Environmental risk evaluation report: Perflunafene [PFD]

(CAS no. 206-94-5)

Chief Scientist's Group report

April 2023

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Dr Robert Bradburne
Chief Scientist

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Executive summary

There is growing regulatory concern at international level about the emissions of per- and polyfluoroalkyl substances (PFAS) to the environment. This is due to their extreme persistence, which could lead to long-term exposure of both people and wildlife. High levels of exposure to certain PFAS 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 known to be used at two UK production facilities. The substance reviewed in this evaluation report is perflunafene, also known as perfluorodecalin or PFD (CAS no. 306-94-5). PFD is a bicyclic perfluoroalkane and is an example of a perfluorocarbon (PFC) comprising only fully fluorinated carbon atoms and no other functional groups. It is a moderately volatile liquid at standard pressure and temperature, with low water solubility. PFD appears to be manufactured for use in a range of industrial, biomedical and cosmetic applications, although detailed information on it uses in the UK is lacking.

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

PFD is not readily biodegradable and there is no evidence that it degrades significantly via abiotic mechanisms. PFD therefore screens as Persistent (P) or very Persistent (vP). There are no valid aquatic bioconcentration data for PFD itself. In the absence of better information and based on Quantitative Structure-Activity Relationship (QSAR) approaches, a reasonable worst case log K_{OW} of 7 is predicted. There is significant uncertainty around this value and whether perfluoroalkanes are within the applicability domain of the models used. The influence of volatility and low water solubility on the aquatic bioaccumulation of PFD is also unclear. However, this log K_{OW} indicates that PFD meets the screening criteria as Bioaccumulative (B) and very Bioaccumulative (vB). Estimates of log K_{OA} suggest that bioaccumulation is unlikely in air-breathing organisms, and this is supported by non-standard mammalian studies which indicate elimination of PFD via exhalation.

Aquatic and mammalian toxicity data on PFD itself are lacking. Read-across arguments in the EU REACH registration dossier refer to studies on other PFCs, but these are not well supported. There is, at present, no conclusive information on PFD to determine whether it meets the toxicity (T) criterion for ecotoxicity. The UK supplier does not identify any classification for PFD that would meet the human health 'T' criteria, although there are

almost no mammalian toxicity data for the substance itself. The substance is not currently self-classified for aquatic hazard under Classification, Labelling and Packaging legislation, but in the absence of reliable information the Environment Agency recommends that the UK supplier self-classifies PFD as Aquatic Chronic 4 on a precautionary basis.

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). PFD screens as P/vP but does not screen as M based on predicted log K_{OC} data, although there is some uncertainty in the estimated value. There is insufficient information to draw a definitive conclusion for T. PFD is a moderately volatile liquid and the influence of volatility is also not considered under the draft PMT criteria. Based on the available information, it is not currently considered to pose a groundwater concern.

Actual emissions from the UK production facility are expected to be low (an assumed 0.5 tonnes/year to air). 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 PFD, a proportion of the overall production volume could eventually end up in the atmosphere (unless specific measures are taken to recover or destroy it).

PFD has the potential for long-range transport in the atmosphere. It is not identified in the Ozone-Depleting Substances (ODS) Substances and Fluorinated Greenhouse Gases (F-gas) regulations. Information suggests, however, that it has a relatively high global warming potential (GWP), with a 100-year GWP ≥ 7 190 $GtCO_2$-eq (see Section 9.5). Although emissions resulting from UK production and use are expected to be low, it is proposed that further information is obtained to clarify these. Additional UK policy consideration of the impact and potential management of PFC (including PFD) emissions more generally, under F-gas or other regulations, is also proposed.

The direct emission estimates and Predicted Environmental Concentrations (PEC) for PFD in Section 10 are based largely on default exposure modelling assumptions. In the absence of more detailed information regarding emissions, use pattern or measured environmental concentrations, there remains significant uncertainty in this assessment. Further refinement would be required to improve its reliability, which could include specific information on UK tonnages, uses, releases, monitoring data and more reliable experimental data on physico-chemical properties to improve the modelling.

Given uncertainty in the level of ecotoxicity posed by this substance, no relevant environmental Predicted No-Effect Concentration (PNEC) values have been calculated to perform a risk characterisation (Section 11). Further information to derive reliable PNEC (and PEC) values would be required to determine environmental risks.

A number of recommendations are made to the UK supplier to improve their data package to allow a more robust assessment of the environmental hazards, exposure and risks posed by PFD, particularly relating 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 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 has informally reviewed several substances that are being used at two known production facilities in the UK, namely AGC Chemicals Europe Ltd of Thornton Cleveleys, Lancashire and F2 Chemicals Ltd of Preston, Lancashire. Based on information provided by these companies, a provisional list of PFAS for further consideration was drawn up. This was narrowed down to the following eight substances which were, at the time, registered at more than 1 tonne per year under the EU REACH Regulation[1] and subsequently also under UK REACH. Additionally a potential substitute for perfluoroctanesulfonic acid (PFOS, which is a known POP) was included that had been identified from UK surface water monitoring. All of the substances chosen for further evaluation are listed below, initially using their EU-registered name:

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

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

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

The additional substance also being considered is:

- 6:2 Chlorinated polyfluorinated ether sulfonate, 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. PFD), 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). As the substance was, at the time of writing, registered under EU REACH, information on the properties and uses substance was obtained from the European Chemicals Agency (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.

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 the hazards, exposure and risks to human health. This is <u>not</u> a formal UK REACH Evaluation.

1 Substance identity

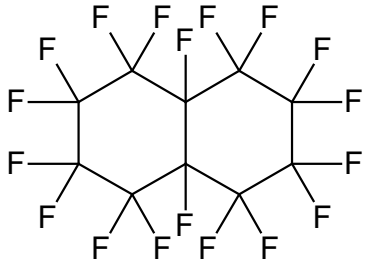
1.1 Name and other identifiers

Table 1.1 Substance identifiers

Public name	Perflunafene (*cis*- and *trans*-)
IUPAC name	1,1,2,2,3,3,4,4,4a,5,5,6,6,7,7,8,8,8a-Octadecafluoronaphthalene
EC number	206-192-4
CAS name	-
CAS number	306-94-5
Index number in Annex VI of the CLP Regulation	-
Molecular formula	$C_{10}F_{18}$
Molecular weight	462 g/mol
SMILES code(s)	C12(C(C(C(C(C1(F)F)(F)F)(F)F)(F)F)(C(C(C(C2(F)F)(F)F)(F)F)(F)F)(F)F)F
Synonyms	Octadecafluorodecahydronaphthalene; Perfluorodecahydronaphthalene. Perfluorodecalin [PFD]*; Perflunafene; PFC-9-1-18; Flutec PC6™; Flutec PP6™; Flutec TG PFD™; Perfluorodecalin-HP™
Type of substance	Mono-constituent

Note: * The substance is generally referred to in the academic literature by the name perfluorodecalin and so we will refer to it as “PFD” for the purposes of this report.

Figure 1.1 Structural formula of PFD



The substance is isomeric because the fluorine atoms attached to the bridging carbon atoms can either be on the same (cis) or opposite (trans) sides of the molecule. We assume that the commercial substance contains both isomers in equal proportions and that although isomerism will affect molecular shape, it is likely to make very little difference to key environmental endpoints. F2 Chemicals Ltd indicates that the cis- and trans-isomers are not present in equal proportions; there is some batch-to-batch variation but it is typically 55-60% trans and 45-40% cis and the proportions of cis and trans in the racemic mixture has an effect on the melting point.

1.2 Structurally related substances

PFD is a bicyclic perfluoroalkane. It is an example of a perfluorocarbon (PFC). Substances in this category have fully fluorinated carbon atoms and lack functional groups such as the acids, ethers or alcohols that characterize other PFAS categories (OECD, 2018).

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

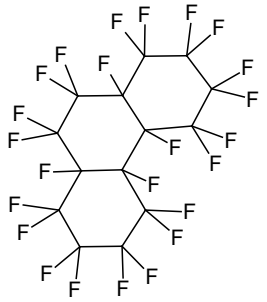
One tricyclic perfluoroalkane with a similar structure was identified, as summarized in Table 1.2. Perfluorophenanthrene, also known as perfluoroperhydrophenanthrene (and abbreviated to PFPh for the purposes of this report) is registered under EU REACH, although the tonnage is confidential (ECHA 2020d). The UK Department of the Environment and Health and Safety Executive reviewed original study reports for this substance in 1985 under the Notification of New Substances (NONS) Regulations. It has an additional perfluorocyclohexane ring compared to PFD.

Additional potential analogues include:

- Perfluorocyclohexane (also known as dodecafluorocyclohexane, CAS no. 355-68-0): This monocyclic substance is not registered under EU REACH, although it is included in ECHA's CLP Inventory (with self-classifications for irritancy) which suggests a level of supply below 1 tonne/year. It is listed in Annex 3 of REACH as a substance predicted to meet the hazard classification criteria for category 1A or 1B carcinogenicity, mutagenicity or reproductive toxicity, or with dispersive or diffuse

use(s) and likely to meet any classification criterion for health or environmental hazards. As no readily available data are available for this substance, it is not considered further.

Table 1.2 Substance identifiers for perfluorophenanthrene

Public name	Perfluorophenanthrene
EC number	400-470-0
CAS number	306-91-2
Structural formula	
Molecular formula	$C_{14}F_{24}$
Molecular weight	624.11 g/mol
SMILES code(s)	C12(C3(C(C(C(C1(C(C(C(C2(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(C(C(C(C3(F)F)(F)F)(F)F)(F)F)(F)F)F
Synonyms	1,1,2,2,3,3,4,4,4a,4b,5,5,6,6,7,7,8,8,8a,9,9,10,10,10a-Tetracosafluoro-phenanthrene; Flutec PP11TM; Perfluorophenanthrene; Perfluoroperhydrophenanthrene

- Perfluorohydrofluorene (also known as docosafluorododecahydrofluorene or docosafluoro-dodecahydro-1H-fluorene and marketed as Flutec PP10^{TM}, CAS no. 307-08-4): This polycyclic substance has a fully fluorinated cyclopentyl ring bridging two perfluorocyclohexane rings, and a molecular weight of 574.09 g/mol. It was registered under EU REACH, and although the registration is no longer active, the submitted data were still available (at the time of writing) on the ECHA public dissemination website (ECHA, 2020). The Environment Agency and Health and Safety Executive also reviewed original study reports for this substance in 1990 under the NONS Regulations. This substance is referred to as PFHF for the purposes of this report.

These substances have different molecular shapes and weights compared to PFD, so are unlikely to be close analogues. However, they provide additional context for some endpoints (particularly in cases where the reliability of the REACH data for PFD cannot be independently verified).

1.3 Transformation products

Information from Section 6 of this report indicates that PFD 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.

2 Analytical chemistry

2.1 Regulatory and academic methods

As they have not self-classified the substance as being ‘dangerous’, the UK supplier does not include analytical details in their EU REACH registration dossier (ECHA, 2020a).

The Environment Agency searched the academic literature for analytical methods for the detection of PFD in the following environmental matrices: water, fresh and marine; soil; sediment; sludge; and air (see Appendix A). No environmental monitoring methods for PFD were identified.

Analytical monitoring of PFD in environmental matrices does not appear to be performed as part of national or international programmes. In particular, it is not present in the following PFAS databases accessed via the NORMAN network website: https://www.norman-network.com/nds/susdat/ [accessed 12 February 2021]:

- PFASTRIER list; and
- PFASNTREV19.

PFD was included in a KEMI PFAS List and OECD PFAS list (OECD, 2018) but 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 PFD.

It is recommended that the UK supplier provides details of their analytical methodology for measuring atmospheric emissions of PFD (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, and the European Chemicals Agency (ECHA) public databases are, at the time of writing, still a relevant source of information about industrial chemicals on the UK market.

According to the ECHA website (ECHA, 2020a), PFD is registered in the EU by Chementors Ltd, Raisio, Finland (a consultancy firm) at an aggregated supply level of 1 to 10 tonnes/year (ECHA, 2020a). The substance is manufactured by F2 Chemicals Ltd, 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. Personal communication with F2 Chemicals Ltd confirms that their annual production tonnage of PFD is within the 1 to 10 tonne/year range.

An overview of uses from the public EU REACH registration dossier is presented in Table 3.1, but this does not provide any information about actual applications. The F2 Chemicals Ltd website http://www.f2chemicals.com/ [accessed August 2020] states that PFD's characteristics include:

- Compatibility with most construction materials;
- excellent chemical and thermal stability;
- high solubility for gases (e.g. oxygen, carbon dioxide);
- non-flammability; and
- limited toxicity.

Due to its inert nature and capacity for dissolving oxygen, PFD can be used in a range of biomedical applications such as eye surgery, wound treatment, liquid breathing (including for premature babies), and organ and tissue storage (source: F2 Chemicals Ltd). Chernysheva and Skliar (2014) mention additional biomedical uses of PFCs as ultrasound and magnetic resonance imaging contrast agents, propellants in inhalation drug delivery, gene delivery applications and as a means to enhance cavitation during ultrasound tissue ablation. The Environment Agency has not sought further information on the use of PFD for these applications. PFD is also an ingredient of a blood substitute that has been used in Russia (Maevsky *et al*., 2005).

Table 3.1 Overview of uses

Life cycle stage	Use(s)
Manufacture	**Manufacture of substance** ERC1: Manufacturing PROC 3: Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions
Formulation	**Formulation at industrial/laboratory sites** ERC2: Formulation into mixture PROC 3: Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions Product category formulated: PC 21: Laboratory chemicals PC 29: Pharmaceuticals Substance supplied as such for this use
Uses at industrial sites	None identified in registration dossier
Uses by professional workers	None identified in registration dossier
Consumer uses	None identified in registration dossier
Article service life	None identified in registration dossier

Source: REACH registration dossier (ECHA, 2020a)

Although not specifically mentioned in the EU REACH registration, a second major application appears to be in the cosmetics industry. The F2 Chemicals Ltd http://www.f2chemicals.com/ [accessed August 2020] states that PFD (along with PFPh) has several useful properties for cosmetic formulations, such as:

- Facilitating emulsion formulation due to its lipophobic and hydrophobic properties (forming a third phase).
- Can be used in colour products for enhanced colour.
- Does not interfere with the normal functions of the skin.
- Has a unique emollient feel.
- Is non-greasy, easy to use, non-irritant, and odourless.
- Enhances appearance, smoothness and softness of the skin.
- Having a high gas dissolving ability (it can be loaded with oxygen).

Suggested applications include:

- Sun creams.
- Anti-ageing creams and gels.
- General purpose creams and gels for the face and neck.
- Lipsticks.
- Eye contour creams & gels.
- Scalp treatment.
- Oxygen masks.
- Two-way cakes.
- Self-foaming products.

Reported uses of PFD in cosmetic products in Denmark include nail polish/care, cleansing wipes, shampoo, conditioner, hair spray/styling, moisturizer, anti-aging products, facial cream, facial cleansing/gels, sunscreen, eye cream, acne treatment, lip balm/plumber (*sic*), acne treatment, masks and scrubs (Danish Environmental Protection Agency, 2018).

The proportion of the tonnage used in biomedical or cosmetics applications within the UK is unknown.

Other miscellaneous uses mentioned in a Wikipedia article https://en.m.wikipedia.org/wiki/Perfluorodecalin [accessed December 2021] include cell culturing, improving microscopy resolution for airspace-containing tissues such as plant leaves, an anti-solvent for the self-organization of perovskite nanocrystals into supercrystals, and a solvent for poly[4,5-difluoro-2,2-bis(trifluoromethyl)-1,3-dioxole-co-tetrafluoroethylene] (“Teflon AF”). The relevance of any of these uses for the UK is unknown.

4 Summary of relevant regulatory activities

4.1 Europe

4.1.1 European Chemicals Agency (ECHA)

The Public Activities Co-ordination Tool (PACT) https://echa.europa.eu/pact (accessed July 2020) provides an overview of the substance-specific activities that EU regulatory authorities are working on under the EU REACH and CLP Regulations. PFD 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 EU REACH restriction proposal (see: https://www.rivm.nl/en/pfas/pfas-restriction-proposal accessed July 2020). The current scope of the work is wide and includes all substances that contain at least one aliphatic -CF_2- or -CF_3 element, PFD is therefore within scope of this initiative (see ECHA Registry of Restriction Intentions: https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e18663449b, accessed October 2021).

4.1.2 European Food Safety Agency (EFSA)

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

A search of EFSA http://www.efsa.europa.eu/ (accessed July 2020) did not identify PFD 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 REACH activities.

PFD 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).

4.1.4 Cosmetics

Use of PFD in cosmetic products is governed by Regulation (EC) No. 1223/2009. Perfluorodecalin is not listed as a prohibited substance under this legislation. Consolidated TEXT: 32009R1223 — EN — 13.08.2019 (europa.eu) (accessed May 2022).

4.2 Regulatory activity outside Europe

4.2.1 United States

The US EPA is planning to carry out tiered toxicity and toxicokinetic testing for a range of PFAS in the near future (Patlewicz *et al.,* 2019). PFD 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)).

PFD is not listed as one of the substances undergoing risk evaluation as part of the 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 PFD as being under assessment under the Prohibition of Certain Toxic Substances Regulations, 2012 https://www.canada.ca/en/environment-climate-change/services/canadian-environmental-protection-act-registry/substances-list/toxic.html (accessed July 2020).

4.2.3 Australia

A search did not identify PFD 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).

4.2.4 New Zealand

A search did not identify PFD 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/screened-chemicals-list/ (accessed July 2020).

4.2.5 Japan

Industrial chemicals are managed under the Chemical Substances Control Law (CSCL), most recently amended in 2009 https://www.nite.go.jp/chem/jcheck/list3.action?category=141&request_locale=en (accessed July 2020). Under the Act there are 3 lists:

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

PFD 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)

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

4.3.2 Greenhouse gases

Fluorinated gases ('F-gases') may contribute to climate change due to their global warming potential and they are often used as substitutes for ozone-depleting substances, because they do not damage the atmospheric ozone layer (EC, 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. PFD is not an F-gas because it is a liquid, although it is moderately volatile.

5 Physico-chemical properties

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

The source of this information is the publicly available EU REACH registration database (ECHA, 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 REACH registration dossiers generally lack sufficient supporting information. The Environment Agency is therefore not always in a position to assign its own reliability scores (except in the case of data presented in academic journals or obtained using quantitative structure-activity relationship (QSAR) models).

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

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

Table 5.1 Summary of physico-chemical properties

Property	Value(s)	Reliability Klimisch score	Reference
Physical state at 20 °C and 101.3 kPa	Clear colourless liquid	Registrant: 2 (key study)	Registration dossier
Melting / freezing point	-7 °C (unknown method, Sargent *et al*., 1970)	Registrant: 2 (key study)	Registration dossier
Boiling point	142 °C (distillation method, Green, 1969)	Registrant: 2 (key study)	Registration dossier
Relative density	1.94 g/m3 at 20 °C (buoyancy method, unnamed report)	Registrant: 2 (key study)	Registration dossier
Vapour pressure	0.88 Pa at 25 °C (unnamed method, unnamed report)	Registrant: 2 (key study)	Registration dossier
Surface tension	17.6 mN/m (capillary rise method, Green, 1969)	Registrant: 2 (key study)	Registration dossier
Water solubility	Insoluble	Registrant: 2 (key study)	Registration dossier
n-Octanol/water partition coefficient (log K_{OW})	5.02 at 25 °C (software prediction using KOWWIN v1.67)	Registrant: 2 (key study)	Registration dossier
Particle size distribution	Data waiver (liquid)		Registration dossier
Stability in organic solvents and identity of relevant degradation products	Stable in all solvents	Registrant: 2 (key study)	Registration dossier
Dissociation constant	Data waiver (‘does not dissociate’)	-	Registration dossier

Note: It is likely that isomerism affects crystal structure, and hence the melting point of the substance. For example, a Wikipedia article: https://en.m.wikipedia.org/wiki/Perfluorodecalin cites a melting point of −3.6 °C for the *cis*-isomer, +18 °C for the *trans*-isomer, and −6.7 °C for a 50/50 mixture (the source is stated to be "Flutec PP Fluorocarbon Liquids", ISC Chemicals Ltd, table E5-2/4, but this cannot be located online). The F2 Chemicals Ltd website: https://f2chemicals.com/flutec_pc6.html cites a melting point of −5 °C. Similar variations may occur for other physico-chemical properties but in the absence of information to the contrary, it is assumed that the data in the table reflect the 50/50 mixture.

5.1 Vapour pressure

5.1.1 Measured data

A vapour pressure of 0.88 kPa at 25 °C was reported in the EU REACH registration dossier (ECHA, 2020a), but no method or experimental details were provided. The study was not GLP compliant. The EU REACH registration assessed the data reliability as Klimisch 2 (reliable with restrictions).

5.1.2 Predicted data

In the absence of full study details, we have considered predicted data.

The ChemSpider database contains predicted vapour pressures for PFD (RSC, 2020a). The US EPA CompTox dashboard contained predicted vapour pressures for PFD generated from ACD/Labs and OPERA software (US EPA, 2020a). Values are presented in Table 5.2. The Environment Agency has converted the values from mmHg to kPa.

Table 5.2 Predicted vapour pressures for PFD

Source	Prediction method	Vapour pressure at 25 °C
ACD/Labs	Not available	0.91 kPa [6.8 mmHg]
EPISuite™ Estimation programme MPBPVP v1.42	Mean of Antoine and Grain Methods BP = 136.69 °C MP = 23.52 °C	0.97 kPa [7.3 mmHg]
OPERA	Global applicability domain: Outside Local applicability domain index: 0.321 Confidence level: 0.375	12.32 kPa [92.4 mmHg]
TEST	Not available	0.17 kPa [1.26 mmHg]

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

- This information was not available for the ACD/labs model. 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 perfluorocarbons (PFCs) (see

Appendix B) (e.g. perfluorohexane) and it is likely that the predicted value for PFD falls within the applicability domain of the model.

- The OPERA model, structural analogues of PFD were included in both the training set and external test sets (e.g. perfluorocyclohexane). PFD is considered outside the global applicability domain and has a low local applicability domain index (< 0.4), and so the prediction is not considered reliable based on the OPERA model applicability domain criteria.
- For the TEST model, structural analogues of PFD were included in both the training set and external test sets (e.g. perfluorocyclohexane). Therefore, predicted values from TEST are considered to be within the applicability domain of the model.

5.1.3 Data from structural analogues

PFPh has a vapour pressure of 0.13 kPa at 70 °C and 4.67 kPa at 100 °C (ECHA, 2020d). These are the same values as those derived from the original study report by the UK under NONS. The vapour pressure at 25 °C will be significantly less than 0.13 kPa.

PFHF has a vapour pressure of 0.113 kPa at 25 °C according to a standard method (ECHA, 2020e). This is the same value as that derived from the original study report by the UK under NONS.

Both substances have a higher molecular weight than PFP, so would be expected to be less volatile.

5.1.4 Additional sources

No additional information was reviewed as part of this evaluation.

5.1.5 Recommended value

The EU REACH registration indicates that the vapour pressure is 0.88 kPa at 25 °C from the key study (ECHA, 2020a). The Environment Agency recommends that the robust study summary is updated to provide full details of the study. This result lies within the range of apparently reliable *in silico* predicted values (0.17 kPa to 0.97 kPa at 25 °C (US EPA, 2020a and RSC, 2020a)). It is also consistent with values for higher molecular weight analogues such as PFPh and PFHF.

The Environment Agency considers that although key details are lacking, the vapour pressure of **0.88 kPa at 25 °C** can be used to derive conclusions for the exposure and risk assessment.

5.2 Surface tension

5.2.1 Measured data

The reported surface tension in the EU REACH registration dossier is approximately 17.4 mN/m at 25 °C (ECHA, 2020a). The reference is Green (1969), and this value is stated to be “for the pure material”. The method was not considered GLP compliant, and no further information was presented. The EU REACH registration gave the study a reliability rating of 2 (reliable with restrictions).

The surface tension of the substance itself is not relevant for this evaluation.

5.2.2 Predicted data

The ChemSpider database (RSC, 2020a) and US EPA CompTox dashboard (US EPA, 2020a) include a prediction of surface tension that is a similar order of magnitude to the reported measured value. 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

PFPh has a surface tension of 19.3 mN/m at 20 °C as the pure substance (ECHA, 2020d). As for PFD, this value is not relevant to this evaluation. However, the NONS dossier supplied to the UK included a study report which showed that the substance has a negligible effect on the surface tension of water at the limit of solubility. The NONS dossier for PFHF included a similar result (ECHA, 2020e).

5.2.4 Additional sources

Chernyshev and Skliar (2014) reported a substantial decrease in the surface tension of deionised water in the presence of perfluoroalkane vapours in an experiment using perfluoropentane and perfluorohexane at 20 °C. The surface tension of the water reduced from 72 mN/M to 64.6 mN/M in the presence of perfluoropentane and 66.7 mN/M in the presence of perfluorohexane.

5.2.5 Recommended value

Although the EU REACH registration reports a surface tension of 17.4 mN/m at 25 °C for PFD, 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.

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 for a surface tension value for substances with a water solubility below 1 mg/L. It is likely that this applies to PFD (Section 5.3.5).

The Environment Agency notes that PFD 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, like its analogue PFPh.

The Environment Agency recommends that the robust study summary for this end point is updated to clarify that a surface tension measurement in aqueous solution is not available (a data waiver could be provided based on limited water solubility).

5.3 Water solubility

5.3.1 Measured data

No experimentally derived water solubility value was presented in the EU REACH registration dossier of PFD. The substance is said to be 'insoluble' with a water solubility of 0.01 mg/L at 20 °C sourced from "other company data, data from various sources, including read-across from similar PFCs" (ECHA, 2020a).

5.3.2 Predicted data

In the absence of an experimental study or specific details about read across, we have considered predicted data.

The ChemSpider database contained estimated water solubilities from EPISuite™ (RSC, 2020a). The US EPA CompTox dashboard contained predicted water solubility endpoint values for generated from TEST and OPERA (US EPA, 2020a). 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 462 g/mol.

Table 5.3 Predicted water solubilities for PFD

EPISuite™	Details	Water Solubility
Water solubility estimate from log Kow (WSKOW v1.41)	Log Kow used: 7.8 (estimated) no melting point equation used	4.9×10^{-5} mg/L at 25 °C
Water solubility estimate from fragments (v1.01 est.)	-	4.62×10^{-7} mg/L
OPERA	Predicted value: 1.07×10^{-5} mol/L	4.94 mg/L

	Global applicability domain: outside Local Applicability domain index: 0.261 Confidence Interval: 0.383	
T.E.S.T.	Not available	1.5 mg/L

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

- Guidance provided with the WSKOWWIN 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 R2 of 0.97, standard deviation of 0.409 and an average deviation of 0.313. The validation set contained several PFCs (see Appendix B) and it is likely that the predicted value for PFD falls within the applicability domain of the model. Nevertheless, but the value should be treated with caution due to the lack of information about the error associated with such estimates.
- For the OPERA model, no close structural analogues of PFD were included in both the training set and external test sets. PFD is considered outside the global applicability domain and has a low local applicability domain index (< 0.4); therefore the prediction is not considered reliable based on the OPERA model applicability domain criteria.
- For the TEST model, no close structural analogues of PFD were included in both the training set and external test sets. Therefore, predicted values from TEST are outside the applicability domain of the model.

5.3.3 Data from structural analogues

PFPh has a water solubility of ≤5 mg/L at 25 °C (ECHA, 2020d). This is the same value as that derived from the original study report by the UK under NONS.

PFHF has a water solubility of <0.012 mg/L at 20 °C using a standard method (ECHA, 2020e). This is the same value as that derived from the original study report by the UK under NONS.

5.3.4 Additional sources

The EU REACH registration of perfluorohexane (a linear PFC with a lower molecular weight than PFD) has a reported measured water solubility of <0.1 mg/L at 25 °C. According to Chernyshev and Skliar (2014), lower molecular weight PFCs such as perfluorohexane form colloids in water, which may involve “liquid droplets, vapour bubbles or a combination of both phases simultaneously.”

Tsai *et al*. (2002), Tsai (2009) and Tsai (2011) roughly estimated the water solubility of several PFCs based on the measured water solubility of tetrafluoromethane. The estimation was performed using a regression equation derived from plotting water

solubility against (predicted) octanol-water partition co-efficient. These values are summarised in Table 5.4.

Table 5.4 Summary of estimated water solubility or perfluorocarbon 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	Tsai (2009)
Perfluorohexane	338	1.0×10^{-5}	3.4	Estimated	Tsai (2009)
Perfluoroheptane	388	5.7×10^{-6}	2.2	Estimated	Tsai (2009)
Perfluorooctane	438	3.1×10^{-6}	1.4	Estimated	Tsai (2009)
Perfluorononane	488	1.7×10^{-6}	0.8	Estimated	Tsai (2009)
Perfluorodecalin (PFD)	**462**	**4.5×10^{-6}**	**2.1**	**Estimated**	**Tsai (2011)**

Note: *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 5.5.5).

5.3.5 Recommended value

The key water solubility value of 0.01 mg/L at 20 °C presented by the EU REACH registration lacks description and documentation of the read across approach used (including source data reliability). The Environment Agency recommends that the robust study summary is updated to provide details of the study and considers the requirements of ECHA's Read Across Assessment Framework (RAAF) (ECHA, 2017a) for any data which have been read-across.

In silico predictions for the water solubility of PFD were between 4.62×10^{-7} and 4.94 mg/L (US EPA, 2020a and RSC, 2020a), although only the lowest value may be considered "reliable", and this is subject to uncertainty. The studies of Tsai *et al*. (2002) and Tsai (2009 and 2011) suggest a water solubility of 2.1 mg/L for PFD, but the Environment Agency considers this value is unreliable. There is only a limit value for a higher molecular weight analogue (PFPh), although this suggests that this type of substance is unlikely to be highly soluble in water.

No aquatic toxicity studies have been performed on the substance itself, so the concentration achievable in aquatic test media is unknown (see Section 7).

Ideally a new water solubility measurement would be performed to provide a more relevant value. It is not known whether PFD can form colloids in water similar to lower molecular weight PFCs (as noted by Chernyshev and Skliar, 2014); this could complicate the measurement. PFD is predicted 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.

The Environment Agency considers that the water solubility of PFD is probably below 1 mg/L at 20 °C, although there is uncertainty in the actual value. Given its polycyclic structure and higher molecular weight, PFD is likely to be less soluble than perfluorohexane (<0.1 mg/L at 25 °C) and is probably close to that for PFHF (<0.012 mg/L at 20 °C). In the absence of better information, a water solubility of **0.01 mg/L at 25 °C** will be used in the assessment as an approximation.

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

Log K_{OW} is an important property for organic substances because it is used in models and hazard assessment as an indicator of partitioning behaviour between water and organic matter.

5.4.1 Measured data

No experimentally derived log K_{OW} value was presented in the EU REACH registration dossier of PFD.

The Chemspider database lists an experimental log K_{OW} value of 7.79 at 25 °C (RSC, 2020a). The Environment Agency considers that there is insufficient detail to allow the value to be fully validated. Ruelle (2000) also reported a measured log K_{OW} of 6.0 for PFD, without further details.

5.4.2 Predicted data

The key study information is a predicted log K_{OW} value of approximately 5.02 at 25 °C that was generated in the EU REACH registration using EPA software (ECHA, 2020a). The EU REACH registration assessed the data reliability as Klimisch score 4 (not assignable).

To assess the relevance of this result, we reviewed additional sources. The ChemSpider database contained estimated log K_{OW} values for PFD from ACD/Labs and EPISuite™ (RSC, 2020a). The US EPA CompTox dashboard contained estimated log K_{OW} values for PFD from EPISuite™, ACD/Labs and OPERA software (US EPA, 2020a). Values are presented in Table 5.5.

Table 5.5 Predicted log K_{OW} values for PFD

Model	Details	Log K_{OW}
ACD/Labs	ACD/LogP ACD/LogD (pH 5.5)	6.03 5.62
EPISuite™	KOWWIN v1.67 estimate (ChemSpider)	7.80
EPISuite™	KOWWIN v1.68 estimate (Environment Agency)	5.68
OPERA	Predicted value: 8.35 Global applicability domain: Outside Local applicability domain index: 0.299 Confidence interval 0.607	8.35

The predicted log K_{OW} values reported in the EU REACH registration for PFD and those contained within the ChemSpider and CompTox dashboard databases are different. The Environment Agency predicted the log K_{OW} value as 5.68 using KOWWIN v1.68 for PFD. This is closer to that derived in the EU REACH registration, though still higher. It is not clear why this value differs from the result reported by ChemSpider using the same method.

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

- For the ACD/labs model this information was not available. Therefore no assessment of the applicability can be performed.
- Guidance provided with the KOWWIN v1.68 model indicates that the relationship between the experimental and predicted values for a validation set of 10 331 compounds was good, with an R^2 of 0.94 and standard deviation of 0.47. The training set contained several PFCs (see Appendix B) and it is likely that the predicted value for PFD falls within the applicability domain of the model but the value should be treated with caution due to the lack of information about the error associated with such estimates.
- For the OPERA model, no close structural analogues of PFD were included in both the training set and external test sets. PFD is considered outside the global applicability domain and has a low local applicability domain index (< 0.4), therefore the prediction is not considered reliable based on the OPERA model applicability domain criteria.

Ruelle (2000) reported a predicted log K_{OW} of 6.69 for PFD. No details were provided.

Tsai (2009 and 2011) estimated a log K_{OW} of 2.85 for PFD using a fragment constant approach, and this study is summarised in Section 5.4.4 as it included additional PFCs. The Environment Agency does not consider it to be reliable.

5.4.3 Data from structural analogues

PFPh has a log K_{OW} of ≥3 according to a standard method (ECHA, 2020d). This is the same value as that derived from the original study report by the UK under NONS.

PFHF has a log K_{OW} of >5.5 at 22 °C according to a standard method (ECHA, 2020e). This is the same value as that derived from the original study report by the UK under NONS.

5.4.4 Additional sources

Tsai (2009 and 2011) estimated the log K_{OW} of several PFCs, including PFD, using a fragment constant approach as summarised in Table 5.6.

Table 5.6 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
Perfluorodecalin (PFD)	**462**	**2.85**

The Environment Agency notes that the predicted value for perfluorohexane (Environment Agency, 2022) is much lower than those estimated using other models. The reliability of these values is therefore highly uncertain but they indicate a general trend of increasing hydrophobicity with longer chain length PFCs.

5.4.5 Recommended value

No experimental value for log K_{OW} was presented in the registration dossier. Instead the EU REACH registration has provided a predicted value of 5.02 without further supporting information. The Environment Agency recommends that the robust study summary is updated to provide details of the method and applicability domain and explains how reliability has been assessed.

Two measured log K_{OW} values (6.0 and 7.79) have been reported in the Chemspider database and by Ruelle (2000), although they cannot be validated.

In silico predictions for the log K_{OW} of PFD were in the range 5.62 to 8.35 (US EPA, 2020a and RSC, 2020a), although most of the predictions cannot be considered reliable. The

Environment Agency considers that the best estimate is likely to be 5.68, obtained using the KOWWIN v1.68 model, although the error associated with this estimate is unknown. This is close to the measured value of 6.0 reported by Ruelle (2000), although this might be coincidental as the reliability of that study is also unknown. However, these values are all higher than the estimate in the EU REACH registration.

Log K_{OW} has been measured using standard methods for the related substances PFPh and PFHF, with values in the range of ≥ 3 to > 5.5. They have higher molecular weights than PFD, so solubility in different solvents is likely to be lower, but they suggest that a high log K_{OW} is possible for this type of substance.

Ideally a new log K_{OW} measurement would be performed to provide a more reliable value for PFD itself. OECD TG 123 (slow-stirring method) is recommended for highly hydrophobic substances, and it has been validated for log K_{OW} values up to 8.2 (OECD, 2006b). As noted in Section 5.3, PFCs can form colloids in water, and it is possible that colloid formation could also occur in n-octanol. There is also potential for PFD to form a third phase, which would make log K_{OW} practically meaningless. Volatility might also be an issue.

It might therefore be more practical to measure the solubility in n-octanol and derive a ratio with the water solubility value as an estimate (although there is currently no reliable water solubility measurement either). However, direct measurements of relevant properties like the fish bioconcentration factor and organic carbon-water partition coefficient would be preferable, and if necessary, a log K_{OW} could be back-calculated from them.

In the absence of a fully reliable measured result, and given the range of available information, it is difficult to derive a log K_{OW} value for further use in this assessment. It may lie in the range 6 to 7, so we have assumed a **log K_{ow} of 7 at 25 °C** for modelling purposes, as a reasonable worst case.

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

Log K_{OA} is 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). It can also be used in the assessment of bioaccumulation in air-breathing organisms.

5.5.1 Measured data

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

5.5.2 Predicted data

The Environment Agency has estimated an n-octanol-air partition coefficient (K_{OA}) using the dimensionless HLC (K_{AW}) of 4.23 (see Section 6.2.2) and a log K_{OW} value of 7 (Section 5.4.5) ($K_{OA} = K_{OW}/K_{AW}$). The resulting log K_{OA} is 2.77. As there is uncertainty in the HLC (K_{AW}), the reliability of the derived K_{OA} value is unknown.

The US EPA CompTox dashboard and ChemSpider database contained predicted K_{OA} values for PFD generated from KOAWIN v1.10 and OPERA software (RSC 2020a; US EPA 2020a). These values are presented in Table 5.7.

Table 5.7 Predicted log K_{OA} for PFD

Source	Details	Log K_{OA}
EPISuite™ Estimation programme KOAWIN v1.1	Log K_{OW} used: 7.8 K_{AW} used: 6.85 (estimated) (ChemSpider)	0.948
EPISuite™ Estimation programme KOAWIN v1.1	Log K_{OW} used: 5.68 K_{AW} used: 6.85 (estimated) (Environment Agency)	-1.17
OPERA	Global applicability domain: Inside Local Applicability domain index: 0.995 Confidence Interval: 0.913	3.26
Calculation	$K_{OA} = K_{OW}/K_{AW}$ Where log K_{AW} is 4.23 and a log K_{OW} is 7	2.77

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

- For the KOAWIN 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 PFD is dependent on the reliability of HENRYWIN and KOWWIN and the presence of structural analogues in their respective data sets. It is not known whether the training set contained structurally similar substances of PFD, so the reliability is uncertain.
- PFD is considered inside the global applicability domain of the OPERA model and has a high local applicability domain index (> 0.6). The prediction could therefore be considered reliable based on the OPERA model applicability domain criteria. However, no close structural analogues of PFD were included in the training and external test sets so this conclusion might be misleading.

5.5.3 Data from structural analogues

There are no measured data for PFPh or PFHF.

5.5.4 Additional sources

No relevant references were identified in the literature search.

5.5.5 Recommended value

No log K_{OA} values are available from 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 0.948 to 3.26, although the reliability of these predictions is uncertain. They also depend on the log K_{OW} value chosen, and a reliable value is not available. The Environment Agency therefore does not consider it appropriate to choose a single value from the estimated data range. This is considered further in the assessment of bioaccumulation in air-breathing organisms (Section 6.3.2).

5.6 Dissociation constant

The EU REACH registration indicates that PFD does not dissociate (ECHA, 2020a). It has no ionisable functional groups so will remain as a neutral compound at environmentally relevant pH.

6 Environmental fate properties

6.1 Degradation

6.1.1 Abiotic degradation

The EU REACH registration dossier for PFD (ECHA, 2020a) states that PFCs have very high stability to strong acid, strong base, oxidisers, reducers and temperature.

6.1.1.1 Hydrolysis

This endpoint is not a REACH information requirement for the tonnage being supplied, but the EU REACH registration states that PFCs do not hydrolyse. The Environment Agency agrees that the lack of hydrolysable groups in the chemical structure and water solubility of around 0.01 mg/L mean that hydrolysis is unlikely to be a significant degradation pathway for PFD.

6.1.1.2 Phototransformation in air

This is not a REACH information requirement for the tonnage being supplied, and there is no relevant information in the EU REACH registration dossier.

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). Further information on atmospheric half-life is provided in Section 9.5.

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

Table 6.1 Predicted photodegradation half-life values for PFD

Source	Atmospheric hydroxylation rate constant	Half-life (days)
EPISuite™ Estimation programme AOPWIN v1.92	0 cm^3/molecule-sec	-
OPERA	1.11 x 10^{-14} cm^3/molecule-sec Global applicability domain: Inside Local Applicability domain index: 0.540 Confidence Interval: 0.593	1 450[a]

Note: [a] Calculated by the Environment Agency using EUSES (v2.03)

AOPWIN v1.92 predicts no indirect photodegradation as the chemical bonds that the QSAR uses to predict hydroxyl radical reaction are not present in PFD. *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 1.92 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 PFD.
- PFD is considered inside the global applicability domain of the OPERA model and has a local applicability domain index of 0.4 to 0.6. This prediction could be considered reliable with restrictions. However, no close structural analogues of PFD were included in the training and external test sets so this conclusion might be misleading.

6.1.1.3 Phototransformation in water

This is not a REACH information requirement for the tonnage being supplied, and there is no relevant information in the EU REACH registration dossier.

6.1.1.4 Phototransformation in soil

This is not a REACH information requirement for the tonnage being supplied, and 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 PFD itself.

The EU REACH registration dossier (ECHA, 2020a) fills this end point through read-across of a study on perfluoroisohexane (PFiHx, CAS no. 355-04-4). This substance has been evaluated in Environment Agency (2023). Very little information is available about the test, which is considered reliable without restriction in the EU REACH registration. It was performed according to OECD TG 310 (Ready Biodegradability - CO_2 in Sealed Vessels (Headspace Test)) and to GLP, with no biodegradation occurring after 28 days. The EU REACH registration concluded that the substance was “not inherently biodegradable” (presumably in the absence of any biodegradation being observed).

The EU REACH registration justified the read-across by stating that “saturated perfluorocarbons form a class that exhibits very similar properties”. The registration dossier makes reference to a document titled ‘Perfluorocarbons as a Category for Read-Across’ to provide further justification. This document provides very limited qualitative reasoning for similarity of perfluorinated substances, but no quantitative information, nor data related to biodegradation.

6.1.2.2 Predicted data

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

6.1.2.3 Data from structural analogues

No biodegradation was observed for PFPh over 28 days in an OECD TG 310 study (ECHA, 2020d). This is similar though not identical to the result provided in the original study report reviewed by the UK under NONS (6 % degradation observed over 28 days in an OECD TG 301D closed bottle test). The same conclusion was reached for PFHF using a standard test method (ECHA, 2020e).

6.1.2.4 Recommended value

Despite the limitations of the read-across argument in the EU REACH registration, the Environment Agency agrees that PFD is not readily biodegradable. This is consistent with experimental data for PFPh and PFHF. The Environment Agency recommends that the robust study summary for this end point is updated using the ECHA RAAF (ECHA, 2017a), using more appropriate analogues and taking account of differences in physico-chemical properties and molecular size.

6.1.3 Biodegradation in sediment

This is not a REACH information requirement for the tonnage being supplied, and there is no relevant information in the EU REACH registration dossier.

6.1.4 Biodegradation in soil

This is not a REACH information requirement for the tonnage being supplied, and there is no relevant information in the EU REACH registration dossier.

6.1.5 Summary and discussion on degradation

There are no measured abiotic degradation data for PFD. Based on the structure and low water solubility, hydrolysis will not be a significant degradation pathway. Degradation in air is also unlikely to be significant (see Section 9.5).

There are also no measured biodegradation data for PFD, but it is considered to be not readily biodegradable based on read-across from related substances. It is likely to be extremely persistent in the environment.

6.2 Environmental distribution

6.2.1 Adsorption/desorption

6.2.1.1 Measured data

This is not a REACH information requirement for the tonnage being supplied, and there is no relevant information in the EU REACH registration dossier (it states that a study is scientifically not necessary, without any details).

6.2.1.2 Predicted data

The Environment Agency has predicted the log K_{OC} for PFD using the preferred log K_{OW} value of 7. This was done in EUSES v2.03 using the "Predominantly hydrophobics" chemical class (the equation is: log K_{OC} = 0.81 log P_{OW} + 0.10). The calculated log K_{OC} was 5.77. 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 PFD means that it is within the applicability domain.

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

Table 6.2 Predicted log K_{OC} for PFD

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	6.87
EPISuite™ Estimation programme KOCWIN v2.0	Molecular Connectivity Index (MCI) method K_{OC} = 5.31 x 10^6 L/kg Log K_{OW} method (estimated log K_{OW} = 5.68) K_{OC} = 8.50 x 10^4 L/kg	6.73 4.93
OPERA	Global applicability domain: Outside Local Applicability domain index: 0.245 Confidence Interval: 0.438	4.38
EUSES model calculation from Log K_{OW}	Log K_{OW} = 7 and 'predominantly hydrophobics" equation	5.77

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) and it is likely that the predicted value for PFD does not fall within the applicability domain of the model. The value should therefore be considered unreliable.
- For the OPERA model, no close structural analogues of PFD were included in both the training set and external test sets. PFD is considered outside the global applicability domain and has a low local applicability domain index (< 0.4), therefore the prediction is not considered reliable based on the OPERA model applicability domain criteria.

6.2.1.3 Data from structural analogues

No relevant information is available for PFPh or PFHF.

6.2.1.4 Recommended value

In the absence of better information, the Environment Agency recommends a log K_{OC} of **5.77** for modelling purposes. This is based on a QSAR which relies on log K_{OW}, and there is significant uncertainty in this value for PFD, both in terms of the input value and the suitability of the available QSARs for this type of substance.

6.2.2 Volatilisation

6.2.2.1 Measured data

This is not a REACH information requirement for the tonnage being supplied, and there is no relevant information in the EU REACH registration dossier.

6.2.2.2 Predicted data

A Henry's law constant (HLC) of 4.07 x 10^7 Pa m³/mol was calculated by the Environment Agency using EUSES (v2.03) and the recommended values of water solubility of 0.01 mg/L at 25 °C and vapour pressure of 0.88 kPa at 25 °C (see Sections 5.1.5 and 5.3.5).

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

Table 6.3 Predicted Henry's Law constant for PFD

Source	Details	HLC (Pa m^3/mol)
EPISuite™ Estimation programme HENRYWIN v.3.1	Bond Method: 1.74 x 10^5 atm m^3/mol Group Method: Incomplete	1.76 x 10^{10}
EPISuite™ Estimation programme HENRYWIN v.3.1	Vapour pressure/water solubility estimate using EPISuite™ derived values: 9.034 x 10^4 atm m^3/mol	9.15 x 10^9
OPERA	Predicted value: 1.54 x 10^{-2} atm m^3/mol Global applicability domain: outside Local Applicability domain index: 0.0923 Confidence Interval: 0.225	1.56 x 10^3
EUSES model calculation	Calculated from water solubility of 0.01 mg/L at 25 °C and vapour pressure of 0.88 kPa at 25 °C	4.07 x 10^7

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) and it is likely that the predicted value for PFD 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 caution.
- For the OPERA model, no close structural analogues of PFD were included in both the training set and external test sets. PFD is considered outside the global applicability domain and has a low local applicability domain index (< 0.4). The prediction is therefore not considered reliable based on the OPERA model applicability domain criteria.

6.2.2.3 Data from structural analogues

No relevant information is available for PFPh or PFHF.

6.2.2.4 Recommended value

The Environment Agency recommends a HLC of **4.07 x 10^7 Pa m^3 mol^{-1}** for modelling purposes calculated from the assumed water solubility value (0.01 mg/L) and measured vapour pressure (0.88 kPa).

This value has been used to derive the dimensionless HLC or air-water partition coefficient (log K_{AW}) of 4.23, which is used in modelling the prediction of long-range transport of PFD (see Section 6.2.4 below).

6.2.3 Distribution modelling

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 PFD has been assessed by the Environment Agency using EPI Suite (US EPA 2019, version 4.11) and is summarised in Table 6.4. 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 summarised in Table 6.6 and Table 10.2.

Table 6.4 Resulting of generic level III fugacity model for PFD

Compartment (percent distribution at steady state)	Emission rate (1 000 kg/h) to air	Emission rate (1 000 kg/h) to water	Emission rate (1 000 kg/h) to soil	Emission rate (1 000 kg/h) to air: water: soil equally
Amount in air (%)	100.0	0.036	97.8	1.14
Amount in water (%)	<0.1	1.29	<0.1	1.27
Amount in soil (%)	<0.1	<0.1	2.15	0.01
Amount in sediment (%)	<0.1	98.7	<0.1	97.6

This modelling suggests that the substance will remain in air if released there, with little deposition. Release under other scenarios results in accumulation in sediment.

The Environment Agency has used the SimpleTreat model in EUSES (v2.03) to predict the following partitioning of PFD in a wastewater treatment plant, based on lack of ready biodegradation and an estimated log K_{OC} of 5.77, as summarised in Table 6.5.

Table 6.5 Predicted partitioning of PFD in a wastewater treatment plant showing fraction of emission to compartment/degraded

Air	10.1%
Water	6.37%
Sludge	83.5%
Biodegradation	0.0%

This model predicts that a significant fraction will partition to air and sludge, with a small fraction emitted to effluent. The reliability of this prediction for this type of substance is unknown, and the significant uncertainties in the partition coefficients also mean that this distribution might not be reliable.

6.2.4 Long-range transport potential

The REACH Guidance (Chapter R.7B, Section R.7.9.4.3) 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 PFD, the Environment Agency has performed calculations using input parameters for PFD indicated in Table 6.6.

The sensitivity of changing the log K_{OW} value was not investigated due to the very high endpoint value used in this assessment. In addition the very long degradation rate used in the input parameters for air, water and soil compartments means that negligible change in the output was expected for PFD.

Table 6.6 Estimated long-range transport potential of PFD

Input Parameter	Value
Molecular mass	462 g/mol
Log K_{AW} [a]	4.23
Log K_{OW}	7.0

Half-life in air (hours)	2.4 x 10^{41}
Half-life in water (hours)[b]	2.4 x 10^{41}
Half-life in soil (hours)	2.4 x 10^{41}
LRTP output parameter	
Characteristic Travel Distance (km)	1 349 987
Transfer Efficiency (%)	1 042
P_{ov} (days)	2.44 x 10^{40}

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

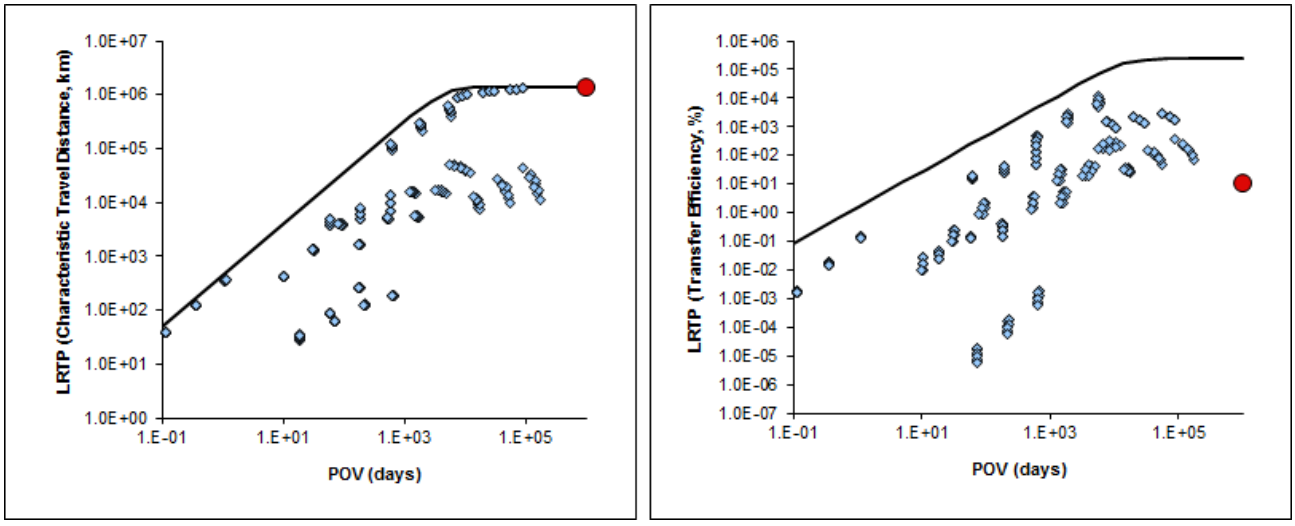
b -The upper bound value for biodegradation of a non-readily biodegradable substance in EUSES is 1 x 10^{40} days to represent infinity (equivalent to 2.4 x 10^{41} hours).

The OECD LRTP screening tool predicts the following outputs:

- Overall persistence (P_{OV})
- 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 OECD LRTP screening tool allows comparisons of these three characteristics for a range of substances, provided in Figure 6.1.

Figure 6.1 Long-range transport potential of PFD (log K_{OW} of 7)



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 PFD 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 PFD due to its physico-chemical characteristics (PFD is more volatile and less water soluble than PFAS such as perfluorooctanoic acid). Due to its low water solubility, removal of PFD 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 PFD 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

PFD has an estimated log K_{OW} of 7 (see Section 5) and so screens as potentially bioaccumulative in aquatic organisms; a log K_{OW} ≥3 is a trigger for secondary poisoning assessment (ECHA, 2016).

The Environment Agency has predicted a fish bioconcentration factor (BCF) of 45 700 L/kg wet weight (ww) for PFD, using a QSAR within the EUSES v2.03 model for the "predominantly hydrophobics" chemical class and a log K_{OW} of 7. This is a widely accepted approach for neutral organic compounds, although it is not known if PFCs were used in the training or test sets of the QSAR, so its reliability for PFD is unknown.

6.3.1.2 Measured data

A fish bioaccumulation study is not a REACH information requirement for the tonnage being supplied. However, the EU REACH registration includes a robust study summary for a fish bioaccumulation study performed with another unidentified substance (citing a fish BCF of ≤30), and states that PFD is "not believed to be bioaccumulative" (ECHA, 2020a). This study is considered further in Section 6.3.1.3. The justification for read-across provided in the registration dossier is that "it is well established that saturated PFCs form a class of chemicals with very similar properties". No other justification is provided.

6.3.1.3 Data from structural analogues

The EU REACH registration dossier for PFD summarises a study which is also included in the EU REACH registration for PFPh (ECHA, 2020d). The original study report study was evaluated by the UK under NONS.

The test was performed in 1984 according to OECD TG 305 C using Common Carp *Cyprinus carpio* that had been acclimatised for 14 days. It is not specified whether the test was performed according to GLP. Fish were stated to have an average weight of 22.4 g, an average length of 9.7 cm and average lipid content of 4.2% (it is not indicated which exact time point these relate to).

Test solutions were prepared with the aid of HCO-20 and F-142D ('Megaface') as dispersants. The study was conducted using flow-through conditions for an 8-week uptake period, with natural water. Two test concentrations were used, with measured values of around 0.08 mg/L for the lower treatment (nominal 0.1 mg/L), and around 0.8 mg/L for the higher treatment (nominal 1 mg/L). There was no depuration period. The test temperature ranged between 23 and 27 °C and oxygen levels between 3.0 and 5.4 mg/L.

The dimensionless BCF was 7.3 to 30 at the lower concentration and 0.2 to 4.7 at the higher concentration, based on whole body concentrations.

The limited information provided in the EU REACH registration dossiers means that it is not possible to independently assess the study validity. However, the Environment Agency still has access to the original test report submitted for NONS, and a more detailed study summary is provided in a confidential annex. It is an old study and consequently there are deficiencies in the methodology used compared to modern standards. For example, there is no depuration period and the number of fish sampled at each time point is lower than a modern test. It is not possible to lipid normalise the result as the reported fish lipid content was only recorded at the start of the test, or correct for fish growth during the study (carp can grow significantly over an 8-week period).

Lower levels of bioaccumulation were seen at the higher test concentration suggesting that this exposure was above the water solubility (as the BCF values would be expected to be consistent at both concentrations). The water solubility of PFD is expected to be around 0.01 mg/L (see Section 5.3.5). Since PFPh has a higher molecular weight, it would be expected to be less soluble in water, and so its water solubility limit is likely to be below 0.01 mg/L. It is therefore likely that the use of dispersants meant that the water solubility limit was exceeded at the lower test concentration in the study. As an example, assuming that the dissolved concentration was around 0.01 mg/L, the BCF values could be up to 300. Overall, in the absence of more accurate water solubility information for PFPh, it is not possible to determine the extent to which the BCF may have been under-estimated. The Environment Agency therefore considers the numerical BCF values to be unreliable. The Environment Agency also notes that PFPh is a larger molecule than PFD as it contains three rather than two perfluorocyclohexane rings. PFPh may therefore be less bioavailable (i.e. PFD may have a higher BCF).

No relevant BCF information is available for PFHF.

6.3.1.4 Other information

The NONS dossier for PFPh includes information on fat solubility from a study report that followed a standard method. The reported solubility was 504 g per 100 g of HB307 solvent (a standardised form of coconut oil) at 37 °C. The NONS dossier for PFHF also reported similar information, with a solubility of 1 102 g per 100 g of HB307 solvent at 37 °C.

The fat solubility endpoint was deleted as an information requirement from chemicals legislation because it was considered redundant since the K_{OW} is essentially a surrogate method to assess the relative solubility of a substance in water and fat. Nevertheless, where available, it provides useful supplementary information about the affinity of substances for fatty tissues.

It is possible that the measurements for PFPh and PFHF were affected by colloid formation in the same way as water solubility, but the data suggest that this type of substance could have significant miscibility in fat.

Perfluorohexane or tetradecafluorohexane (CAS no. 355-42-0) is not a close analogue of PFD because it is a linear substance. However, it has a relatively high solubility in n-octanol, which is a surrogate for lipid (≥ 3.0 g/L at 20 ° C) and so also points to a potential affinity for fat (ECHA, 2020f).

6.3.1.5 Recommended value

The EU REACH registration considers that PFD has a low bioaccumulation potential in fish. However, in contrast, the Environment Agency considers that the study used for read-across is not reliable, and the arguments about its use for PFD are unsubstantiated. PFD screens as potentially bioaccumulative in aquatic organisms, based on a likely log K_{OW} of 7. There is also evidence from both lower and higher molecular weight PFCs that this type of substance may have significant solubility in fat. It is therefore premature to dismiss a bioaccumulation concern, and a precautionary assumption would be to use the estimated fish BCF of **45 700 L/kg ww** derived from the estimated log K_{OW}.

Although not a REACH requirement for the level of supply, the Environment Agency recommends that the robust study summary for this endpoint is updated to provide further details of the study, clearly assess its reliability and state which substance was tested. More detailed reasoning should also be provided to justify the read-across from PFPh (or other substances) in accordance with the ECHA Read Across Assessment Framework (RAAF) (ECHA, 2017a), taking account of any expected trends in bioaccumulation in relation to molecular size.

6.3.2 Terrestrial bioaccumulation

The EU REACH registration has not assessed the potential for terrestrial bioaccumulation as this is not a standard 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. Section 5 discusses the available estimates for K_{OA}, which range from 0.948 to 3.26 with a value of 2.77 derived using a log K_{OW} value of 7.0. There is uncertainty in the log K_{OW} value used in the estimations.

These values suggest that PFD does not meet the screening criteria for bioaccumulation in air-breathing organisms.

There is no measured information on the bioaccumulation of PFD in earthworms. The Environment Agency has predicted an earthworm BCF for PFD using the assumed log K_{OW} value of 7.0 with a QSAR within the EUSES v2.03 model for the “predominantly hydrophobics” chemical class. The calculated BCF was 120 000 L/kg ww. This QSAR which was derived from data on a small number of organochlorine compounds and so it is unlikely that PFCs are within the applicability domain.

6.3.2.2 Other information

The EU REACH registration cites a paper by Clark *et al.* (1975) about the use of perfluorinated compounds as red blood cell substitutes, arguing that this class of chemicals is not bioaccumulated since "*compounds containing only carbon and fluorine … do not remain indefinitely in the liver and spleen*."

The Environment Agency has been unable to obtain the full article for this study, but it and related studies are discussed in Section 8.1. Of these, Yokoyama *et al*. (1975) and Okamoto *et al*. (1975) tested the elimination of PFD from laboratory mammals. While these studies are old, did not use standard protocols and have several limitations, both indicate that PFD does not have a long half-life in test animals, with excretion occurring via exhalation.

6.3.3 Summary and discussion of bioaccumulation

There are no measured fish bioaccumulation data for PFD itself. 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 for PFCs like PFD may not be appropriate, as they may have a tendency to form colloids. Nevertheless, there is evidence that both lower and higher molecular PFCs can have significant lipid solubility, and so PFD could be bioaccumulative in aquatic organisms based on its assumed log K_{OW}. This would need to be considered if the substance exceeds its current low level of commercial supply.

For risk assessment purposes, the Environment Agency recommends deriving the BCF value using the QSAR in EUSES, where this is needed. Using the assumed log K_{OW} value (7), the fish BCF is predicted to be 45 700 L/kg ww.

Estimates of log K_{OA} are affected 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 from mammalian studies that injected various PFCs (including PFD) into the blood stream.

7 Ecotoxicology

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

7.1 Aquatic compartment (including sediment)

7.1.1 Fish

7.1.1.1 Short-term (acute) toxicity

This is not a standard information requirement under REACH Annex 7 for substances registered below 10 tonnes/year. However, the EU REACH registration dossier includes a robust study summary for an acute fish test, conducted in 1989 according to OECD TG 203 and in compliance with GLP (ECHA, 2020a). The substance identity is not stated (Batch 51178/B is cited), and the summary refers to “read-across based on grouping of substances (category approach)”.

The test solution was prepared with the aid of a dispersant (Megaface F142-D), and the study was conducted as a limit test at 100 mg/L, which was the highest concentration that could be tested because of the very low solubility of the material in water and the toxicity of the vehicle at high concentrations. The test species was Rainbow Trout (*Salmo gairdneri*, now known as *Oncorhynchus mykiss*), with 20 fish per each group in a semi-static test system (with daily renewal). The reported hardness was 350 mg/L as $CaCO_3$ (noted as slightly higher than recommended, but not considered to have had an effect), the test temperature was 14 ± 1°C and the dissolved oxygen concentration was ≥9.8 mg/L.

No adverse effects were observed and the 96-h LC_{50} was >100 mg/L (nominal).

It is not possible to establish the validity of the test from the limited information provided. For example, the water solubility of PFD is likely to be around 0.01 mg/L, and the nominal test concentration exceeds this by 4 orders of magnitude. The actual test concentration is not reported.

Given the uncertainty in the log K_{OW} value, the Environment Agency does not consider that QSARs would give reliable results.

Neither PFPh nor PFHF have adverse effects on fish up to 100 mg/L in short-term tests (ECHA, 2020d; ECHA, 2020e); these data were previously accepted by the UK under NONS. The NONS data for PFHF appear to be the source of the information for PFD (and PFPh). The Environment Agency notes that PFHF is a larger molecule than PFD, and so may be less bioavailable.

Although not a REACH requirement for the level of supply, the Environment Agency recommends that the robust study summary for this endpoint is updated to provide further

details of the study, clearly assess its reliability and state which substance was tested. More detailed reasoning should also be provided to justify any read-across in accordance with the ECHA RAAF (ECHA, 2017a), taking account of any expected trends in bioaccumulation in relation to molecular size.

7.1.1.2 Long-term (chronic toxicity)

This is not a standard information requirement under REACH Annex 7 for substances registered below 10 tonnes/year. The EU REACH registration dossier includes a statement saying that a study is not scientifically necessary as other information is available, without providing additional details (ECHA, 2020).

7.1.2 Aquatic invertebrates

7.1.2.1 Short-term (acute) toxicity

This is a standard information requirement under REACH Annex 7 for substances registered below 10 tonnes/year.

The EU REACH registration dossier (ECHA, 2020) refers to an attachment which "*makes clear [that] this material is essentially non-toxic to a wide range of organism and does not bioaccumulate*." It also provides a robust study summary for an acute *Daphnia* immobilisation test, conducted in 1989 according to OECD TG 202 and in compliance with GLP. The substance identity is not stated (Batch 51178/B is cited), and the summary refers to "read-across based on grouping of substances (category approach)".

The test solution was prepared with the aid of a dispersant (Megaface F142-D). The test species was the cladoceran crustacean *Daphnia magna* (water flea), in a static test system (group size not stated). The reported hardness was 350 mg/L as $CaCO_3$ (noted as slightly higher than recommended, but not considered to have had an effect), the test temperature was 21 ± 1°C (no information is provided on the dissolved oxygen concentration).

No adverse effects were observed and the 48-h EC_{50} was >0.1 mg/L (nominal).

It is not possible to establish the validity of the test from the limited information provided. For example, the water solubility of PFD is likely to be around 0.01 mg/L, and the nominal test concentration exceeds this by an order of magnitude. The actual test concentration is not reported.

Given the uncertainty in the log K_{OW} value, the Environment Agency does not consider that QSARs would give reliable results.

The same *Daphnia* result appears to be used in the EU REACH registrations for both PFPh and PFHF (ECHA, 2020d; ECHA, 2020e). Under NONS, no acute invertebrate data were provided for PFPh based on a technical argument that the use of an auxiliary solvent

leads to emulsion formation, which separates within 1 to 2 hours. Aeration would maintain a homogeneous dispersion, but this is not possible in a daphnid test as the organisms become trapped at the surface.

The NONS data for PFHF appear to be the source of the information for PFD (and PFPh). The Environment Agency notes that PFHF is a larger molecule than PFD, and so may be less bioavailable.

The Environment Agency recommends that a study according to OECD TG 202 should be performed as a limit test up to the water solubility limit of PFD. Alternatively, the robust study summary for this endpoint should be updated to provide further details of the study, clearly assess its reliability and state which substance was tested. More detailed reasoning should also be provided to justify any read-across in accordance with the ECHA RAAF (ECHA, 2017a), taking account of any expected trends in bioaccumulation in relation to molecular size.

7.1.2.2 Long-term (chronic toxicity)

This is not a standard information requirement under REACH Annex VII for substances registered below 10 tonnes/year.

7.1.3 Algae and aquatic plants

This is a standard information requirement under REACH Annex 7 for substances registered below 10 tonnes/year. However, the EU REACH registration dossier includes a statement saying that a study is not scientifically necessary as other information is available, without providing additional details (ECHA, 2020a).

The Environment Agency recommends that a study according to OECD TG 201 should be performed. Alternatively, the robust study summary for this endpoint should be updated to provide more detailed reasoning to justify any read-across in accordance with the ECHA RAAF (ECHA, 2017a), taking account of any expected trends in bioaccumulation in relation to molecular size.

7.1.4 Sediment organisms

This is not a standard information requirement under REACH Annex 7 for substances registered below 10 tonnes/year.

7.1.5 Other aquatic organisms

No other data are available.

7.2 Terrestrial compartment

This is not a standard information requirement under REACH Annex 7 for substances registered below 10 tonnes/year. The EU REACH registration dossier includes a statement saying that a study is not scientifically necessary as other information is available, without providing additional details (ECHA, 2020a).

7.3 Microbiological activity in sewage treatment systems

This is not a standard information requirement under REACH Annex 7 for substances registered below 10 tonnes/year. However, the EU REACH registration dossier includes a robust study summary for an activated sludge respiration inhibition test, conducted in 1989 according to OECD TG 209 and in compliance with GLP (ECHA, 2020a). The substance identity is not stated, and the summary refers to “read-across based on grouping of substances (category approach)”.

The test used a static design with activated sludge from a predominantly domestic sewage source. The reported hardness was 350 mg/L as $CaCO_3$, and the pH was 6.0 to 8.5 (no other abiotic parameters are summarised). 3,5-Dichlorophenol was used as the positive control, and gave a 3-h IC_{50} of 15 mg/L.

No adverse effects were observed and the 3-h IC_{50} was >100 mg/L (nominal).

It is not possible to establish the validity of the test from the limited information provided. For example, the water solubility of PFD is likely to be around 0.01 mg/L, and the nominal test concentration exceeds this by 4 orders of magnitude. The actual test concentration is not reported.

No data are available for PFPh (ECHA, 2020d). The NONS data for PFHF appear to be the source of the information for PFD (ECHA, 2020a). The Environment Agency notes that PFHF is a larger molecule than PFD, and so may be less bioavailable.

Although not a REACH requirement for the level of supply, the Environment Agency recommends that the robust study summary for this endpoint is updated to provide further details of the study, clearly assess its reliability and state which substance was tested. More detailed reasoning should also be provided to justify any read-across in accordance with the ECHA RAAF (ECHA, 2017a), taking account of any expected trends in bioaccumulation in relation to molecular size.

7.4 Atmospheric effects

This is not a standard information requirement under REACH Annex 7 for substances registered below 10 tonnes/year. PFD is a liquid, so biotic effects via airborne exposure are unlikely. The greenhouse gas hazard is considered further in Section 9.5.

7.5 Summary of ecotoxicology

No ecotoxicity studies are available for PFD. The EU REACH registration relies on read across from three short-term toxicity studies (for fish, *Daphnia* and sewage micro-organisms) performed on a higher molecular weight substance (PFHF) to conclude that the substance is effectively biologically inert. No data are provided for the algal/aquatic plant toxicity endpoint, even though this is a standard information requirement for the level of supply.

The long-term effects of PFD on wildlife, if any, are unknown. Given its likely very high persistence and potential for high miscibility in fat (see Section 6.3.1.4), the Environment Agency considers that the argumentation for this conclusion requires substantial revision, and ideally more robust support from long-term toxicity studies on relevant species. This needs consideration if the substance exceeds its current low level of commercial supply.

8 Mammalian toxicology

The following information is taken directly from the ECHA public dissemination website entry for PFD (ECHA, 2020a). No human health hazard assessment has been undertaken. The focus is on those longer-term endpoints which are potentially relevant for determination of the substance as Toxic ('T') according to the REACH Annex 13 criteria (see Section 9.3) or for a wildlife secondary poisoning assessment. With the exception of an *in vitro* gene mutation study in bacteria, these types of study are not a standard information requirement under REACH Annex 7 for substances registered below 10 tonnes/year.

The study details and their reliability (Klimisch) scores are as presented in the public EU REACH registration dossier and the Environment Agency has not evaluated this information. The same comments about sources of data, reliability scoring and use of supplemental information apply as for Section 5.

PFD is used in both medical and cosmetic applications, including as a blood substitute. 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 sought confirmation of this.

8.1 Toxicokinetics

No toxicokinetics studies on the registered substance have been included in the EU REACH registration dossier (ECHA, 2020a). The EU REACH registration mentions a read-across case based on "aggregated data from various published studies on PFCs" but the source substances are not named individually and few other details are provided. The case for the endpoint is largely based on the EU REACH registration's general assumption and experience from medical applications that PFCs are not expected to be absorbed or metabolised in terrestrial mammals to any significant extent (due to their hydrophobic and lipophobic properties) and will be excreted via the lungs (based on studies in which they are introduced into the blood stream). PFCs injected into the blood stream tend to briefly accumulate in the liver and spleen. Investigations into medical applications indicate they are not metabolised.

Given the relevance of toxicokinetics to the bioaccumulation assessment (see Section 6), and because the EU REACH registration references a study by Clark *et al.* (1975) for that endpoint, and related data in other registration dossiers, the Environment Agency performed a limited literature search for additional information. A brief summary is provided below:

- Flaim (1994) states that intravenous PFC emulsions are cleared from the blood through a process involving phagocytosis of emulsion particles by reticuloendothelial macrophages (RES) and ultimate elimination through the lung in expired air. The rate

of PFC elimination from the RES is proportional to the vapour pressure of the PFC, inversely proportional to molecular weight and positively influenced by lipophilicity. Dose-dependent respiratory excretion occurs with no evidence of metabolic products. Repeated administration of high doses of PFC emulsion may lead to a saturation of the RES-mediated clearance capacity, resulting in a redistribution of PFC to non-RES tissues. Intravenous injection is not a relevant exposure route for wildlife.

- Okamoto *et al.* (1975) noted "*that the long term retention of [PFCs] in body tissues has been the main impediment for their use as the substitute of blood*". Based on this, they measured the distribution and retention of 5 fluorochemicals in rabbits, rats and mice using a series of experiments to assess possible candidates for artificial blood. As noted in Section 6.3.2, a study by Okamoto *et al*. (1975) is referenced in the EU REACH registration dossier. Tests were performed as emulsions using 20% w/v perfluorodecalin and three different emulsifiers: 4% w/v Plauronic F-68 (described as a commercial polyoxyethylene-polyoxypropylene copolymer), 2% w/v egg-yolk phospholid and 2% w/v perfluorooctane-sulfonyl-amido-dimethylaminopropane-N-oxide (FNNO). The other substances were perfluorotributylamine, perfluoro-1-methyldecalin, perfluoro-N,N-diethylcyclohexylamine and 2H-nonacosafluoro-3,6,9,12-tetraoxa-5,8,11-methylpentadecane (Freon E4).
    - The first experiment used male rabbits (strain not indicated) weighing 2.2 to 3 kg to test the effect of different emulsifiers on elimination time. The substance emulsion was injected into an ear vein, with a 4 g/kg bodyweight (bw) dose used for PFD. Blood samples (1 to 2 mL) were taken at 0, 6, 24, 48, 72 and 96 hours. Results are only reported as a graph in the paper, and indicate that about 20% of PFD in the egg-yolk phospholipid emulsion remained after 96 hours in male rabbits compared to virtually complete elimination of PFD in the FNNO emulsion after 24 hours. The results are stated to be the mean of "at least 3 rabbits". The authors suggest that the variation seen with different emulsifiers could be due to differing emulsion stability within the organism.
    - A second experiment investigated the effect of emulsion particle size on the elimination of the fluorochemicals in rabbits using fine (average particle diameter 0.095 µm) and coarse (average particle diameter 0.3 µm) particles. The separation appears to have been done using a centrifuge, but this is not clear in the paper. This test used perfluorotributylamine, perfluoro-1-methyldecalin and Freon E4 (but not PFD) at a dose of 12 g/kg bw. The same animal weight and injection method as the first experiment were used. Results are reported in two graphs, which indicate that the finer emulsion was more slowly eliminated and accumulated less in the liver compared to the coarser one.
    - A third experiment investigated the distribution of three fluorochemicals in rabbit organ tissue. This was performed using an injected dose of 12 g/kg bw using "at least 5 rabbits" per chemical, with the distribution assessed after one week. The same animal weight and injection method as the first experiment were used. Sixteen different tissues were analysed (brain, heart, lung, liver, spleen, kidney,

adrenal, pancreas, small intestine, stomach, colon, femoral marrow, muscle, adipose tissue, bile and eyeball). Only perfluorotributylamine, perfluoro-1-methyldecalin and Freon E4 appear to have been assessed (i.e. not PFD). The paper reports that similar results are seen for the chemicals with 40% of the deposition occurring in the liver, spleen and lung. The highest concentrations were found in the spleen, femoral marrow and liver.

- Based on the distribution in rabbits, a fourth experiment assessed the excretion of 3 of the substances from specific organs of mice over 8 weeks. This was conducted using male dd-strain mice weighing between 15 to 20 g and an injected dose of 4 g/kg bw (injection site not specified). Analysis was performed on the liver, spleen, lung and kidney of “at least 4 mice” at 48 h, 1,2, 4 and 8 weeks. The results showed that perfluoro-1-methyldecalin was the most quickly eliminated (PFD was not tested).
- In a fifth experiment male Wistar rats weighing 200 to 250 g were used to compare the elimination of PFD and perfluoro-1-methyldecalin from specific organs using an injected dose of 8 g/kg bw (injection site not specified). Concentrations were analysed in liver, spleen and lungs with measurements in “at least 5 rats” made at 1, 2 and 4 weeks. Results, based on the sum of the concentrations in the three organs, indicate 26% of PFD remained after 1 week, 9% after 2 weeks and it was almost completely eliminated 4 weeks after injection. For comparison, around 52 to 55% of perfluoro-1-methyldecalin was detected at 1 to 2 weeks, with 31% after 4 weeks (21% and 10% in the liver and spleen).

The conclusion drawn from these studies was that of the five substances tested, the elimination rate of PFD was the most rapid. The form of elimination was not investigated in this study, and instead the paper cites a second study by the authors (Yokoyama *et al.*, 1975), which is described below.

The Environment Agency notes that the Okamoto *et al*. (1975) study is very old, was not performed to a standard protocol and used a small number of animals. Nevertheless, it provides a useful insight into the possible target organs of PFD, as well as an indication of the comparative rates of elimination. A half-life for PFD cannot be reliably calculated from the rat experiment as it is unclear whether any substance was present in other parts of the rat which were not analysed (for example, the rabbit experiment suggested bone marrow may be a significant target, but the elimination kinetics are unknown). One further aspect is the slower elimination of the egg-yolk phospholid emulsion.

- Yokoyama *et al.* (1975) studied the elimination rat of 6 fluorinated substances in male Wistar rats. These were PFD, perfluoro-1-methyldecalin, perfluorotributylamine, perfluoro-N-methyldibutylamine, perfluoro-N,N-diethylcyclohexylamine and perfluoro-2-isopentylpyran. The total number of animals per chemical was not stated, but 8 to 10 rats were sampled at each time point. Animals weighing 140 to 160 g were injected in the tail vein with an emulsion of the PFC as a yolk phospholipid aqueous suspension

(4 g/kg bw). Prior to injection the solutions had been filtered using a 0.45 μm filter to ensure that emulsion particle size was below this value (the paper indicates that the resulting average particle diameter was 0.1 to 0.2 μm). Depuration was studied over 14 days by measuring PFC concentration in urine, faeces and blood, the latter by sacrificing animals (and removing all blood). Samples were taken at 3 hours, and 1, 2, 4, 7 and 14 days. Expired air from the animal chambers was passed through Freon E4 to absorb the PFCs, and also sampled at the same time points. Chemical analysis was performed using gas chromatography, although the detection limits are not stated. Only perfluorotributylamine was detected in the urine and faeces during depuration, with all other chemicals detected solely in the blood. In the blood, rapid elimination of PFD, perfluoro-1-methyldecalin and perfluorotributylamine was observed, with less than 50% PFD present after 24 hours, and no detection after 7 days. As excretion was still occurring after 7 days, the authors noted that the excretion rate was not related to blood levels of the substances. Instead it was suggested to relate in part to the vapour pressure of a substance. The measured half-lives were 7.2 days for PFD, 109 days for perfluoro-1-methyldecalin, 895.2 days for perfluorotributylamine, 22.5 days for perfluoro-N-methyldibutylamine, 62.4 days for perfluoro-N,N-diethylcyclohexylamine and 38.2 days for perfluoro-2-isopentylpyran. Additional experiments were performed using 2 g/kg bw and 8 g/kg bw doses of PFD, resulting in half-lives of 4.2 days and 12.2 days respectively, indicating that the elimination rate constant was dependent on initial dose. Elimination was observed to be exponential. These two tests appear to have used fewer animals.

The Environment Agency notes that the study is very old and was not performed to a standard protocol. Yokoyama *et al.* (1975) did, however, appear to use a larger number of animals than Okamoto *et al*. (1975). For PFD, the calculated half-life is based on the total amount excreted (i.e. via expiration, urine and faeces), rather than any measurement of remaining substance in the body. Given the volatility of the substances, this could potentially underestimate the half-lives. The experiment does provide relative half-lives and suggests that the excretion of PFD may be relatively fast. The results from additional doses tested suggest concentration dependence, although given some of the other uncertainties in the study, this cannot be confirmed.

- In a more recent review paper, Cabrales & Intaglietta (2013) state that PFC excretion has been an important consideration in parenteral use (medical adminstration that is not oral). They note that the rate of *in vivo* excretion is principally determined by molecular weight (lower weight PFCs are more rapidly excreted).

- A further cited article in some of the F2 registrations is Clark *et al.* (1975). The Environment Agency has been unable to obtain the full article. Based on the abstract this appears to be a review of perfluorinated substances as gas carriers (artificial blood). The abstract states that "*perfluorinated substances … have reasonably short dwell times in the liver*" but no further details are provided (the main issue appears to be restricting the use of high vapour substances which can cause pulmonary gas embolism).

8.2 Repeated dose toxicity

The EU REACH registration (ECHA, 2020a) states that “decades of experience handling saturated perfluorocarbons have indicated no toxic effects for any of these substances, though no specific repeated dose testing has been performed that we are aware of. Their use in medical applications in the blood, lungs and eyes supports the data.”

The EU REACH registration also includes the results of a non-guideline short-term repeated dose toxicity study via the inhalation route performed in 1992 using octafluoropropane (CAS no. 76-19-7), which was not in compliance with GLP. It was a limit test which exposed guinea pigs to 10% test substance in air (around 113 000 ppm) continuously for 10 days. No clinical, gross pathological or behavioural effects were observed and there was no mortality. No observations were made about feeding behaviour, urinalysis or ophthalmological findings, and haematological and clinical biochemistry findings were not specified. The ratio of liver and adrenal weight to body weight increased in females, but these were considered unrelated to the treatment; interstitial pneumonitis was found to be present in all control and test animals. The EU REACH registration therefore considers this study to be unreliable (Klimisch 3) because non-pathogen-free subjects were used. The Environment Agency notes that the substance is a gas, and since PFD is a liquid and has a different molecular structure, the relevance of this study is unclear.

8.3 Mutagenicity

The EU REACH registration (ECHA, 2020a) states that “...an Ames test for PFD indicates it has no genetic toxicity. Decades of experience handling saturated perfluorocarbons have further indicated no toxic effects for any of these substances. Their use in medical applications - in which PFD is the most commonly used example - in the blood, lungs and eyes supports the data.”

The negative in vitro bacterial reverse mutation assay (Ames) test was performed in 1979 using Salmonella typhimurium (strains TA 1535, TA 1537, TA 98 and TA 100) in the presence and absence of rat liver homogenate as the metabolic activation system. A standard test guideline was not available, and the test was not performed in compliance with GLP. No cytotoxicity was reported. The conclusion was that the test material had no ability to induce mutations under the test conditions. The EU REACH registration considers it reliable with restrictions (Klimisch 2). Other studies and read across arguments are made in the registration, but these have not been summarised for the purposes of this evaluation.

The EU REACH registration also includes the results of a negative in vivo mouse micronucleus test performed in 1984 using octafluoropropane (CAS no. 76-19-7) in an OECD TG 474 study in compliance with GLP. The species strain was Swiss CD-1. The conclusion was that the test material not genetically toxic. The EU REACH registration

considers it reliable without restriction (Klimisch 1). The Environment Agency notes that the substance is a gas.

8.4 Carcinogenicity

No carcinogenicity studies are available in the EU REACH registration dossier ECHA, 2020a). The EU REACH registration states that PFD is not a carcinogen because "...decades of experience handling saturated perfluorocarbons have indicated no toxic effects for any of these substances, which has been confirmed by Ames testing by contract laboratories including HRC, SRI Int, Safepharm and Toxicol on representative substances from the class. Their use in medical applications in the blood, lungs and eyes further supports the data".

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

No reproduction toxicity studies are available in the EU REACH registration dossier ECHA, 2020a). The EU REACH registration states that they are not scientifically necessary for PFD because it "...has been used in various medical applications, both in trials and in routine use, in human subjects, for some forty years, indicating this material has zero toxicity to humans."

8.6 Summary of mammalian toxicology

Evidence from old non-standard studies suggests that PFD does not have a long half-life in test animals, with excretion occurring via exhalation following administration to the blood stream by injection.

No standard regulatory mammalian toxicity studies are available for PFD for the endpoints considered in this report. Only an old non-standard Ames test is available. The EU REACH registration relies on generic read across arguments from other PFCs (including one *in vivo* micronucleus study from a lower molecular weight gas) and general medical experience to conclude that the substance is effectively biologically inert.

Given its likely very high persistence and potential for high miscibility in fat (see Section 6.3.1.4), the Environment Agency considers that the argumentation for this conclusion requires review by relevant regulatory bodies.

9 Environmental hazard assessment

9.1 Classification and labelling

9.1.1 Harmonised classification

PFD does not have a harmonised classification in Annex VI of the European Classification, Labelling and Packaging (CLP) legislation 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 identify any hazards, and no environmental hazards are identified on ECHA's CLP Inventory: https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/127671 [accessed May 2022].

9.1.3 Conclusions for classification and labelling

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

The estimated log K_{OW} is above 4, indicating that PFD meets the bioaccumulation criterion for the purposes of hazard classification.

No experimental acute or chronic aquatic toxicity data are available on PFD itself. The EU REACH registration claims that the substance is not toxic to aquatic organisms based on generic read across from another PFC, although the data for that substance are limited. The long-term effects of PFD on wildlife, if any, are unknown. Given its likely very high persistence and potential for high miscibility in fat (see Section 6.3.1.4), the Environment Agency considers that a 'safety net' classification with Aquatic Chronic 4 would be warranted on a precautionary basis.

The human health hazard classification has not been considered in this report.

9.2 Assessment of environmental endocrine disrupting (ED) properties

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

9.3 PBT and vPvB assessment

The EU REACH Registration dossier for PFD (ECHA, 2020a) states that "the substance is not PBT/vPvB" with the following justification:

"Perfluorodecalin is an inert, relatively volatile (for its molecular weight) liquid, essentially insoluble in water. It is rapidly lost from water and soil by evaporation. Testing on perfluorocarbons for medical applications indicates they do not bioaccumulate, they are essentially harmless and they are rapidly lost from the human body."

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

Persistence: There are no measured abiotic degradation data for PFD. Based on the structure and low water solubility, hydrolysis will not be a significant degradation pathway.

There are no measured biodegradation data for PFD, but it is considered to be not readily biodegradable based on read across from related substances in which zero or close to zero degradation was observed in standard studies over 28 days.

PFD therefore meets the screening criterion for being potentially persistent (P) or very persistent (vP).

No environmental half-life data for water, sediment or soil are available for comparison with the definitive criteria in REACH Annex 13 but, due to the stability of the carbon-fluorine bond, the Environment Agency considers it highly likely that the substance will be extremely persistent if released into the environment.

Distribution modelling suggests that the atmosphere may be an important sink if the substance is released to air (see Section 6). Several studies suggest that the atmospheric half-life of PFD exceeds 1 000 years.

Bioaccumulation: There are no studies on the bioaccumulation of PFD in aquatic organisms for comparison with the definitive criteria in REACH Annex 13. As discussed in Section 5.4.5, there is significant uncertainty regarding the log K_{OW} of PFD, but it seems likely that the log K_{OW} will be above 5, and the Environment Agency has used a log K_{OW} of 7 for the purposes of this report. This exceeds the Annex 13 screening criterion for being potentially bioaccumulative (B) ($K_{OW} \leq 4.5$) and very bioaccumulative (vB) ($K_{OW} \geq 5$).

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 for PFCs like PFD may not be appropriate, as they may have a tendency to form colloids. Nevertheless, there is evidence that both lower and higher molecular PFCs can have significant lipid solubility, and so PFD could be bioaccumulative in aquatic organisms based on its assumed log K_{OW}.

In terms of bioaccumulation in air breathing organisms, the screening criteria are a log K_{OW} > 2 and log K_{OA} > 5 (ECHA, 2017b). With a proposed log K_{OW} of 7 for PFD the log K_{OW} criterion is met. In Section 6.3.2.1 the range of estimated K_{OA} is 0.948 to 3.26 with a value of 2.77 derived using a log K_{OW} value of 7.0. While there is uncertainty regarding the derived K_{OA} values, the data currently suggest that PFD does not meet the log K_{OA} screening criterion. This is consistent with limited, non-standard and very old data suggesting elimination of the substance from laboratory mammals is relatively rapid.

Toxicity: No ecotoxicity studies are available for PFD. The EU REACH registration relies on read across from three short-term toxicity studies (for fish, *Daphnia* and sewage micro-organisms) performed on a higher molecular weight substance (PFHF) to conclude that the substance is effectively biologically inert. No data are provided for the algal/aquatic plant toxicity endpoint, and the long-term effects of PFD on wildlife, if any, are unknown.

Based on the limited available aquatic toxicity read-across information, the substance may not meet the screening toxicity (T) criterion (short-term L(E)C_{50} < 0.1 mg/L). However, given its likely very high persistence and potential for high miscibility in fat (see Section 6.3.1.4) further testing would be warranted, particularly if the supply level exceeds 10 tonnes/year.

PFD is not classified in the EU REACH registration for any human health hazard that would meet the T criterion.

Overall conclusion: PFD screens as potentially P/vP, and is likely to be extremely persistent in the environment. It screens as potentially B and vB. There is insufficient information to draw a definitive conclusion for 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 draft 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: PFD meets the screening criterion for being P or vP (see section 9.3).

Mobility: An experimental log K_{OC} value is not available. A predicted log K_{OC} of 5.77 has been used as an approximation for this evaluation (see Section 6), which does not meet

the draft criterion as being mobile (M) (log K_{OC} ≤ 4). However, there is significant uncertainty in this value for PFD, both in terms of the K_{OW} input value and the suitability of the available QSARs for this type of substance. A definitive log K_{OC} value from a relevant soil study should be considered if the level of supply exceeds 10 tonnes/year.

Toxicity: There is currently insufficient information to make a conclusion relating to T (see Section 9.3).

Overall conclusion: PFD screens as potentially P/vP, and is likely to be extremely persistent in the environment. It does not screen as M based on predicted log K_{OC} data, although there is some uncertainty in the estimated value. There is insufficient information to draw a definitive conclusion for T.

PFD is a moderately volatile liquid, and the influence of volatility is not considered under the draft 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, 2020d).

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 PFD are listed in Table 9.1. These values are sourced from the Fifth Assessment Report of the IPCC (IPCC, 2013). PFD is shown in **bold italics**.

Table 9.1 Global Warming Potential of PFCs

Perfluoroalkane	Trade name	Atmospheric lifetime years	Atmospheric lifetime days	GWP (100 years) as CO_2 equivalent
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
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 (PFD)	***PFC-91-18***	***2 000***	***-***	***7 190***
Perfluorodecalin (cis)	***-***	***2 000***	***-***	***7 240***
Perfluorodecalin (trans)	***-***	***2 000***	***-***	***6 290***
Perfluoroethene	PFC-1114	-	1.1	<1
Perfluoropropene	PFC-1216	-	4.9	<1
Perfluorobuta-1,3-diene	-	-	1.1	<1
Perfluorobut-1-ene	-	-	6	<1
Perfluorobut-2-ene	-	-	31	2
Perfluorocyclopentene	-	-	31	2

Note: The IPCC Fourth Assessment Report (Forster *et al* 2007) reported a GWP for PFD of > 7 500 (100-year time horizon), based on research by Shine *et al* (2005). It also stated that the substance has an atmospheric lifetime of >1 000 years, indicating that this is a lower limit (Forster *et al* 2007). A more recent study by LeBris *et al* (2017) provided an atmospheric lifetime of 8 030 years for *cis*-PFD and 7 440 years for *trans*-PFD.

PFD is not one of the PFCs currently listed in the Ozone-Depleting Substances (ODS) Substances and Fluorinated Greenhouse Gases (F-gas) Regulations (see: https://www.gov.uk/guidance/fluorinated-gases-f-gases). However, the above information suggests it has a relatively high GWP. A qualitative risk characterisation for the atmosphere is included in 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.

Available hazard data are discussed in Sections 7, 8 and 9. The EU REACH registration considers the substance to be non-hazardous and has not derived PNECs. The Environment Agency considers that the substance could be classified for aquatic hazard in the absence of reliable information (see Section 9.1.3), which would oblige the supplier to perform an exposure and risk assessment under UK REACH. The Environment Agency notes however that the available public information is currently insufficiently detailed to allow the derivation of environmental PNECs following the REACH guidance (ECHA, 2008b). The Environment Agency therefore recommends that further supporting information is added to the REACH registration dossier relating to the ecotoxicity and mammalian toxicology endpoints, so that a firmer judgement can be made about the need for derivation of PNECs - and also DNELs for human health risk assessment.

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

PFD is not (self-)classified in the EU REACH registration as hazardous, so the EU REACH registration does not include any assessment of environmental exposure. The Environment Agency considers that, in the absence of reliable information, the substance could be classified as Aquatic Chronic 4 for environmental hazards (see Section 9.1.3). The Environment Agency has therefore 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

PFD is manufactured at a single site (F2 Chemicals Ltd, Lea Lane, Lea Town, Preston, Lancashire PR4 0RZ) in the range of 1 to 10 tonnes/year.

The other registered use mentioned in the registration dossier is formulation into a mixture. The company's website suggests that it is used in biomedical applications and in cosmetics (see Section 3). The Environment Agency does not have information on the tonnage split between these uses. Consumption by UK businesses is also likely to be significantly lower than the EU level of supply

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 is high potential for release to wastewaters or direct to surface waters in some of the substance's applications, but no information is currently available.

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. Releases may occur from sewage sludge spreading.

Routes of emission to air

According to the company's environmental permit, environmental releases from the production facility 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 identity and quantity of individual substances is not stated.

Given that PFD is a moderately volatile liquid, there may be some potential for release to air in some of the substance's applications, but no information is currently available. As the substance is supplied on the EU market in the range 1 to 10 tonnes/year, the amount supplied to the UK market will be significantly lower (perhaps in the region of 0.1 to 1 tonne/year).

10.1.2 Release assumptions made by the Environment Agency

The Environment Agency has received actual production volume data from the UK supplier, which is in the range 1 to 10 tonnes/year. In the absence of detailed information on tonnage splits and releases for downstream uses, it is not appropriate to consider other parts of the life cycle.

The environmental release fractions for the Environmental Release Category (ERC) for manufacture can be based on the default worst case assumptions in the 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 to air	Environmental release fraction used in the exposure assessment to wastewater	Environmental release fraction used in the exposure assessment to soil	Regional volume of use (tonnes/ year)	Fraction of main local source	Number of emission days/ year (local)
ERC1: Manufacture of the substance	**0.05**	**0.06**	**0.0**	**10**	**1**	**20[a]**

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

Assuming that production is at the upper limit of the current tonnage band (9.99 tonnes/year), the adoption of these highly conservative assumptions indicates a worst-case emission from the manufacture of PFD of 0.5 tonnes/year to air and 0.6 tonnes/year to wastewater for both local and regional scales. However, this essentially assumes that there is no abatement on site. The Environment Agency notes that:

- The site reports total PFC emissions of 6 tonnes/year to air. Given the registered tonnage bracket, the Environment Agency anticipates that PFD would comprise a small proportion of these emissions.
- The site permit does not require wastewater emissions to be reported. The Environment Agency notes that the UK supplier 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 10.2.1 to the European Union System for the Evaluation of Substances (EUSES) computer program (v2.0.3) (ECHA, 2020b). 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 of England (approximately 56 million people, based on Office for National Statistics data: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/bulletins/annualmidyearpopulationestimates/mid2019 (accessed July 2020) (the equivalent figures for the UK are around 16% for land area and 30% for population). The continental environment is the size of 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, except for the local environment.

The key properties of PFD 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.

Table 10.2 Substance-specific input parameters for the EUSES model

Parameter	Values used in this evaluation
Physical state	Liquid
Molecular weight	462 g/mol
Vapour pressure at 25 °C, kPa	0.88
Water solubility at 25 °C, mg/L	0.01
Octanol-water partition coefficient (log K_{ow})	7.0
Chemical class for K_{OC}-QSAR	Predominantly hydrophobics
Organic carbon-water partition coefficient (log K_{OC})	5.77
Suspended matter–water partitioning coefficient (log $K_{SUSP-WATER}$)	4.77
BCF_{fish} (L/kg ww^{-1})	45 700
$BCF_{earthworm}$ (L/kg ww^{-1})	1.2×10^5
Half-life for degradation in air, hours	2.4×10^{40} k_{OH} = 0 cm^3/molecule/s
Biodegradability	Not readily biodegradable
Sewage treatment works removal rate: Air Sludge	 10.1 % 83.5 %

In the absence of an emission to wastewater treatment works or direct emission to fresh/marine water, soil or groundwater, no PECs for freshwater or marine, soil compartments, groundwater or secondary poisoning have been derived. A qualitative assessment is presented below for compartments other than air where a local and regional PEC have been derived.

10.2.3.1 Air

The local air compartment is assumed to receive emissions from the process and via volatilisation from the WWTWs. The local PEC for air represents the concentration at 100 m from the emission source and is estimated to be 6.41×10^{-3} mg/m^3 for the manufacturing site. The regional PEC is the same value as there is one source of emission in the region.

10.2.3.2 *Other compartments*

The manufacture of PFD only includes the emission to air at local and regional scale, so the majority of the exposure pathways are not relevant for this substance i.e.:

- Direct release of PFD to fresh / marine water and environmental distribution with sediment assuming equilibrium partitioning.

- Release to wastewater treatment works and distribution to air, sewage sludge and effluent discharge to freshwater and marine water.

The deposition of PFD from the atmosphere to surface media is not predicted to be a significant pathway for a substance with low water solubility that is highly volatile. Therefore, PECs for PFD in water, soil, sediment and biota are expected to be very low for a moderately volatile liquid emitted directly to the atmosphere.

10.1.4 Monitoring data

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

10.1.5 Discussion

The derivation of the modelled PECs for PFD 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 WWTP 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, this assessment is considered indicative of potential release and exposure of PFD 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

In the absence of information to clarify the (eco)toxicity of PFD, no relevant Predicted No Effect Concentration (PNEC) for the environment or Derived No Effect Level (DNEL) for human health have been derived. Also, no PEC values have been calculated in the exposure assessment to allow for a formal risk characterisation. On the basis of expected limited emissions/releases into the environment, environmental risks from PFD are likely to be low, but this would benefit from further clarification by the UK supplier.

PFD is not one of the PFCs currently listed in the Ozone-Depleting Substances (ODS) Substances and Fluorinated Greenhouse Gases (F-gas) Regulations. However, it does have a significant global warming potential (see Section 9.5). Worst-case releases to air from the production site are predicted to be around 0.5 tonnes/year, although this is likely to be over-estimated. In addition, a proportion of the amount supplied for biomedical and cosmetic applications may evaporate and hence be released to air in a diffuse manner. In the absence of better information on releases in a UK context, the Environment Agency notes a concern for this hazard but considers that the contribution of PFD to global warming will be relatively small in the context of other sources of greenhouse gases.

The question of whether there could be additional information gathered or management of PFD and PFC emissions more generally, under F-gas or other regulations, warrants further UK policy consideration.

12 Conclusion and recommendations

12.1 Conclusion

PFD is a bicyclic perfluoroalkane, containing only carbon and fluorine atoms. It is registered under EU REACH by a single company at a supply level of 1 to 10 tonnes/year. As it is produced in the UK, the UK REACH registration tonnage will be the same. The main uses appear to be for biomedical and cosmetic products, and the scale of use within the UK is likely to be around 1 tonne/year or less as the UK market is smaller than the EU.

There is very little measured property data for PFD and most of the conclusions drawn in the EU REACH registration dossier are based on information for other PFCs (including substances with different molecular weights and shapes). It is a moderately volatile liquid at standard pressure and temperature, with a low water solubility and relatively high predicted K_{OW} value. There is significant uncertainty in these physico-chemical properties, especially as this type of substance may form colloids in various solvents.

Given its likely very high persistence and potential for high miscibility in fat (based on data for similar substances), the Environment Agency considers that classification with Aquatic Chronic 4 would be warranted on a precautionary basis due to the lack of any reliable aquatic toxicity data. PFD screens as potentially vPvB. There is insufficient information to draw a definitive conclusion for T. It therefore does not currently meet the draft PMT criteria, but the actual K_{OC} value is unknown. PFD also has a significant GWP.

The primary emission within the UK is likely to be to the atmosphere from the production site. It has not been possible to produce a comprehensive risk assessment for the environment due to the lack of information on emissions from downstream use and the limited data available on (eco)toxicological hazards. GWP is a concern, but PFD is likely to make a relatively small contribution to global warming compared to other sources of greenhouse gases.

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 PFD:

- Details of an appropriate analytical methodology for measuring PFD (and related PFC) emissions to air (see Section 2.1).
- Confirmation of the scale of supply within the UK and a clearer description of uses within the registration dossier (Section 3).

- Vapour pressure: The robust study summary should be updated to provide full details of the key study (Section 5.1).
- Surface tension: The information provided should be for an aqueous solution, so the robust study summary for this end point should be updated to clarify that a surface tension measurement in aqueous solution is not available (a data waiver could be provided) (Section 5.2).
- Water solubility: The robust study summary should be updated to provide full details of the key study and consider the requirements of ECHA's RAAF. Ideally a new water solubility measurement would be performed to provide a more relevant value, including an assessment of colloid formation (Section 5.3).
- Log K_{OW}: The robust study summary should be updated to provide details of the prediction method and applicability domain and explain how reliability has been assessed. Further QSAR models and read across approaches should also be considered. If feasible, a measured log K_{OW} value should be obtained, e.g. OECD TG 123 (slow-stirring method) or the ratio of solubility in water and in n-octanol (Section 5.4).
- Ready biodegradation: The robust study summary should be updated with further details of the reported study, including the test methodology and controls used. Further information should also be included to confirm the validity of the read-across of the biodegradation data from perfluoroisohexane to PFD using the ECHA RAAF to assess differences between the two chemicals. More appropriate analogues could also be selected (Section 6.1.2).
- Log K_{OC}: There is significant uncertainty in this value for PFD, both in terms of the K_{OW} input value and the suitability of the available QSARs for this type of substance. A definitive log K_{OC} value from a relevant soil study should be considered if the level of supply exceeds 10 tonnes/year (Section 6.2.1).
- Fish bioaccumulation: The robust study summary could provide further details of the study, clearly assess its reliability and state which substance was tested. More detailed reasoning should also be provided in the REACH registration dossier to justify the read-across from PFPh (or other substances) in accordance with the ECHA RAAF, taking account of any expected trends in bioaccumulation in relation to molecular size. A definitive bioconcentration study should be considered if the level of supply exceeds 10 tonnes/year since the substance screens as vPvB (Section 6.3).
- Acute fish toxicity: The robust study summary for this endpoint could be updated to provide further details of the study, clearly assess its reliability and state which substance was tested. More detailed reasoning should also be provided to justify any read-across in accordance with the ECHA RAAF, taking account of any expected trends in bioaccumulation in relation to molecular size (Section 7.1.1).
- Acute *Daphnia* toxicity: A study according to OECD TG 202 should be performed as a limit test up to the water solubility limit of PFD. Alternatively, the robust study summary should be updated to provide further details of the reported study, clearly assess its reliability and state which substance was tested. More detailed reasoning should also be provided to justify any read-across in accordance with the ECHA RAAF, taking account of any expected trends in relation to molecular size (Section 7.1.2).

- Algal toxicity: A study according to OECD TG 201 should be performed. Alternatively, the robust study summary should be updated to provide more detailed reasoning to justify any read-across in accordance with the ECHA RAAF, taking account of any expected trends in relation to molecular size (Section 7.1.3).
- Sewage micro-organisms: The robust study summary could be updated to provide further details of the study, clearly assess its reliability and state which substance was tested. More detailed reasoning should also be provided to justify any read-across in accordance with the ECHA RAAF, taking account of any expected trends in relation to molecular size (Section 7.3).
- In the absence of suitable ecotoxicological data, self-classification with Aquatic Chronic 4 would be warranted on a precautionary basis (Section 9.1).
- Further information is required to better understand and provide improved quantitative estimates of emissions and the levels of PFD in the UK environment. This could include specific information on UK tonnages, uses and releases, more reliable experimental data for physico-chemical properties used in modelling and/or by incorporating PFD into monitoring programmes in relevant environmental media/compartments (Section 10).
- Based on clarification of the PBT/vPvB characteristics of PFD (Section 9.3), its hazards (Section 9.6) and emissions (Section 10), there should be further consideration of whether and how the substance should be managed based on any hazards or risks determined (Section 11).

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

The Environment Agency 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.

The question of whether there could be additional information gathered or management of PFC (including PFD) emissions more generally, under F-gas or other regulations, warrants further UK policy consideration.

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14 List of abbreviations

%	Percentage
B	Bioaccumulative
BCF	Bioconcentration factor
BMF	Biomagnification factor
CAS	Chemical Abstracts Service
C&L	Classification and Labelling [Inventory]
CLP	Classification, Labelling and Packaging [Regulation]
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
m/z	Mass to charge ratio
mg	Milligram
min	Minute
mL	Millilitre
mol	Mole
MS	Mass spectrometry
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
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

p	Statistical probability
Pa	Pascal
PACT	Public Activities Co-ordination Tool
PBT	Persistent, Bioaccumulative and Toxic
PC	Product category
PEC	Predicted environmental concentration
PFAS	Per- and polyfluorinated alkyl substances
PFCAs	Perfluoroalkyl carboxylic acids
PFOS	Perfluorooctane sulfonic acid
pg	Picogramme
pKa	Acid dissociation constant
PMT	Persistent, Mobile and Toxic
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
RAAF	ECHA Read Across Assessment Framework (see ECHA, 2017a)
RCR	Risk characterisation ratio
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals (EU Regulation No. 1907/2006)
RMOA	Risk Management Option Analysis [REACH]

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

Appendix A: Literature search

A literature search was undertaken by the Environment Agency on the 20th April 2020 to identify published information relevant to the assessment of PFD. 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
306-94-5	303	17
Perflunafene	0	2
Perfluorodecalin	800	875
Octadecafluorodecahydroaphthalene	0	11
Perfluorodecahydroaphthalene	2	9
Total unique records	**802**	**889**

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

Appendix B: QSAR models

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

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

Table B.1 QSAR model outline

Name	Brief description
ACD/Labs	Predicts physicochemical properties via the Percepta Platform: https://www.acdlabs.com/products/percepta-platform/.
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 TEST does not report K_{OW} values and uses a different database for surface tension. (US EPA, 2016).

EPISuite™

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

Table B.2 EPISuite™ PFCs included in training and validation sets

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

Open Structure-activity/property Relationship App (OPERA)

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

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

- If a chemical is considered outside the global AD and has a low local AD index (< 0.4), the prediction can be unreliable.
- If a chemical is considered outside the global AD but the local AD index is average (0.4 - 0.6), the query chemical is on the boundary of the training set but has quite similar neighbours (average reliability). If the local AD index is high (> 0.6), the prediction can be trusted.

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

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

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

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

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

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