Justification Document for the Selection of a CoRAP Substance

Group Name: Hydrofluoroethers

EC	CAS	Substance public name
435-790-1	297730-93-9	3-ethoxy-1,1,1,2,3,4,4,5,5,6,6,6-dodecafluoro-2-(trifluoromethyl)-hexane (HFE-7500)
484-450-7	-	3M(TM) NOVEC(TM) ENGINEERED FLUID (HFE-7000)
422-270-2	-	1,1,1,2,2,3,3,4,4-nonafluoro-4-methoxybutane; 1,1,1,2,3,3-hexafluoro-3-methoxy-2-(trifluoromethyl)propane (HFE-7100)
484-410-9	-	2-Ethoxy-3,3,4,4,5-pentafluoro-2,5-bis[(1,2,2,2-tetrafluoro-1-trifluoromethyl)ethyl] tetrahydrofuran (HFE-7800)

Authority: Spanish Ministry for the Ecological Transition

Date: 19/03/2019

Cover Note

This document has been prepared by the evaluating Member State given in the CoRAP update.

1 IDENTITY OF THE SUBSTANCES WITHIN THE GROUP

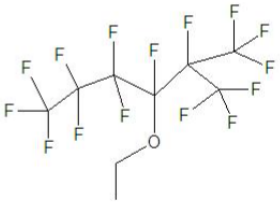
1.1 Other identifiers of the substances within the group

These substances are registered under the REACH process.

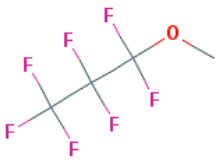
EC name (public)	IUPAC name (public)	Index number in Annex VI of the CLP Regulation:	Molecular formula:	Molecular weight or molecular weight range:	Synonyms:
3-ethoxy-1,1,1,2,3,4,4,5,5,6,6,6-dodecafluoro-2-(trifluoromethyl)-hexane	3-ethoxy-1,1,1,2,3,4,4,5,5,6,6,6-dodecafluoro-2-(trifluoromethyl)-hexane	603-224-00-2			
[No public or meaningful name is available]	[No public or meaningful name is available]				
1,1,1,2,2,3,3,4,4-nonafluoro-4-methoxybutane; 1,1,1,2,3,3-hexafluoro-3-methoxy-2-(trifluoromethyl)propane	1,1,1,2,2,3,3,4,4-nonafluoro-4-methoxybutane; 1,1,1,2,3,3-hexafluoro-3-methoxy-2-(trifluoromethyl)propane				
2-Ethoxy-3,3,4,4,5-pentafluoro-2,5-bis[(1,2,2,2-tetrafluoro-1-trifluoromethyl)ethyl] tetrahydrofuran	2-Ethoxy-3,3,4,4,5-pentafluoro-2,5-bis[(1,2,2,2-tetrafluoro-1-trifluoromethyl)ethyl] tetrahydrofuran				

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

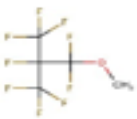
Structural formulas:



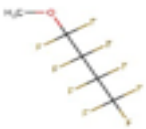
435-790-1

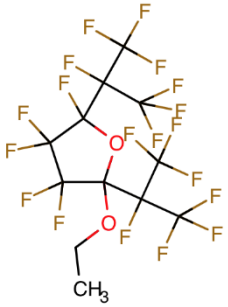


484-450-7



422-270-2





484-410-9

1.2 Similar substances/grouping possibilities

Hydrofluoroethers are a group of substances which have a per- and/or polyfluorinated region, an ether group and a hydrocarbon region.

The substances in this group differ in the length and branching of the fluorinated carbon chain. Furthermore, in most of the substances the fluorinated region is perfluorinated but in others some of the carbons are only partially fluorinated. The position of the ether linkage is either between two fluorinated groups or between a fluorinated and a hydrocarbon group.

2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table: Completed or ongoing processes

other processes	**RMOA**	**REACH process**			**Authorisation**		**Restriction**	**h C&L**	**process under other EU legislation**		**previous legislation**		**Stockholm convention**	**other processes EU legislation**
EC entries		CCH	TPE	SEV	candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	PPP	BPR	NONS	RAR	POPs	
435-790-1				yes				yes			Yes			
484-450-7											Yes			
422-270-2											Yes			
484-410-9											Yes			

The Substance Evaluation of HFE-7500 started in 2018.

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

Table: Harmonised classification

Index No	International Chemical Identification	EC No	CAS No	Classification		Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)		
603-224-00-2	3-ethoxy-1,1,1,2,3,4,4,5,5,6,6,6-dodecafluoro-2-(trifluoromethyl)-hexane	435-790-1	297730-93-9	Aquatic Chronic 4	H413	H413	

3.1.2 Self classification

- In the registration the following additional classifications are included:

EC no.	Classification		Spec. Conc. Limits, M-factors
	Hazard Class and Category Code(s)	Hazard statement code(s)	
435-790-1	No additional classifications compared to the harmonised one		
484-450-7	Not classified		
422-270-2	Not classified		
484-410-9	Aquatic Chronic 4	H413	

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:

EC no.	Classification		Spec. Conc. Limits, M-factors
	Hazard Class and Category Code(s)	Hazard statement code(s)	
435-790-1	Skin irrit. 2 Eye Irrit. 2 STOT SE 3	H315 H319 H335 (lungs, inhalation)	-
484-450-7	Not classified		
422-270-2	Aquatic Chronic 4	H413	-
484-410-9	No additional classifications		

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

None.

3.2 Environmental hazard assessment/PBT assessment

Persistence:

Based on available biodegradation screening studies and BIOWIN QSAR predictions the substances are not readily biodegradable, and thus, they all screen for potential P/vP. The four substances have a perfluorinated region to which a methyl or ethyl group is connected via ether linkage. Poly- and perfluorinated organic compounds are known to be highly persistence due to the high stability of carbon fluorine bonds (Siegemund et al. 2000). Therefore, the four HFEs are expected to be very persistent. Possibility of using read across from other poly- and perfluorinated compounds already identified as vP is under assessment regarding the current CoRAP evaluation process of HFE-7500.

Furthermore, based on the available information, the substances are highly volatile based on Henry's Law constants and have long atmospheric half-lives (e.g. Goto et al 2000, Wang et al 2014). Therefore, they have potential for long-range transport.

Table: Overview of ready biodegradability data and read across

EC	Substance name	Readily biodegradable (yes/no)	Based on
435-790-1	HFE-7500	No	*0-1% degradation after 28d (OECD 301D)*
484-450-7	HFE-7000	No	not ready biodegradable (EPISUITE)
422-270-2	HFE-7100	No	*-6-13% degradation after 28d (test material analysis), -7-22% degradation (oxygen consumption) (OECD 301D)*
484-410-9	HFE-7800	No	-

Bioaccumulation

Based on the available BCF value of 5200 in fish measured in a reliable OECD 305 study, HFE-7500 fulfils the criteria for B and vB.

HFE-7800 has a log Kow above 6.5 and hence, it screens for potential B/vB. Further information on its bioaccumulation in aquatic organisms may be needed to conclude.

HFE-7000 and HFE-7100 have log Kow values below 4.5 and log Koa values below 2, and thus, do not fulfil the screening criteria for B/vB for aquatic and air-breathing organisms. However, other perfluorinated substances are known to accumulate in terrestrial organisms through protein binding (e.g. ECHA 2012a, 2012b, 2012c, 2013). Therefore, further information on the potential for bioaccumulation is needed for these substances.

Table: Overview of bioaccumulation data

EC	Substance name	Log Kow	Log Koa	BCF
435-790-1	HFE-7500	6 (shake flask)	1.88 (KOAWIN)	5200 (OECD 305)
484-450-7	HFE-7000	3.53 (HPLC)	1.79 (KOAWIN)	27 (BCFBAF)
422-270-2	HFE-7100	3.53-4.11 (HPLC)	1.63-1.74 (KOAWIN)	37-144 (OECD 305, study disregarded by the registrant due to major methodological deficiencies) 63-160 (BCFBAF)
484-410-9	HFE-7800	> 6.5 (HPLC) 7.51 (KOWWIN)	4.67 (KOAWIN)	7460 (BCFBAF)

Aquatic toxicity

For HFE-7500, no reliable aquatic toxicity data is available. Based on the predicted chronic values for fish and daphnia, the substance could potentially fulfil the criterion for T based on aquatic toxicity.

For HFE-700 and HFE-7800 acute tests with fish, daphnia and algae are reported. No significant effects were observed. However, there is very little information available on the tests and hence their reliability cannot be evaluated. Furthermore, HFE-7800 has a very low solubility, and therefore, chronic testing would be more relevant for the substance.

Based on the available acute data on HFE-7100, the substance seems to have low acute toxicity to aquatic organisms.

Table: Overview of aquatic toxicity data

EC	Substance name	Toxicity acute	Toxicity chronic
435-790-1	HFE-7500	Fish: no reliable data Daphnia: no reliable data Algae: no reliable data	Fish: ChV 0.013 mg/L (ECOSAR) Daphnia: ChV 0.019 mg/L (ECOSAR) Algae: ChV 0.146 mg/L (ECOSAR)
484-450-7	HFE-7000	Fish: 96h LC50 > 1.5 mg/L (guideline not indicated in the dissemination site) Daphnia: 48h EC50 > 1.3 mg/L (OECD 202) 48h EC50 0.74 mg/L (study disregarded by the registrant) Algae: 72h ErC50 > 2.9 mg/L (guideline not indicated in the dissemination site)	Fish: ChV 4.34 mg/L (ECOSAR) Daphnia: ChV 2.89 mg/L (ECOSAR) Algae: 72h NOErC 2.9mg/L (guideline not indicated in the dissemination site)

EC	Substance name	Toxicity acute	Toxicity chronic
422-270-2	HFE-7100	Fish: 96h LC50 > 7.9 mg/L (OECD 203) Daphnia: 48h EC50 > 10.0 mg/L (OECD 202) Algae: 96h ErC50 > 8.9 mg/L (OECD 201)	Fish: ChV 1.817 mg/L (ECOSAR) Daphnia: ChV 1.382 mg/L (ECOSAR) Algae: 96h NOErC 8.9 mg/L (OECD 201)
484-410-9	HFE-7800	Fish: 96h LC50 > 0.032 mg/L (guideline not indicated in the dissemination site) Daphnia: 48h EC50 > 0.024 mg/L (guideline not indicated in the dissemination site) Algae: 72h ErC50 > 0.054 mg/L (guideline not indicated in the dissemination site)	Fish: ChV < 0.001 mg/L(ECOSAR) Daphnia: ChV 0.002 mg/L (ECOSAR) Algae: 72h NOErC 0.054 mg/L (guideline not indicated in the dissemination site) ChV 0.023 mgL (ECOSAR)

3.3 Human Health hazard assessment

Human health data not screened.

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES[1]

4.1 Tonnage and registration status

Table: Tonnage and registration status

from ECHA dissemination site*

EC no.	Substance name	Registration status	Tonnage (t/y)
435-790-1	HFE-7500	Full registration + NONS	0-10 tpa (Full reg.) Confidential (NONS)
484-450-7	HFE-7000	NONS	Confidential
422-270-2	HFE-7100	Full registration + NONS	1+ tpa (Full reg.) Confidential (NONS)
484-410-9	HFE-7800	NONS	Confidential

*the total tonnage band has been calculated by excluding the intermediate uses, for details see the Manual for Dissemination and Confidentiality under REACH Regulation (section 2.6.11):

https://echa.europa.eu/documents/10162/22308542/manual_dissemination_en.pdf/7e0b87c2-2681-4380-8389-cd655569d9f0

4.2 Overview of uses

Based on the registration information HFE-7500 is used as functional fluid (heat transfer fluid) at industrial sites and by professional workers. Article service-life in vehicles and electrical/electronic articles is reported. The substance is mainly used in closed systems but some of the uses take place in more open systems.

For HFE-7000, HFE-7100 and HFE-7800 no public information on uses is included in the ECHA dissemination site. However, similar uses as those of HFE-7500 can be expected.

Hydrofluoroethers (HFEs) are being used as third generation replacements to chlorofluorocarbons (CFCs), hydrochlorofluorocarbons (HCFCs) and perfluorocarbons (PFCs) because of their nearly zero stratospheric ozone depletion and relatively low global warming potential (Tsai, W-T, 2005). However, there are other properties (i.e. high volatility and long atmospheric lifetime) that should also be considered.

HFEs have been developed for commercial and industrial uses as refrigerant, cleaning solvent, foaming agent and dry etching agent (Tsai, W-T, 2005):

- Refrigerants: CFCs were used in domestic refrigerators, freezers and air conditioners. As these substances have been targeted as GHGs in the Kyoto Protocol, HFEs will gradually increase with its more extensive applications because of their lower cost than HFCs.

[1] As of 06 March 2019.

- Cleaning solvent: it is necessary to use HFCs (phase-out under Montreal Protocol) or HFEs as cleaning solvents in the some precision processes or equipment. HFE 7500 among others HFEs could be termed as dense non-aqueous phase liquid (DNAPL), examples of which could include trichloroethylene and perchloroethylene, from a leakage or illegal dumping.
- Blowing agent: According to the thermal conductivity, some HFEs are potential alternatives to the traditional blowing agents (CFCs).
- Dry etching agent (process of removing exposed SiO 2 thin-film in the pattern formed by photoresist exposure and development): used in substitution of PFCs in semiconductor industry.
- Other applications: carrier solvents for coatings, and lubricants or friction-reduction agents on devices such as surgical knife blades

Table: Uses

Part 1:

Substance: EC 435-790-1						
☐ Manufacture	☐ Formulation	☒ Industrial use	☒ Professional use	☐ Consumer use	☒ Article service life	☒ Closed system
Substance: EC 484-450-7 (no information on uses is available at the ECHA dissemination site)						
☐ Manufacture	☐ Formulation	☐ Industrial use	☐ Professional use	☐ Consumer use	☐ Article service life	☐ Closed system
Substance: EC 422-270-2 (no information on uses is available at the ECHA dissemination site)						
☐ Manufacture	☐ Formulation	☐ Industrial use	☐ Professional use	☐ Consumer use	☐ Article service life	☐ Closed system
Substance: EC 484-410-0 (no information on uses is available at the ECHA dissemination site)						
☐ Manufacture	☐ Formulation	☐ Industrial use	☐ Professional use	☐ Consumer use	☐ Article service life	☐ Closed system

Part 2:

Substance1: EC 435-790-1 (HFE-7500)

	Use(s)	Technical function
Uses as intermediate		
Formulation		
Uses at industrial sites	Functional fluid at industrial site	
Uses by professional workers	Widespread use of functional fluid (indoor and outdoor)	
Consumer Uses		
Article service life	Widespread use of articles* with low release (indoor and outdoor)	Refrigerants, cleaning solvents, blowing agents

*****Article Category: vehicles covered by End of Life Vehicles (ELV) directive, machinery, mechanical appliances, electrical/electronic articles covered by the Waste Electrical and Electronic Equipment (WEEE) directive

Substance 2: EC 484-450-7 (HFE-7000). no information on use(s) nor technical function is available at the ECHA dissemination site. Tsai (2005) indicates cleaning solvent as a probable use.

Substance 3: EC 422-270-2 (HFE-7100). no information on use(s) nor technical function is available at the ECHA dissemination site. Tsai (2005) indicates cleaning solvent as a probable use.

Substance 4: EC 484-410-9 (HFE-7800). no information on use(s) nor technical function is available at the ECHA dissemination site.

Part 3: The potential for exposure is high for

Substance name	Humans	Environment
HFE-7500 (EC 435-790-1)	☐	☐
HFE-7100 (EC 422-270-2)	☐	☐
HFE-7800 (EC 484-410-9)	☐	☐
HFE-7000 (EC 484-450-7)	☐	☐

5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE OR GROUP

5.1. Legal basis for the proposal

☐ Article 44(2) (refined prioritisation criteria for substance evaluation)

☒ Article 45(5) (Member State priority)

5.2. Selection criteria met (why the substance or group qualifies for being in CoRAP)

☐ Fulfils criteria as CMR/ Suspected CMR

☐ Fulfils criteria as Sensitiser/ Suspected sensitiser

☐ Fulfils criteria as potential endocrine disrupter

☒ Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB

☐ Fulfils criteria high (aggregated) tonnage (*tpa > 1000*)

☒ Fulfils exposure criteria

☐ Fulfils MS's (national) priorities

5.3 Initial grounds for concern to be clarified under Substance Evaluation

Hazard based concerns		
CMR ☐ C ☐ M ☐ R	Suspected CMR[1] ☐ C ☐ M ☐ R	☐ Potential endocrine disruptor
☐ Sensitiser	☐ Suspected Sensitiser[2]	
☐ PBT/vPvB	☒ Suspected PBT/vPvB[1]	☐ Other (please specify):
Exposure/risk based concerns		
☐ Wide dispersive use	☐ Consumer use	☐ Exposure of sensitive populations
☐ Exposure of environment	☐ Exposure of workers	☐ Cumulative exposure
☐ High RCR	☐ High (aggregated) tonnage	☐ Other (please specify below)

[2] CMR/Sensitiser: known carcinogenic and/or mutagenic and/or reprotoxic properties/known sensitising properties (according to CLP harmonized or registrant self-classification or CLP Inventory)
Suspected CMR/Suspected sensitiser: suspected carcinogenic and/or mutagenic and/or reprotoxic properties/suspected sensitising properties (not classified according to CLP harmonized or registrant self-classification)
Suspected PBT: Potentially Persistent, Bioaccumulative and Toxic

The SEv of HFE-7500 is ongoing by the ES MSCA based on initial concern on suspected PBT/vPvB properties. The other registered HFEs are very similar to HFE-7500 and are expected to have similar environmental fate and effects or follow a predictable pattern. Therefore, evaluation of the substances considering the whole group is expected to lead to a more time- and cost effective assessment. In addition, it may reduce the need for animal testing.

HFEs belong to the wider group of per- and polyfluorinated substances (PFAS), and therefore could be included in the EU Strategy on per- and polyfluorinated substances which is currently under special consideration in the EU (CARACAL – Competent Authorities' Session - 12 June 2018).

PBT/vPvB concern:

Based on the biodegradation screening tests, QSAR models and molecular structures containing perfluorinated fragments, the four registered HFEs are expected to be very persistent. Possibility to use read across from other perfluorinated substances in the persistence assessment will be explored under the current CoRAP process. If it is not possible to firmly conclude on vP based on the available information, further information on degradation may be needed.

Based on the available data, HFE-7500 fulfils the criteria for B and vB.

Based on the measured log Kow above 6.5, HFE-7800 screens for B/vB. The remaining two substances have log Kow values below 4.5 but there is a concern on potential bioaccumulation via protein binding. Bioaccumulation potential in air-breathing organisms of HFEs cannot currently be reliably estimated due to lack of experimental data and lack of understanding of the influence of protein binding on bioaccumulation.

In conclusion, further information/assessment on the bioaccumulation of HFE-7800, HFE-7000 and HFE-7100 is needed.

There is no chronic toxicity data on aquatic organisms and hence based on the available information it is not possible to conclude whether the substances fulfil the criterion for T_{eco}. Further information on aquatic toxicity may be needed.

Other environmental concerns:

Based on the available data on water solubility and log Koc values, some HFEs, especially the ones with shorter fluorinated carbon chain, e.g. HFE-7000 and HFE-7100, may have high mobility in the environment. On the other hand, HFEs have high volatility and long atmospheric half-lives, and thus, they may be subject to long-range transport via air. These environmental fate and distribution properties together with the expected high persistence can be considered a concern, and further information and/or evaluation is needed to remove or confirm the concerns.

5.4 Indication of information that may need to be requested to clarifyfy the concern

☐ Information on toxicological properties	☐ Information on physico-chemical properties
☒ Information on fate and behaviour	☒ Information on exposure
☒ Information on ecotoxicological properties	☒ Information on uses

☐ Information on ED potential	☐ Other (provide further details below)
Further information on degradation, bioaccumulation and aquatic toxicity of HFEs may be needed to conclude on the suspected PBT/vPvB concern and/or potential other concerns related to high persistence and high mobility. Possibility to read across and grouping with other poly- and perfluorinated substances will be assessed. Further information on uses and exposure may also be needed to assess the concern on potential wide dispersive uses.	

5.5 Potential follow-up and link to risk management

☐ Harmonised C&L	☒ Restriction	☒ Authorisation	☐ Other (provide further details)
If the PBT/vPvB concern is confirmed for some or all of the substances, a risk management options analysis shall be carried out. If PBT/vPvB concern is not confirmed, the possibility to identify some of the substances as SVHCs on the basis of Art. 57f criteria will be assessed. Potential follow-up options are authorisation and/or restriction.			

REFERENCES

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