Justification Document for the Selection of a CoRAP Substance

Substance Name (public name):	Diethyl Ether
EC Number:	200-467-2
CAS Number:	60-29-7
Authority:	France
Date:	21/03/2017

Cover Note

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

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1 IDENTITY OF THE SUBSTANCE

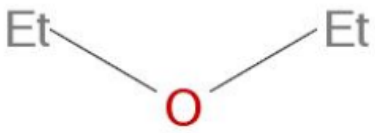
1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	diethyl ether
IUPAC name (public):	1,1'-oxydiethane
Index number in Annex VI of the CLP Regulation:	603-022-00-4
Molecular formula:	C4H10O
Molecular weight or molecular weight range:	74.1216
Synonyms:	1,1'-oxydiethane 1,1-oxydiethane DIETHYL ETHER Diethyl Ether Anhydrous (stabilized with BHT) Diethylether ETHANE,1,1'-OXYBIS- ether ethoxy-ethane Ethoxyethane Ethylenzene éter dietílico

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

Structural formula:



1.2 Similar substances/grouping possibilities

Structural formula:

Chemical name	Diethyl ether (DEE)	Diisopropylether (DIPE)	Dimethylether (DME)
	Target chemical	Read across	Read across
CAS no	60-29-7	108-20-3	115-10-6
EC no	200-467-2	203-560-6	204-065-8

Read across substance:

EC number:	203-560-6
EC name (public):	Diisopropylether
CAS number:	108-20-3
CAS name (public):	
IUPAC name (public):	2,2'-oxydipropane
Index number in Annex VI of the CLP Regulation:	603-045-00-X
Molecular formula:	C6H14O
Molecular weight or molecular weight range:	102.18
Synonyms:	diisopropyl ether 2,2'-Oxy-bis-propane 2,2'-oxydipropane 2-isopropoxypropane 2-propan-2-yloxypropane Di-isopropyl ether Diisopropyl ether Diisopropylether Isopropyl ether Isopropyl Ether (stabilized with HQ) Propane, 2,2'-oxybis-

Read across substance:

EC number:	204-065-8
EC name (public):	Dimethylether
CAS number:	115-10-6
CAS name (public):	
IUPAC name (public):	dimethyl ether
Index number in Annex VI of the CLP Regulation:	603-019-00-8
Molecular formula:	C2H6O
Molecular weight or molecular weight range:	46.07
Synonyms:	

2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table: Completed or ongoing processes

RMOA	☐ Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	☐ Compliance check, Final decision
		☒ Testing proposal
		☐ CoRAP and Substance Evaluation
	Authorisation	☐ Candidate List
		☐ Annex XIV
	Restri -ction	☐ Annex XVII
Harmonised C&L	☐ Annex VI (CLP) (see section 3.1)	

Processes under other EU legislation	☐ Plant Protection Products Regulation Regulation (EC) No 1107/2009
	☐ Biocidal Product Regulation Regulation (EU) 528/2012 and amendments
Previous legislation	☐ Dangerous substances Directive Directive 67/548/EEC (NONS)
	☐ Existing Substances Regulation Regulation 793/93/EEC (RAR/RRS)
(UNEP) Stockholm convention (POPs Protocol)	☐ Assessment
	☐ In relevant Annex
Other processes / EU legislation	☒ Other (provide further details below)
Medicinal product legislations: Diethyl ether is used as a medicinal active substance.	

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)		
603-022-00-4	diethyl ether ether	200-467-2	60-29-7	Flam. Liq. 1	H224		
				Acute Tox. 4 *	H302		
				STOT SE 3	H336		

3.1.2 Self classification

- In the registration: substance is listed in Annex VI to regulation (EC) No 1272/2008 under Index-No 603-022-00-4. No deviation.

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

  Eye Irrit. 2 (H319)
  Carc. 2 (H351)
  Skin irrit. 2 (H315)

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

None

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

4.1 Tonnage and registration status

Table: Tonnage and registration status

From ECHA dissemination site		
☒ Full registration(s) (Art. 10)	☐ Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per dissemination site)		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☐ 100 – 1000 tpa
☒ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	☐ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential
One joint submission		

4.2 Overview of uses

This substance is used in the following products: fuels, laboratory chemicals, explosives and extraction agents. This substance has an industrial use resulting in manufacture of another substance (use of intermediates).

This substance is manufactured and/or imported in the European Economic Area in 1 000 - 10 000 tonnes per year.

Table: Uses

Part 1:

☒ Manufacture	☒ Formulation	☒ Industrial use	☒ Professional use	☒ Consumer use	☐ Article service life	☐ Closed system

[1] *Dissemination site was accessed in April 2016.*

Part 2:

	Use(s)
Uses as intermediate	
Formulation	Fuels
Uses at industrial sites	Manufacture or use as reaction or extraction solvent (laboratory chemicals, extraction agents, fuels) Laboratory chemicals
Uses by professional workers	Manufacture of smokeless gunpowder (explosives) Laboratory chemicals Using material as fuel sources, limited exposure to unburned product to be expected
Consumer Uses	Use as fuel by consumers
Article service life	

Part 3: There is high potential for exposure of

☒ Humans	☒ Environment

5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

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 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 below)
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

Since the lead registrant does not provide any data for skin irritation/corrosion in the registration dossier whereas some data on this endpoint are available on ECHA website it appears that a CCh is needed prior to evaluation of the substance.

A read across with DIPE and DME is used by the registrants except for carcinogenicity. The read-across seems justified since they all belong to the category of aliphatic esters and are considered to be members of a homologous series of aliphatic ethers. Properties of DEE are expected to lie between those of the smaller DME and the larger DIPE (supported by their known physicochemical properties). However a study by Belpoggi *et al.* (2002) on DIPE showed an increase of hemolymphoreticular neoplasia in males and females of tests groups (two doses + one control).

Additionally, as acetaldehyde, one of the main metabolite of diethylether, has a harmonized classification proposal under examination at this time as a carcinogen and mutagen, these concerns needs to be further investigated for DEE also since data for the substance are limited or show equivocal results.

Concerning reprotoxicity, the substance was reported to decrease fertility and induce foetotoxicity at high concentrations. A TPE for DEE is still under examination, which could clarify the concern for reprotoxicity. If not, this concern may remain for the evaluation of the substance.

Therefore the potential for carcinogenicity, mutagenicity and reprotoxicity of diethyl ether should be further evaluated.

Additionally since the substance is among other uses used in fuels there is a wide dispersive use of the substance, a potential environamental release and an exposure of the consumers to this substance which overall represent a concern related to the exposure to this substance.

5.4 Preliminary indication of information that may need to be requested to clarify 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)
Several concerns were identified for the DEE especially carcinogenicity which need to be clarified under a substance evaluation procedure.	

5.5 Potential follow-up and link to risk management

☒ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)
After reviewing the data available, eMSCA believes that DEE classification for eye irritant should be envisaged by registrant or further elaborated (3 *in vivo* studies with methodological limitations show irritation, one *in vitro* and one *in vivo* exhibit eye irritation). Despite the fact that this endpoint is not a priority endpoint for CLH. After clarifying the concerns for carcinogenicity and reprotoxicity they may also lead to a CLH proposal.			