Justification Document for the Selection of a CoRAP Substance

Substance Name (Public Name):	Oxydiethylene dinitrate
Chemical Group:	Organic
EC Number:	211-745-8
CAS Number:	693-21-0
Submitted by:	Italian MSCA
Date:	22/03/2016

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):	Oxydiethylene dinitrate
IUPAC name (public):	oxydiethane-2,1-diyl dinitrate
Index number in Annex VI of the CLP Regulation:	603-033-00-4 603-033-01-1 [>25 % Phlegmatiser]
Molecular formula:	$C_4H_8N_2O_7$
Molecular weight or molecular weight range:	196.1155
Synonyms:	*DEGN*

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

Structural formula:

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[1]
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	

[1] Entry no 59.

Other processes / EU legislation	☒ Other (provide further details below)

Other processes/EU legislation: Substance is included to the Annex III: LIST OF SUBSTANCES WHICH COSMETIC PRODUCTS MUST NOT CONTAIN EXCEPT SUBJECT TO THE RESTRICTIONS LAID DOWN (reference no 7) of the Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products.

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

1. **Oxydiethylendinitrate, diethylene glycol dinitrate, digol dinitrate**

Index number: 603-033-00-4

CLP criteria:

Unst. Expl; H200: Unstable explosives.
Acute Tox. 2; H330: Fatal if inhaled.
Acute Tox. 1; H310: Fatal in contact with skin.
Acute Tox. 2; H300: Fatal if swallowed.
STOT RE 2; H373: May cause damage to organs through prolonged or repeated exposure.
Aquatic Chronic 3; H412: Harmful to aquatic life with long lasting effects.

DSD criteria:

E; R3: Extreme risk of explosion by shock, friction, fire or other sources of ignition.
T+; R26/27/28: Very toxic by inhalation, in contact with skin and if swallowed.
R33: Danger of cumulative effects.
R52-53: Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

2. **Oxydiethylene dinitrate, diethylene glycol dinitrate, digol dinitrate [>25 % phlegmatiser]**

Index number: 603-033-01-1

CLP criteria:

Expl. 1.1; H201: Explosive; mass explosion hazard.
Acute Tox. 2; H330: Fatal if inhaled.
Acute Tox. 1; H310: Fatal in contact with skin.
Acute Tox. 2; H300: Fatal if swallowed.
STOT RE 2; H373: May cause damage to organs through prolonged or repeated exposure.
Aquatic Chronic 3; H412: Harmful to aquatic life with long lasting effects.

DSD criteria:

n/a

3.1.2 Self classification

- In the registration

  No deviation from section 2.1.

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

  No deviation from section 2.1.

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

n/a

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES[2]

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
There is an individual and a joint submission.		

4.2 Overview of uses

Table: Uses

Part 1:

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

Industrial use:

- Use Propellants with DEGDN as plasticizer

PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing)
ERC 5: Industrial use resulting in inclusion into or onto a matrix

[2] *The ECHA dissemination site was accessed 19.05.2015.*

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[3] ☒ C ☐ M ☒ R	☒ Potential endocrine disruptor
☐ Sensitiser	☐ Suspected Sensitiser[3]	
☐ PBT/vPvB	☒ Suspected PBT/vPvB[3]	☐ 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)

[3] 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 registration dossier contained chronic toxicity study using read across substance that was administered to rats by feeding. The study was conducted equivalent or similar to the OECD 452 with reliability 2 and not GLP compliant.

- The result indicated the incidence of neoplastic changes at the highest dose group in males (363 mg/kg/day) and females (434 mg/kg/day). These were hepatocellular carcinoma and cholangiofibrosis in the liver, and cell tumors in the testis (pressure on the tubules, aspermatogeneis).

The registration dossier contained reproductive toxicity study with reliability 2 and not GLP compliant. The study was conducted using read across substance in rats and equivalent or similar to OECD 416, USFDA guidelines (1966).

- The result indicated severe aspermatogenesis (408 mg / kg / day), mild-moderate increases in the amounts of interstitial tissue in testes in the F2a generation that resulted sever infertility in the F2a generation, and all litter parameters except male / female ratios were reduced in the high dose F1a litters (452 mg / kg / day).
- All litter parameters except male / female ratios were reduced in the high dose (452 mg TNG / kg / day) F1a litters.
- The food intake of the F1b dams was ~65 % that of the corresponding control dams. Their gestational product (litter size x litter weight) was ~62 % that of those control dams.

Being the effects of the reproductive toxicity study on spermatogenesis and in testes, the endocrine disruption properties should be investigated to better understanding the mode of action.

The registration dossier contained developmental toxicity study using read across substance in rats. The study was conducted equivalent or similar to the FDA guideline (1966) with reliability 2 and no GLP compliant.

- The result indicated the incidence of unossified and incompletely ossified hyoid bones at the highest dose group 59.3 mg/kg/day that was increased compared to the low 0.9 mg/kg/day and mid dose group 6.4 mg/kg/day and significantly increased compared to the control group.

The RCR for

- PROC 8b is close to 1 via inhalation exposure and above 1 via dermal exposure.
- PROC 3 is close to 1 via inhalation exposure and also the combined RCR is close to 1.

Therefore, the potential risk of the registered substance for carcinogenicity, reproductive toxicity, and exposure concern can be investigated under substance evaluation.

Suspected PBT properties:

Although estimated aquatic BCF is 3.16 L/kg (EPIWIN), the estimated (KOAWIN) Log K_{OA} is 5.78, this value has to be further clarified to assess bioaccumulation potential in air-breathing organisms. Read-across based on study for Nitroglycerin has been used in the documentation of persistency, $DT_{50(water)}$ > 1 year.

Therefore, within the SEv process, PBT concern should be further clarified.

5.4 Preliminary indication of information that may need to be requested t 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 ED potential	☐ Other (provide further details below)
Depends on the outcome of evaluation	

5.5 Potential follow-up and link to risk management

☐ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)
Depends on the outcome of evaluation			