Agency evaluation of HFP considers that there is significant uncertainty in the log K_{OW} and recommends a log K_{OW} of 2.0 at 25°C for modelling purposes with a range of 1.5 to 2.5 for the purposes of sensitivity analysis (Environment Agency, 2023a).

- No key studies on the toxicity to terrestrial organisms are included in the EU REACH registration for perfluoroethane (ECHA, 2020b). The EU REACH registration for perfluoroethane also refers to data waiving, although no justification is available online (ECHA, 2020b).

7.2.2 Predicted data

For PFP, the Environment Agency calculated a 14-d LC_{50} of 270 ppm for earthworms in ECOSAR™ v1.11 as part of the EPISuite™ platform (US EPA, 2012), using the log K_{OW} of 2.8 and water solubility of 6.4 mg/L recommended in this evaluation (see Sections 5.4 and 5.3). To account for the uncertainty associated with the log K_{OW} for PFP (see Section 5.4), this input parameter was varied to 2.5 and 3.1, which led to 14-d LC_{50} values of 290 ppm and 251 ppm, respectively, for earthworms. However, no PFCs are included in the model training set (US EPA, 2012) and it is not clear therefore that PFP is within the applicability domain, so these values should be treated with caution.

No further predicted data were available on ChemSpider (RSC, 2020a) or US EPA CompTox (US EPA, 2020a) for PFP.

7.2.3 Recommendations

Overall, despite a lack of certainty over the applicability of the QSAR models for PFCs, the data indicate that the substance is likely to have a low acute toxicity to earthworms with all predicted LC_{50} values for PFP and the analogue HFP being above 100 ppm. The substance is not readily biodegradable, but HLC (see Section 6.2.2) and the distribution modelling (see Section 6.2.3) also suggest that PFP will mostly volatilise to air and there is little potential for exposure to soil (see Section 10.1). The log K_{OC} of 2.12 to 2.93 (see Section 6.2.1) also indicates relatively low soil sorption potential. Therefore, toxicity to terrestrial organisms is unlikely. This information supports the data waiver in the EU REACH registration according to the specific and general rules for adaptation of testing set out in Annex 9 and Annex 11 of REACH.

The Environment Agency currently considers that no information on soil-dwelling organisms is required. The Environment Agency recommends that the additional

information on the exposure assessment and the K_{OC} is added to the justification for the data waiving. The Environment Agency also suggests that appropriate formats are used for the analogue and any QSAR approaches for the references made to terrestrial toxicity studies in the CSR as set out in the read-across assessment framework (ECHA, 2017b) and Chapter 6 of the guidance on REACH information requirements relating to QSARs and grouping of chemicals (ECHA, 2008a).

7.3 Microbiological activity in sewage treatment systems

No relevant information is available in the EU REACH registration (ECHA, 2020a). This is a standard information requirement under REACH Annex 8 for substances registered at 10 tonnes/year or more. The EU REACH registration refers to data waiving because the EU REACH registration considers that there is no emission to a sewage treatment plant. Information from the environmental permit and use pattern for F2 Chemicals Ltd suggest that emissions to wastewater could occur but are negligible according to personal communication from the UK supplier (see Section 10.1.1). The Environment Agency also notes that microbial toxicity is unlikely because the substance is highly volatile and is expected to mostly partition from water to air in a wastewater treatment plant (see Section 6.2.3). This information supports the data waiver according to the specific and general rules for adaptation of standard testing in Annex 8 and Annex 9 of REACH. The Environment Agency recommends that the high volatility of the substance and the distribution modelling are added to the justification for the data waiving.

7.4 Atmospheric effects

The Environment Agency notes that PFP is a gas. No data about biotic effects (e.g. to plants) from aerial exposure are available in the online REACH registration (ECHA, 2020a), but this is not a standard information requirement.

The available data in the EU REACH registration dossier suggest that PFP 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 public EU REACH registration for PFP (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 poisoning assessment. No human health hazard assessment has currently been undertaken. The study details and their reliability (Klimisch) scores are as presented in the EU REACH registration and the Environment Agency has not evaluated this information.

Aside from some OECD genotoxicity studies, the on-line EU registration and F2's CSR does not include any standard regulatory studies on the registered substance itself. The EU REACH registration states that PFCs have been used in numerous medical applications and sufficient data exists for humans and other animals such that further testing is unnecessary. For each mammalian toxicology endpoint below, F2 refer to a weight-of-evidence case based on grouping of substances (category approach) or read-across to other PFCs. They also cite a number of literature studies, mostly on other PFCs but a few do mention testing with PFP (usually referred to as octafluoropropane). The key mammalian toxicity information is summarised below.

8.1 Toxicokinetics

The EU REACH registration for PFP (ECHA, 2020a) states that a toxicokinetics study is scientifically not necessary and that other information is available. The CSR refers to a number of papers in the public domain which are not reviewed in detail here, however brief summaries are provided below:

Yamanouchi (1975) looked at perfluorodecalin (CAS 306-94-5) a larger bi-cyclic $C_{10}F_{18}$ molecule than PFP, as a 'blood extender' through direct injection as an emulsion into the blood stream of male Wistar rats (initial concentration not reported). Perfluorodecalin concentrations in the liver, spleen, bone marrow and adipose declined steadily after 1, 2 and 4 weeks and at 3 months. In addition the author looked at fluoride ion concentrations in the femur, liver, plasma and urine, and found no significant change compared to the control. The study summarises that:

- No change in the fluoride content in rats given perfluorodecalin was found.
- mass spectrum of perfluorodecalin infused was perfectly coincident with that of perfluorodecalin retained in the organs.
- perfluorodecalin was expelled through expiration only in unaltered form
- perfluorodecalin was not converted to other related compounds and also was not decomposed *in vivo*.

F2 propose that this suggests a lack of the catabolism of perfluorodecalin and they would expect PFP to be eliminated faster as it has a considerably higher vapour pressure. This was supported by reference to an abstract from Hutter *et al.* (1999) referring to PFP as

octafluoropropane, which reported results from an elimination model verified by data from a Phase 1 clinical trial of 10 healthy human subjects: 'Despite the high affinity of octafluoropropane for tissue, the model predicted that nearly 100% of the material would be exhaled from the lungs within 6 minutes'.

The CSR also refers to a study by Killam *et al.* (1999) which reported that octafluoropropane (or OFP) '...was rapidly exhaled though the lungs after an IV [intravenous] injection such that a maximum of less than 10% of the total dose appeared in the venous blood samples. Statistical moment analysis showed rapid OFP elimination with mean residence times of 46, 41 and 38 seconds for the three doses, and mean total recoveries for the exhaled OFP were 111%, 100.5% and 121.6%, respectively'.

One further report is referenced in the CSR (Platts and Fraser, 2011) where PFP was investigated for use as a diagnostic imaging agent. In this application the material is encapsulated in lipid-shelled microbubbles and injected directly into human bloodstream. Although numbers of individuals and concentrations tested are not reported, the paper notes generally that: 'The octafluoropropane [i.e. PFP] gas is not metabolised and is excreted unchanged in the lungs. The mean half-life is 1.3 minutes in healthy subjects and 1.9 minutes in people with chronic airflow limitation. The lipid shell is metabolised by the usual process of fatty acid metabolism'. This study is discussed further at Section 6.3.1.2.

As a summary of ADME (adsorption, distribution, metabolism, excretion) test results from the public domain, the EU REACH registration concludes that PFCs will be poorly adsorbed in organisms as they are both lipophobic and hydrophobic, although they acknowledge that data are lacking in this area and most testing has been for medical applications where PFCs are introduced directly into the body.

They state that the available references indicate that PFCs already in the blood stream tends to accumulate briefly in the liver and spleen but these chemicals are known for their inertness - being stable up to around 400°C; they are resistant to strong acids, bases, oxidants and reducing agents and there are no reports of them being metabolised.

In relation to excretion, F2 summarise that when PFCs are administered directly into the blood they are excreted by expiration. The rate of expiration appears to be a function of the vapour pressure and the excretion half-life for PFP is reported as less than 2 minutes.

8.2 Repeated dose toxicity

No oral or dermal repeated dose toxicity studies on PFP are presented in the EU REACH registration (ECHA, 2020a). The CSR states that these studies are not technically feasible as the material is a gas. In their on-line EU registration, F2 state that there is good evidence that the substance has no long term toxicology, partly based on decades of use of this class of compound in medical applications, and therefore no testing is required. Some relevant literature articles supporting this view are also cited in the CSR including:

Qi Yu, et al. (2014); Yokoyama K, et al. (1978); Platts D.G. and Fraser J.F. (2011); Abou-Chebl A., et al. (2011) and Walker, G.M., et al. (2003).

The on-line EU registration does report a short-term repeated dose inhalation toxicity study in guinea pigs using PFP (Unnamed, 1992). In this study male and female guinea pigs (10 per sex) were exposed continuously to *circa* 10% v/v octafluoropropane (113 000 ppm or mg/L) in air for 10 days. There was analytical verification of the concentration by infrared spectrometry and gas-liquid chromatography (IR-GLC). No adverse effects relating to PFP were reported, however some animals in the test and control groups were sacrificed on day 6 due to illness. All control and test subjects were later found to have interstitial pneumonitis and so the EU REACH registration considered the study to be Klimisch 3 (unreliable) although it did provide indications that effects were not due to PFP.

8.3 Mutagenicity

The EU REACH registration (ECHA, 2020a) states that decades of experience of handling and use of saturated PFCs in medical applications in the blood, lungs and eyes supports their view that no adverse genotoxic effects would be observed.

One *in-vitro* gene mutation study in bacteria using PFP is reported in the on-line dossier. Details are given in the Table 8.1 Summary of mutagenicity endpointsbelow.

Table 8.1 Summary of mutagenicity endpoints

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
OECD 471 (bacterial reverse mutation assay) Stated to be GLP compliant	*Salmonella typhimurium* strains TA 1535, TA 1537, TA 98 and TA 100, with and without metabolic activation	PFP applied as a gas at concentrations of 5, 10, 20, 40 and 80% v/v in air. Positive controls used: 9-aminoacridine, 2-nitrofluorene, N-ethyl-N-nitro-N-nitrosoguanidine, 2-aminoanthracene	Negative for genotoxicity; also no cytotoxicity seen. Positive control validity confirmed. It was concluded that PFP shows no evidence of mutagenic activity when tested in this bacterial system.	Registrant: 1 (reliable without restriction)	Unnamed (1991), cited in ECHA (2020a)

8.4 Carcinogenicity

The following study was reported in the public EU registration dossier for PFP (ECHA, 2020a).

Table 8.2 Summary of carcinogenicity endpoints

Method	Species	Brief study details	Results	Reliability (Klimisch) score	Reference
Mammalian erythrocyte micronucleus test, OECD TG 474 Conducted to GLP	Mouse (male and female) 15 animals per sex per dose	Singe oral gavage at 2026 mg PFP/ml in 1% methyl cellulose to give total dose of 40520 mg/kg. Bone marrow smears taken at 24, 48 and 72 hours examined for micronuclei and ratio of polychromatic to normochromatic erythrocytes.	Negative toxic and genotoxic effects. Testing concluded that PFP is not geneticall y toxic	Registrant : 1 (reliable without restriction)	Unnamed (1984), cited in ECHA (2020a)

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

The public EU REACH registration dossier for PFP does not include any reproductive toxicity studies on the registered substance but a weight-of-evidence and read-across case has been made based on an in-house summary review report (Unnamed, 2017 cited in ECHA, 2020a). This also refers to five other published papers on PFCs which are the same as cited at 8.2 above and do not appear to specifically cover reproductive effects.

The EU REACH registration states however that this review offers '...good evidence that the substance is not toxic to reproduction, partly based on decades of use of this class of compound in medical applications, and therefore no testing is required'.

8.6 Summary of mammalian toxicology

The EU registration dossier for PFP concludes that overall no mammalian reproductive or developmental toxicity effects are expected to occur in parental or offspring mammals at a NOEL of up to 10 000 mg/kg bw/day (nominal). This appears to be a weight-of-evidence conclusion rather than based on any particular studies. Due to this apparent lack of toxicity, no Derived No-Effect Level (DNEL) has been proposed in the EU REACH registration.

The published papers do appear to indicate that saturated PFCs, including PFP, are relatively inert and stable to metabolic processes. Whilst such PFCs may accumulate briefly in certain tissues such the liver and spleen, they also appear to be rapidly excreted unchanged via the lungs and this rate is expected to increase along with the substance

vapour pressure. The EU REACH registration reports an excretion half-life for PFP of less than 2 minutes. The available non-regulatory *in-vitro* studies that have been conducted with PFP do not indicate any adverse genotoxic effect.

A paper also reviewed by the Environment Agency, Chernyshev and Skliar (2014) (and references therein) also states that saturated PFCs have ‘unique properties’ including general biological inertness leading to a low level of toxicity, weak intermolecular interactions and high gas solubility, which have proved useful in biomedical applications. These include use as an ultrasound and magnetic resonance imaging contrast agent, blood substitute, liquid ventilation, a propellant in inhalation drug delivery, gene delivery applications and as a means to enhance cavitation during ultrasound tissue ablation. These applications have presumably been associated with various clinical trials, with underlying toxicological information that has been evaluated by an appropriate regulatory authority.

The Environment Agency has not evaluated the available mammalian toxicity information further at this stage.

9 Environmental hazard assessment

9.1 Classification and labelling

9.1.1 Harmonised classification

There is no current harmonized entry for PFP in Annex VI of the Classification, Labelling and Packaging (CLP) Regulation (EC) No 1272/2008, nor a mandatory classification under GB CLP.

9.1.2 Self classification

The EU REACH registration dossier (ECHA, 2020a) does not propose any human health or environmental hazard classes (there is a classification for physical effects: H280: 'Contains gas under pressure; may explode if heated' – for cylinders containing PFP gas.)

In ECHA's Classification and Labelling (C&L) Inventory, the aggregated self-classifications include the following additional hazard classes (ECHA, 2020e):

- H281: Contains refrigerated gas; may cause cryogenic burns or injury.
- H336: May cause drowsiness or dizziness.
- STOT RE 2, H373: May cause damage to liver, kidney, blood, the central nervous and cardiovascular systems through prolonged or repeated exposure.

Only 1 of >76 Notifiers included these additional hazard classes. The basis for the specific target organ toxicity statement is unknown.

9.1.3 Conclusions for environmental classification and labelling

PFP is not readily biodegradable and there is no evidence that it degrades significantly via abiotic mechanisms (see Section 6). It is therefore considered to be "not rapidly degradable" for the purposes of hazard classification.

An aquatic bioaccumulation study is not available. The EU REACH registration states that the bioaccumulation of PFP is 'very low' based on read across from other PFCs and toxicokinetic information (see Section 6.3.1.2). The Environment Agency considers the log K_{OW} of PFP to be around 3 (range 2.5 to 3.5) at 25 °C. There is some uncertainty surrounding this endpoint (see Section 5.4). However, since the highest log K_{OW} value in this range is less than 4, PFP does not meet the CLP bioaccumulation criterion for the purposes of hazard classification.

No acute or chronic aquatic toxicity data are available on PFP itself. As it is a gas and aqueous exposure is considered minimal, the EU REACH registration claims that such testing is not scientifically warranted. The Environment Agency has considered the exposure-based waiver arguments, along with ecotoxicity information on PFP analogues and from QSAR models in Section 7.1. Although there are a number of uncertainties, the Environment Agency considers that PFP is unlikely to pose either an acute or chronic hazard to aquatic life.

Based on the currently available information, the Environment Agency agrees that PFP does not currently require classification for aquatic hazards according to the CLP criteria.

Physical or human health hazard classifications for PFP have not been considered in this report.

9.2 Assessment of endocrine disrupting (ED) properties

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

9.3 PBT and vPvB assessment

The EU REACH registration (ECHA, 2020a) stated that the substance is not PBT/vPvB with the following justification:

“[PFP] is a hydrophobic, lipophobic gas. It has a very low solubility in water, and all the evidence suggests it is rapidly lost from soil and sediment. Studies on saturated PFCs, mostly looking at their use in medical applications, in both animals and humans, have shown no sign that they are metabolised in the body and consistently indicate that they do not accumulate in the body. Tests on [PFP] itself indicate that when injected into the blood (encapsulated in microbubbles) it has a half-life in the human body of under 2 minutes.

[PFP] will enter the atmosphere very quickly, and human exposure will be restricted to contact with the gas and inhalation.”

Further consideration by the Environment Agency in relation each of the REACH Annex 13 PBT/vPvB criteria is provided below.

Persistence:

PFP is not readily biodegradable and there is no evidence that it degrades via abiotic mechanisms (see Section 6). PFP therefore meets the screening criterion for being potentially persistent (P) or very persistent (vP). No environmental half-life data are available for comparison with the definitive criteria in REACH Annex 13 but, due to the

stability of the saturated C-F bonds, all indications are that the molecule will be very persistent if released into the environment.

Bioaccumulation:

There are no studies on the bioaccumulation of PFP in aquatic organisms for comparison with the definitive criteria in REACH Annex 13. The EU REACH registration states that the bioaccumulation of PFP is 'very low' based on read across from other PFCs and toxicokinetic information. The Environment Agency considers the log K_{OW} of PFP to be around 3 (range 2.5 to 3.5) at 25 °C. There is some uncertainty surrounding this endpoint (see Section 6.4) but this log K_{OW} is less than the REACH screening criterion (≤ 4.5) for being potentially bioaccumulative (B) in aquatic organisms.

In terms of bioaccumulation in air-breathing organisms, the screening criteria are a log K_{OW} > 2 and log K_{OA} > 5 (ECHA, 2017c). With a proposed log K_{OW} of 3 for PFP (range 2.5 to 3.5) the log K_{OW} criterion is met. In Section 6.3.2.1 the estimated K_{OA} is around 0.98. There is some uncertainty regarding the derived K_{OA} values, but the data currently suggest that PFP does not meet the log K_{OA} screening criterion for bioaccumulation in air-breathing organisms. Given that PFP is a gas, significant uptake by air-breathing organisms other than by inhalation is not expected. Toxicokinetic information from published studies on medical applications of PFP also indicates low retention in mammalian tissues even following direct intravenous injection (excretion half-life < 2 days in humans).

Overall PFP is not considered to meet the REACH Annex 13 B or vB criteria.

Toxicity:

No acute or chronic aquatic toxicity data on PFP itself are presented in the EU registration dossier. As it is a gas and aqueous exposure is considered minimal, the EU REACH registration claims that such testing is not scientifically warranted. The Environment Agency has considered the exposure-based waiver arguments, along with ecotoxicity information on PFP analogues and from QSAR models in Section 7.1. Although there are a number of uncertainties, the Environment Agency considers that PFP is unlikely to meet the REACH Annex 13 criterion for ecotoxicity (T) of a NOEC of < 0.01 mg/L, or the acute screening criterion for being potentially 'T' (L/EC_{50} < 0.1 mg/L).

In terms of mammalian toxicology, few data are available on PFP itself in the EU registration dossier. Instead various weight of evidence and read-across proposals have been made based on a broad category approach using information on other PFCs (Section 8). The EU REACH registration has not proposed any mammalian hazards for PFP or self-classifications that would meet the T criterion based on mammalian toxicity (see Section 9.1). However, the suitability of the weight of evidence and read-across arguments presented have not been considered by the Environment Agency.

No avian toxicity data are available but this is not a requirement for substances with this tonnage and risk profile.

No information is available on the ED potential of PFP.

Overall conclusion:

PFP is considered to be vP but does not screen as B/vB or (based on currently available information) as T.

9.4 Groundwater hazard

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

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

Persistence:

PFP meets the screening criterion for being P or vP (see Section 9.3).

Mobility:

An experimental log K_{OC} value is not available. The Environment Agency suggests that a log K_{OC} of 2.53 (range 2.12 to 2.93) could be used as an approximation (see Section 6.2.1). PFP would therefore meet the draft criterion as being mobile (M) (log $K_{OC} \leq 4$) or very mobile (vM) (log $K_{OC} \leq 3$). A definitive log K_{OC} value is not available from a relevant soil study, so there is some uncertainty in this assessment. In addition, since PFP is a gas, a K_{OC} may be meaningless.

Toxicity:

The Environment Agency considers that PFP is unlikely to meet the REACH Annex 13 T criterion based on aquatic toxicity information. The EU REACH registration has not proposed any mammalian hazards for PFP or self-classifications that would meet the T criterion based on mammalian toxicity. However, the suitability of the weight of evidence and read-across arguments presented have not been considered by the Environment Agency (see Section 9.3).

Overall conclusion:

PFP is considered to be vP and potentially M, but it is not currently considered to meet the T criteria. PFP is a gas at normal environmental temperatures and pressures, and the influence of volatility is not currently considered under the PMT criteria.

9.5 Greenhouse gas hazard

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

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 in the homologous series relevant to PFP are listed in Table 9.1 below. These values are sourced from the Fifth Assessment Report of the IPCC (IPCC, 2013). PFP is included (in ***bold italics***).

The Ozone-Depleting Substances (ODS) Substances and Fluorinated Greenhouse Gases (F-gas) Regulations quotes a GWP for PFP of 8 830 $GtCO_2$-eq which is slightly lower than that reported by the IPCC (2014) below.

Table 9.1 Global warming potential of PFCs

Perfluoroalkane	Trade name	Atmospheric lifetime		GWP (100 years) as CO_2 equivalent
		years	days	
Tetrafluoromethane	PFC14	50 000	-	6 630
Perfluoroethane	PFC116	10 000	-	11 100
-	PFC-c216	3 000	-	9 200
Perfluoropropane	**PFC-218**	**2 600**	**-**	**8 900[a]**
Perfluorocyclobutane	PFC-318	3 200	-	9 540
Perfluorobutane	PFC-31-10	2 600	-	9 200
Perfluoropentane	PFC-41-12	4 100	-	8 550
Perfluorohexane	PFC-51-14	3 100	-	7 910
Perfluoroheptane	PFC-61-16	3 000	-	7 820
Perfluorooctane	PFC-71-18	3 000	-	7 620
Perfluorodecalin	PFC-91-18	2 000	-	7 190

Note: a - An earlier review article by Tsai *et al*. (2002) gave a 100-year GWP of 7 000 (relative to 1 for carbon dioxide). The IPCC Fourth Assessment Report gave a 100-year GWP of 8 830 $GtCO_2$-eq (Forster *et al.* 2007).

The 10-year GWP for PFP of 8 900 $GtCO_2$-eq is relatively high compared to other PFCs.

A qualitative risk characterisation for the atmosphere is included at Section 11.

9.6 Limit values

9.6.1 Predicted No Effect Concentration (PNEC) derivation

A PNEC is an indication of an acceptable environmental concentration based on evidence from (eco)toxicity studies.

The available hazard information is discussed in Sections 7, 8 and 9. The EU REACH registration considers the substance to be non-hazardous and has not derived PNECs. No acute or chronic aquatic, terrestrial or mammalian toxicity data on PFP itself are presented in the EU registration dossier. As PFP is a gas and aqueous and soil exposure is considered minimal, the EU REACH registration claims that such testing is not scientifically warranted. The Environment Agency has considered the exposure-based waiver arguments, along with ecotoxicity information on PFP analogues and from QSAR models in Section 8. The Environment Agency agrees that PFP is likely to pose a low hazard to wildlife and so derivation of environmental PNECs according to the REACH guidance (ECHA, 2008b) is not currently required.

The Environment Agency notes that the EU REACH registration has not currently determined a DNEL for use in human health risk assessment as they do not consider PFP to be hazardous to human health.

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

A CSR was available in the EU REACH registration dossier, but since PFP is not self-classified by the UK supplier as hazardous, no assessment of environmental exposure was performed. The Environment Agency agrees that PFP is unlikely to pose either an acute or chronic hazard to aquatic life and does not currently require classification for aquatic hazards according to the CLP criteria (see Section 9.1.3). Nevertheless, the Environment Agency has prepared an environmental exposure assessment based on information in the EU REACH registration dossier, the environmental permit and information provided on the F2 Chemicals Ltd website. This has been done to help decide on the priority for further work - it does not affect the company's responsibilities to demonstrate safe use for their substance.

10.1 Environment

10.1.1 Short description of emission scenarios and measures for reducing emissions to the environment

PFP is manufactured at F2 Chemicals Ltd, Lea Lane, Lea Town, Preston, Lancashire PR4 0RZ. PFP is also registered by other companies in the EU in the range of 100 to 1 000 tonnes/year.

Other uses in the EU REACH registration dossier are:

- Formulation into a mixture.
    - Formulation, Transfer and (Re-)Filling.
- Use as intermediate.
- Use of non-reactive processing aid at industrial site (no inclusion into or onto article).
    - Calibration of analysis equipment.
    - Solvent in polymerisation process.
- Use of reactive processing aid at industrial site (no inclusion into or onto article).
    - Industrial use as cleaning/etching reagent.
- Use at industrial site leading to inclusion into/onto article.
    - Use for electronic component manufacture.
- Use of functional fluid at industrial site.
    - Refrigerant.
- Widespread use of functional fluid (outdoor).
    - Use gas to refill refrigeration equipment, refrigerant gas.

10.1.1.1 Routes of emission to surface water

There are no direct releases to surface water or groundwater at the manufacturing site, based on the environmental permit information and use pattern. Emissions to wastewater are noted as being from ‘spent scrubber liquors, rainwater from the scrubber and DHF (dilute hydrofluoric acid) areas’. The total effluent emissions are estimated at 20 m^3/day which primarily comprises ‘wash-down from production vessels and spent scrubber liquors’. There is no on-site treatment, and the effluent is discharged off-site to a municipal sewage treatment plant at Clifton Marsh.

There may be some potential for release to wastewaters or direct to surface waters in some of the substance’s applications but no specific information is currently available.

10.1.1.2 Routes of emission to land

There are no direct releases to soil at the manufacturing site, based on the environmental permit information and use pattern.

No information is currently available about potential routes of emission to land from the use of the substance.

10.1.1.3 Routes of emission to air

According to the company’s environmental permit, environmental releases can be expected to be primarily to the air compartment. The company reports (total) releases of volatile organic compounds – assumed to be PFCs – in the region of 6 tonnes/year to air although the exact identity and quantity of individual substances is not stated.

The substance is a gas, so there is likely to be release to air from some of the substance’s applications but no information is currently available.

10.1.2 Release assumptions made by the Environment Agency

The Environment Agency has received actual production volume data from F2 Chemicals Ltd. However, for the purposes of this evaluation, it can be assumed as an extreme worst case that PFP could be produced at up to 400 tonnes/year, which is the maximum capacity of the plant (see Section 3; this is stated to be for all products and so is unlikely to be realistic). There are no other UK producers.

In the absence of detailed information about uses, the Environment Agency assumes that all registered uses occur in the UK, at a supply volume of 100 tonnes/year, which is 10% of the upper limit of the EU registered annual tonnage (consumption by UK businesses is likely to be significantly lower than the EU level of supply). This also assumes that 25% of 400 tonnes/year of PFP production is supplied to the UK market. The supply volume of 100 tonnes/year has been split equally between the 8 EU registered uses. In addition, the environmental release fractions for each Environmental Release Category (ERC) are

based on the default worst case assumptions in ECHA's R.16. Guidance Document (ECHA, 2016), as summarised in Table 10.1.

Table 10.1 Uses and environmental releases for F2 Chemicals use only

Use Type and ERC	Environmental release fraction used in the exposure assessment			Regional volume of use (tonnes/ year)	Fraction of main local source	Number of emission days/year (local)
	to air	to wastewater	to soil			
ERC1: *Manufacture of the substance*	0.05	0.06	0	400	1	20[a]
ERC2: *Formulation, Transfer and (Re-) Filling*	0.025	0.02	0.0001	12.5	1	20[a]
ERC4: *Calibration of analysis equipment*	1	1	0.05	12.5	1	20[a]
ERC4: *Solvent in polymerisation process*	1	1	0.05	12.5	1	20[a]
ERC5: *Use for electronic component manufacture*	0.5	0.5	0.01	12.5	1	20[a]
ERC6a: *Use of intermediate*	0.05	0.02	0.001	12.5	1	20[a]
ERC6b: *Industrial use as cleaning/etching reagent*	0.001	0.05	2.5×10^{-4}	12.5	1	20[a]
ERC7: *Refrigerant*	0.05	0.05	0.05	12.5	1	20[a]
ERC9b: *Use gas to refill refrigeration equipment, refrigerant gas*	0.05	0.05	0.05	1.25[b]	0.002[b]	365[b]

Note: a - This is the default emission rate for the tonnage band in the R.16 Guidance Document (ECHA, 2016).

b - This is the default regional tonnage (10%) and emission rate for widespread use in the R.16 Guidance Document (ECHA, 2016).

The adoption of these highly conservative assumptions indicates a worst case emission from the manufacture of PFP of 20 tonnes/year to air and 24 tonnes/year to wastewater for

both regional and local scales. However, this essentially assumes that there is no abatement on site.

- The site reports total PFC emissions of 6 tonnes/year to air. Given the registered tonnage bracket, the Environment Agency anticipates that PFP could comprise a large proportion of these emissions. A reasonable worst case assumption is therefore that the emission to air from PFP is 6 tonnes/year at the local and regional scales from manufacturing (i.e. PFP accounts for all of the reported emission to air). This is equivalent to a release factor of 1.5% assuming a production volume of 400 tonnes/year.
- The site permit does not require wastewater emissions to be reported. Given the ratio of the reported and estimated air emissions (which differ by a factor of 3.3), a more realistic reasonable worst case release to wastewater might be in the region of 7 tonnes/year for the local and regional scales from manufacturing based on the extreme worst case tonnage. However, the Environment Agency notes that the manufacterer has said that emissions to wastewater are “negligible”. The Environment Agency would prefer a quantitative estimate and recommends that the basis for this statement is explained, but for the purposes of this assessment, zero release to wastewater is assumed for this site.

10.1.3 Predicted Environmental Concentrations (PECs)

Chemical concentrations can be predicted for various environmental compartments by inputting the environmental releases mentioned in Section 10.1.2 to the European Union System for the Evaluation of Substances (EUSES) computer program (v2.0.3). This is the best model currently available for assessing environmental exposure of novel chemicals in a standardised way.

In the following discussion, the 'local' environment is considered to be an area close to a site of release (e.g. the manufacturing site). The 'regional’ PEC is a background concentration arising from direct emissions of the substance from industrial processes and diffuse emissions as a consequence of the use of end products within a highly developed region, 200 km × 200 km in area, with 20 million inhabitants. The ‘regional’ scenario is equivalent to around 31% of the land area (130,279 km²) and 36% of the population (approximately 56 million people[2]) of England.[3] The continental environment is the size of

[2] https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/bulletins/annualmidyearpopulationestimates/mid2019 (accessed July 2020)

[3] The equivalent figures for the UK are around 16% for land area and 30% for population.

the EU and is generally used for mass balance purposes. The assessment is generic, representing a realistic worst case approach for a hypothetical environment that broadly reflects average European conditions. It is not intended to represent any specific part of the UK, with the exception of the local environment.

The key properties of PFP used in the EUSES calculations are summarised in Table 10.2. Unless stated otherwise, all other partitioning coefficients are derived using the log K_{OW} using the hydrophobic QSAR contained within the model (see Section 6).

The local and regional PECs are summarised in Table 10.3 and Table 10.4 below.

Table 10.2 Substance-specific input parameters for the EUSES model

Parameter	Values used in this evaluation
Physical state	Gas
Molecular weight, g/mol	188
Vapour pressure at 25 °C, kPa	767
Water solubility at 25 °C, mg/L	6.56
Octanol-water partition coefficient (log K_{OW})	2.8 (range of 2.5 to 3.1)
Chemical class for K_{OC}-QSAR	Predominantly hydrophobics
Organic carbon-water partition coefficient (log K_{OC})	2.53 (range of 2.12 to 2.61)
Suspended matter–water partitioning coefficient (log $K_{SUSP-WATER}$)	1.53 (range of 1.12 to 2.61)
BCF_{fish} (L/kgww^{-1})	47.9
$BCF_{earthworm}$ (L/kgww^{-1})	8.41
Half-life for degradation in air, hours	1 x 10^{40} k_{OH} = 0 cm^3/molecule/s
Biodegradability	Not readily biodegradable
Sewage treatment works removal rate: Air Sludge	 92.2 % 2.95 %

In the absence of an emission to wastewater treatment works or direct emission to fresh / marine water or soil or groundwater from manufacturing, no PECs for freshwater or marine, soil compartments, groundwater or secondary poisoning have been derived for manufacturing.

10.1.3.1 Fresh surface water

Concentrations are estimated in sewage effluent from a 'standard' sewage treatment plant (STPs) for each life cycle step, based on the influent concentration and the partitioning properties described in Section 6. The concentration in the receiving water is calculated by assuming a default dilution factor of 10. The PEC_{local} is made up of a local water concentration (C_{local}) resulting from the relevant process emission, added to the $PEC_{regional}$.

The regional and local PEC values for freshwater have been estimated in Table 10.3 and Table 10.4.

10.1.3.2 Freshwater sediment

The PEC for sediment can be derived from the PEC_{local} for surface water using the suspended matter–water partitioning coefficient (see Table 10.2) assuming equilibrium partitioning.

The regional and local PEC values for freshwater sediment have been estimated in Table 10.3 and Table 10.4.

10.1.3.3 WWTP micro-organisms

PECs for WWTPs are based on effluent concentrations arising from direct releases. A PEC_{WWTP} has been estimated for each part of the life cycle (see Table 10.3).

10.1.3.4 Groundwater

As described under Section 9.4, local PECs for groundwater can be estimated for agricultural land that accepts sewage sludge from the STP that treats effluent (see Table 10.3). The porewater concentration for agricultural soil is used to represent groundwater. The predicted regional concentration (Table 10.4) for groundwater is lower than the water solubility of 6.56 mg/L (see Section 5.3.5).

10.1.3.5 Air

The local air compartment is assumed to receive emissions from the process and via volatilisation from the WWTP. Local PECs for air represent the concentration 100 m from the emission source, and have been estimated for each use pattern (see Table 10.3) and the regional PEC is also presented in Table 10.4.

As a gas, removal of PFP from the atmosphere through precipitation is not likely to be a significant process and rainwater concentrations are likely to be low.

10.1.3.6 Soil (including sewage sludge)

At both local and regional scales, EUSES takes into account the application of sewage sludge containing the substance (specifically from the Clifton Marsh STP in this case) and atmospheric deposition. Direct releases to soil are only included at the regional scale –

industrial soil is not considered a protection target for direct releases at local scale and no direct releases to soil are permitted at local scale.

Three different soil PECs are calculated in EUSES: soil (PEC_{soil}), agricultural soil ($PEC_{agr,soil}$) and grassland ($PEC_{grassland}$). These vary in terms of the depth of soil considered and the duration and/or route of exposure which include the repeated application of sludge from a WWTPs that occurs over a 10 year period and aerial deposition from atmosphere. The 30-day average for soil represents the PEC for soil organisms, while the 180-day averages for agricultural and grassland soils are used to estimate exposure of farmed animals and people through the food chain. The various local soil PECs are summarised in Table 10.3.

At the regional level the soil concentration in unpolluted or 'natural' soil is used as the background concentration, to avoid double counting of application through sludge. The estimated regional concentrations for the soil compartment are summarised in Table 10.4.

10.1.3.7 Secondary poisoning in the freshwater food chain

If a substance accumulates in the food chain, it might reach a concentration in food that could cause toxic effects in a predator that eats that food. This is referred to as secondary poisoning.

Since the substance is highly persistent and was initially thought to be potentially bioaccumulative, PECs for fish-eating predators were calculated and are presented in Table 10.3. These are estimated from the surface water concentration (annual average PEC) using the fish BCF and biomagnification factors (BMFs) estimated from the log K_{OW} and assumes that the predator gets half of its food from a local site and half from the region.

10.1.3.8 Secondary poisoning in the terrestrial food chain

The EUSES model estimates concentrations in earthworms using an estimated earthworm BCF and the pore water concentration of the substance in agricultural soil. The resulting values are presented in Table 10.3 Local PECs. The Environment Agency considers that results derived from the estimated $BCF_{earthworm}$ should be treated cautiously as its reliability for use with PFCs is not known.

Table 10.3 Local PECs

Life cycle stage	Compartment	PEC_{local}	Unit
ERC1: Manufacture of the substance	Air	2.7	mg/m^3
ERC2: (Formulation, Transfer and (Re-) Filling)	Fresh surface water (annual average)	1.71×10^{-3}	mg/L
	Freshwater sediment	0.179	mg/kg ww
	Air	2.7	mg/m^3
	Agricultural soil – 30 day average	1.66×10^{-3}	mg/kg ww

Life cycle stage	Compartment	PEC_{local}	Unit
	Agricultural soil – 180 day average	5.44×10^{-4}	mg/kg ww
	Grassland - 180 days	3.66×10^{-4}	mg/kg ww
	Groundwater*	4.97×10^{-7}	mg/L
	WWTP	0.305	mg/L
	Concentration in fish (fresh water)	1.77×10^{-3}	mg/kg ww
	Concentration in earthworms	4.07×10^{-5}	mg/kg
ERC4: (Calibration of analysis equipment) refrigerant gas)	Fresh surface water (annual average)	0.0835	mg/L
	Freshwater sediment	8.93	mg/kg ww
	Air	2.71	mg/m^3
	Agricultural soil – 30 day average	0.0673	mg/kg ww
	Agricultural soil – 180 day average	0.0115	mg/kg ww
	Grassland - 180 days	2.56×10^{-3}	mg/kg ww
	Groundwater*	1.05×10^{-5}	mg/L
	WWTP	15.2	mg/L
	Concentration in fish (fresh water)	2	mg/kg ww
	Concentration in earthworms	6.48×10^{-4}	mg/kg
ERC4: (Solvent in polymerisation process) equipment,	Fresh surface water (annual average)	0.0835	mg/L
	Freshwater sediment	8.93	mg/kg ww
	Air	2.71	mg/m^3
	Agricultural soil – 30 day average	0.0673	mg/kg ww
	Agricultural soil – 180 day average	0.0115	mg/kg ww
	Grassland - 180 days	2.56×10^{-3}	mg/kg ww
	Groundwater*	1.05×10^{-5}	mg/L
	WWTP	15.2	mg/L
	Concentration in fish (fresh water)	2	mg/kg ww
	Concentration in earthworms	6.48×10^{-4}	mg/kg
ERC5: (Use for electronic component manufacture)	Fresh surface water (annual average)	0.0418	mg/L
	Freshwater sediment	4.46	mg/kg ww
	Air	2.7	mg/m^3
	Agricultural soil – 30 day average	0.0338	mg/kg ww
	Agricultural soil – 180 day average	5.91×10^{-3}	mg/kg ww
	Grassland - 180 days	1.44×10^{-3}	mg/kg ww
	Groundwater*	5.39×10^{-6}	mg/L
	WWTP	7.62	mg/L
	Concentration in fish (fresh water)	1	mg/kg ww
	Concentration in earthworms	3.44×10^{-4}	mg/kg
ERC6a: Use of intermediate	Fresh surface water (annual average)	1.71×10^{-3}	mg/L
	Freshwater sediment	0.179	mg/kg ww
	Air	2.7	mg/m^3
	Agricultural soil – 30 day average	1.66×10^{-3}	mg/kg ww
	Agricultural soil – 180 day average	5.44×10^{-4}	mg/kg ww

Life cycle stage	Compartment	PEC_{local}	Unit
	Grassland - 180 days	3.66×10^{-4}	mg/kg ww
	Groundwater*	4.97×10^{-7}	mg/L
	WWTP	0.305	mg/L
	Concentration in fish (fresh water)	0.0417	mg/kg ww
	Concentration in earthworms	5.28×10^{-5}	mg/kg
ERC6b: (Industrial use as cleaning/etching reagent) refrigeration	Fresh surface water (annual average)	4.21×10^{-3}	mg/L
	Freshwater sediment	0.447	mg/kg ww
	Air	2.7	mg/m^3
	Agricultural soil – 30 day average	3.67×10^{-3}	mg/kg ww
	Agricultural soil – 180 day average	8.79×10^{-4}	mg/kg ww
	Grassland - 180 days	4.33×10^{-4}	mg/kg ww
	Groundwater*	8.02×10^{-7}	mg/L
	WWTP	0.762	mg/L
	Concentration in fish (fresh water)	0.102	mg/kg ww
	Concentration in earthworms	7.1×10^{-5}	mg/kg
ERC7: (Refrigerant)	Fresh surface water (annual average)	4.21×10^{-3}	mg/L
	Freshwater sediment	0.447	mg/kg ww
	Air	2.7	mg/m^3
	Agricultural soil – 30 day average	3.67×10^{-3}	mg/kg ww
	Agricultural soil – 180 day average	8.79×10^{-4}	mg/kg ww
	Grassland - 180 days	4.33×10^{-4}	mg/kg ww
	Groundwater*	8.03×10^{-7}	mg/L
	WWTP	0.762	mg/L
	Concentration in fish (fresh water)	0.102	mg/kg ww
	Concentration in earthworms	7.1×10^{-5}	mg/kg
ERC9b: (Use gas to refill refrigeration equipment, refrigerant gas)	Fresh surface water (annual average)	3.79×10^{-5}	mg/L
	Freshwater sediment	2.22×10^{-4}	mg/kg ww
	Air	2.7	mg/m^3
	Agricultural soil – 30 day average	3.21×10^{-4}	mg/kg ww
	Agricultural soil – 180 day average	3.21×10^{-4}	mg/kg ww
	Grassland - 180 days	3.21×10^{-4}	mg/kg ww
	Groundwater*	2.93×10^{-7}	mg/L
	WWTP	8.35×10^{-5}	mg/L
	Concentration in fish (fresh water)	0.027	mg/kg ww
	Concentration in earthworms	4.07×10^{-5}	mg/kg

Note: ww – wet weight
dw – dry weight
* The porewater concentration for agricultural soil is used to represent groundwater.

Table 10.4 Regional PECs

Compartment	$PEC_{regional}$	Unit
Fresh surface water	3.71×10^{-5}	mg/L
Freshwater sediment	2.42×10^{-4}	mg/kg ww
Marine water	3.74×10^{-6}	mg/L
Marine sediment	2.27×10^{-5}	mg/kg ww
Air	2.7	mg/m^3
Agricultural soil	4×10^{-4}	mg/kg ww
Natural soil	3.21×10^{-4}	mg/kg ww
Industrial soil	2.14×10^{-3}	mg/kg w
Groundwater*	8.04×10^{-6}	mg/L

Note: dw – dry weight

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

10.1.4 Sensitivity analysis

10.1.4.1 Log K_{ow}

There is uncertainty regarding the reliability of several of the input parameters for EUSES, in particular key physico-chemical and fate properties of PFP. To determine the effect on local and regional PEC generation, the log K_{OW} of PFP has been varied within the range 2.5 to 3.1.

Changing the K_{OW} had no effect on the air concentration as would be expected for this property. Reducing K_{OW} had the effect of increasing the surface water PEC accordingly whist decreasing the soil, sediment and groundwater PECs. This effect is to be expected as partitioning to soil and sediment increases with increasing K_{OC} which is derived from K_{OW}.

Although an increase / decrease in PECs was observed from the modification to K_{OW} in the range described in Section 5, the surface water PECs are generally in the same order of magnitude, although the freshwater sediment PEC is very sensitive to K_{OW} / K_{OC}.

10.1.4.2 Future climate scenarios

The default temperature of environmental compartment is 12 °C and default value of 10 has been used as a dilution factor for STP effluent[4]. The sensitivity of the modelled PECs to potential changes under future climate change scenarios has been considered to highlight whether pre-emptive controls may be necessary.

Research into UK climate change projections has been published by the Met Office[5] for different warming levels including; 1.5 °C, 2 °C and 4 °C and highlighted that the average temperature over the most recent decade (2009-2018) has been on average 0.3 °C warmer than the 1981-2010 average and 0.9 °C warmer than the 1961-1990 average. Increasing the environmental compartment temperature to 16 °C had no effect on the generated 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.

The Environment Agency (2013) reported that a default dilution factor value of 10 is insufficiently protective of a great deal of surface watercourses in England. In addition, dry weather is also likely to become more frequent in summer months, which will reduce river flows. A dilution factor (DF) of 2 was recommended by Environment Agency (2013) to be protective of surface watercourses.

Reducing the dilution factor from 10 to 5 and also 2 increased the surface water and freshwater sediment PEC values. For example, changing the DF from 10 to 2, the PEC_{local} for freshwater, freshwater sediment and fish increased by 5 times of that reported in Table 11.3.

10.1.4.3 Discussion

An increase / decrease in PECs was observed from the modification of K_{OW} in the range described in Section 3, although the surface water PECs are generally in the same order of magnitude, the freshwater sediment PEC is very sensitive to K_{OW} / K_{OC} changes.

---

[4] Experimentally derived chemical properties will usually be measured at a standard temperature, which is different from the temperature used in the models of EUSES. For most chemicals and most properties, a temperature correction will not be necessary between the standard 20 or 25 degrees and the environmental temperature used in the system (by default 12 degrees Celsius in the environment and 15 degrees in the WWTP.

[5] https://www.metoffice.gov.uk/research/approach/collaboration/ukcp/index (accessed 27 July 2020)

Information from the Met Office as summarised above indicates the future climate will experience periods of drought. In this situation, where there is less dilution in surface water courses, this could lead to potentially higher concentrations in environmental media. In the exposure assessment, a decrease in the default dilution factor from 10 to 5 and 2 has the effect of increasing the surface water and sediment PECs and the freshwater fish concentrations accordingly. This parameter change only affects surface water media after mixing with effluent from the wastewater treatment plant and partitioning with the surface water sediment and concentrations in fish.

10.1.5 Monitoring data

No monitoring data were identified in the EU REACH registration dossier, academic literature or internal Environment Agency monitoring network.

10.1.6 Discussion

The derivation of the modelled PECs for PFP is influenced by a range of uncertainties including:

- Emission uncertainty (use pattern, emission scenarios and volumes);
- Parameter uncertainty (predicted physico-chemical and fate inputs, dilution factor);
- Modelling uncertainty (modelled WWTWs removal); and
- Monitoring data uncertainty (no measurements available).

In the absence of more detailed information regarding emissions, use pattern and measured environmental concentrations, there remains significant uncertainty in this assessment. Therefore, PECs derived in this evaluation are considered indicative of potential release and exposure of PFP in the environment.

Further refinement would be required to improve the reliability of this assessment. This could include specific information on UK tonnages, uses and releases, monitoring data and more reliable experimental data for physico-chemical properties.

11 Risk characterisation

11.1 Risks to aquatic and terrestrial compartments

No relevant environmental PNEC values are currently available to perform a risk characterisation using the PECs derived in the exposure assessment.

11.2 Risks to human health via the environment

Although not the focus of this report, no relevant human health DNEL values are currently available to perform a risk characterisation using the PEC's derived in the exposure assessment.

11.3 Risks to the atmosphere

The Environment Agency notes that PFP has a significant global warming potential, with a 100-year GWP in the order of 8 800 to 8 900 $GtCO_2$-eq. (see Section 9.5).

Through the Environmental Permitting Regulations, the permitting regime does require applicants to assess the GWP of their site emissions, but as long as Best Available Techniques are being used to control emissions, there is no requirement to reduce emissions in response to the site's GWP. The maximum emission of PFP from the manufacturing site is assumed to be 6 tonnes/year as a worst case (see Section 10.1). This would be an equivalent emission of CO_2 of 53 400 tonnes[6] using the CO_2 equivalent.

Emissions from other uses within the UK have not been considered due to lack of information. This is an information gap. However, given the physico-chemical properties of PFP, it seems plausible that most of the production volume (up to a theoretical maximum of 400 tonnes/year) could eventually end up in the atmosphere (unless specific measures are taken to destroy waste). The Environment Agency notes that some potential downstream user industries (e.g. the semi-conductor industry) have exemptions from some F-gas controls.

[6] https://www.gov.uk/guidance/calculate-the-carbon-dioxide-equivalent-quantity-of-an-f-gas

12 Conclusions and recommendations

12.1 Conclusion

PFP is a perfluoroalkane and an example of a perfluorocarbon (PFC) containing only carbon and fluorine atoms. It is a gas at standard pressure and temperature and any primary emissions are expected to be to the atmosphere.

PFP is produced for use in a wide range of uses including as a processing, etching and cleaning aid, coolant and solvent in semi-conductor and electrical equipment manufacture. Releases occur to air during manufacture at a single UK site, potentially up to a level of around 6 tonnes/year (although the actual amounts are likely to be lower). Small releases may occur at downstream user sites, again mostly to air, although this has not been quantified.

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

- PFP is not readily biodegradable and there is no evidence that it degrades significantly via abiotic or biotic mechanisms. It is considered likely to be very persistent (vP), with a long atmospheric half-life.
- There are no valid experimental log K_{OW} or aquatic bioconcentration data for PFP itself, however log K_{OW} estimates and other information indicate that it does not screen as potentially bioaccumulative or very bioaccumulative (B/vB). As PFP is volatile, fish bioconcentration studies could be difficult to perform and the standard B/vB triggers and criteria may also not be relevant. There are some indications of retention in mammalian tissues (possibly non-lipid mediated) but also of elimination by exhalation of similar high vapour pressure PFCs in mammalian studies. Overall it is concluded that PFP is unlikely to bioaccumulate in aquatic or air-breathing organisms.
- There are no ecotoxicity data on PFP itself to determine whether it meets the 'T' criteria for ecotoxicity. However, as PFP is a gas its high volatility could make standard ecotoxicological testing difficult to perform. Information from QSAR models and suggested analogues of PFP indicates that the acute and chronic aquatic toxicity for fully saturated perfluoroalkanes is expected to be low. The UK supplier has not proposed any aquatic hazard self-classification for PFP under CLP and similarly they do not identify any classifications or toxicity that would meet human health T criteria. Whilst there are some uncertainties with the assumptions made, the information considered in Sections 7 and 8 indicates overall that PFP is unlikely to exhibit significant (eco)toxicity and no PNEC values have been determined for use in environmental risk assessment. A number of recommendations are made, however, for the company to provide further scientific support and justification for their data-waiving and read-across justifications and to update their registration dossier accordingly.
- Overall PFP screens as vP but does not screen as B/vB or (based on currently available information) as T.

- 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). PFP is considered to be vP and screens as potentially mobile (M) and so in theory it poses a potential concern relating to the contamination of groundwaters. However, the influence of volatility is not currently considered under these criteria and environmental distribution modelling indicates that PFP is expected to partition predominantly to air rather than to soil or water.
- Once in the atmosphere, available information suggests that PFP has the potential for long-range transport. It is also a greenhouse gas identified in the Ozone-Depleting Substances (ODS) Substances and Fluorinated Greenhouse Gases (F-gas) regulations. It therefore presents a risk to the environment once emitted to the atmosphere and is expected to have a significant 100-year global warming potential (GWP) in the order of 8 800 to 8 900 $GtCO_2$-eq. No data about biotic effects (e.g. to plants) from aerial exposure are available.
- The Environmental Permitting Regulations do require applicants to assess the GWP of their site emissions, but as long as Best Available Techniques are being used to control emissions, there is no requirement to further monitor or reduce emissions in response to the site's GWP. The maximum emission of PFP from the manufacturing site is assumed to be up to 6 tonnes/year as a conservative worst case. This would be an equivalent emission of CO_2 of 53 400 tonnes using the CO_2 equivalent.
- Emissions from other uses within the UK have not been considered due to lack of information. This is an information gap. However, given the physico-chemical properties of PFP, it seems plausible that most of the production volume could eventually end up in the atmosphere (unless specific measures are taken to destroy waste). The Environment Agency notes that some potential downstream user industries (e.g. the semi-conductor industry) have exemptions from some F-gas controls.

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, exposure and risks posed by PFP:

- Details should be provided of appropriate analytical methodology for measuring PFP (and related PFC) emissions to air (see Section 2.1).
- Further detail in the RSS relating to the absence of surface tension, noting this should be for an aqueous solution (Section 5.2).
- Further information in the RSS to support a reliable water solubility value for PFP (Section 5.3).
- Further information in the RSS to support a reliable log K_{OW} value for PFP, ideally based on measured data (Section 5.4).

- Information to clarify the estimated log K_{OC}, noting this is based largely upon the log K_{OW}, so if further information is supplied to clarify that value, then further consideration should be given to the calculated log K_{OC} (Section 6.2.1).
- Information to clarify and support a reliable Henry's Law constant for PFP and to update the RSS accordingly (Section 6.2.2).
- In relation to short-term (acute) ecotoxicological endpoints for fish, aquatic invertebrates, algae, sewage treatment microorganisms as well as sediment-dwelling and terrestrial organisms. Further information should be included to support any exposure-based justification for data waiving. In addition, it is recommended that further information be included to justify any analogue or read-across approaches used taking in to account the guidance in ECHA, 2017b. Any use of QSAR or grouping approaches should also utilise the appropriate reporting formats and guidance as set out ECHA, 2008a (Section 7).
- Additionally, any data waivers for long-term (chronic) ecotoxicological endpoints should be clearly justified in accordance with ECHA's guidance on adaptation of long-term aquatic toxicity testing (ECHA, 2020f) (Section 7).
- The Environment Agency has not fully considered the mammalian toxicology information presented in the EU REACH registration and CSR (Section 8). However, the UK supplier may wish to include additional information and more detailed RSS on the available testing for related substances to support the current data waiving. As above, it is recommended that this should consider the relevant ECHA guidance relating to QSARs and grouping of chemicals (ECHA, 2008a) and the read-across assessment framework (ECHA, 2017b). Any additional references and regulatory information on the safety of PFP when used in medical devices or procedures could also be included.
- Further information to substantiate the statement that there are 'negligible' emissions of PFP to wastewater at the manufacturing site (Section 10.1.2).
- More detailed information relating to the UK tonnage, use pattern and releases/emissions of PFP to each environmental compartment, and/or more reliable experimental data on its physico-chemical properties in order to refine the current worst case modelled exposure estimates. This could include incorporation of PFP into monitoring programmes in relevant environmental media (Section 10.1).

PFP has a high Global Warming Potential. 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 proposed PMT/vPvM criteria are not an official hazard category under UK REACH. Development of a Government policy on the risk management implications for substances with PMT/vPvM properties could be considered.

PFP has a high Global Warming Potential and is listed as a PFC under F-gas legislation. The environmental permit for F2's manufacturing site has a requirement to report annual releases of volatile organic compounds (VOCs) to air, but only a total figure is provided. No specific monitoring data relating to PFP were identified in the EU REACH registration dossier, academic literature or internal Environment Agency monitoring networks. There could be consideration of whether more detailed information on emissions to air from all stages of its life cycle, as well as further efforts to monitor and minimise releases are warranted for PFP under UK F-gas Regulations.

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.

13 References

Abou-Chebl, A., Sung, G., Barbut, D., Torbey, M., 2011. Local brain temperature reduction through intranasal cooling with the RhinoChill device: preliminary safety data in brain-injured patients. Stroke, 42(8), 2164-2169. https://doi.org/10.1161/STROKEAHA.110.613000 (Accessed July 2020).

Arp, H.P.H. and Hale, S.E. 2019. Improvement of Guidance and Methods for the Identification and Assessment of PM/PMT Substances; FKZ 3716 67 416 0. German Environmental Agency (UBA), Dessau-Rosslau, Germany.

Bartos, S., Laush, C., Scharfenberg, J. and Kantamaneni R., 2007. Reducing greenhouse gas emissions from magnesium die casting. Journal of Cleaner Production, 15, 979-987.

Brown J., 1963. Physical properties of perfluoropropane. Journal of Chemical Engineering. Vol 8, 106-108.

Cai B., Liu H., Kou F., Yang Y., Yao B., Chen X., Wong D., Zhang L., Li J., Kuang G., Chen L., Zheng J., Guan D. and Shan Y., 2018. Estimating perfluorocarbon emission factors for industrial rare-earth metal electrolysis. Resources, Conservation & Recycling, 136, 315–323.

Chernyshev V. and Skliar M., 2014. Surface tension of water in the presence of perfluorocarbon vapours. Soft Matter, 10, 1937-1943.

Crowder G., Taylor Z., Reed T. and Young J., 1967. Vapour Pressures and Triple Point Temperatures for Several Pure Fluorocarbons. Journal of Chemical and Engineering Data, 12, 481-485.

Culbertson, J., Prins, J. and Grimsrud, E., 2000. Improvements in the detection and analysis of CF -containing 3 compounds in the background atmosphere by gas chromatography–high-resolution mass spectrometry. Journal of Chromatography, 903, 261–265.

EC, 2015. Fluorinated Greenhouse Gases Policy and Documentation. EC. https://ec.europa.eu/clima/policies/f-gas_en (Accessed July 2020)

EC, 2007. Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). European Commission. https://ec.europa.eu/environment/chemicals/reach/reach_en.htm (Accessed October 2020)

ECHA, 2008a. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.6: QSARs and grouping of chemicals. May 2008. European Chemicals Agency, Helsinki, Finland.

https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9 (Accessed November 2020)

ECHA, 2008b. Guidance on information requirements and chemical safety assessment. Chapter R.10: Characterisation of dose [concentration]-response for environment. May 2008. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/documents/10162/13632/information_requirements_r10_en.pdf/bb902be7-a503-4ab7-9036-d866b8ddce69 (Accessed February 2021)

ECHA, 2011. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.4: Evaluation of Available Information. Version 1.1. December 2011. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/documents/10162/13643/information_requirements_r4_en.pdf/d6395ad2-1596-4708-ba86-0136686d205e (Accessed July 2020)

ECHA, 2012. REACH registration dossier for docosafluorododecahydrofluorene. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/registration-dossier/-/registered-dossier/2659/1/2. Last modified 06 July 2012. (Accessed February 2021)

ECHA, 2013. Support document for identification of pentadecafluorooctanoic acid (PFOA) as a substance of very high concern. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/documents/10162/8059e342-1092-410f-bd85-80118a5526f5 (Accessed July 2020).

ECHA, 2016. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.16: Environmental Exposure Assessment. Version 3.0. February 2016. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/documents/10162/13632/information_requirements_r16_en.pdf (Accessed July 2020)

ECHA, 2017a. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.7a: Endpoint Specific Guidance. Version 6.0. July 2017. European Chemicals Agency, Helsinki, Finland. https://www.echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf (Accessed July 2020)

ECHA, 2017b. Read-Across Assessment Framework (RAAF) and ENV appendices. [online]. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

ECHA, 2017c. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.11: PBT/vPvB assessment. Version 3. June 2017. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/documents/10162/13632/information_requirements_r11_en.pdf (Accessed February 2021)

ECHA, 2017d. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.7b: Endpoint Specific Guidance. Version 4.0. June 2017. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/documents/10162/17224/information_requirements_r7b_en.pdf/ (Accessed February 2021)

ECHA, 2019. EUSES - European Union System for the Evaluation of Substances. Version 2.0.3. https://echa.europa.eu/support/dossier-submission-tools/euses

ECHA, 2020a. REACH online registration for octafluoropropane. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/registration-dossier/-/registered-dossier/18075. (Accessed 9 June 2020)

ECHA, 2020b. REACH online registration for perfluroethane. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/registration-dossier/-/registered-dossier/10719/1. (Accessed February 2021).

ECHA, 2020c. EUSES- European Union System for the Evaluation of Substances. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/support/dossier-submission-tools/euses. (Accessed July 2020)

ECHA, 2020d. REACH registration dossier for hexafluoropropene. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/registration-dossier/-/registered-dossier/15192/1/2. (Accessed February 2021).

ECHA, 2020e. Classification and Labelling (C&L) Inventory entry for PFP. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/76358 (Accessed February 2021)

ECHA, 2020f. Adaptation of long-term aquatic toxicity testing under Annex IX to REACH. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/documents/10162/0/010820_adaptation_long_term_aquatic_toxicity_testing_en.pdf/6bba61b1-61ef-23c7-939a-95bed1b5cf3d?utm_source=echa-weekly&utm_medium=email&utm_campaign=weekly&utm_content=20200805&_cldee=c3RldmUuZHVuZ2V5QGVudmlyb2. (Accessed August 2020).

ECHA, 2020g. PACT- Public Activities Coordination Tool. European Chemicals Agency, Helsinki, Finland. https://echa.europa.eu/pact (Accessed July 2020)

Environment Agency, 2023a. Environmental risk evaluation report. Hexafluoropropene [HFP] (CAS no. 116-15-4). Environment Agency, Bristol.

Environment Agency 2023b. Environmental risk evaluation report. Perfluoroisohexane [PFiHx] (CAS no. 354-04-4). Environment Agency, Bristol.

Environment Canada, 2012. Ecological Screening Assessment Report. Long-Chain (C9-C20) Perfluorocarboxylic Acids, their Salts and their Precursors.

F2 Chemicals Ltd, 2020. Webpage on Octafluoropropane. http://www.f2chemicals.com/octafluoropropane.html (Accessed August 2020)

Forster, P., V. Ramaswamy, P. Artaxo, T. Berntsen, R. Betts, D. Fahey, J. Haywood, J. Lean, D. Lowe, G. Myhre, J. Nganga, R. Prinn, G. Raga, M. Schulz & R. Van Dorland (2008): Changes in Atmospheric Constituents and in Radiative Forcing. Climate Change 2007: The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the IPCC, S. Solomon et al. (eds.), Cambridge University Press, Cambridge, UK, Chapter 2. http://www.cambridge.org/catalogue/catalogue.asp?isbn=9780521705967 (Accessed December 2020)

Hansch, C., Leo, A., Hoekman, D. H. 1995. Exploring QSAR: hydrophobic, electronic, and steric constants. American Chemical Society. Washington. 1995. 348.

Hutter, J. C., Luu, H. M., Mehlhaff, P. M., Killam, A. L., and Dittrich, H. C. 1999. Physiologically based pharmacokinetic model for fluorocarbon elimination after the administration of an octafluoropropane-albumin microsphere sonographic contrast agent, Journal of Ultrasound Medicine, 18(1), 1-11.

IPCC, 2014: Climate Change 2014: Synthesis Report. Contribution of Working Groups I, II and III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change [Core Writing Team, R.K. Pachauri and L.A. Meyer (eds.)]. IPCC, Geneva, Switzerland, 151 pp. https://www.ipcc.ch/assessment-report/ar5/ (Accessed December 2020)

Jasper, J. J., 1972. The Surface Tension of Pure Liquid Compounds. J. Phys. Chem. Ref. Data, 1, 841-1009

Killam, A. L., Mehlhaff, P.M., Zavorskas, P. A., Greener Y., and McFerran, B. A., 1999. Tissue Distribution of 125 I-Labeled albumin in rats, and whole blood and exhaled elimination kinetics of octafluoropropane in anesthetized canines following intravenous administration of Optison® (FS069). International Journal of Toxicology, 18 (1), 49-63.

Lowe K., Anthony P., Davey, M. and Power J., 1999. Culture of cells at perfluorocarbon-aqueous interfaces. Artificial Cells, Blood Substitutes, and Biotechnology, 27(3), 255-261.

Martin T., 2016. User's Guide for TEST (version 4.2) (Toxicity Estimation Software Tool) A Program to Estimate Toxicity from Molecular Structure. US EPA, Washington, DC.

Mayo-Bean K., Moran K., Meylan B. and Ranslow P., 2012. Methodology Document for the ECOlogical Structure-Activity Relationship Model (ECOSAR) Class Program: MS-Windows Version 1.11. US EPA, Washington, DC.

Meylan, W. M., and Howard, P. H. 2005 Estimating octanol-air partition coefficients with octanol-water partition coefficients and Henry's law constants. Chemosphere, 61, 5, 640-4.

Mühle J., Ganesan A., Miller B., Salameh P., Harth C., Greally B., Rigby M., Porter L., Steele L., Trudinger C., Krummel P., O'Doherty S., Fraser P., Simmonds P., Prinn R. and Weiss R., 2010. Perfluorocarbons in the global atmosphere: tetrafluoromethane, hexafluoroethane, and octafluoropropane. Atmos. Chem. Phys., 10, 2010, 5145–5164. http://www.atmos-chem-phys.net/10/5145/2010/acp-10-5145-2010.pdf (Accessed December 2020)

Nelson D., Zahniser M. and Kolb C., 1993. OH Reaction Kinetics and Atmospheric Lifetimes of CF3CFHCF3 and CF3CH2Br. Geophys Research Lett, 20, 197-200.

NICNAS, 1992. Full Public Report File No. NA/46 Perfluoropropane. National Industrial Chemicals and Assessment Scheme, Sydney, Australia. https://www.industrialchemicals.gov.au/sites/default/files/NA46%20Public%20Report%20PDF.pdf (Accessed April 2021).

OECD, 1995a. Test No. 105: Water Solubility, OECD Guidelines for the Testing of Chemicals, Section 1, OECD Publishing, Paris. Available from https://doi.org/10.1787/9789264069589-en (Accessed July 2020)

OECD, 1995b. Test No. 107: Partition Coefficient (n-octanol/water): Shake Flask Method, OECD Guidelines for the Testing of Chemicals, Section 1, OECD Publishing, Paris. https://doi.org/10.1787/9789264069626-en (Accessed July 2020)

OECD, 2004a. Test No. 111, Partition Coefficient (n-octanol/water), HPLC Method, OECD Guidelines for the Testing of Chemicals, Section 1, OECD Publishing, Paris. https://doi.org/10.1787/9789264069701-en (Accessed July 2020)

OECD, 2004b. Test No. 117, Hydrolysis as a Function of pH, OECD Guidelines for the Testing of Chemicals, Section 1, OECD Publishing, Paris. https://doi.org/10.1787/9789264069824-en (Accessed July 2020)

OECD, 2006. Test No. 104: Vapour Pressure, OECD Guidelines for the Testing of Chemicals, Section 1, OECD Publishing, Paris. https://doi.org/10.1787/20745753 (Accessed July 2020).

OECD, 2009. The OECD Pov and LRTP Screening Tool (Version 2.2). http://www.oecd.org/chemicalsafety/risk-assessment/oecdpovandlrtpscreeningtool. htm (Accessed July 2020).

OECD, 2014. Test No. 310, Ready Biodegradability - CO2 in sealed vessels (Headspace Test), OECD Guidelines for the Testing of Chemicals, Section 3, OECD Publishing, Paris. https://doi.org/10.1787/9789264069626-en (Accessed July 2020)

OECD, 2018. Toward a new comprehensive global database of per- and polyfluoroalkyl substances (PFASs): summary report on updating the OECD 2007 list of per- and polyfluoroalkyl substances (PFASs). Series on Risk Management No. 39. JT03431231. Paris: Organisation for Economic Co-operation and Development.

http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV-JM-MONO(2018)7&doclanguage=en (Accessed July 2020)

Okamoto H., Yamanouchi K. and Yokoyama K., 1975. Retention of Perfluorochemicals in Circulating Blood and Organs of Animals After Intravenous Injection of Their Emulsions. Chemical and Pharmaceutical Bulletin (Tokyo), 23(7), 1452-7. doi: 10.1248/cpb.23.1452

Patlewicz G., Richard A., Williams A., Grulke C., Sams R., Lambert J., Noyes P., DeVito M., Hines R., Strynar M., Guiseppi-Elie A. and Thomas R. [2019]. A Chemical Category-Based Prioritization Approach for Selecting 75 Per- and Polyfluoroalkyl Substances (PFAS) for Tiered Toxicity and Toxicokinetic Testing. Environmental Health Perspectives, 127(1), 14501. doi: 10.1289/EHP4555

Platts D. & Fraser J., 2011. Contrast echocardiography in critical care: echoes of the future? A review of the role of microsphere contrast echocardiography. Critical Care and Resuscitation, 13(1), 44-55.

PUBCHEM, 2020a. National Center for Biotechnology Information. PubChem Database. Octafluoropropane, Source=Hazardous Substances Data Bank (HSDB). https://pubchem.ncbi.nlm.nih.gov/source/hsdb/8074

Qi Yu, Kun Liu, Li Su, Xin Xia and Xun Xu, 2014. Perfluorocarbon Liquid: Its Application in Vitreoretinal Surgery and Related Ocular Inflammation. BioMed Research International, 2014. Article ID 250323

RSC, 2020a. Royal Society of Chemistry. ChemSpider. Version 2020.0.18.0. http://www.chemspider.com/Chemical-Structure.6192.html. (Accessed July 2020)

RSC, 2020b. Royal Society of Chemistry. ChemSpider. Version 2020.0.18.0. http://www.chemspider.com/Chemical-Structure.6191.html. (Accessed July 2020)

Sabljic, A., Güsten, H., Verhaar, H., and Hermens, J., 1995, QSAR modelling of soil sorption. Improvements and systematics of log K_{OC} vs. log K_{OW} correlations. Chemosphere, 31, 4489–4514.

Tsai W-T, Chen H. and Hsien W-Y, 2002. A review of uses, environmental hazards and recovery/recycle technologies of perfluorocarbons (PFCs) emissions from the semiconductor manufacturing processes. Journal of Loss Prevention in the Process Industries, 15 (2), 65-75. https://doi.org/10.1016/S0950-4230(01)00067-5 (Accessed July 2020)

Tsai W-T., 2009. Environmental hazards and health risk of common liquid perfluoro-n-alkanes, potent greenhouse gases. Environment International, 35 (2), 418-424. https://doi.org/10.1016/j.envint.2008.08.009 (Accessed July 2020)

US EPA, 2012. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.1. United States Environmental Protection Agency, Washington, DC, USA.

US EPA, 2016. User's Guide for TEST (Toxicity Estimation Software Tool), EPA/600/R-16/058, United States Environmental Protection Agency, Washington, DC, USA. https://www.epa.gov/sites/production/files/2016-05/documents/600r16058.pdf (Accessed July 2020).

US EPA, 2020a. U.S. Environmental Protection Agency. CompTox Chemicals Dashboard. https://comptox.epa.gov/dashboard/DTXSID9052503 (Accessed July 2020)

US EPA, 2020b. U.S. Environmental Protection Agency. CompTox Chemicals Dashboard. https://comptox.epa.gov/dashboard/DTXSID2026949 (Accessed July, 2020)

US EPA, 2020c. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.11]. United States Environmental Protection Agency, Washington, DC, USA.

US EPA, 2020d. Toxicity Estimation Software Tool (TEST): Training and Prediction Sets. https://www.epa.gov/chemical-research/toxicity-estimation-software-tool-test. (Accessed December 2020)

US EPA, 2020e. Overview of Greenhouse Gases - Emissions of Fluorinated Gases. United States Environmental Protection Agency. https://www.epa.gov/ghgemissions/overview-greenhouse-gases#f-gases (Accessed December 2020)

Walker, G.M., Kasem, K.F., O'Toole, S.J., Watt, A., Skeoch, C.H., Davis, C.F., 2003. Early perfluorodecalin lung distension in infants with congenital diaphragmatic hernia. J Pediatr Surg., 38(1), 17-20. https://doi.org/10.1053/jpsu.2003.50002. PMID: 12592611 (Accessed July 2020)

Mansouri, K., Grulke, C., Richard, A., Judson, R., Williams, A., 2016. An Automated Curation Procedure for Addressing Chemical Errors and inconsistencies in public datasets used in QSAR modelling [online]. SAR and QSAR in Environmental Research, 27, 911-937. https://doi.org/10.1080/1062936X.2016.1253611 (Accessed July 2020).

Williams, A., Grulke, C. and Edwards, J. 2017. The CompTox Chemistry Dashboard: A Community Data Resource for Environmental Chemistry. Journal of Chemical Information and Modelling, 9, 61. https://doi.org/10.1186/s13321-017-0247-6 (Accessed July 2020)

Yalkowsky S. and Dannenfelser R., 1992. The AQUASOL database of Aqueous Solubility. Version 5. Tucson, AZ: Univ AZ, College of Pharmacy. Not publicly accessible.

Yamanouchi, K., and Yokoyama, K., 1975. The Biological Inertness of Perfluorocarbons In Vivo, in Proceedings of the Xth International Congress for Nutrition: Symposium on Perfluorochemical Artificial Blood, Kyoto, p91

Yokoyama, K., Yamanouchi, K. and Murashima R., 1975. Excretion of Perfluorochemicals After Intravenous Injection of their Emulsion. Chemical and Pharmaceutical Bulletin (Tokyo), 23(6), 1368-1373. https://doi.org/10.1248/cpb.23.1368 (Accessed July 2020).

Yokoyama K., Yamanouch K., Ohyanagii H. and Mitsuno T., 1978. Fate of Perfluorochemicals in Animals after Intravenous Injection or Hemodilution with their Emulsions. Chem. Pharm. Bull., 26 (3), 956-966.

14 List of abbreviations

%	Percentage
B	Bioaccumulative
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
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
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
MATC	Maximum Acceptable Toxicant Concentration
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
PFC	Perfluorocarbon
PFCA	Perfluoroalkyl carboxylic acids
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
STOT-RE	Specific target organ toxicity - repeat exposure (a class of hazard classification)
SVHC	Substance of Very High Concern
t	Tonne
T.E.S.T	Toxicity Estimation Software Tool
TG	Test Guideline
TSCA	Toxic Substances Control Act
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
wwt	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 PFP. 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
76-19-7	866	117
Octafluoropropane	76	571
Perfluoropropane	416	1430
Total unique records	**1098**	**2008**

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*., 2016).

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

Table C.1 QSAR model outline

Name	Brief description
ACD/Labs	Predicts physicochemical properties via the Percepta Platform[7].
EPISuite ™ Estimation Programs Interface Suite ™ for Microsoft© Windows	A Windows®-based suite of physical/chemical, environmental fate and ecotoxicity property estimation programs developed by the US EPA and Syracuse Research Corp. It uses a single input (typically a SMILES string) to run the following estimation programs: AOPWIN™, AEROWIN™, BCFBAF™, BioHCwin, BIOWIN™, ECOSAR™, HENRYWIN™, HYDROWIN™, KOAWIN™, KOCWIN™, KOWWIN™, LEV3EPI™, MPBPWIN™, STPWIN™, WATERNT™, WSKOWWIN™ and WVOLWIN™.
OPEn structure-activity/property Relationship App (OPERA)	Open source suite of QSAR models providing predictions and additional information including applicability domain and accuracy assessment, as described in Williams *et al*. (2017). All models were built on curated data and standardized chemical structures as described in Williams *et al*. (2016). All OPERA properties are predicted under ambient conditions of 760 mmHg (103 kPa) at 25 °C.
T.E.S.T. Toxicity Estimation Software Tool	US EPA software application for estimating the toxicity of chemicals using QSAR methods. EPISuite™ is the model used to generate some physico-chemical data, although T.E.S.T. does not report K_{OW} values and uses a different database for surface tension. (US EPA, 2016).

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

EPISuite™

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

Table C.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 fromfragments (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) (https://www.epa.gov/chemical-research/toxicity-estimation-software-tool-test)

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 SuiteTM. 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 SuiteTM.

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

Would you like to find out more about us or your environment?

Then call us on

03708 506 506 (Monday to Friday, 8am to 6pm)

Email: enquiries@environment-agency.gov.uk

Or visit our website

www.gov.uk/environment-agency

incident hotline

0800 807060 **(24 hours)**

floodline

0345 988 1188 **(24 hours)**

Find out about call charges (https://www.gov.uk/call-charges)

Environment first

Are you viewing this onscreen? Please consider the environment and only print if absolutely necessary. If you are reading a paper copy, please don’t forget to reuse and recycle.