federal public service
HEALTH, FOOD CHAIN SAFETY
AND ENVIRONMENT

SUBSTANCE EVALUATION CONCLUSION

as required by REACH article 48

and

EVALUATION REPORT

for

Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine

aka "FC-770"

EC No 473-390-7

Evaluating Member State : Belgium

Dated : May 2022

Evaluating Member State Competent Authority

Belgian CA

Belgian Federal Public Service Health, Food Chain Safety and Environment,
Risk Management Service

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Year of evaluation in CoRAP : 2016

Before concluding the substance evaluation a Decision to request further information was issued on 21 August 2018.

Further information on registered substances here:

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

DISCLAIMER

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

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

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

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

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Part A. CONCLUSION

1. CONCERN(S) SUBJECT TO EVALUATION

The Substance, Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine (FC-770) was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB properties;
- Exposure of the environment;
- Wide dispersive use.

The assessment under substance evaluation was targeted on the environmental and ecotoxicological properties of the Substance. No additional concerns were identified during this evaluation.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Not applicable.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the Substance has led the evaluating Member State to the following conclusions, as summarised in the table below.

Table 1: Conclusion of Substance Evaluation

CONCLUSION OF SUBSTANCE EVALUATION Conclusions	Tick box
Need for follow-up regulatory action at EU level	X
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	X
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised classification and labelling

Not applicable.

4.1.2. Identification as a substance of very high concern

The vP and vB criteria according to annex XIII of REACH are considered fulfilled. The eMSCA plans to proceed with the identification of the Substance as an SVHC according to Article 57(e) of REACH.

4.1.3. Restriction

Not applicable.

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Not applicable.

5.2. Other actions

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS

Indication of a tentative plan is not a formal commitment by the evaluating Member State. A commitment to prepare a REACH SVHC Annex XV dossier should be made via the registry of intentions.

Table 2: Tentative plan for follow-up actions

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**
RMOA	April 2022	BE CA
SVHC identification	August 2022	BE CA

Part B. SUBSTANCE EVALUATION

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

The Substance, Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine (or FC-770) was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB properties;
- Exposure of the environment;
- Wide dispersive use.

The assessment under substance evaluation was targeted on the environmental and ecotoxicological properties of the Substance.

No additional concerns were identified during this evaluation.

Table 3: Evaluated endpoints

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Suspected PBT/vPvB	Concern confirmed. The vP criterion is considered to be fulfilled. The vB criterion is considered to be fulfilled for aquatic organisms as the BCF is greater than 5000 L/kg. The human T criterion is considered to be not fulfilled. In absence of long-term studies with aquatic organisms it is not possible to conclude whether the environmental T criterion is met.
Exposure of the environment Wide dispersive use	Concern confirmed. Considering the described uses exposure of the environment cannot be avoided and the use is considered to be wide dispersive.
Additional endpoints evaluated	
Toxicokinetics (in the context of PBT assessment)	No indication that the bioaccumulation potential in air-breathers is high based on current information. However, some uncertainties remain regarding the available toxicokinetic data for B assessment.
Acute toxicity and Corrosion/Irritation	Concern refuted
Sensitisation	Concern refuted (not skin sensitizing)
Repeated dose toxicity (in the context of PBT assessment)	Concern refuted (not toxic after repeated dose exposure via the oral route)
Mutagenicity (in the context of PBT assessment)	Concern refuted (T criteria for human health are not met)
Toxicity to reproduction (in the context of PBT assessment)	Concern refuted (T criteria for human health are not met)

7.2. Procedure

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to suspected PBT/vPvB, exposure of the environment and wide dispersive use, the Substance, Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine (or FC-770) was included in the Community rolling action plan (CoRAP) for substance evaluation pursuant to Article 44(2) of REACH to be evaluated in 2016. The updated CoRAP was published on the ECHA website on 22 March 2016. The Competent Authority of Belgium was appointed to carry out the evaluation.

Pursuant to Article 45(4) of REACH, the Competent Authority of Belgium has initiated the substance evaluation for Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine, (EC No 473-390-7) based on registration(s) submitted by the Registrant(s) and other relevant and available information.

The evaluating MSCA considered that further information was required to clarify the suspected PBT/vPvB concern. Therefore, it prepared a draft decision pursuant to Article 46(1) of REACH to request further information. It submitted a draft decision to ECHA on 17 March 2017.

A unanimous agreement of the Member State Committee on the draft decision was reached in its MSC-60 meeting. ECHA notified the registrant(s) of the decision pursuant to Article 51(6) of REACH on 21 August 2018 requesting a bioaccumulation in aquatic species study (OECD TG 305).

In accordance with Article 46(2) of REACH, the registrant(s) updated their dossier on 28 November 2019 with a bioaccumulation in aquatic species study applying aqueous exposure. In accordance with Article 46(3) of REACH, the evaluating Member State started the second round of the evaluation without undue delay.

In accordance with Article 46(4) of REACH, the evaluating Member State finished its evaluation activities within 12 months of the information being submitted.

7.3. Identity of the substance

Table 4: Substance identity

SUBSTANCE IDENTITY	
Public name:	Reaction mass of 2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine and 2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine
EC number:	473-390-7
CAS number:	1093615-61-2 (mentioned in the registration dossier)
Index number in Annex VI of the CLP Regulation:	/
Molecular formula:	$C_7F_{15}NO$
Molecular weight range:	399.0 g/mol
Synonyms:	FC-770

Type of substance ☐ Mono-constituent ☒ Multi-constituent ☐ UVCB

Structural formula of the constituents :

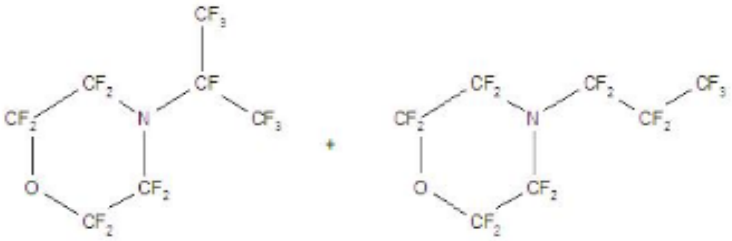

Table 5: Constituents

Constituent			
Constituents	**Typical concentration**	**Concentration range**	**Remarks**
2,2,3,3,5,5,6,6-octafluoro-4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)morpholine	Confidential	Confidential	Synonym : 4-perfluoro-isopropylmorpholine
2,2,3,3,5,5,6,6-octafluoro-4-(heptafluoropropyl)morpholine	Confidential	Confidential	Synonym : 4-perfluoro-n-propylmorpholine

7.4. Physico-chemical properties

Table 6: Physico-chemical properties

Values for the individual constituents are not available. Considering their chemical structures it is reasonable to accept that the values in the table are valid for the individual constituents as well as for the substance as a whole.

OVERVIEW OF PHYSICO-CHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20 °C and 101.3 kPa	Liquid
Density	1.80 kg/L at 20 °C (OECD TG 109)
Melting point	-127 °C at 101.3 kPa
Boiling point	96 °C at 101.3 kPa (OECD TG 103)
Vapour pressure	6750 Pa at 20 °C (OECD TG 104; Key value) 5070 Pa at 20 °C (ASTM E-1719-97)
Water solubility	66.2 µg/L at 23 °C (equiv. to OECD TG 105) = 1.66×10^{-7} mol/L at 23 °C
Partition coefficient n-octanol/water (log Kow)	5.7 at 23 °C Applying solubility ratio method
Kinematic viscosity	0.786 mm^2/s at 25 °C
Oxidising properties	Substance shows no oxidising properties
Granulometry	Substance is not a solid

7.5. Manufacture and uses

7.5.1. Quantities

Table 7: Aggregated tonnage*

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☒ 10 – 100 t	☐ 100 – 1000 t	☐ 1000- 10,000 t	☒ 10,000-50,000 t
☒ 50,000 – 100,000 t	☒ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☒ > 1000,000 t	☐ Confidential

*Dissemination website checked on 1 October 2021 (ECHA, 2021)

7.5.2. Overview of uses

Table 8: Overview of uses*

USES Life cycle stage	
Manufacture	ERC1 : Manufacture of the substance PROC2: Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment conditions PROC3 : Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions PROC8b : Transfer of substance or mixture (charging and discharging) at dedicated facilities PROC15 : Use as laboratory reagent
Formulation	ERC2 : Formulation into mixture PROC8b : Transfer of substance or mixture (charging and discharging) at dedicated facilities
Uses at industrial sites	ERC7 : Use of functional fluid at industrial site PROC1 : Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions PROC8b : Transfer of substance or mixture (charging and discharging) at dedicated facilities PROC15 : Use as laboratory reagent
Uses by professional workers	ERC9a : Widespread use of functional fluid (indoor) PROC1 : Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions PROC8b : Transfer of substance or mixture (charging and discharging) at dedicated facilities PROC15 : Use as laboratory reagent

Article service life	ERC10a : Widespread use of articles with low release (outdoor) ERC11a : Widespread use of articles with low release (indoor) PROC21 : Low energy manipulation of substances bound in materials and/or articles
Consumer uses	/

*Dissemination website checked on 1 October 2021 (ECHA, 2021)

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Not applicable.

7.6.2. Self-classification

- In the registration(s):

  Specific for "Cell crude of FC-770"
  - Acute Tox. 4; H302: Harmful if swallowed
  - Acute Tox. 3; H311: Toxic in contact with skin
  - Eye Irrit. 2; H319: Causes serious eye irritation

7.7. Environmental fate properties

7.7.1. Degradation

7.7.1.1. Abiotic degradation

7.7.1.1.1. Hydrolysis

A hydrolysis study is not performed with the Substance. Based on the chemical functionalities of the two main constituents of the Substance, the eMSCA considers that hydrolysis does not take place. During manufacture of the Substance, very harsh reaction conditions are applied and the Substance as the end product of the synthesis is demonstrated to be very stable. Therefore, any chemical transformation under environmental conditions (e.g. ring opening or hydrolysis) is highly unlikely to occur.
It is also noted that the Substance does not contain functional groups for which hydrolysis can be estimated by the QSAR model HYDROWIN v2.00 of the EPI Suite tool (US EPA, 2000).

7.7.1.1.2. Phototransformation in air

The susceptibility of the Substance to phototransformation in air has not been experimentally examined. However, the structural analog perfluoro-N-methylmorpholine (PNMM) was resistant to direct photolysis under medium pressure mercury lamp irradiation as well as to indirect photolysis by hydroxyl radicals and singlet oxygen atoms (University thesis, 1993, Registration dossier). The dissipation half-life of PNMM was calculated to be >1000 years. PNMM differs from the Substance only in the alkyl chain attached to the morpholinic nitrogen. Comparison of the UV spectra of the Substance and PNMM shows very little difference in the absorption cross sections and therefore similar susceptibility to direct photolysis is assumed. Further, it is considered that perfluoroalkyl chains are inert to oxidative processes. Therefore, it is appropriate to conclude that the Substance is very stable in the air compartment with a half-life assessed to be 1000 years or longer. In publicly available literature (Prather, 2001) atmospheric lifetimes of 3200 and 4100 years

are reported for perfluorocyclobutane and perfluoropentane. These data confirm that in general perfluorinated compounds are extremely stable in the atmosphere and there is no reason to assume that the Substance behaves differently.

It is also noted that the Substance does not contain functional groups that allow the QSAR model AOP v1.92 of the EPI Suite tool (US EPA, 2000) to estimate a reaction rate constant or a half-life for reaction with hydroxyl radicals or ozone.

7.7.1.1.3. Phototransformation in water

Phototransformation in water is not experimentally tested. There are no indications that this type of degradation process is relevant for the Substance.

7.7.1.1.4. Summary on abiotic degradation

Experimental data on the abiotic degradation of the Substance are not available. Nevertheless, no indications are found that the Substance will degrade to a relevant extent under environmentally abiotic conditions.

7.7.1.2. Biotic degradation

In general, the stability of organic fluorine compounds has been described by Siegemund *et al*. (2012). This author concludes that *"when all valences of a carbon chain are satisfied by fluorine, the zigzag-shaped carbon skeleton is twisted out of its plane in the form of a helix. This situation allows the electronegative fluorine substituents to envelope the carbon skeleton completely and shield it from chemical attack. Several other properties of the C-F bond contribute to the fact that highly fluorinated compounds belong to the most stable organic compounds. These include polarizability and high bond energies, which increase with increasing substitution by fluorine. The influence of fluorine is greatest in highly fluorinated and perfluorinated compounds."* These observations strongly suggest that also the Substance will not degrade at all under environmental conditions.

For the Substance only one experimental biodegradation study is available: a ready biodegradation test according to OECD Guideline 310 (headspace test). In this test 0 % degradation was found after 28 days, and therefore it is concluded that the Substance is not readily biodegradable. Moreover, the total lack of biodegradation in this test is fully in line with the overall observation that all perfluorinated compounds are extremely stable.

A simulation study is not available for the Substance.

The EPI Suite tool (US EPA, 2000) includes several BIOWIN models that provide degradation timeframes for primary and ultimate degradation of chemicals. According to REACH Guidance R.11. (ECHA, 2017a) the combination of estimates from BIOWIN 2, 3 and 6 can be used as screening criteria that indicate whether compounds are potentially (very) persistent. If the BIOWIN 2 or 6 score is less than 0.5 in combination with a BIOWIN 3 score less than 2.25, one should conclude that the substance is potentially (very) persistent.

For the constituents of the Substance the following estimates are found:

- BIOWIN 2: 0.0000 (<0.5) ➔ Does not biodegrade fast;
- BIOWIN 3: 0.2682 (<2.25) ➔ Ultimate biodegradation longer than months;
- BIOWIN 6: 0.0000 (<0.5) ➔ Not readily degradable.

The estimated values are far below the screening criteria and it is concluded that the Substance is potentially (very) persistent. Furthermore, these models estimate the ether and the tertiary amine functionalities in the Substance to decrease the biodegradation potential compared with perfluorinated compounds without nitrogen or oxygen in their carbon chain.

On the other hand, the BIOWIN models cannot be expected to predict the biodegradability of perfluorinated compounds with high reliability. The reason is that the training data set is not fully implemented for perfluorinated compounds. In particular, there is no fragment coefficient for -CF_2- moieties in models 2 and 3 and perfluorinated compounds are not represented in the training set.

It is noted that the Biodegradation/Biocatalysis Pathway Prediction System from EAWAG (EAWAG BBD software, 2010) does not present a result for the Substance constituents. Apparently, biodegradation of perfluorinated compounds is hardly or not reported in scientific literature. This observation suggests that it is highly unlikely that biodegradation of perfluorinated substances takes place under environmentally relevant conditions.

7.7.1.3. Summary on degradation

Although experimental studies on degradation with the Substance are very scarce and a simulation study has not been performed, the eMSCA concludes that the Substance meets the very persistent criteria in water, sediment and soil of REACH Annex XIII. This conclusion is underpinned by several arguments.

In the ready biodegradation study according to OECD TG 310 no degradation whatsoever is found and the lack of biodegradation is supported by QSAR predictions.

Perfluoroalkyl compounds all share high resistance to environmental and metabolic degradation. This resistance to degradation is primarily due to the high electronegativity and low polarisability of fluorine, which results in the strongest covalent bond known in organic chemistry: the C-F bond (Kissa, 2001). The C-F bond is resistant to acids, bases, oxidation and reduction, and also high temperatures. Multiple C-F bonds on the same geminal carbon lead to additional strengthening of the C-F bond. The strong electron withdrawing effect of the fluorine atoms in perfluoroalkyl moieties also strengthens the skeletal bonds in the carbon chain (O'Hagan, 2008). It is not expected that the length of the perfluoroalkyl chain has any major impact on the inherent stability of PFASs.
For the following perfluorinated compounds that were assessed in the framework of the REACH Regulation it has been concluded that they meet the vP criterion: PFOA (ECHA, 2013), C_9-C_{14} PFCAs (ECHA, 2015, ECHA, 2012a, ECHA, 2012b, ECHA, 2012c, ECHA, 2012d, ECHA, 2012e), PFDA (ECHA, 2016) and PFHxS (ECHA, 2017b).

7.7.2. Environmental distribution

A reliable determination of key physico-chemical properties is of paramount importance in the assessment of the distribution of substances in environmental compartments. In contrast to other organic substances, the uncharged perfluorinated compounds tend to be at the same time very hydrophobic and also rather lipophobic what makes that their concentrations in all condensed environmental compartments (water, sediment and soil) probably remain quite low. Because of the unusual properties of these compounds it is often difficult to execute the usual physico-chemical tests in a reliable way and the resulting values should be used with care.

The eMSCA makes the following observations in relation to key physico-chemical properties. Values for the individual constituents are not available. Considering their chemical structures it is reasonable to accept that the values in the table are valid for the individual constituents as well as for the substance as a whole.

<u>Volatility</u>

The vapour pressure of the Substance was examined in two studies and the eMSCA considers the study according to OECD Guideline 104 to be the most reliable one. Based on this study the vapour pressure was found to be 6750 Pa at 20 °C. The other study according to a US protocol resulted in a value of 5070 Pa and is thus in line with the key study. Also the estimation with EPI Suite is in line with the key study as it predicts a vapour pressure of 31200 Pa at 25 °C.

A vapour pressure of 6750 Pa (at 20 °C) is accepted as a reliable and correct estimate. This vapour pressure corresponds with a concentration in air of 1105 g/m³ (=2.77 mole/m³).

Water solubility

The water solubility of the Substance was measured using a scientifically valid method that is equivalent to OECD Guideline 105 and the test was conducted under GLP protocol. Based on this test the water solubility was found to be 66 µg/L (= $1.66x10^{-4}$ mole/m³). This value is in line with the estimated water solubility from EPI Suite of 228 µg/L (WATERNT program v1.01).

Partitioning octanol-water

The log K_{ow}-value of 5.7 (K_{ow} = 501187) that is reported in the registration dossier is not measured via the shake flask or slow-stirring method, but was determined via the ratio of the solubilities in octanol and water. There is no reference to the study that examined the solubility of the Substance in octanol. However, based on the water solubility of the Substance and the reported log Kow-value of 5.7, the solubility in octanol is calculated to be 33.1 g/L (83.2 mole/m³).

Partitioning air-water

The dimensionless Henry's law constant (HLCt) was measured experimentally by analytically quantifying the concentration of the Substance in both the headspace and the water phase of a sealed vial after equilibration. The resulting measured dimensionless HLCt of 42400 (= 1030 atm·m³/mole) is rather high given the measured values for the volatility (2.77 mole/m³) and the water solubility ($1.66x10^{-4}$ mole/m³). Based on the separate values, one would expect a dimensionless HLCt of 16700.

Partitioning octanol-air

The log K_{oa}-value is not experimentally measured but can be derived from the relationship $K_{oa} = K_{ow}/K_{aw}$ or log K_{oa} = log K_{ow} – log K_{aw}. Based on the measured dimensionless Henry's law constant one can derive a log K_{oa}-value of 1.07 (= 5.7 – 4.63).

7.7.2.1. Adsorption/desorption

An experimental adsorption/desorption study to determine the K_{oc}-value is not available as the practical execution of the test is very challenging. In absence of an experimentally determined K_{oc}, it is best to use a QSAR method to assess the adsorption potential.

EPI Suite (US EPA, 2000) provides two approaches to estimate the K_{oc}. In general the Molecular Connectivity Index method seems to be more reliable than the method based on the log K_{ow}. The MCI method predicts a K_{oc} of 21930 L/kg (log K_{oc} = 4.34).

7.7.2.2. Distribution modelling

The distribution of the Substance in environmental compartments can be assessed with different modelling programs. All these models have in common that they are based on the methodology developed by Donald Mackay and co-workers. One such program is the fugacity module embedded in EPI Suite (US EPA, 2000). This is a rather simple model that does not allow to change default parameters that describe the environmental compartments. More flexible and thus more complex models are the new EQC model developed by the Canadian Environmental Modelling Centre (CEMC, Trent University) and EUSES (ECHA). In the last two programs the assessor has more options to change default values and he can adapt the assessment taking into account the use of the substance under investigation.

Three programs were used to examine quantitatively the distribution of the Substance in the environment.

EPI Suite

In one of the submodules of EPI Suite, the volatilisation rate and the corresponding half-lives for standardized rivers and lakes are estimated. The half-life in a standard river is estimated to be 2 hours, and the estimated half-life in a standard lake is predicted to be 8 days. These half-life values cannot be used to evaluate the distribution in the environment as the deposition process from air to water or soil is not considered.

In the framework of distribution modelling the level III fugacity module is much more instructive. Such a model predicts the partitioning of a chemical between air, soil, water and sediment using a combination of default environmental parameters and an initial release pattern that can be chosen by the user. In this way, the eMSCA examined the probable distribution of the Substance and, as could be expected, the predicted distribution depends on the compartment to which the substance is initially released. Three scenarios were developed, namely initial release to respectively only air, only water and only soil. Taking into account the use scenarios that are described in the registration dossier, the first scenario seems by far to be the most realistic one. The various resulting mass distributions are provided in table 9.

Table 9: EPI Suite distribution modelling (Level III Fugacity model)

Only release to air (ppm)			
Air	Water	Soil	Sediment
999,960	< 1	40	< 1
Only release to water (ppm)			
Air	Water	Soil	Sediment
62,000	260,000	2	678,000
Only release to soil (ppm)			
Air	Water	Soil	Sediment
979,000	< 1	21,000	< 1

If direct releases are only to the air, the Substance will stay in the air compartment and its presence in other compartments will be negligible. If direct releases take place to surface water, the sediment is estimated to form the main sink. If the release is to soil the major part of the substance will evaporate into the air compartment. It should be noted that according to the use of the Substance as mentioned in the registration dossier the last two scenarios, i.e. release to water and soil are unlikely to occur in practice.

NewEQC Level III fugacity model

NewEQC incorporates advances in the science of chemical partitioning and reactivity as compared to the original EQC fugacity model. The NewEQC model specifically includes improved treatment of input partitioning and reactivity data, temperature dependence, and sensitivity/uncertainty analysis, as well as providing full user control over a range of substance partitioning parameters.

Based on the assumption that 100 % of the emission is directed to the air compartment and assuming a production volume of 250 t/y the relative distribution between compartments is provided in table 10.

Table 10: NewEQC Level III Fugacity modelling

Air (gas phase)	99.996 %
Aerosol in gas phase	$2x10^{-6}$ %
Water	$5x10^{-6}$ %

Soil (gas filled pores)	$4x10^{-3}$ %
Adsorbed to soil	$5x10^{-4}$ %
Sediment	$4x10^{-5}$ %
Biota	$1x10^{-7}$ %

The half-time for transport from soil to air was predicted to be 1.59 hours, which is many orders of magnitude shorter than transport from air to soils (1610 days) or from air to water (461,000 years).

As already indicated, this analysis is based on the reasonable assumption that all emissions are to the atmosphere.

EUSES

In order to verify the analysis made with the NewEQC fugacity model, the environmental distribution was also estimated with EUSES.

EUSES is a user-friendly computer program that allows to estimate the risks posed by chemicals to man and the environment in a quantified manner. To achieve this purpose several submodules are implemented in the program, one of them being a method to predict the environmental distribution based on the estimated releases and emissions of substances and this on different spatial scales. Therefore, EUSES can be used to get an estimation of to what extent the various environmental compartments will be impacted by the release of the Substance. EUSES also allows to assess the influence of the assumptions that are made regarding the emission pattern.

The eMSCA took as a starting point the emission pattern described in EUSES for the most prominent use of the Substance, namely use as a heat transfer agent. The emission patterns for the production step as well as for the industrial use step were considered. EUSES provides different release fractions for these two steps. For the production step the TGD/EUSES provides the following release fractions : air = 0.05; wastewater = 0.003; industrial soil = 0.0001, while for the industrial use step the release fractions are : air = 0.001; wastewater = 0.005; industrial soil = 0.01. By considering both scenarios separately one can assess the impact of the underlying assumptions on the quantitative prediction of the distribution.

EUSES allows to estimate the environmental distribution on different spatial scales going from the local scale in a sewage treatment plant (STP) up to the global scale. For the smallest scale (i.e. an STP) EUSES predicts the distribution as follows: air = 33%; water = 4%; sludge = 63%. This result is substantially determined by the adsorption behaviour of a substance and unfortunately that property is not experimentally examined for the Substance. So, there remains substantial uncertainty on the reliability of this specific estimation.

When considering the distribution estimation for the larger scales, the initial assumptions on the release pattern become less and less influential, and at the largest scale the release patterns do not make a difference anymore.

For the various spatial scales EUSES predicts the relative mass distribution of the Substance in percentage as shown in table 11.

Table 11: EUSES environmental distribution modelling

	Air	**Agricultural soil**	**Natural soil**	**Freshwater**	**Sediment**
Regional scale	82	18	0.4	$3x10^{-4}$	$8x10^{-3}$
Continental scale (=EU)	99.74	0.23	0.03	$4x10^{-6}$	$9x10^{-5}$
Global scale	99.9	/	0.09	$9x10^{-3}$	$7x10^{-4}$

The eMSCA concludes that the environmental distribution estimated with EUSES is fully in line with the predictions from the NewEQC model. Over time when a steady state situation is established more than 99 % of the Substance will reside in the air and less than 1 % will be found in condensed states. As indicated by the EPI Suite model, the sediment compartment could only form temporarily the main sink in case that direct releases take place to surface water.

7.7.3. Bioaccumulation

7.7.3.1. Aquatic bioaccumulation

Screening information

The Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11, v3.0 (page 68), points out that if the log K_{ow} of a substance is greater than 4.5 the substance is potentially (very) bioaccumulative for aquatic organisms.

For FC-770 a log K_{ow} value of 5.7 has been calculated based on its solubility in water and in n-octanol. Further EPI Suite v4.1 predicts log K_{ow} values for the isopropyl and n-propyl constituent of respectively 4.55 and 4.70. The small difference between these two values can be attributed to the fact that the perfluorinated isopropyl fragment is not recognized by the model while on the contrary the perfluorinated n-propyl fragment is recognized. As these values are greater than 4.5, the eMSCA concludes that both constituents screen as potentially (very) bioaccumulative for aquatic organisms.

QSAR estimations

It is verified whether QSAR models could deliver useful estimations of the bioaccumulation potential of FC-770.

At this moment the BCFBAF module in EPI Suite (US EPA) is not recommended for perfluorinated substances and the maximum number of fluorine atoms in any individual compound is 8, while FC-770 contains 15 fluorine atoms. None of the BCF models in VEGA (VEGA HUB 2022) can be applied due to a lack of similar substances in the training sets. The BCF baseline model of CATALOGIC (LMC 2022) cannot be used as FC-770 is out of the structural and mechanistic domain.

Therefore it is concluded that at the moment QSAR estimations do not provide reliable information on the bioaccumulation potential of the Substance.

Experimental information

In the framework of the Substance Evaluation process, a Decision was sent to the registrant(s) of the Substance requesting to perform a bioaccumulation study on aquatic organisms according to OECD Guideline 305 (OECD 2012). The registrant(s) carried out a pilot BCF study that was not executed under GLP conditions and which is indicated in the registration dossier to be reliable with restrictions.

The pilot BCF study with the Substance was performed in closed glass aspirator bottles with a volume of 13.2 L without a headspace. Considering the extremely high measured dimensionless Henry's law constant for the Substance, namely 42400, it was clear that avoiding headspaces in the test bottles would be essential in order to be able to establish appropriate substance concentrations in the water phase. One can calculate that employing 13.2 L aspirator bottles a headspace volume of 300 µL already causes the substance concentration to drop with ca 50% in the water medium. So, one foresaw that relatively minute headspace volume variations in the test bottles will lead to substantially varying substance concentrations in the water phase. In order to find out how an appropriate stable substance concentration could be achieved in the test system three preliminary tests were run proceeding to the BCF study. Whatever test set-up was applied in these preliminary tests, one found that time weighted average concentrations in water were systematically 3 to 6 times lower than the nominal starting concentration. In view of this observation, it was decided to run the BCF study at a nominal substance concentration of 100 µg/L.

The actual BCF study was carried out with freshwater under flow-through conditions using *Lepomis macrochirus* (common name bluegill). The test substance was not radiolabelled as specific chemical analysis by gas chromatography was considered to be effective. The uptake duration was 28 days, with fish being sampled on exposure days 7, 14, 21, 27 and 28. A 14-day depuration phase followed with sampling on days 3, 7 and 14. Control chambers were sampled on exposure day 28 and depuration day 14 only.

The test conditions during the study are described in table 12.

Table 12: Test conditions

Nominal test item concentration	100 µg/L; Purity 98.5 %; No radiolabelling.
Vehicles	Methyl tert-butyl ether (2.4 µL/L); Dimethylformamide (100 µg/L).
Temperature	21.8 – 22.3 °C
Flow rate	38 exchanges/day
pH	7.8
Dissolved oxygen	7.5 - 9.2 mg/L
Hardness	140 - 144 mg $CaCO_3$/L
TOC	< 1 mg/L (in 4 weeks prior to the test)
Apparatus	13.2 L glass bottles without headspace
Number of fish per vessel	6
Acclimation period	14 days
Uptake period	28 days
Depuration period	14 days
Fish weight at study initiation	2.24 g
Fish weight at study termination	2.45 g
Biomass loading rate	ca. 1 g/L

The applied nominal test concentration was thus 100 µg/L while it is expected that the concentrations to which the fish are exposed in reality are lower. Indeed, it is in practice difficult to reduce the headspace to 0 and to avoid all leaks in the test chambers and one has to open the test system from time to time for feeding, cleaning and sampling operations. Based on these observations the test item concentrations in water as given in table 13 are considered to be accurate.

The measured concentrations in fish and in the water medium at the various sampling points are reported in table 13.

Table 13: Measured tissue and water concentrations

Sampling day	Mean tissue concentration and standard deviation (µg/kg wet weight)	Mean water concentration and standard deviation (µg/L)
Uptake day 0, hour 0	-	24.1 ± 4.1
Uptake day 0, hour 4	-	14.6 ± 2.1
Uptake day 1	-	14.8 ± 0.8
Uptake day 7	66300 ± 8500	11.8 ± 4.0
Uptake day 14	52700 ± 22010	6.0 ± 0.32
Uptake day 21	132800 ± 7500	30.7 ± 3.2
Uptake day 27	116500 ± 18300	7.0 ± 2.1
Uptake day 28	94000 ± 18300	7.9 ± 5.6

Depuration day 3	88800 ± 36700	-
Depuration day 7	76100 ± 16500	-
Depuration day 14	36300	-

In a first instance these raw data were used to determine a kinetic BCF. In order to do so the sequential method approach (OECD TG 305, annex 5, § 4) was applied and resulted in a depuration rate constant k_2 of 0.0633/d. It is noted that in this study fish growth is minimal and corresponds with a growth dilution rate constant k_g of 0.0012/d. Using the depuration rate constant in combination with the measured fish tissue concentrations an uptake rate constant k_1 of 607/d was calculated. Combination of these two rate constants leads to a BCF_k (k_1/k_2) of 9585 with a 95 % confidence interval of 5492-16726.

It is noted that the substance concentrations in the water medium in the various test bottles differ a lot. The lowest concentration in water was 6.0 µg/L, the highest value was 30.7 µg/L and the simple mean of the daily water concentrations was 14.6 µg/L. One of the validity criteria of the OECD 305 test with aqueous exposure (OECD 305, § 24) states that the concentration of the test substance should be maintained within 20 % of the mean value. Despite the fact that a stable test concentration could not be generated, the eMSCA considers that the results of the study are relevant and should be used in the determination of the BCF. In this study the substantial variation in exposure concentration between the bottles is caused by subtle differences in the bottle set-up and their operation conditions and not by erroneous analysis of the water samples. Although the precision is rather poor, the calculated BCF_k is estimated to be accurate and not biased. Because the lower boundary of the 95 % confidence interval is calculated to be 5492 and thus still greater than the very bioaccumulative criterion (BCF >5000) for aquatic organisms, it is appropriate to conclude that the Substance meets the vB criterion for aquatic organisms.

Besides a kinetic BCF_k also a steady-state BCF_{ss} could be determined. In this experiment it is not clear when steady state can be considered to be reached or whether steady-state is reached at all, but comparing the concentrations in water and in the fish at all sampling points during uptake (i.e. at day 7, 14, 21, 27, 28), regardless whether steady-state would be established or not, one comes to the following average BCFs: arithmetic mean = 9454 L/kg; geometric mean = 8418 L/kg; median value = 8783 L/kg. It is to be noted that the real BCF_{ss} can only be greater than the BCFs derived in this way and so this confirms that the Substance meets the vB criterion for aquatic organisms.

In ECHA's PBT/vPvB guidance (ECHA 2017a, § 4.1.2.9) it is stated that uptake rates are rather similar for neutral organic compounds and as a result the elimination rate is the discriminating factor in the bioaccumulation potential of such compounds. It is also recognized that the uptake rate constant depends on the fish wet weight and in ECHA 2017c, § 7.10.4.1. the following formula is given to establish the expected uptake rate constant: $k_1 = (520\pm40)*\text{fish wet weight}^{(-0.32\pm0.03)}$ L/kg/d. Assuming linear growth during the test, the fish weight at the start of depuration is estimated here at 2.38 g. Based on this fish weight, one can calculate the uptake rate constant to be in the 354-436 L/kg/d range. Consequently, one can conclude that if the depuration rate constant is less than 0.0708/d (= 354/5000), the very bioaccumulative criterion would be fulfilled. In this study the depuration rate constant was found to be 0.0607/d and so this observation confirms that the Substance meets the very bioaccumulative criterion for aquatic organisms. Besides, it should be noted that in this analysis the variable exposure conditions employed in the test do not affect the result and as such it represents a reliable additional argument in assessing the bioaccumulation potential.

It is noted that in this study fish mortality is observed in the test chambers and even to a greater extent in the control chambers without test item. Mortality also did not associate with measured exposure concentrations. Therefore, it is reasonable to assume that fish mortality is not caused by the test item but is triggered by the experimental set-up. In order to check whether the circumstances that caused fish mortality also had an influence on the determined BCFs, the BCFs were recalculated omitting those replicates where some fish did not survive (i.e. replicates for exposure days 14 and 27 and depuration days 7 and 14). Proceeding in this way an arithmetic mean BCF of 7281 L/kg and a depuration rate

constant k_2 of 0.019/d was found. The eMSCA notes that based on this alternative approach the vB criteria are still met and consequently that the observed mortality in some replicates is not a reason to reject the study or its results.

In the determination of a BCF it is the customary approach to take into account the lipid content of the fish that are employed in the study. Paragraph 2 of the OECD TG 305 mentions that the BCF should be expressed on a 5% lipid content basis. Unfortunately, it was in practice not possible to find out the lipid content of the fish used in this test and thus the estimated BCF_k of 9585 represents a non-normalized value. The eMSCA finds that normalization of the BCF would only lead to a different end conclusion regarding the fulfilment of the very bioaccumulative criterion if the mean lipid content of the fish had been greater than 9.585 %. This condition is considered to be highly unlikely, especially since the observed mortality and morbidity indicate stressful conditions for the fish.

Based on this study one cannot definitively conclude which mechanism causes the observed bioaccumulation. The eMSCA is of the opinion that storage in lipids is the most likely route because the log K_{ow} of FC-770 is 5.7 and one may reasonably assume that organisms are not at all able to metabolize these very stable perfluorinated compounds. Although FC-770 is an amine it is a very weak base because of the great electron withdrawing effect of the fluorine atoms. Being predominantly a neutral molecule FC-770 is unlikely to bind to proteins.

7.7.3.2. Terrestrial bioaccumulation

An experimental bioaccumulation study with air-breathers is not available.

Based on the measured dimensionless Henry's law constant a log K_{oa} value of 1.07 was found.

As the log K_{oa} is far less than the threshold value set in the PBT guidance (ECHA, 2017a) for bioaccumulation in air-breathing organisms (log K_{oa} = 5), one may assume that the bioaccumulation potential for these species is very low.

7.7.3.3. Summary and discussion of bioaccumulation

Based on an experimental bioaccumulation study with fish, the eMSCA concludes that the Substance shows a high potential for bioaccumulation and that the vB criterion of REACH Annex XIII (BCF >5000) for aquatic organisms is met.

Regarding the bioaccumulation potential for terrestrial organisms one can only refer to a screening criterion, i.e. the log K_{oa}. The estimated log K_{oa} of the Substance is far less than the threshold value mentioned in the PBT guidance. Therefore, the Substance is not expected to be bioaccumulative for air-breathers. However, this screening information cannot be fully confirmed by available information on toxicological and pharmacokinetic studies in mammals as uncertainties remain regarding available toxicokinetic data (see section 7.9.1 Toxicokinetics).

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

7.8.1.1. Fish

A semi-static short-term fish test with *Danio rerio* was carried out according to OECD Guideline 203 using 10 litre sealed glass containers with a fill volume of 9.5 litres. The loading rate of the test substance was 100 mg/L which is far above its water solubility (i.e. 0.066 mg/L). Test solutions were prepared daily by stirring for approximately 1 hour in air-tight vessels. After a stabilisation period of 5-25 minutes, the Water Accommodated Fraction (WAF) was collected by siphoning and used for the test. The final test solutions were all clear and colourless.

Concentrations of the Substance in the fresh solutions were 0.159 mg/L and 0.214 mg/L at 0 and 72 hours, respectively. The Substance concentrations in the test solutions after 24 hours were all below the limit of quantitation (LoQ). As the rate at which the Substance disappears from the test vessel is not monitored, it is also not possible to estimate a reliable time weighted average and to present a sensible value for LC_{50}. One can only conclude qualitatively that in this test no mortality is observed.

A long-term test on fish is not available. One may assume that the execution of a long-term test will encounter the same kind of practical difficulties as the short-term test.

7.8.1.2. Aquatic invertebrates

A semi-static acute immobilisation test was performed with *Daphnia magna* according to OECD Guideline 202 using 100-mL sealed glass containers. A limit test was conducted with an initial loading rate of 100 mg/L which is far above the Substance's water solubility (i.e. 0.066 mg/L). The test solutions were prepared each day by stirring for approximately 1 hour in air-tight vessels. After a stabilisation period of 5-25 minutes, the Water Accommodated Fraction (WAF) was collected by siphoning and used for the test. The final test solutions were all clear and colourless.

The actual Substance concentrations to which the Daphnia were exposed are unknown since the Substance concentrations in the test solutions after 24 hours were all below the limit of quantitation (LoQ). The concentration of Substance in the fresh solutions were 0.1 mg/L and in one case <LoQ. As the rate at which the Substance disappears from the test vessel is not monitored, it is also not possible to estimate a reliable time weighted average and to present a sensible EC_{50} value. One can only conclude that in this test limited immobilization (5%) is observed in the exposed organisms.

A long-term test on aquatic invertebrates is not available. One may assume that the execution of a long-term test will encounter the same kind of practical difficulties as the short-term test.

7.8.1.3. Algae and aquatic plants

An algae growth inhibition test was performed using *Pseudokirchnerella subcapitata* in freshwater under static conditions (OECD Guideline 201) using 100 mL septum-sealed glass bottles. The Substance concentration corresponded to an initial loading rate of 100 mg/L which is far above its water solubility (i.e. 0.066 mg/L).

The test solutions were prepared by stirring a loading rate of 100 mg/L for approximately 1 hour in air-tight vessels. After a stabilisation period of 5-20 minutes, the Water Accommodated Fraction (WAF) was collected by siphoning and used for the test. The final test solutions were all clear and colourless. The Substance concentration on day 0 was 0.479 mg/L but the samples after 24 hours were <LoQ. As the rate at which the Substance disappears from the test vessel is not monitored, it is also not possible to estimate a reliable time weighted average and to present a sensible value for $EC_{50.}$

Growth during the 0-24 hour period was 29% inhibited versus the controls, but recovered by 48 hours. Overall, no significant effects on the algae growth rate were observed at 48 hours.

7.8.1.4. Sediment organisms

No data available.

7.8.1.5. Other aquatic organisms

No data available.

7.8.2. Terrestrial compartment

No data available.

7.8.3. Microbiological activity in sewage treatment systems

In a static respiration inhibition test performed with activated sludge of predominantly domestic sewage (study according to OECD Guideline 209), no reduction in respiration rate was recorded. The nominal concentration of the test item was 1000 mg/L, which is far above the water solubility of the Substance (i.e. 0.066 mg/L). Therefore, the eMSCA concludes that the Substance shows no toxicity for microorganisms at saturation. EC_{50} (3h) is considered to be >0.066 mg/L.

7.8.4. PNEC derivation and other hazard conclusions

Not applicable.

7.8.5. Conclusions for classification and labelling

Strictly applying the CLP rules the Substance should be classified as aquatic chronic category 4. Indeed, the Substance shows no acute toxicity for aquatic organisms up to the water solubility, but it is not readily biodegradable and it has an experimentally determined BCF greater than 500 L/kg. This classification cannot be removed as long as there is no proven lack of long-term toxicity at 1 mg/L and currently no long-term experimental NOEC values are available.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

Table 14: Studies on absorption, distribution, metabolism and excretion

Method	Result	Remarks	Reference
In vivo In 3 male rats (Sprague-Dawley) Single dose : 1000 mg/kg bw Oral gavage to fasted	Absorption : test article not quantifiable in serum, liver or urine samples Distribution : /	Rel. 2 Test material : FC-770 Purity : 94,2%	Registration dossier (Study report, 2015)
In vivo In male rats (Sprague-Dawley) : 3/dose Single dose : 100, 300 and 1000 mg/kg bw Gavage	Absorption : test article not quantifiable in serum, liver or urine samples Distribution : / Excretion : in feces (19-27%)	Rel. 2 Test material : FC-770 Purity : 94,2%	Registration dossier (Study report, 2015)

In this non GLP-experiment single doses of the Substance up to 1000 mg/kg bw were administered. Monitoring of serum, liver, urine and faeces took place up to 48 hours after administration. In serum, liver and urine no quantifiable levels of test item were found.

The test item was quantifiable in fecal samples but only up to 27 % of the administered dose. As the concentration in fat tissue was not measured and because most of the applied test item was not retrieved analytically, this experiment does not allow to provide a full picture of the toxicokinetic behaviour of the Substance in mammals.

7.9.2. Acute toxicity and Corrosion/Irritation

7.9.2.1. Acute toxicity – oral route

Table 15: Study on acute toxicity after oral administration

Method	Result	Remarks	Reference
OECD TG 423 In female rats (Wistar) : 3/dose Dose : 2000 mg/kg bw Gavage	LD_{50} >2000 mg/kg bw No mortality No abnormalities in clinical observations, bw and at macroscopic examination	Rel. 1 Test material : FC-770 Purity : 94,5%	Registration dossier (Study report, 2007)

Based on the available study the eMSCA concludes that the Substance is not acutely toxic via the oral route.

7.9.2.2. Acute toxicity – dermal route

No information available.

7.9.2.3. Acute toxicity – inhalation route

Table 16: Study on acute toxicity after inhalation exposure

Method	Result	Remarks	Reference
OECD TG 403 In Rats (Wistar) : 5/sex/dose Dose : 20.6 ± 1.7 mg/l (nominal conc. of 21.5 mg/l) Exposure of 4 h Vapour	LC_{50} >20 mg/l No mortality No abnormalities in clinical and at macroscopic examination Slight bw loss	Rel. 1 Test material : FC-770 Purity : 94,5%	Registration dossier (Study report, 2007)

Based on the available study the eMSCA concludes that the Substance is not acutely toxic via the inhalation route.

7.9.2.4. Skin irritation

Table 17: Study on skin irritation

Method	Result	Remarks	Reference
OECD TG 404 In male rabbits (New Zealand White) : 3/dose Dose : 0.5 ml of undiluted substance Exposure of 4h	Overall irritation score : 0 Score of 0 at all timepoints	Rel. 1 Test material : FC-770 Purity : 94,5%	Registration dossier (Study report, 2007)

Method	Result	Remarks	Reference
Semiocclusive			

Based on the available study the eMSCA concludes that the Substance is not irritating.

7.9.2.5. Eye irritation

Table 18: Study on eye irritation

Method	Result	Remarks	Reference
OECD TG 405 In rabbits (New Zealand White) : 3 animals Dose : 0.1 ml Exposure of 24h	Overall irritation score : 0 A score of 1 for redness was observed at 1h. All other assessments were scored 0.	Rel. 1 Test material : FC-770 Purity : 94,5%	Registration dossier (Study report, 2007)

Based on the available study the eMSCA concludes that the Substance is not irritating.

7.9.3. Sensitisation

7.9.3.1. Skin sensitisation

Table 19: Study on skin sensitisation

Method	Result	Remarks	Reference
OECD TG 429 (LLNA) In female mice (CBA; inbred, SPH quality) : 5/dose An additional group of animals was treated with 100% test substance conc. Conc. : 0 and 100%	Stimulation index : 3.0 in the treated group (2.5 for the additional group) vs 1.0 for control group Disintegrations per minute (DPM) : 466 DPM in treated group (312 DPM for the additional group) vs 154 DPM in control group	Rel. 1 Test material : FC-770 Purity : 94,5%	Registration dossier (Study report, 2007)

Based on the available study the eMSCA concludes that the Substance is not skin sensitizing.

7.9.3.2. Respiratory sensitisation

No information available.

7.9.4. Repeated dose toxicity

7.9.4.1. Repeated dose exposure – oral route

Table 20: Study on repeated dose toxicity after oral administration

Method	Result	Remarks	Reference
OECD TG 407 (28-day)	NOAEL : 1000 mg/kg bw/d No effects observed for clinical signs, bw, bwg	Rel. 1 Test material :	Registration dossier (Study report, 2007)

Method	Result	Remarks	Reference
In rats (White, outbred, SPH quality) : 5/dose Doses : 250, 500 and 1000 mg/kg bw/d Gavage	Some haematological and clinical biochemistry findings (decreased WBC, increased RBC count, increased haemoglobin and haematocrit levels, increased activated partial prothromboplastin time, decreased ASAT, increased glucose) but all these findings are within the physiological range. Organ weight : slight changes in males at 250 and 500 mg/kg bw/d at the end of treatment and at 1000 mg/kg bw/d at the end of the recovery period. However these modifications were within the physiological range.	FC-770 Purity : 94,5%	

The eMSCA considers that the substance is not toxic after repeated dose exposure via the oral route. The eMSCA accepts a NOAEL of 1000 mg/kg bw/d.

7.9.4.2. Repeated dose exposure – dermal route

No information available.

7.9.4.3. Repeated dose exposure – inhalation route

Table 21: Studies on repeated dose toxicity after inhalation exposure

Method	Result	Remarks	Reference
OECD TG 413 (90-day) In rats (Sprague-Dawley CD) : 10/sex/dose Doses : 4971, 15094, 49589 ppm Vapour	NOAEL : 49589 ppm No treatment related effects	Rel. 1 Read across Test material : perfluoro-N-methylmorpholine	Registration dossier (Study report, 1993)
OECD TG 413 (90-day) In rats (CD (SD) BR-Sprague-Dawley) : 10/sex/group Doses : 0, 5000, 15000, 50000 ppm Vapour	NOAEL : ca. 49821 ppm No treatment related effects observed	Rel. 2 Read across Test material (CAS number) : perfluorohexane (1064697-81-9)	Registration dossier (Study report, 1992)

The eMSCA does not accept the read-across approach as presented in the registration dossier(s). There is however no identified concern, so no further testing for this endpoint was asked.

7.9.5. Mutagenicity

Table 22: *In vitro* genotoxicity studies

Method	Result	Remarks	Reference
OECD TG 473 (*In vitro* mammalian chromosome aberration test) Peripheral human lymphocytes	Genotoxicity : negative with and without S9 Cytotoxicity : no	Rel. 1 Test material : FC-770	Registration dossier (Study report, 2006)

Method	Result	Remarks	Reference
With and without met. act. Test conc. : without S9 : 10, 33 and 100 µg/ml and with S9 : 10, 33, 66 and 100 µg/ml. + negative and positive controls		Purity : 94,5%	
OECD TG 471 (Bacterial reverse mutation assay) S. Typhimurium TA 1535, TA 1537, Ta 98 and TA 100 With and without met. act. Test conc. : 10 to 5000 µg/ml. + negative and positive controls	Genotoxicity : negative Cytotoxicity : no	Rel. 1 Test material : FC-770 Purity : 94,5%	Registration dossier (Study report, 2006)
OECD TG 476 (*In vitro* mammalian cell gene mutation test) Mouse lymphoma L5178Y cells With and without met. act. Test conc. : 0.03 to 300 µg/mL + vehicle and positive control	Genotoxicity : no Cytotoxicity : no, but tested up to precipitating concentrations	Rel. 1 Test material : FC-770 Purity : 94%	Registration dossier (Study report, 2011)

Based on the available information, the eMSCA concludes that no further testing is needed under this Substance Evaluation.

7.9.6. Carcinogenicity

No information available.

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

Table 23: Study on toxicity to reproduction

Method	Result	Remarks	Reference
OECD TG 421 (reproduction/developmental toxicity screening test) In rats (Sprague-Dawley): 10/sex/dose Doses : 0, 100, 500 and 1000 mg/kg bw/d Gavage Exposure of 4w for males (commencing 2w prior mating) and for females 2w prior mating and continued until at least day 4 of lactation)	NOEL : ≥1000 mg/kg bw/d for adult and reproductive parameters Parental animals : No treatment related effects observed No abnormalities in mating performance, fertility, duration of gestation, litter size and survival, and litter and pup weights Offspring : No effects on viability, clinical signs, bw, sexual maturation, organ weights, gross pathology, histopathology. (however inconsistency with the section "details on results" which mentions no data for sexual maturation, organ weights, gross pathology and histopathology) Pup weights were comparable across all groups, no difference about	Rel. 1 Test material : FC-770 Purity : 94%	Registration dossier (Study report, 2011)

Method	Result	Remarks	Reference
	viability		

The eMSCA accepts a NOEL of >1000 mg/kg bw/d for this endpoint.

7.9.8. Hazard assessment of physico-chemical properties

Not evaluated.

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

Not evaluated.

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

Based on the available information, the self-classification proposed by the registrant is sufficient to cover the observed effects:

(Considering the specific composition of "Cell crude of FC-770")

Acute Tox. 4; H302: Harmful if swallowed;
Acute Tox. 3; H311: Toxic in contact with skin;
Eye Irrit. 2; H319: Causes serious eye irritation, SCL ≥10%.

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.11. PBT and vPvB assessment

The Substance consists of two constituents whose chemical structures are very similar. One constituent contains a perfluorinated isopropyl substituent while the other constituent contains a perfluorinated n-propyl substituent. Considering their very similar structures, the eMSCA concludes that their physico-chemical properties and also their PBT/vPvB properties will hardly diverge. This conclusion is underpinned by the QSAR estimations in EPI Suite (US EPA, 2000). All the estimated numerical values differ hardly or are even equal.

7.11.1. Persistence

Although simulation tests are not available for the Substance, the eMSCA concludes that the Substance is very persistent in all environmental compartments, based on the weight of evidence.

An OECD TG 310 ready biodegradation test on the Substance gave 0 % degradation after 28 days, indicating that the Substance is not readily biodegradable. This is supported by QSAR predictions.

Also for the air compartment, there are no indications that this perfluorinated substance can be degraded abiotically.

The stability of organic fluorine compounds has been described by Siegemund et al. (2012), indicating that no environmental degradation is expected for perfluorinated compounds.

A whole series of perfluorinated substances has already been examined in the past and identified as meeting the vP criterion and for none of these substances a mechanism was found that leads to degradation in relevant environmental circumstances. Therefore, the eMSCA considers that the Substance meets the vP criterion of REACH Annex XIII and just like other perfluorinated substances, must be classified as very persistent.

7.11.2. Bioaccumulation

The Substance screens as bioaccumulative according to ECHA REACH Guidance R.11. (ECHA, 2017a) based on its log K_{ow} >4.5.

One experimental bioaccumulation study is available for the Substance, namely a study on the aquatic species bluegill which resulted in a kinetic BCF_k of 9585. Although this study is a pilot study, and not a definitive study according to GLP rules, and considering the fact that the study shows some technical shortcomings, the eMSCA is of the opinion that the study is sufficiently reliable and that it forms an acceptable basis to conclude that the Substance meets the vB criterion of REACH Annex XIII for aquatic organisms.

Based on the currently available data (estimated log K_{oa} <5 and results from the toxicological and pharmacokinetic studies in mammals), the bioaccumulation potential for terrestrial organisms and mammals is expected to be low. However, this screening information cannot be fully confirmed by available information on toxicological and pharmacokinetic studies in mammals as uncertainties remain regarding available toxicokinetic data (see section 7.9.1 Toxicokinetics).

7.11.3. Toxicity

Human Health

The Substance is not classified for the endpoints carcinogenicity, mutagenicity or reproduction toxicity. In the oral repeated dose study a NOAEL of 1000 mg/kgbw/d was established and the substance is not classified as STOT RE. Therefore, the substance does not meet the human T criterion.

Environment

In the various short-term toxicity studies with aquatic organisms no effects were observed. However, the actual exposure levels in these tests are not clear. Further, no long-term toxicity tests are available and therefore, it cannot be ruled out that effects would occur after long-term exposure as it is most likely that the Substance does not have time to reach steady-state in a short time.

Therefore, the eMSCA considers that it is currently not possible to conclude whether the T criterion for the environment is met.

7.11.4. Overall conclusion

The Substance meets the vPvB criterion for aquatic organisms.

7.12. Exposure assessment

The usual exposure assessment (estimation of PECs) is not executed. However, the relative distribution of the Substance between the various environmental compartments is evaluated. (see § 7.7.2.2.)

7.13. Risk characterisation

Risk characterisation was not performed in this substance evaluation.

7.14. References

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7.15. Abbreviations

ASTM :	American Society for Testing and Materials
B :	bioaccumulative
BCF :	bioconcentration factor
CA :	Competent Authority
CLP :	Classification, Labelling and Packaging
Conc. :	concentration
CoRAP :	Community Rolling Action Plan
EC_{50} :	concentration that causes 50 % of the effect
ECHA :	European Chemicals Agency
ED :	endocrine disruption
eMSCA :	evaluating Member State Competent Authority
EU :	European Union
EUSES :	European Union System for the Evaluation of Substances
GLP :	Good Laboratory Practice
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
LC_{50} :	concentration that is lethal for 50 % of the organisms
LD_{50} :	dose that is lethal for 50 % of the organisms
LLNA :	Local Lymph Node Assay
NOAEL :	No Observed Adverse Effect Level
NOEC :	No Observed Effect Concentration
NOEL :	No Observed Effect Level
OECD :	Organisation for Economic Co-operation and Development
P :	persistent
PBT :	persistent, bioaccumulative and toxic
PEC :	Predicted Environmental Concentration
PFCA :	perfluorocarboxylic acid
PFHxS :	perfluorohexane-1-sulphonic acid
PFOA :	perfluorooctanoic acid
PNEC :	Predicted No Effect Concentration
QSAR :	Quantitative Structure-Activity Relationship
REACH :	Regulation No 1907/2006 concerning Registration, Evaluation, Authorisation and Restriction of Chemicals
STOT RE :	specific target organ toxicity – repeated exposure
SVHC :	Substance of Very High Concern
T :	toxic
TG :	Test Guideline
TGD :	Technical Guidance Document
TOC :	total organic carbon
vB :	very bioaccumulative
vP :	very persistent
vPvB :	very persistent and very bioaccumulative