LATVIJAS VIDES, ĢEOLOĢIJAS UN METEOROLOĢIJAS CENTRS

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Ethylene Carbonate

EC No 202-510-0

CAS No 96-49-1

Evaluating Member State(s): Latvia

Dated: 15.08.2019

Template Version 2.1
March 2015

Evaluating Member State Competent Authority

Latvian Environment, Geology and Meteorology Centre
Maskavas iela 165
Rīga, LV-1019, Latvia
Tel: +371 67032600
Fax: +371 67145154
Email: lvgmc@lvgmc.lv

Year of evaluation in CoRAP: 2018

Member State concluded the evaluation without any further need to ask more information from the registrants under Article 46(1) decision.

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

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Ethylene Carbonate was originally selected for substance evaluation in order to clarify concerns about:

- Suspected CMR/reprotoxic properties

- Exposure/Wide dispersive use (workers, professional and industrial users), high tonnage.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Compliance check (CCH) final decisions (Decision number: CCH-D-2114290256-46-01/F; CCH-D-2114290254-40-01/F; CCH-D-2114290253-52-01/F). Information available here: https://echa.europa.eu/information-on-chemicals/dossier-evaluation-status/-/dislist/substance/100.002.283

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

4. FOLLOW-UP AT EU LEVEL

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

Not applicable.

4.1.1. Harmonised Classification and Labelling

Not applicable.

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

Not applicable.

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

Table 2

REASON FOR REMOVED CONCERN The concern could be removed because	Tick box
Clarification of hazard properties/exposure	X
Actions by the registrants to ensure safety, as reflected in the registration dossiers (e.g. change in supported uses, applied risk management measures, etc.)	

Taking into account the new information in the updated registration dossier and additional clarifications provided by the Registrant, the evaluating Member State was able to conclude on every concerned endpoint and found no potential, inadequately controlled risks. Hence, the evaluating Member State concludes that the initial concerns can be removed and there is no need for follow-up action at EU level.

5.2. Other actions

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Not applicable.

Part B. Substance evaluation

7. EVALUATION REPORT

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to exposure to workers, professional and industrial users and possible CMR/reprotoxic properties ethylene carbonate, CAS No 96-49-1 (No 202-510-0) was included in the Community rolling action plan (CoRAP) for substance evaluation according to Article 44(2) of the REACH Regulation to be evaluated in 2018. The CoRAP was published on the ECHA website on 20 March 2018. The Competent Authority of Latvia initiated the substance evaluation for ethylene carbonate.

7.1. Overview of the substance evaluation performed

Ethylene Carbonate was originally selected for substance evaluation in order to clarify concerns about:

- Suspected CMR/reprotoxic properties

- Exposure/Wide dispersive use (workers, professional and industrial users), high tonnage.

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
CMR/reprotoxic properties	Concern not substantiated. No further action.
Exposure assessment and risk characterisation for workers, professional and industrial users	Acceptable. No further action.

7.2. Procedure

Pursuant to Article 44(2) of the REACH Regulation, Ethylene Carbonate was included on the Community rolling action plan (CoRAP) for evaluation in 2018. The Competent Authority of Latvia (eMSCA) was appointed to carry out the evaluation.

The evaluation was based on the information provided in the registrations dossiers.

The evaluation of Ethylene Carbonate was targeted at human health endpoints and focused on the initial grounds for concern for the inclusion of the substance in the CoRAP. Environmental hazard endpoints were not examined. During the process, fluent communication was established between the eMSCA and the Lead registrant

Following evaluation of the available information the eMSCA considered that no new information needs to be requested under this substance evaluation to clarify the concerns and concluded substance evaluation process.

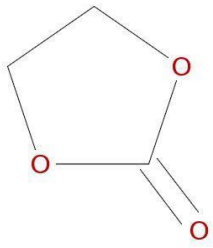
7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	Ethylene carbonate
EC number:	202-510-0
CAS number:	96-49-1
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	C3H4O3
Molecular weight range:	88.06
Synonyms:	Ethylene carbonate

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

Structural formula:



7.4. Physico-chemical properties

Table 5

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Solid, Colorless low-melting solid.
Melting/freezing point	36°C at 101 325 Pa Weight of evidence approach based on 3 peer-reviewed values from handbooks.
Boiling point	247°C at 101 325 Pa Weight of evidence approach based on 3 peer-reviewed values from handbooks.
Density	1.32 g/cm^3 at 40 °C Weight of evidence approach based on 3 peer-reviewed values from handbooks.
Vapour pressure	1 Pa at 20°C Weight of evidence approach based on 3 peer-reviewed values from handbooks and 2 estimated values using calculation methods (US EPA EPI Suite software).
Water solubility	0.778 mg/L at 20°C Experimental data according to EU test method A.6 using flask method (Registration dossier, study report, 2010)
Partition coefficient n-octanol/water (Log Kow)	0.11 at 20°C Data is calculated based on EU test method A.8, using the shake flask method (Registration dossier, study report, 2010)
Flammability	Non flammable Experimental data according to EU test methods A.10, A.12 and A.13 (Registration dossier, study report, 2010).
Explosive properties	Non explosive In accordance with column 2 of REACH Annex VII, the study is not required, no chemical groups associated with explosive properties present in molecule.
Oxidising properties	Non oxidising

	In accordance wit column 2 of REACH Annex VII, the study is not required, on the basis on chemicals structure: no halogen atoms chemically bonded to oxygen or nitrogen.
Granulometry	In accordance with column 2 of REACH Annex VII, the study is not required: the substance is marketed or used in a non solid or granular form.
Stability in organic solvents and identity of relevant degradation products	In accordance with column 1 of REACH Annex IX, the study is not required, as the stability of the substance is not considered to be critical.
Dissociation constant	3.86 pKa at 20°C According to guideline OECD 112 using the titration method (Registration dossier, study report, 2010).

7.5. Manufacture and uses

7.5.1. Quantities

Table 6

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

7.5.2. Overview of uses

Table 7

USES	Use(s)
Uses as intermediate	01 – Manufacture of Substance
Formulation	02 – Formulation & (Re)packing of Substances and Mixtures
Uses at industrial sites	03a - Uses in Coatings: Industrial 04a – Uses in Cleaning Agents: Industrial 05a – Uses in laboratories: Industrial 06a – Polymer processing: Industrial 07a – Uses as processing aid: Industrial 08a – Uses as functional fluids: Industrial 09a – Uses as lubricant: Industrial 10a – Manufacturing of enamel: Industrial 11a – Uses in electrical wire enamelling: Industrial
Uses by professional workers	04b - Uses in Cleaning Agents: Professional 12a – Uses in agrochemicals: Professional 05b – Uses in laboratories: Professional 06b – Polymer processing: Professional 07b – Uses as processing aid: Professional

	08b – Uses as functional fluids: Professional 09b – Uses as lubricant: Professional
Consumer uses	13a – waterborne latex wall paint 14a - remover

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

No harmonised classification.

7.6.2. Self-classification

- In the registration(s)*:*

Eye Irrit. 2; H319: Causes serious eye irritation
Acute Tox.4; H302: Harmful if swallowed
STOT RE 2; H373: May cause damage to organs (Kidney, oral)

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

Eye Dam. 1; H318: Causes serious eye damage
STOT SE 3; H335: May cause respiratory irritation
Skin Irrit. 2; H315: Causes skin irritation

7.7. Environmental fate properties

Not evaluated.

7.8. Environmental hazard assessment

Not evaluated.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

The substance is absorbed easily by oral and inhalation routes taking into account that the ethylene carbonate is water- soluble and represents a small molecule. Following, it will readily dissolve into the gastrointestinal fluid and blood. When the substance is airborne, a high amount will be absorbed by inhalation. An oral absorption of 50 % is assumed as well as 100% respiratory absorption is proposed as a worst case.

Based on its high water solubility, dermal uptake is expected to be moderate to high as the substance will easily dissolve into the surface moisture of the skin. The dermal uptake is favoured by molecule size and a low vapour pressure of the substance. Dermal absorption of 50% is assumed.

Wide distribution throughout the body is expected as the substance is relatively small and water-soluble. Ethylene carbonate follows the metabolic pathway where cyclic organic carbonates are metabolized to their respective glycols and CO_2.The ethylene carbonate is primarily excreted via exhalation as CO_2 (57%), to a lower amount via the urine (27%) and only marginally via feces (2%). The half-life of ethylene carbonate is estimated to be 0.25 h or lower, and no bioaccumulation is expected.

It can be assumed that the metabolite of ethylene carbonate - ethylene glycol has similar toxicokinetic profile taking into account size and structural similarities of both molecules. Based on the available information, the eMSCA can support these conclusions.

7.9.2. Acute toxicity and Corrosion/Irritation

The substance is not acute toxic by dermal and inhalation routes.

As regards the oral toxicity, it is indicated that the ethylene glycol, the main metabolite of ethylene carbonate is classified for acute toxicity category 4, H302 (harmful if swallowed) according to the Annex VI of EC 1272/2008. Based on these considerations, ethylene carbonate should also be classified for acute oral toxicity category 4.

The substance is not a skin irritant, but it shall be classified as an eye irritant category 2, H319 (causes serious eye irritation) according to criteria of EC 1272/2008, and based on the available information, the eMSCA can support this conclusion. No relevant information is available concerning respiratory system.

7.9.3. Sensitisation

Ethylene carbonate should not be classified as a skin sensitiser, and based on the available information, the eMSCA can support this conclusion. No data are available to decide on the classification for respiratory sensitisation.

7.9.4. Repeated dose toxicity

It is concluded that the ethylene carbonate should be classified as STOT RE Category 2, H373 (kidney) substance according to the CLP regulation. This conclusion is based on read-across data from its metabolite ethylene glycol used for the risk characterization of ethylene carbonate. Relevance to human health is substantiated, and based on the available information, the eMSCA can support this conclusion.

7.9.5. Mutagenicity

Three in vitro key studies on mutagenicity are submitted by the registrants:

- bacterial reverse mutation assay with S. typhimurium TA 1535, TA 1537, TA 98 and TA 100 as well as with E. coli WP2 uvr A with and without metabolic activation performed according to OECD Guideline 471 (Registration dossier, study report, 2016) (reliability 1). Dose levels between 50 and 5000 µg/plate of ethylene carbonate have been tested, and a number of positive controls with sodium azide. were applied. No cytotoxicity and no genotoxicity were observed.
- mammalian chromosome aberration test with Chinese hamster lung fibroblasts (V79) with and without metabolic activation performed according to OECD Guideline 473 (Registration dossier, study report, 2000) (reliability 2). Dose levels between 27.8 and 890.0 µg/mL of ethylene carbonate have been tested, and positive controls with ethylmethanesulphonate and cyclophosphamide applied. No cytotoxicity and no genotoxicity were observed.
- mammalian cell gene mutation assay with mouse lymphoma L5178Y cells with and without metabolic activation performed according to OECD Guideline 476 (Registration dossier, study report, 2000)(reliability 1). Dose levels between 55.6, and 890.0 µg/mL of ethylene carbonate have been tested, and a positive control with methylmethanesulphonate is applied. No genotoxicity was observed. Cytotoxicity indicated at the maximal concentration tested (890.0 µg/mL).

In addition, three supportive bacterial reverse mutation assays with S. typhimurium (with reliability 2), one in vitro mammalian cell gene mutation assay with Chinese hamster Ovary cells (reliability 1), one in vitro mammalian cell transformation assay with BALB/3T3 mouse

cells (reliability 2) and one DNA damage and repair assay - unscheduled DNA synthesis in mammalian cells (hepatocytes of adult male F344 rats) in vitro (reliability 2) are provided. No genotoxicity was observed.

No in vivo and no human data are available.

The eMSCA concludes that based on the available data there is no concern for mutagenicity and no information needs to be requested under this substance evaluation.

7.9.6. Carcinogenicity

Only two supportive studies on carcinogenicity by oral route in rats assessed as "not reliable" (Klimisch score 3 and 4) are provided by the registrants. In one of them Charles River CD rats both males and females were fed with ethylene carbonate in diet containing approximately 1250, 2000 and 2500 mg/kg bw/day of the substance for 18 months (Ulland et al., 1973; Weisburger EK et al., 1981). No neoplastic effects were observed. The NOAEL for females was estimated to be ~2500 mg/kg bw/day or 50000 ppm (the highest concentration tested) and 1250 mg/kg bw/day (or 25000 ppm) for males due to nephrotoxicity.

No data are available on carcinogenicity after exposure via inhalation, dermal or other routes as well as no human data are available. The eMSCA concludes that based on the available data on mutagenicity in combination with carcinogenicity, there is no concern for carcinogenicity and no information needs to be requested under this substance evaluation.

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

Effects on fertility

No human data are available. The registrants provided two key studies assessed as reliability 2 studies on a metabolite of ethylene carbonate - ethylene glycol - used for the risk characterization of ethylene carbonate as read-across. In one of them, a three-generation study on Fischer 344 rats, both males and females were fed 40, 200 and 1000 mg ethylene glycol/kg/day in diet (DePass *et al*., 1986). The NOAEL for parental animals and for offsprings was found to be >1000 mg/kg/day as no reproductive effects were found.

In the second study on CD-1 male and female mice doses of approximately 500, 1000 and 2000 mg ethylene glycol/kg/day were administered with drinking water for 18 weeks (1 week prior to cohabitation, 14 weeks of cohabitation, and 3 weeks thereafter)(Registration dossier, study report, 1984). The NOAEL for fertility was estimated to be 1000 mg/kg bw/day for parental and F1 male and female mice. Exposure at highest dose resulted in a small but significant decrease in the number of litters per breeding pair, in the number of live pups per pair and in the live pup weight. In addition, distinct facial deformities and other malformations were reported for a significant number of pups (shortened nasal, parietal and/or frontal bones of the skull, fused ribs). eMSCA concludes that NOAEL for developmental effects can be set as 1000 mg/kg bw/day as well. F1 animals with continued exposure to ethylene glycol exhibited decreased mating and fertility indices relative to control group handled in the same manner. There were no effects on litter size, pup weight or sex ratio.

Effects on development

No human data are available. With respect to animal studies, one key study on Sprague-Dawley rats conducted according to OECD Guideline 414 and characterised as reliability 2 study is available (Registration dossier, study report, 1991) Ethylene carbonate was administered once daily by oral gavage on days 6-15 of gestation at doses: 750, 1500 and

3000 mg/kg bw/day. The vehicle control was used as well covering 27 animals in each of the test groups. The NOEL for maternal toxicity was determined to be 1500 mg/kg bw/day and the NOEL for developmental toxicity - 750 mg/kg bw/day.

The signs of maternal toxicity in the higest dose group included post dose salivation during various intervals of the study and statistically significant decrease in the group mean dam body weight changes. Statistically significant decreases were observed in the group mean fetal body weights in the 1500 and 3000 mg/kg/day dose groups. These decreases were considered biologically significant and related to the administration of the test substance. A statistically significant increase was observed in the total number of foetal malformation and in the number of litters with malformations in the 3000 mg/kg dose group (skeletal malformations in the vertebrae and sternebrae, incomplete ossification of the 1st, 2nd, 3rd or 4th sternebrae and unossification of the 6th sternebrae, etc.), however, it can be attributed to maternal toxicity. On the other hand, part of the same statistically significant malformations, namely, incomplete ossification or unossification of the sternebrae are observed at the 1500 mg/kg/day dose group.

A number of registrants have provided one other key study with reliability 2 on New Zealand White rabbits with ethylene glycol in drinking water (Tyl et al.,1993). Animals were treated by oral gavage given doses of 100, 500, 1000 and 2000 mg/kg/day from gestation day 6 - 19. The NOAEL for maternal toxicity was found to be 1000 mg/kg/bw/day and the NOAEL for developmental toxicity was found to be 2000 mg/kg bw/day.

In a supportive study assessed as reliability 2 study on CD-1 mice the animals were given daily doses of 50, 150, 500 or 1500 ethylene glycol mg/kg/day by oral gavage from gestation day 6 – 15 (Tyl, 1989). The NOELs were found to be 1500 mg/kg bw/day for maternal toxicity and 150 mg/kg bw/day for developmental toxicity. Exposure of pregnant mice to ethylene glycol during organogenesis by gavage produced developmental toxicity but no maternal toxicity at doses of 500 and 1500 mg/kg/day.

Conclusions on reproductive toxicity

Weight of evidence analysis concerning effects on fertility shows that the ethylene carbonate should not be classified for reproductive toxicity based on read-across to ethylene glycol. Only in one study on mice at the highest dose of 2000 mg/kg/day some signs of fertility impairment are indicated, however, OECD Test Guideline for repeated dose toxicity studies by the oral route suggests using the upper dose of 1000 mg/kg/day as a limit dose (CLP Regulations, point 3.7.2.5.9).

With regard to developmental toxicity, the eMSCA considers that a number of statistically significant developmental effects observed in on Sprague-Dawley rats at the dose of 1500 mg/kg/day, being the NOEL for maternal toxicity, formally suggests the classification of ethylene carbonate as Repr. 2, H361d (suspected of damaging the unborn child). The NOAEL for developmental toxicity is estimated to be 750 mg/kg bw/day. Conclusion on developmental toxicity is supported by developmental effects indicated in the study on CD-1 mice. However, the developmental effects were not shown in New Zealand White rabbits.

The newest investigations, both in vivo and in vitro, have established that the developmental toxicity of ethylene glycol in rats is related to the accumulation of glycolic acid in the blood and metabolic acidosis. When ethylene glycol was administered orally to rats and rabbits at a developmentally toxic dose (1000 mg/ kg bw/day) glycolic acid was found to be preferentially distributed into the rat embryo compared to the maternal blood (embryo/blood concentration 1.54) whereas this was not the case in the rabbit (embryo/blood concentration 0.31) (Registration dossier, study report, 2008, 2011).

Recent investigation demonstrated that uptake of glycolic acid into the rat embryo occurs predominantly by a specific, pH-dependent, active uptake transporter protein, consistent with the proton-linked monocarboxylate transporters (Registration dossier, study report, 2014) having two isoforms (Registration dossier, study report, 2016). The new and unpublished results indicate that polarity of these isoforms in the mouse and rat placenta

syncytiotrophoblast is opposite to that in the rabbit and human placenta (Registration dossier, study report 2018). Since ethylene glycol is not a developmental toxicant in the rabbit and taking into account species dependant toxicokinetics of the substance in placenta, no classification for developmental toxicity is warranted under CLP Regulation (paragraph 3.7.2.3.2 of CLP).

The validity of the proposed read-across is strengthened by the similarity in the toxicological profiles of both substances, indicating that ethylene carbonate as well as ethylene glycol do not exhibit systemic toxicity. In order to support this evidence, an in vitro hydrolysis study was performed by Ehmer in 2015. In this study, propylene carbonate was incubated in Wistar rat blood over a time span of 30 minutes. The positive control item ethylene carbonate was also incubated in Wistar rat blood over a time span of 30 minutes. 35.5 % of the start concentration remained after 5 minutes of incubation. After 30 minutes 15.5% of the start concentration was observed. The hydrolysis product ethylene glycol was formed simultaneously from the reference item at concentrations that corresponded to its turnover/hydrolysis. The calculated half-life value for ethylene carbonate was 3.533 minutes. This corresponds to a turnover of 0.14 µmol/(ml x min). For both compounds the formation of the corresponding glycols was observed simultaneously.

7.9.8. Hazard assessment of physico-chemical properties

Based on the available data, ethylene carbonate is not explosive, flammable or oxidising substance.

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

Table 8

CRITICAL DNELS/DMELS					
Endpoint of concern	**Type of effect**	**Critical study(ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL/ DMEL**	**Justification/ Remarks**
Workers					
Developmental toxicity / teratogenicity	Long-term - systemic effects (dermal route)	Developmental study on Sprague-Dawley rats by oral gavage (Registration dossier, study report, 1991)	NOAEL: 750 mg/kg bw/day	DNEL: 15 mg/kg bw/day	AF=50 (oral to dermal extrapolation "1" x interspecies "10" x intraspecies "5" x exposure duration "1" (teratogenecity study))
Developmental toxicity / teratogenicity	Long-term - systemic effects (inhalation route)	Developmental study on Sprague-Dawley rats by oral gavage (Registration dossier, study report, 1991)	NOAEC: 661 mg/m³	DNEL: 53 mg/m³	AF=12.5 (interspecies "2.5" x intraspecies "5" x exposure duration "1" (teratogenecity study))
General population					

Developmental toxicity / teratogenicity	Long-term - systemic effects (dermal route)	Developmental study on Sprague-Dawley rats by oral gavage (Registration dossier, study report, 1991)	NOAEL: 750 mg/kg bw/day	DNEL: 7.5 mg/kg bw/day	AF=100 (oral to dermal extrapolation "1" x interspecies "10" x intraspecies "10" x exposure duration "1" (teratogenecity study))
Developmental toxicity / teratogenicity	Long-term - systemic effects (inhalation route)	Developmental study on Sprague-Dawley rats by oral gavage (Registration dossier, study report, 1991)	NOAEC: 326 mg/m³	DNEL: 13 mg/m³	AF=25 (interspecies "2.5" x intraspecies "10" x exposure duration "1" (teratogenicity study))

* the dose descriptor starting point = 750 mg/kg bw/day x 1/(0.38 m³/kg bw/d) x 6.7 m³/10 m³ x 0.5 = 661 mg/m³, where:

- NOAEL for developmental toxicity through oral route 750 mg/kg bw/day
- route-to-route extrapolation factor from oral to inhalation "1"
- a standard breathing volume for the rat 0.38 m3/kg bw/d for 8 hours exposure
- correction factor for 8 hours exposure of workers – basic caloric demand 6.7 m³
- correction factor for 8 hours exposure of workers – caloric demand under light activity 10 m³
- correction factor for difference of the bioavailability via the inhalation route (100%) and oral route (50%) – "0.5"

** the dose descriptor starting point = 750 mg/kg bw/day x 1 /1.15 m³/kg bw/d x 0.5 = 326 mg/m³, where:

- route-to-route extrapolation factor from oral to inhalation "1"
- a standard breathing volume for the rat 1.15 m³/kg bw/d for 24 hours exposure
- correction factor for difference of the bioavailability via the inhalation route (100%) and oral route (50%) – "0.5"

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

There is no harmonised classification according to CLP regulation.

Self-classification in the registration dossiers:

- Eye Irrit. 2; H319: Causes serious eye irritation
- Acute Tox.4; H302: Harmful if swallowed
- STOT RE 2; H373: May cause damage to organs (Kidney, oral)

Additional self-classification notified in the C&L Inventory:

- Eye Dam. 1; H318: Causes serious eye damage
- STOT SE 3; H335: May cause respiratory irritation
- Skin Irrit. 2; H315: Causes skin irritation

Human health hazard assessment is summarised in sections 7.9.1 – 7.9.9 above. No need for harmonised classification on CMR properties of the substance is identified by eMSCA .

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated

7.11. PBT and VPVB assessment

Not evaluated

7.12. Exposure assessment

Confidential annex.

7.12.1. Environment

Not evaluated.

7.12.2. Combined exposure assessment

Not evaluated.

7.13. Risk characterisation

7.13.1. Human health

7.13.1.1. Workers

Risk characterisation for workers is based on possible risk from long-term exposure having potential to cause developmental effects. The related reference values - DNELs for inhalation and dermal exposure are applied. It is considered that oral exposure cannot cause any concern in occupational environment. In addition, risk from acute short-term exposure is assessed based on the same DNELs for long-term exposure as DNELs for short term exposure were not quantifiable based on the available data.

Risk characterisation for developmental toxicity / teratogenicity (long-term exposure)

		Manufacturing and distribution of ethylene carbonate	Formulation and (re)packing of ethylene carbonate and mixtures	Industrial uses	Professional uses
Inhalation exposure	The highest exposure concentration estimated (mg/m³)	7.71	11.01	11.01	11.01
	DNEL (mg/m³)	53			
	RCR	**0.15**	**0.21**	**0.21**	**0.21**
Dermal exposure	The highest exposure concentration estimated (mg/kg	1.37	2.74	2.83	2.83

	bw/day)				
	DNEL (mg/kg bw/day)	15			
	RCR	**0.09**	**0.18**	**0.19**	**0.19**
Total exposure	The highest exposure concentration estimated (mg/kg bw/day)	1.74	3.27	3.27	3.40
	DNEL (mg/kg bw/day)	15			
	RCR	**0.12**	**0.22**	**0.22**	**0.23**

Risk characterisation for acute short-term exposure

		Manufacturing and distribution of ethylene carbonate	Formulation and (re)packing of ethylene carbonate and mixtures	Industrial uses	Professional uses
Inhalation exposure	The highest exposure concentration estimated (mg/m³)	15.41	22.02	22.02	22.02
	DNEL (mg/m³)	53			
	RCR	**0.29**	**0.42**	**0.42**	**0.42**
Dermal exposure	The highest exposure concentration estimated (mg/kg bw/day)	2.74	2.74	4.28	5.66
	DNEL (mg/kg bw/day)	15			
	RCR	**0.18**	**0.18**	**0.29**	**0.38**
Total exposure	The highest exposure concentration estimated (mg/kg	3.48	3.83	6.18	6.80

	bw/day)				
	DNEL (mg/kg bw/day)	15			
	RCR	**0.23**	**0.26**	**0.41**	**0.45**

According to the eMSCA's evaluation, the Risk Characterisation Ratio (RCR = Exposure concentration/DNEL) for workers is well below "1" for all usages both for long-term and short-term exposure based on the highest exposure estimate within each use. Following, all other PROCs included in the specific use do not pose long – term or short-term risk for workers.

7.13.1.2. Consumers

Risk characterisation for consumers is based on possible risk from long-term exposure having potential to cause developmental effects. The related reference values - DNELs for inhalation and dermal exposure are applied. It is considered that oral exposure cannot cause concern for consumers taking into account the foreseen applications of consumers` products containing ethylene carbonate.

Risk characterisation for developmental toxicity / teratogenicity (long-term exposure)

		Exposure from use of waterborne latex wall paint	Exposure from use of removers
Inhalation exposure	The highest exposure concentration estimated (mg/m³)	0.0094	0.01
	DNEL (mg/m³)	13	
	RCR	**0.0007**	**0.0008**
Dermal exposure	The highest exposure concentration estimated (mg/kg bw/day)	0.036	0.072
	DNEL (mg/kg bw/day)	7.5	
	RCR	**0.005**	**0.01**
Total exposure	**RCR**	**0.006**	**0.01**
Total exposure from combined use	**RCR**	**0.02**	

According to the eMSCA's evaluation, the RCR for consumers is very low and well below "1" for both usages as well as for the possible combined use of waterborne latex wall paints and removers.

The initial concerns on exposure and corresponding risks are now clarified.

7.13.1.3. Indirect exposure of humans via the environment

Not applicable.

7.14. References

Corley, R.A., Wilson, D.M., Hard, G.C., Stebbins, K.E., Bartels, M.J., Soelberg, J.J., Dryzga, M.D., Gingell, R., McMartin, K.E., Snellings, W.M. 2008: Dosimetry considerations in the enhanced sensitivity of male Wistar rats to chronic ethylene glycol-induced nephrotoxicity. (publication), Toxicol. Appl. Pharmacol. 228, 165 - 178.

DePass, L.R., Woodside, M.D., Maronpot, R., Weil, C.S. 1986: Three-Generation Reproduction and Dominant Lethal Mutagenesis Studies of Ethylene Glycol in the Rat. (publication), Fundamental and Applied Toxicology 7, 566 - 572.

OECD Screening Information Dataset (SIDS) (2004). SIDS Initial Assessment Report for SIAM 19.; Organization for Economic Cooperation and Development (OECD).

Robinson et al. 1990: Subacute and subchronic toxicity of ethylene glycol administered in drinking water to Sprague-Dawley rats (publication), DRUG AND CHEMICAL TOXICOLOGY, 13(1), 43-70.

Tyl RW, Price CJ, Marr MC, Myers CB, Seely JC, Heindel JJ, Schwetz BA 1993: Developmental Toxicity Evaluation of Ethylene Glycol by Gavage in New Zealand White Rabbits. (publication), Fundamental and Applied Toxicology 20: 402-412.

Tyl RW 1989: Developmental Toxicity Evaluation of Ethylene Glycol Administered by Gavage to CD-1 Mice: Determination of a "No Observable Effect Level" (NOEL). (study report), 1989.

Ulland B, Weisburger EK, and Weisburger JH 1973: Chronic Toxicity and Carcinogenicity of Industrial Chemicals and Pesticides (publication), Toxicol Appl Pharmacol 25: 446.

U.S. National Library of Medicine 2009: Ethylene Carbonate, CAS: 96-49-1 (review article or handbook), NLM, OXNET, Hazardous Substance Databank (HSDB).

Weisburger EK Ulland BM, Nam J, Gart JJ, Weisburger JH 1981: Carcinogenicity tests of certain environmental and industrial chemicals (publication), J Nat Cancer Inst 67: 75-88.

7.15. Abbreviations

AF - Assessment factor

eMSCA – evaluating Member State Competent Authority

CMR - Carcinogenic, mutagenic or toxic to reproduction

CSR - Chemical Safety Report

DNEL - Derived no-effect level

LEV - Local Exhaust Ventilation

NOAEC - No observed adverse effect concentration

NOEL - No observed effect level

OECD - Organisation for Economic Co-operation and Development

OC – Occupational conditions

PPE - Personal protective equipment

PROC – Process category

RCR – Risk Characterisation Ratio

RMM – Risk Management Measure