Justification Document for the Selection of a CoRAP Substance

Substance Name (public name): dichloromethane

EC Number: 200-838-9

CAS Number: 75-09-2

Authority: 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

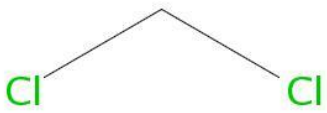
1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	dichloromethane
IUPAC name (public):	dichloromethane
Index number in Annex VI of the CLP Regulation:	602-004-00-3
Molecular formula:	CH_2Cl_2
Molecular weight or molecular weight range:	84.9
Synonyms:	-

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

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)		
602-004-00-3	**dichloromethane; methylene chloride**	200-838-9	75-09-2	**Carc. 2**	**H351: Suspected of causing cancer.**	-	

3.1.2 Self classification

- In the registration:

  Joint submission:

  Skin Irrit. 2, H315: Causes skin irritation.

  Eye Irrit. 2, H319: Causes serious eye irritation.

  Carc. 2, H351: Suspected of causing cancer <state route of exposure if it is conclusively proven that no other routs of exposure cause the hazard>. Route of exposure: Inhalation.

  STOT Single Exp. 3, H336: May cause drowsiness or dizziness. Affected organs: central nervous system. Route of exposure: Inhalation.

  Individual submission:

  No deviations from the harmonised classification.

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

  Ox. Liq. 1, H271

  Ox. Gas 1, H270

  Ox. Sol. 1, H271

  Met. Corr. 1, H290

Ozone 1, EUH059
Expl. 1.1, H200
Flam. Gas 1, H220
Flam. Aerosol 1, H222
Flam. Liq. 1, H224
Flam. Sol. 1, H228
Org. Perox. A, H240
Self-react. A, H241
Water-react. 1, H260
Self-heat. 1, H251
Pyr. Sol. 1, H250
Pyr. Liq. 1, H250
Press. Gas., H280
Acute Tox. 1, H300
Acute Tox. 1, H310
Acute Tox. 1, H330
Acute Tox. 4, H302
Eye Dam. 1, H318
Skin Corr. 1A, H314
Eye Irrit. 2B, H320
Skin Sens. 1, H317
Resp. Sens. 1, H334
Asp. Tox. 1, H304
Carc. 2, H350 (Inhalation)
Carc. 2, H351 (Oral)
Carc. 2, H351 (Inhalation)
Muta. 1A, H340 (Oral)
Muta. 2, H341
Repr. 1A, H360 (Oral) (test)
Lact., H362
STOT SE 1, H370 (CNS/Nervous system...)
STOT SE 1, H370 (test) (Oral)
STOT RE 1, H372 (test/Central nervous...) (Oral)
STOT RE 2, H373 (not specified/not provided)
STOT RE 2, H373 (Blood, skin and...)
STOT RE 2, H373 (CNS, blood, liv...) (Inhalation, Ora...)
STOT RE 2, H373 (S.N.C., liver -...) (Inhalation, Ora...)
STOT RE 2, H373 (liver, blood) (Oral)

STOT SE 3, H335 (not specified/not available)

STOT SE 3, H335 (Blood, skin and...)

STOT SE 3, H335 (respiratory tra/respiratory sys...) (Inhalation)

STOT SE 3, H335 (lung) (Inhalation)

STOT SE 3, H336 (brain) (Inhalation)

STOT SE 3, H336 (not available/unknown/not provided)

STOT SE 3, H336 (Affected Organs)

STOT SE 3, H336 (Narcotic effect...)

STOT SE 3, H336 (central nervous system…) (Inhalation)

Aquatic Acute 2, H401

Aquatic Chronic 1

Aquatic Chronic 2, H411

Aquatic Chronic 3, H412

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

Not applicable.

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

[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)
The OECD Guideline 416 (Two-Generation Reproduction Toxicity Study) study (Nitschke KD et al., 1988) has been provided concluding that at concentrations as high as 1500 ppm (ca. 5300		

[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

mg/m^3) dichloromethane did not affect any of the reproductive parameters examined. However, the study does not cover several important parameters, such as organ weights, sperm parameters, estrous cyclicity, implantation sites and histopathology.

Additionally, in a supporting study for carcinogenicity endpoint (Disseminated study report, 1986) it was found that during a two-week exposure period at 3500 ppm, dichloromethane caused a statistically significant ($p<0.05$) increase in the length of the oestrus cycle and elevated serum prolactin concentrations in femal e Sprague-Dawley rats.

Therefore due to the lack of important parameters for reproductive toxicity and the possible effect of the substance to the oestrus cycle the toxicity of dichloromethane to reproduction is not clear and should be further clarified during substance evaluation.

In a developmental toxicity study (Schwetz BA et al., 1975) similar to OECD Guideline 414 examining the effects of maternally inhaled methylene chloride on embryonal and fetal development in rats and mice, foetal skeletal variations were observed which may have been caused by hypoxia as increased carboxyhaemoglobin levels were seen in the dams and hypoxia is known to affect the developing foetus. As a result the level of 4300 mg/m^3 (ca. 1250 ppm) was established to be a LOAEC for developmental toxicity (mild foetotoxicity) and for slight maternal toxicity. However, it should be noted, that LOAEC value in this study does not correlate with the findings in the reprotoxicity study (2-gen).

Dichloromethane is thought to readily transfer across the blood-brain barrier by passive diffusion, as evidenced by the detection of radioactivity in brain tissue 48 hours after exposures of rats to radiolabeled dichloromethane at concentrations of 50, 500, or 1500 ppm for 6 hours (McKenna et al., 1982). It can be transferred across the placenta, and small amounts can be excreted in urine or in milk. Historically it is demonstrated that dichloromethane has transient sedative and anesthetic properties in humans (Mattsson et al. (1990)).Due to this it is not possible to conclude that the skeletal variations were caused by hypoxia and maternal toxicity. Therefore possible developmental toxicity of the substance can not be excluded.

Dichloromethane was found to be genotoxic *in vitro*. A reliable *in vivo* study conducted according to OECD Guideline 474 is available and showed negative results for mutagenicity. There are no reliable studies that would examine DNA breakages based on which it would be possible to conclude on the genotoxic properties of the substance. However, in the endpoint summary for genetic toxicity it is mentioned that DNA damage was detected in the liver and lung using the alkaline single cell gel electrophoresis (SCG) assay.

Additionally classifications as Muta. 1A and 2 have been notified in the C&L inventory.

There was some evidence of carcinogenicity of dichloromethane for male F344/N rats and clear evidence of carcinogenicity of dichloromethane for female F344/N rats as shown by increased incidences of benign neoplasms of the mammary gland (Mennear JH et al., 1988). Additionally, marginally increased incidences in exposed groups of rats included adrenal gland pheochromocytomas and interstitial cell tumors of the testis in males and pituitary gland adenomas/carcinomas in both sexes. However these effects were not dose-related and incidences were not considered compound related. Tumors´ types show a possible relationship with disturbed endocrine function and raise the possibility of a hormonal mechanism.

There is a single case referred in the dossier(s) that dichloromethane may have produced asthma or reactive airways dysfunction syndrome in a worker (Sallie, B. et al., 1996). However the Registrant(s) has concluded that in view of the solvent's extensive, widespread and long-standing use, and the scarcity of published evidence in the area of skin or respiratory sensitization indicates that dichloromethane does not possess any significant sensitising potential.

Based on the above mentioned substance may have respiratory sensitising properties, that should be clarified durng the substance evaluation.

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)

Additional epidemiological or test data regarding the respiratory sensitisation could be considered necessary to clarify the concern.
Reproductive and developmental toxicity study(s) could be considered to clarify the concern.
For the mutagenicity endpoint data for *in vivo* genotoxicity is needed to conclude on the genotoxic properties of the substance that could lead to revision of the classification.
The above only reflects the most probable information to be requested to clarify the suspected concerns, other options are however still open.

5.5 Potential follow-up and link to risk management

☒ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)

Revision of the harmonised classification and labelling could be triggered following SEv.