LATVIJAS VIDES, ĢEOLOĢIJAS UN METEOROLOĢIJAS CENTRS

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Methyl Vinyl Ether

EC No 203-475-4

CAS No 107-25-5

Evaluating Member State(s): Latvia

Dated: 30.08.2019

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2018

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

Methyl vinyl ether was originally selected for substance evaluation in order to clarify concerns about:

- Suspected reprotoxic properties

- Exposure of sensitive populations, consumers and workers (industrial and professional uses).

- Other exposure/risk based concern

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Methyl vinyl ether was evaluated under OECD HPV programme as a part of the chemical category of vinyl ethers (OECD SIDS, 2006).

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

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.

5.2. Other actions

Not applicable.

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

Not applicable.

Part B. Substance evaluation

7. EVALUATION REPORT

According to Article 45(4) of the REACH Regulation Competent Authority of Latvia has initiated substance evaluation for methyl vinyl ether EC No 203-475-4 (CAS No 107-58-5), based on a registration submitted by the concerned registrant.

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 reprotoxic properties methyl vinyl ether 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.

7.1. Overview of the substance evaluation performed

Methyl vinyl ether was originally selected for substance evaluation in order to clarify concerns about:

- Suspected reprotoxic properties

- Exposure of sensitive populations, consumers and workers (industrial and professional use).

- Other exposure/risk based concern

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Reprotoxic properties	Concern not substantiated. No further action.
Exposure of sensitive populations, consumers and workers (industrial and professional use).	Concern not substantiated. No further action.

7.2. Procedure

Pursuant to Article 44(2) of the REACH Regulation, Methyl vinyl ether 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 of Methyl vinyl ether was targeted at human health endpoints and focused on the grounds for concern that were included in the justification document for the inclusion of the substance in the CoRAP. During the process, communication was established between the eMSCA and the lead registrant. On 8 February 2018 the Registrant submitted to ECHA an update of the registration dossier containing the information that was previously required under compliance check. This new information has been assessed by the eMSCA. Finally, on 18.03.2019 the eMSCA has concluded that the new information submitted by the registrants clarifies the concerns.Thus there was no need to prepare a decision to request further information under substance evaluation.

7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	Methyl vinyl ether
EC number:	203-457-4
CAS number:	1017-25-5
Index number in Annex VI of the CLP Regulation:	603-021-00-9
Molecular formula:	C3H6O
Molecular weight range:	58.0791
Synonyms:	Methyl vinyl ether; Ethene, methoxy-;

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	Gaseous, colourless gas with a sweet penetrating odour.
Vapour pressure	1691.7 hPa at 20°C, The vapour pressure is determined in a weight-of-evidence approach of two experimental BASF-studies and two secondary sources, Knovel and HSDB
Water solubility	17.1 g/l at 25 °C, The water solubility is determined in a weight-of-evidence approach of an experimental BASF-study and two secondary sources, SRC PhysProp and HSDB
Partition coefficient n-octanol/water (Log Kow)	0.42 at 25 °C,

	The partition coefficient n-octanol / water is determined in a weight-of-evidence approach of two secondary sources, SRC PhysProp and Knovel and a scientifically accepted calculation model, EPIWIN.
Flammability	Extremely flammable, The flammability of the substance as well as its explosion limits are derived in a weight-of-evidence approach integrating information from three secondary sources, HSDB, GESTIS and Hommel.
Explosive properties	Not applicable, In accordance with section 1 of REACH Annex XI, the explosiveness does not need to be performed as the substance is a gas.
Oxidising properties	Non oxidising, In accordance with column 2 of REACH Annex VII, the oxidising properties do not need to be tested, because the substance is incapable of reacting exothermically with combustible materials on the basis of the chemical structure.
Granulometry	In accordance with column 2 of REACH Annex VII, the particle size distribution (Granulometrie) study does not need to be performed as 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 test does not need to be conducted because the stability of the substance is not considered as critical.
Dissociation constant	In accordance with section 1 of REACH Annex XI, the dissociation constant study does not need to be performed because the substance does not contain any ionic structure.
Melting/freezing point	-122 °C at 101.3 kPa The melting point is determined in a weight-of-evidence approach integrating information from four secondary sources, 3 peer-reviewed sources, HSDB, Kirk-Othmer and Ullmann's and one authoritative sources, GESTIS.
Boiling point	5.69 °C at 101.3 kPa, The boiling point is determined in a weight-of-evidence approach of two experimental studies of BASF and three secondary sources, Kirk-Othmer, Roempp and Hommel.
Density	0.0024 g/cm³ resp. 2.414 g/l at 20 °C, Calculated based on the ideal gas law and its molecular weight.
Auto flammability	210 °C at 1013 hPa, The auto flammability is determined in a weight-of-evidence approach integrating information from three secondary sources, Ullmann's, Hommel and GESTIS.
Flash point	In accordance with section 1 of REACH Annex XI, the flash point does not need to be tested as the substance is s gas.

Surface tension	In accordance with column 2 of REACH Annex VII, the surface tension of the substance does not need to be tested because due its chemical structure, no surface activity is predicted.
Viscosity	In accordance with section 2 of REACH Annex XI, the viscosity does not need to be performed as the substance is a gas.
Storage stability and reactivity towards container material	In accordance with section 1 of REACH Annex XI, the UN test in Part III, sub-section 37.4 does not need to be conducted as the substance is a gas.

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
☐ 100 + tpa				

7.5.2. Overview of uses

Table 7

USES	Use(s)
Uses as intermediate	01 – Manufacture and distribution of substance
Formulation	02 – Formulation & (Re)packing of Substances and Mixtures
Uses at industrial sites	03 – Use as intermediate: Industrial 04 - Manufacture of polymers, resins: Industrial
Uses by professional workers	05 - Use as an adhesive/sealant in the health care industry: Professional
Consumer Uses	06 - Use as an adhesive/sealant in the health care industry: Consumer use

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Table 8

HARMONISED CLASSIFICATION ACCORDING TO ANNEX VI OF CLP REGULATION (REGULATION (EC) 1272/2008)							
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)		
603-021-00-9	methyl vinyl ether	203-475-4	107-25-5	Flam. Gas 1 Press. Gas	H220		D U

7.6.2. Self-classification

- In the registration(s)*:*

Flam. Gas 1 H220: Extremely flammable gas.
Liquefied gas H280: Contains gas under pressure; may explode if heated.
Aquatic Chronic 3 H412: Harmful to aquatic life with long lasting effects.

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

None.

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 rapidly after inhalation as well as hydrolyzes immediately and completely in gastric acid. It is suggested that vinyl ethers may undergo microsomal oxidation to unstable epoxides. In vitro tests only isobutanol was detected in the active microsome incubations.

7.9.2. Acute toxicity and Corrosion/Irritation

No data are available for the oral route of exposure (studies technically not feasible).

No mortality and no clinical signs were found in 10 male and 10 female rats within 14 days after exposure for 4 h to the dose level of 5.3 mg/L. Also at a dose level of 20165 ppm (48 mg/L) no mortality and no clinical signs were detected in rats exposed for 4 h (post exposure period 14 days). In both studies no macroscopic findings were seen at necropsy.

No systemic clinical signs and no mortality were reported after 24 h occlusive exposure to 8 mL/kg bw (ca. 5000 mg/kg bw; cold liquid) in two New Zealand White rabbits; the acute dermal LD50 is considered to be > 5000 mg/kg bw.

The eMSCA supports the conclusion that the substance is not acutely toxic by dermal and inhalation routes, and based on the available information. Neither further information nor additional classification is required.

In a study on skin irritation of MVE there was no erythema, edema, or other irritation in any of 6 New Zealand White rabbits one hour and 1, 2, 3, 7, 10, or 14 days after exposure (occlusive for 4 h) to 0.5 mL of undiluted, cold liquid test substance.

The instillation of 0.1 mL undiluted, cold liquid to the eye resulted only in minor transient conjunctival irritation in 5/6 New Zealand White rabbits 24 h after application; the effects were fully reversible within 24 h (Registartion dossier, study report, 1990).

The eMSCA supports the conclusion that the substance is not a skin or eye irritant and neither further information nor additional classification is required.

7.9.3. Sensitisation

There are no animal or human data available with regard to the skin or respiratory sensitisation potential of methyl vinyl ether. Due to very high volatility and immediate vaporization of vinyl methyl ether at room temperature (boiling point 6°C at 1013 hPa) such studies are technically not feasible. No further information or additional classification is required.

7.9.4. Repeated dose toxicity

No data are available on the oral or dermal route of exposure (studies technically not feasible). The acute toxicity after inhalation is very low (LC50 > 64000 ppm).

With respect to assessment of repeated dose toxicity through inhalation route, Wistar rats were exposed 28 days (6 hrs/day, 5 days/week) to methoxyethene (Registration dossier, study report, 1989). The study was performed according to OECD Guideline 412 (Subacute Inhalation Toxicity: 28-Day Study) and characterized as reliability 1 study. The highest dose level tested was assumed to be the NOAEC value for repeated dose toxicity (1500 ppm or 3.613 mg/L = 3613 mg/m^3) and adopted for further exposure assessment in relation to long-term systemic effects by the registrants. In addition, the NOAEC for local effects - atrophy of olfactory epithelium - was determined to be 3500 ppm (8.431 mg/L or 8431 mg/m^3). This value was adopted for further exposure assessment in relation to long-term local effects by the registrants.

Based on the mentioned sub-acute inhalation study in rats it is concluded that the methyl vinyl ether shall not be classified for repeated dose toxicity according to CLP Regulation. The eMSCA supports this conclusion and neither further information nor additional classification is required.

7.9.5. Mutagenicity

Three in vitro key studies on mutagenicity have been reported in the IUCLID dataset:

- bacterial reverse mutation assay with S. typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation performed similarly to OECD Guideline 471 (Registration dossier, study report, 1979) (reliability 2). Different vapour concentrations up to 25 % of methyl vinyl ether giving cytotoxicity effects have been tested. A negative control as well as a positive controls with sodium azide etc. were applied. No genotoxicity was observed. Atmospheres containing 25% of the test substance were cytotoxic.

- bacterial reverse mutation assay with S. typhimurium TA98, TA100, TA1535, TA1537 and E.coli WP2 uvrA with and without metabolic activation performed similarly to OECD Guideline 471 (Araki, 1994) (reliability 2). Tests were performed

at cytotoxic vapour concentration levels or at the maximum vapour concentration of 50 % of methyl vinyl ether vapour (more detailed information is not given). A negative control as well as a positive control with 1,3-butadiene (gas) were applied. No genotoxicity was observed.

- mammalian cell gene mutation assay with Chinese hamster Ovary cells (CHO) with and without metabolic activation performed according to OECD Guideline 476 (Registration dossier, study report, 2017) (reliability 1). Different concentrations of liquid methyl vinyl ether starting from 1250 µg/ml and ending with 20000 µg/ml at 4-hour exposure have been applied. Both negative control and positive controls with 7,12-dimethylbenzanthracene and ethylmethanesulphonate were used as well. Cytotoxicity was detected at higher concentration levels, but no genotoxicity was observed.

In addition, two supportive in vivo studies have been reported in the IUCLID dataset:

- CD-1 male and female mice erythrocyte micronucleus (chromosome aberration) assay by vapour inhalation (5000 and 25000 ppm (12 and 60 mg/L, respectively); 5 animals per dose and per sex; 6 h/day for 5 days) performed similarly to OECD Guideline 474 and assessed as reliability 2 study (Registration dossier, study report, 1987). Mitomycin C was applied as a positive control substance by intraperitoneal administration in parallel with negative control. Neither genotoxicity nor cytotoxicity effects were detected in erythrocytes from bone marrow.

- Swiss Webster male and female mice erythrocyte micronucleus (chromosome aberration) assay by vapour inhalation (5000, 10000, and 19500 ppm (12, 24, and 47 mg/L, respectively); 5 mice per sex and dose, single 6-hour whole-body vapor exposure) performed similarly to OECD Guideline 474 and assessed as reliability 2 study (Registration dossier, study report, 1990). Triethylenemelamine was applied as a positive control by intraperitoneal administration in parallel with negative control. Neither genotoxicity nor cytotoxicity effects were detected in this assay.

No human data are available.

The eMSCA supports the conclusion made by the Registrant(s) that according to the available data methyl vinyl ether shall not be classified for mutagenicity according to the criteria of the CLP Regulation Thus, neither further information nor additional classification is required.

7.9.6. Carcinogenicity

No data are available on carcinogenicity after exposure via oral, inhalation, dermal or other routes as well as no human data are available. The registrants claim that methyl vinyl ether as well as structurally related substances ethyl vinyl ether, isobutyl vinyl ether and hydroxybutylvinylether were not mutagenic in the Ames test with bacteria or in mammalian cell systems both in the absence and presence of metabolic activation in vitro and in vivo tests. Besides, at room temperature methyl vinyl ether is an extremely flammable gas and may generate explosive atmosphere. The substance is practically exclusively used as intermediate in the manufacture of vinyl ether polymers and co-polymers.

The eMSCA states that firm conclusion on potential carcinogenicity of methyl vinyl ether cannot be made due to lack of data. However, considering the waiving arguments (eg. technically difficult to test orally due to high volatility and immediate vaporization at room temperature) by the Registrant(s), no further information is requested in this substance evaluation.

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

Effects on fertility

No animal data as well as no human data are avialable.

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 (reliability 2 study) is available in the dossier (Registration dossier, study report, 1994; Registration dossier, study report, 2005). The methyl vinyl ether was administered by inhalation (whole body) once daily 6 hours per day on days 6-15 of gestation applying the following nominal concentrations: 0, 5000, 10000 and 19500 ppm (0, 12, 24 and 47 mg/L, respectively). Gestational body weight and body weight gains were reduced during the exposure period in all exposure groups. The relative liver weight was increased in all exposure groups. So, maternal toxicity was shown at all exposure levels. There were no effects of exposure on gestational parameters including resorptions, pre- and post-implantation losses, percentages of live fetuses, and sex ratios. There was no effect of exposure on fetal body weights/litter as well as there were no statistically significant effects of exposure on the incidence of visceral, keletal or external malformations of fetuses. The LOAEC for maternal toxicity was determined to be 50000 ppm (12 mg/L) (the lowest dose tested). As statistically significant fetal abnormalities were not reported, the highest concentration tested – 195000 ppm (47 mg/L) is attributed to NOAEC for developmental toxicity, however, the registrants adopted the 5000 ppm (12 mg/L or 12000 mg/m^3) as NOAEC for further exposure assessment in relation to developmental toxicity.

The registrants provide reasoning why a further pre-natal developmental toxicity study according to OECD Guideline 414 in a second species as well as a two-generation reproduction toxicity study according to OECD Guideline 416 or an extended one-generation reproductive toxicity study according to OECD Guideline 443 is not needed based on exposure considerations outlined in REACH Regulation (Annex IX and Annex X: reproductive toxicity testing may be omitted, if relevant human exposure can be excluded in accordance with Annex XI, section 3). The substance is not incorporated in an article and the manufacturer can demonstrate and document for all relevant scenarios that throughout the life cycle the substance is manufactured and used under strictly controlled conditions. Exposure to methyl vinyl ether is limited to occasional sampling tasks for quality control only. All other operations are performed in fully closed systems.

Conclusions on reproductive toxicity

Based on the single developmental toxicity key study on Sprague-Dawley rats (Registration dossier, study report, 1994; Registration dossier, study report, 2005) methyl vinyl ether should not be classified for reproductive toxicity according to CLP Regulation. The eMSCA considers this statement justified. This conclusion is without prejudice to any further regulatory work that ECHA may initiate at a later stage.

7.9.8. Hazard assessment of physico-chemical properties

At room temperature methyl vinyl ether is an extremely flammable gas and may generate explosive atmosphere. It is chemically unstable at a temperature greater than 20 °C and/or a pressure greater than 101.3 kPa. The substance shall be classified as Flam. Gas 1, Chem. Unst. Gas B (Hazard statement: H220: Extremely flammable gas, H231: May react explosively even in the absence of air at elevated pressure and/or temperature) according to CLP Regulation.

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

Table 9

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					
Repeated dose toxicity	Long-term - systemic effects (inhalation route)	Sub-acute inhalation study in Wistar rats (Registration dossier, study report, 1989)	NOAEC: 3613 mg/m³	DNEL: 24.2 mg/m³	AF=75 (default AF for dose – response relationship "1" x default AF for time extrapolation from subacute to chronic exposure "6" x interspecies AF "2.5" x intraspecies AF "5" x default AF for remaining uncertainties "1")
Repeated dose toxicity	Long-term - local effects (inhalation route)	Sub-acute inhalation study in Wistar rats: local effects on the olfactory epithelium (Registration dossier, study report, 1989)	NOAEC: 8431 mg/m³	DNEL: 339 mg/m³	AF=12.5 (default AF for dose – response relationship "1" x interspecies AF "2.5" x intraspecies AF "5" x default AF for remaining uncertainties "1")
Developmental toxicity	Long-term - systemic effects (inhalation route)	Developmental study on Sprague-Dawley rats by inhalation exposure (Registration dossier, study report,1994)	NOAEC: 12000 mg/m³	-	DNEL was not established as the critical endpoint is repeated dose toxicity
General population					

Repeated dose toxicity	Long-term - systemic effects (total uptake)	Sub-acute inhalation study in Wistar rats (Registration dossier, study report, 1989)	NOAEC: 3613 mg/m³ NOAEL: 748 mg/kg bw/day ***	DNEL: 5 mg/kg bw/day	AF=150 (default AF for dose – response relationship "1" x default AF for time extrapolation from subacute to chronic exposure "6" x interspecies AF "2.5" x intraspecies AF "10" x default AF for remaining uncertainties "1")
Repeated dose toxicity	Long-term - local effects (total uptake)	Sub-acute inhalation study in Wistar rats: local effects on the olfactory epithelium (Registration dossier, study report, 1989)	NOAEC: 8431 mg/m³ NOAEL: 1746 mg/kg bw/day ****	DNEL: 70 mg/kg bw/day	AF=25 (default AF for dose – response relationship "1" x interspecies AF "2.5" x intraspecies AF "10" x default AF for remaining uncertainties "1")

* 3613 x 6h/8h x 6.7 m^3/10 m^3 / AF = 3613 x 0.75 x 0.67 / 75 = 24.2 mg/m^3 , where:

6 h exposure duration in the test with rats

6h/8h extrapolation to 8 h exposure of workers

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

** 8431 x 6h/8h x 6.7 m^3/10 m^3 / AF = 8431 x 0.75 x 0.67 / 12.5 = 339 mg/m^3 , where:

6 h exposure duration in the test with rats

6h/8h extrapolation to 8 h exposure of workers

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

*** 3613 x 5d/7d x 1 x 0.29 m^3/kg bw = 3613 x 0.714 x 0.29 = 748 mg/kg bw/day , where:

- 5d 7d extrapolation from 5 days animal test to 7 days exposure of general population

- „1" extrapolation from inhalation to oral absorption
- 0.29 m^3/ kg bw rat respiratory volume for 6 h exposure

****8431 x 5d/7d x 1 x 0.29 m^3/kg bw = 8431 x 0.714 x 0.29 = 1746 mg/kg bw/day , where:

- 5d/7d extrapolation from 5 days animal test to 7 days exposure of general population
- „1" extrapolation from inhalation to oral absorption
- 0.29 m^3/ kg bw rat respiratory volume for 6 h exposure

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

HARMONISED CLASSIFICATION ACCORDING TO ANNEX VI OF CLP REGULATION (REGULATION (EC) 1272/2008)							
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)		
603-021-00-9	methyl vinyl ether	203-475-4	107-25-5	Flam. Gas 1 Press. Gas	H220		D U

The current harmonised classification above is sufficient.

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.11. PBT and VPVB assessment

Not evaluated.

7.12. Exposure assessment

In confidential annex, which is removed from this public version of the report.

7.13. Risk characterisation

7.13.1. Human health

7.13.1.1. Workers

Risk characterisation for workers is based on the critical endpoint – repeated dose toxicity having potential to cause adverse effects through inhalation exposure route. The related reference values - DNEL for inhalation exposure is applied. Both the long-term systemic and local exposure is considered. Taking into account the physico-chemical properties of the substance (very high volatility and immediate vaporization of vinyl methyl ether at

room temperature - boiling point 6°C at 1013 hPa) it is considered that dermal and oral exposure cannot cause any concern in occupational environment.

Risk characterisation for repeated dose toxicity (long-term systemic exposure)

		Manufacturing of methyl vinyl ether	Charging and discharging of substance and mixtures	Use as an intermediate	Use of monomer in polymerization processes (resins)	Use in laboratories
Inhalation exposure	The highest exposure concentration estimated (mg/m³)	12.1	18.15	12.1	18.15	12.1
	DNEL (mg/m³)	24.2				
	RCR	**0.5**	**0.75**	**0.5**	**0.75**	**0.5**

Risk characterisation for repeated dose toxicity (long-term local exposure)

		Manufacturing of methyl vinyl ether	Charging and discharging of substance and mixtures	Use as an intermediate	Use of monomer in polymerization processes (resins)	Use in laboratories
Inhalation exposure	The highest exposure concentration estimated (mg/m³)	12.1	18.15	12.1	18.15	12.1
	DNEL (mg/m³)	339				
	RCR	**0.04**	**0.05**	**0.04**	**0.05**	**0.04**

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 systemic and long-term local exposure based on the highest exposure estimate within each use. Following, all other PROCs included in the specific use do not pose long – term systemic or local risk for workers. So the intial concern for worker exposure has been removed.

7.13.1.2. Consumers

Not applicable as no consumers` use is expected.

Consumer exposure to residual MVE is considered to be negligible, since most of the marketed vinyl ether polymers and co-polymers are heat-treated and potentially existing residual MVE is expected to evaporate during this process.

7.13.1.3. Indirect exposure of humans via the environment

Risk characterisation for general population is based on the critical endpoint – repeated dose toxicity having potential to cause adverse effects through indirect exposure of man via foods, drinking water and air estimated as combined daily exposure. The related reference values - DNEL for daily uptake is applied. Both the long-term systemic and local exposure is considered.

Risk characterisation for repeated dose toxicity (long-term systemic exposure)

		Manufacturing of methyl vinyl ether	Charging and discharging of substance and mixtures	Use as an intermediate	Use of monomer in polymerization processes (resins)	Use in laboratories
Indirect exposure of man via foods, drinking water and air	The total regional exposure concentration estimated (mg/kg bw/day)	3.45E-6	Not estimated	3.45E-6	3.45E-6	3.45E-6
	DNEL (mg/ kg bw/day)	5.0				
	RCR	**6.9E-7**	**-**	**6.9E-7**	**6.9E-7**	**6.9E-7**

Risk characterisation for repeated dose toxicity (long-term local exposure)

		Manufacturing of methyl vinyl ether	Charging and discharging of substance and mixtures	Use as an intermediate	Use of monomer in polymerization processes (resins)	Use in laboratories
Indirect exposure of man via foods, drinking water and air	The total regional exposure concentration estimated (mg/kg bw/day)	3.45E-6	Not estimated	3.45E-6	3.45E-6	3.45E-6
	DNEL (mg/ kg	70.0				

	bw/day)					
	RCR	**4.9E-8**	**-**	**4.9E-8**	**4.9E-8**	**4.9E-8**

According to the eMSCA's evaluation, the Risk Characterisation Ratio (RCR = Exposure concentration/DNEL) for general population (indirect man via environment exposure) is extremely low and well below "1" for all usages assessed both for long-term systemic and long-term local exposure. Following, no long – term systemic or local risk for general population is in place. So the initial concern for consumer exposure has been removed.

7.14. References

Araki A 1994: Improved method for mutagenicity testing of gaseous compounds by using a gas sampling bag (publication), Mutat Res 307: 335-344.

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

OECD SIDS, SIAM 23, 17-20 October 2006, DE/ICCA, SIAP Vinyl Ethers

7.15. Abbreviations

AF - Assessment factor

CHO – Chinese hamster Ovary cells

eMSCA – evaluating Member State Competent Authority

CMR - Carcinogenic, mutagenic or toxic to reproduction

DNEL - Derived no-effect level

LEV - Local Exhaust Ventilation

LC50 - Lethal concentration

LOAEC - Lowest observed adverse effect concentration

NOAEC - No observed adverse effect concentration

NOAEL - No observed adverse effect level

OECD - Organisation for Economic Co-operation and Development

PPE – personal protective equipment

RCR – Risk Characterisation Ratio

SVHC - Substance of very high concern

WCS – workers contributing scenarios