SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

ethyl methacrylate

EC No 202-597-5

CAS No 97-63-2

Evaluating Member State(s): Italy

Dated: 29 August 2019

Template Version 2.1
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Evaluating Member State Competent Authority

MSCA Italy National Institute of Health on behalf of Ministry of Health
Viale Regina Elena, 299 - 00161 Rome, Italy.
In cooperation with Italian National Institute for Environmental Protection and Research (ISPRA).
Via Brancati, 48 - 00144 Rome, Italy

Tel.: +390649902061
FAX: +390649902286
Email: leonello.attias@iss.it

Year of evaluation in CoRAP: 2014

Before concluding the substance evaluation a Decision to request further information was issued on: 19 August 2016.

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

Ethyl methacrylate (EMA) was originally selected for substance evaluation in order to clarify concerns about:

- Suspected C, M
- Sensitiser
- Exposure/Wide dispersive use
- consumer user
- high (aggregated) tonnage

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

None.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating MSCA (eMSCA) 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

Skin sensitisation:

The available data show that the substance should be classified as Skin. Sens. 1B. However since the substance already has a harmonised classification as Skin. Sens. 1, a revision of the harmonised classification is not considered necessary, as in terms of the appropriate risk management measures there is no difference between the two classifications. Thus a harmonised classification as Skin. Sens. 1B would not have an impact on the safe use of the substance.

5.2. Other actions

Mutagenicity:

The requests for information under substance evaluation to address the concern for mutagenicity have been addressed by the registrant(s) by proposing a category approach based on scenario 6 of the current Read across assessment framework (RAAF) (i.e., different compounds have the same type of effect based on a common mode of action, including absence of effects for every member of the category (ECHA, 2017)). In the opinion of eMSCA, the hypothesis of the applicability of this scenario is not acceptable because the mutagenicity potential of methyl methacrylate (MMA), one of the member of the category, cannot be excluded. MMA was evaluated under substance evaluation by Franch MSCA (ANSES, 2018). In that evaluation, the concern for mutagenicity identified for MMA was not completely clarified, as the potential risk was considered sufficiently addressed by proposing a revision of the harmonised classification, including classification for respiratory sensitization Cat.1. Hence, since the mutagenicity potential of MMA is not clarified, the eMSCA considers the read-across proposed by the registrant(s) for EMA, as not acceptable and sufficient to conclude on mutagenicity potential of EMA. The eMSCA also notes that the studies, which were requested under substance evaluation are also standard information requirements under REACH. As a consequence, the eMSCA concludes that for the endpoint mutagenicity, there are potential data gaps for standard information requirements, which can be better addressed under compliance check (CCH) process. Therefore the eMSCA recommends ECHA to consider this substance for prioritisation for CCH.

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

Not applicable.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

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

- Human health/Suspected CM
- Sensitiser
- Exposure/Wide dispersive use
- Consumer use
- High (aggregated) tonnage

The Substance evaluation started on 27 April 2014.

Table 2

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Endpoint 1 Suspected CM	The read-across applied by registrant(s) was not accepted by eMSCA, therefore the initial concern about mutagenicity and carcinogenicity could not be completely clarified. The eMSCA considers that there are potential standard data gaps for mutagenicity endpoint(for details see also section 7.9.5 and 7.9.6) and recommends ECHA to consider this substance in the prioritisation for CCH.
Endpoint 2 Skin sens	The substance could be classified as Skin. Sens. 1B. However since the substance already has a harmonised classification as Skin. Sens. 1, a revision of the harmonised classification is not considered a priority, as in terms of the appropriate risk management measures there is no difference between the two classifications and thus a harmonised classification as Skin. Sens. 1B would not have an impact on the safe use of the substance.
Endpoint 3 Exposure/Wide dispersive use	No further information required.
Endpoint 4 Consumer use	No public registered data indicating whether or in which chemical products the substance might be used. However consumers could be exposed through the use of polymers that contain the substance. This exposure is considered to be very low. The eMSCA recommends the registrants to provide a quantitative exposure assessment for consumer uses.

Endpoint 5 High (aggregated) tonnage	No further information is required.

7.2. Procedure

The evaluation of EMA has started on April 2014.
The initial grounds for concern relating to: human health/suspected carcinogenicity and mutagenicity, sensitiser, exposure/wide dispersive use, consumer user, high (aggregated) tonnage.
The eMSCA considered that further information was required to clarify the above mentioned concerns. Therefore, it prepared a draft decision pursuant to Article 46(1) of the REACH Regulation to request further information. It submitted the draft decision to ECHA on 26 March 2015.
A unanimous agreement of the Member State Committee on the draft decision was reached on 23 May 2016 in a written procedure launched on 13 May 2016. ECHA took the decision on pursuant to Article 51(6) of the REACH Regulation.

The following tests were requested:

1.in vitro gene mutation study in bacteria (test method: Bacterial reverse mutation test, OECD 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102, as specified in section III;
2. *in vitro* Mammalian Cell Micronucleus study (test method: OECD 487);
3. *in vitro* gene mutation study in mammalian cells (test method: OECD 476 or OECD 490), provided that both studies requested under 1. and 2. have negative results;
4. update of the registration dossier with relevant and available information on skin sensitization.

Subsequently the registrant(s) provided only adaptations for the requested information in updated dossier. In particular a new category approach was submitted.

The eMSCA evaluated the information submitted and concluded that it is not sufficient to conclude on the mutagenicity potential of EMA and further information would be needed. However since the necessary information is also standard information requirement under REACH, it was considered that these data gaps would be better addressed under CCH. Therefore the eMSCA decided to conclude this substance evaluation and recommend ECHA to consider this substance in prioritisation for CCH.

7.3. Identity of the substance

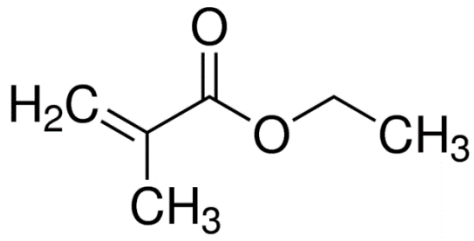
Table 3

SUBSTANCE IDENTITY	
Public name:	Ethyl methacrylate
EC number:	202-597-5
CAS number:	97-63-2
Index number in Annex VI of the CLP Regulation:	607-071-00-2
Molecular formula:	C6H10O2
Molecular weight range:	
Synonyms:	2-Methyl-2-propenoic acid, ethyl ester 2-Methyl-acrylic acid ethyl ester

	2-Methylpropenoic acid, ethyl ester 2-Propenoic acid, 2-methyl ethylester Ethyl-2-methyl-2-propenoate Ethyl-2-methylacrylate Ethyl-2-methylpropenoate Ethyl-alpha-Methylmethylacrylate Ethyl-methylacrylate Methacrylic acid, ethyl ester Prop-2-enoate, 2-methyl-, ethyl

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

Structural formula:



7.4. Physico-chemical properties

Table 4

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	liquid
Vapour pressure	20 hPa at 20 °C
Water solubility	4.69 g/L at 20 °C
Partition coefficient n-octanol/water (Log Kow)	1.87 at 20 °C
Flammability	Waived: there are no chemical groups associated with flammable properties present in the molecule.
Explosive properties	Waived: there are no chemical groups associated with explosive properties present in the molecule.
Oxidising properties	Waived: there are no oxidizing groups in the structure of the molecule.
Granulometry	Waived: the substance is a liquid at 20 °C.
Stability in organic solvents and identity of relevant degradation products	Waived: the stability of the substance is not considered as critical.
Dissociation constant	Waived: the test substance does not dissociate based on structural alerts.

7.5. Manufacture and uses

7.5.1. Quantities

Table 5

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

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

This substance is used by consumers, in articles, by professional workers (widespread uses), in formulation or re-packing, at industrial sites and in manufacturing.
For Consumer Uses ECHA has no public registered data indicating whether or in which chemical products the substance might be used. However, in the Chemical Safety Report (CSR) is reported that all consumer uses are polymer uses.

Table 6

USES	
	Use(s)
Uses as intermediate	Industrial use of manufacturing of substances as intermediate in closed systems with minimal release.
Formulation	PROC 1: Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions PROC 2: Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment conditions PROC 3: Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions PROC 4: Chemical production where opportunity for exposure arises PROC 5: Mixing or blending in batch processes PROC 8a: Transfer of substance or mixture (charging and discharging) at non-dedicated facilities PROC 8b: Transfer of substance or mixture (charging and discharging) at dedicated facilities PROC 9: Transfer of substance or mixture into small containers (dedicated filling line, including weighing) PROC 14: Tabletting, compression, extrusion, pelletisation, granulation PROC 15: Use as laboratory reagent Uses advised against: mixtures containing liquid monomer intended to come into contact with skin or nails.

Uses at industrial sites	PROC 1: Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions PROC 2: Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment conditions PROC 3: Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions PROC 4: Chemical production where opportunity for exposure arises PROC 5: Mixing or blending in batch processes PROC 6: Calendering operations PROC 8a: Transfer of substance or mixture (charging and discharging) at non-dedicated facilities PROC 8b: Transfer of substance or mixture (charging and discharging) at dedicated facilities PROC 9: Transfer of substance or mixture into small containers (dedicated filling line, including weighing) PROC 14: Tabletting, compression, extrusion, pelletisation, granulation PROC 21: Low energy manipulation of substances bound in materials and/or articles
Uses by professional workers	ERC8a: Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) ERC8b: Widespread use of reactive processing aid (no inclusion into or onto article, indoor) ERC8c: Widespread use leading to inclusion into/onto article (indoor) ERC8d: Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor) ERC8e: Widespread use of reactive processing aid (no inclusion into or onto article, outdoor) ERC8f: Widespread use leading to inclusion into/onto article (outdoor) PROC 2: Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment conditions PROC 3: Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment conditions PROC 4: Chemical production where opportunity for exposure arises PROC 5: Mixing or blending in batch processes PROC 6: Calendering operations PROC 8a: Transfer of substance or mixture (charging and discharging) at non-dedicated facilities PROC 8b: Transfer of substance or mixture (charging and discharging) at dedicated facilities PROC 9: Transfer of substance or mixture into small containers (dedicated filling line, including weighing) PROC 10: Roller application or brushing PROC 11: Non industrial spraying PROC 12: Use of blowing agents in manufacture of foam PROC 13: Treatment of articles by dipping and pouring PROC 14: Tabletting, compression, extrusion, pelletisation, granulation PROC 15: Use as laboratory reagent PROC 17: Lubrication at high energy conditions in metal working operations

	PROC 18: General greasing / lubrication at high kinetic energy conditions PROC 19: Hand-mixing with intimate contact and only PPE available. PROC 21: Low energy manipulation of substances bound in materials and/or articles PROC 23: Open processing and transfer operations with minerals/metals at elevated temperature PROC 24: High (mechanical) energy work-up of substances bound in materials and/or articles Uses advised against: mixtures containing liquid monomer intended to come into contact with skin or nails.
Consumer Uses	ECHA has no public registered data indicating whether or in which chemical products the substance might be used. However, in the CSR is reported that all consumer uses have to be considered as polymer uses. Uses advised against: mixtures containing liquid monomer intended to come into contact with skin or nails.
Article service life	ERC8b: Widespread use of reactive processing aid (no inclusion into or onto article, indoor) ERC8c: Widespread use leading to inclusion into/onto article (indoor) ERC8e: Widespread use of reactive processing aid (no inclusion into or onto article, outdoor) ERC8f: Widespread use leading to inclusion into/onto article (outdoor)

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

The substance is currently listed on Annex VI of CLP Regulation ((EC) No 1272/2008).

Table 7

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)**		
607-071-00-2	ethyl methacrylate	202-597-5	97-63-2	Flam.Liq. 2 Skin Irrit. 2 Eye Irrit. 2 Skin Sens. 1 STOT SE 3	H225 H315 H319 H317 H335		Note D

7.6.2. Self-classification

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

Skin Sens. 1B H317

7.7. Environmental fate properties

Hydrolysis of EMA is not expected to play an important role in the abiotic degradation since it is relatively slow within normal pH regimes in the aquatic environments. After exposure to the air EMA will be rapidly degraded by photochemical processes. EMA is readily biodegradable and based on a log Kow of 1.87, bioaccumulation of EMA is expected to be low.

7.7.1. Degradation

EMA, like other lower methacrylate esters, is hydrolytically stable at neutral and acidic pH. According to OECD test guideline 111, the half-life is ~ 2400 days at pH 7 and ~ 4800 days at pH 3. Under normal environmental conditions, abiotic degradation by hydrolysis is not expected to be a very important removal process in the environment.

Regarding phototrasformation in air, EMA is expected to photodegrade in the atmosphere either by reaction with photo-chemically produced hydroxyl radicals or by reaction with ozone. The reaction half-life for the atmospheric oxidation of EMA by hydroxyl radicals range has been estimated to be 19.5 h. For the reaction with ozone an atmospheric half-life of approximately one day has been calculated for all lower methacrylate esters, including EMA. A combined reaction half-life is calculated to be 10.8 h.

Concerning biotic degradation, a key study with reliability was performed according to a standard test protocol (OECD test guideline 301D, Ready Biodegradability Closed Bottle test). With an initial test substance concentration of 3.2 mg/l, 79.1% of EMA was biodegraded after 21 d, meeting the ten day window.
The registrant(s) concluded that the substance is readily biodegradable and based on the available information, the eMSCA can support this conclusion.

Concerning water, sediment and soil simulation tests the registrant(s) proposed a data waiving. Based on the available information, the eMSCA does not see any concern for these compartments.

7.7.2. Environmental distribution

The adsorption coefficient Koc has been calculated to be 1100 from a regression of the measured koc values for methacrylic acid (MAA), MMA and isobutyl methacrylate (iBMA). Due to the low value of log Koc the adsorption to solid soil phase is expected to be low. With respect to the aqueos compartment the calculated Henry's Law constant H at 25 °C and 1013 hPa is 19.5 Pa m3/mol (HENRYWIN calculation, v. 4.00). Due to the high value of H the substance will tend to evaporate from the water surface to the atmosphere.

For the determination of environmental distribution of the registered substance the registrant(s) proposed a Mackay Level III simulation. EMA when released to air or water, will predominantly remain in the environmental compartment into which it was released.

7.7.3. Bioaccumulation

The measured octanol/water partition coefficient (log Kow of 1.87) is low, indicating a low potential for bioaccumulation and low tendency of adsorption to soil and sediment. Concerning bioaccumulation the registrant(s) proposed a data waiving. As the substance has a low potential for bioaccumulation, the eMSCA does not see any concern for bioaccumulation in aquatic species.

The calculated bioconcentration factor for EMA, based on a log Kow of 1.87 is 8 (calculated according to Veith et al. 1979).

The registrant(s) concluded the substance is not bioaccumulative and based on the available information, the eMSCA can support this conclusion.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

7.8.1.1. Fish

The acute toxicity of EMA to fish is low. In a acute test to *Oncorhynchus mykiss* the results showed a 96h LC50 of 100 mg/L. The chronic toxcitity of the read-across substance MMA was found to be a NOEC of 9.4 mg/L in an Early Life Stage study with *Danio rerio*.

7.8.1.2. Aquatic invertebrates

Aquatic invertebrate are the most sensitive species to EMA. The short-term toxicity test to *Daphnia magna* showed a 48hr EC50 of >66 mg/L. The long-term endpoint was a 21d NOEC for reproduction of 18 mg/L for *Daphnia magna*.

7.8.1.3. Algae and aquatic plants

The only reliable toxicity test on algae was a limit test for the effects of EMA to *Pseudokirchneriella subcapitata*. Resuts showed a 72h ErC50 > 110 mg/L and a NOErC of 110 mg/L.

7.8.1.4. Sediment organisms

No information. Since no significant exposure to substance is expected in this compartment the eMSCA concludes that there is no concern for benthic organisms.

7.8.1.5. Other aquatic organisms

The registrant(s) did not report any information.

7.8.2. Terrestrial compartment

The registrant(s) provided a data waiving for toxicity on all three terrestrial taxonomic groups (soil macro-organisms, soil micro-organisms and terrestrial plants), with a justification based on exposure considerations. As indicated in the registration dossier, there is nosignificant director indirect exposure to soil compartment. Moreover, EMA has a low adsorptive and bioaccumulative potential. Therefore, evidence presented in the registration dossier with regard to physicochemical data, environmental fate properties and exposure pattern of this substance supports that a relevant distribution into soil compartment and a significant exposure of the terrestrial organisms can be considered unlikely.

Based on the available information, the eMSCA considers that there is no concern for terrestrial compartment.

7.8.3. Microbiological activity in sewage treatment systems

The registrant(s) provide a key study, performed according to the ISO 8192 Guideline (Test for inhibition of oxygen consumption by activated sludge) and in compliance with GLP criteria. Activated sludge inhibition data are indicated for EMA, after a contact time of 30 minutes, EC50 of 1000-1800 mg / L.

7.8.4. PNEC derivation and other hazard conclusions

Table 8

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	PNEC aqua (freshwater): 1.8 mg/L	Assessment factor: 10 Extrapolation method: assessment factor The derivation of the PNEC aqua freshwater can be based on three long term NOECs to EMA from species representing three trophic levels. An assessment factor of 10 was applied to the long term value of the most sensitive species, *Daphnia magna* (NOEC 18 mg/L)
Marine water	PNEC aqua (marine waters): 0.18 mg/L	Assessment factor: 100 Extrapolation method: assessment factor The eMSCA considers that the study with marine organisms, provided by the registrant(s), is not reliable, therefore PNEC should be based only on freshwater data and the appropriate assessment factor of 100 should be used accordingly
Intermittent releases to water	PNEC aqua (intermittent releases): 1.8 mg/L	Assessment factor: - Extrapolation method: - The eMSCA can support the registrant(s) conclusion to adopt the chronic PNEC as, if the default approach is used to derive the PNEC for intermittent releases from acute data, this value is lower than the chronic PNEC and, hence, is not appropriate

Sediments (freshwater)	PNEC sediment (sediment freshwater): 44.77 mg/Kg ww	Assessment factor: - Extrapolation method: EPM The calculation of the PNEC sediment is based on the EPM utilising PNEC freshwater. The resulting PNEC sediment, recalculated by eMSCA, differs from the value in the CSR (40 mg/Kg dw)
Sediments (marine water)	PNEC sediment (sediment marine water): 4.48 mg/Kg ww	Assessment factor: - Extrapolation method: EPM The Registrans do not report the PNEC sediment as no exposure of sediment is expected. The eMSCA disagrees with this conclusion and performs the calculation of the PNEC sediment based on the EPM utilising PNEC marine water
Sewage treatment plant	PNEC STP:10 mg/L	Assessment factor: 100 Extrapolation method: assessment factor PNEC STP The PNEC microorganisms is calculated from the EC50 value of an is ISO 8192 study test which occurred between 1000 and 1800 mg/L. AF 100 applied in accordance with ECHA Guidance on information requirements and chemical safety assessment Chapter R10:Characterisation of dose [concentration]-response for environment, 2008
Soil	PNEC soil: 1.47mg/kg soil dw	Assessment factor: - Extrapolation method: partition coefficient No toxicity data are available on soil organisms. Therefore, PNEC soil was derived using equilibrium partitioning method (EPM). It is only noted that the resulting PNEC soil, recalculated by eMSCA, differs from the value in the CSR (40.08 mg/Kg dw instead of 1.47 mg/kg soil dw).
Air	no hazard identified	
Secondary poisoning	no potential for bioaccumulation	Since the substance exhibits a low log Kow (1.87), is readily biodegradable and rapidly metabolised in rodents and

		humans, secondary poisoning is unlikely to be a relevant route of exposure.

7.8.5. Conclusions for environmental classification and labelling

EMA is readily biodegradable and based on the available information of low aquatic ecotoxicity. Hence, the eMSCA considers that classification for acute or chronic environmental hazard according to the current criteria of Regulation EC No 1272/2008,is not warranted.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

Methacrylate esters are absorbed to a greater or lesser extent by all routes and are subsequently rapidly hydrolysed by carboxylesterases to MAA and the respective alcohol. Clearance of the parent ester from the body is in the order of minutes for the short chain esters to tens of minutes for the longer esters. The primary metabolites, MAA and the corresponding alcohol, are also subsequently cleared rapidly from blood by standard physiological pathways, with the majority of the administered dose being exhaled as CO2. In the case of MAA the systemic half-life in rats is only 1.7 minutes. On the basis of the rapid metabolism and short half-lives a systemic accumulation of the esters and their metabolites is not expected.

Local effects resulting from the hydrolysis of the ester to the irritant and corrosive metabolite MAA are only observed following inhalation exposure in rodents and this has been shown to be due to the localised concentration of high levels of non-specific esterases in the Bowman's glands of the nasal olfactory tissues. This combination of highly efficient mechanisms of absorption/deposition and localised enzyme activity does not occur in the case of the dermal and oral routes so localised tissue corrosion would not be expected to occur. In summarising the available PBPK data on MMA SCOEL concluded that "Extensive PBPK modelling work has predicted that on kinetic grounds for a given level of exposure to MMA human nasal olfactory epithelium will be at least 3 times less sensitive than that of rats to the toxicity of MMA" (SCOEL, 2005). Local effects are not anticipated as a result of the localised concentration of the corresponding alcohol since the alcohols themselves do not produce local effects.

Overall there is a high level of confidence in the toxicokinetic and toxicodynamic assessment for these chemicals based upon *in vitro* and *in vivo* studies in rodents and human tissues. This is further supported by clear trends across the category consistent with predicted trends based on recognised QSAR based models. In terms of the overall relevance of the findings in animals to humans there is a high degree of confidence since the same toxicokinetic/dynamic processes are known to occur in humans. In the case of dermal exposure there is robust *in vitro* data based upon measurements in animal and human skin supported by an established QSAR model that shows that dermal absorption, and therefore risk, of these esters is lower in humans than in rodents. In the case of inhalation exposure well recognised morphological and physiological differences between rodents and humans have been confirmed for the methyl ester to indicate a lower sensitivity of humans than rodents to the local effects in the upper respiratory tract. This is consistent with findings in limited studies in clinical volunteers and by cross-sectional studies in workers with long-term exposure to concentrations of MMA vapour well in excess of the effect concentration in rodents. There is a high level of confidence that the findings for MMA can be equally applied to the ethyl ester. This is based upon the close structural similarity and physico-chemical properties supported by robust PBPK observations and effect data in animals.

Overall, therefore, the eMSCA considers the available toxicodynamic data sufficiently adequate, particularly since this is consistent with the general trend within the category and the predicted limited opportunity for exposure. In conclusion therefore, there is a high level of confidence in the toxicokinetic assessment for the category of C1-C8 methacrylate esters.

7.9.2. Acute toxicity and Corrosion/Irritation

7.9.2.1 Acute toxicity

Based on results of studies in animals and by analogy to human data with MMA, EMA is classified as irritant to the respiratory tract the registrant(s) concluded the substance is STOT Single Exp.3, H335: May cause respiratory irritation and based on the available information, the eMSCA can support this conclusion.

7.9.2.2. Irritation

7.9.2.3 Skin

The registrant(s) concluded the substance is Skin Irrit 2 and based on the available information, the eMSCA can support this conclusion.

7.9.3. Sensitisation

7.9.3.1 Skin sensitisation

In a standard LLNA assay with reliability 1 and considered as the key study, groups of mice were exposed to 25%, 50% or 100% EMA in vehicle (Acetone/Olive Oil). At those doses, respectively, the recorded stimulation indices (S.I.) were 0.93, 1.41 and 3.85. The EC3 value derived from these data is 82.6%; a result that would categorise EMA as a weak sensitiser.

On the basis of the study presented, the registrant(s) concluded that the substance is Skin Sens. 1B and based on the available information, the eMSCA support this conclusion. However the revision of the harmonised classification is not considered necessary, as in terms of the appropriate risk management measures there is no difference between the two classifications and thus a reclassification as Skin. Sens. 1B does not add administrative value.

7.9.4. Repeated dose toxicity

Not relevant.

7.9.5. Mutagenicity

In vitro data
Experimental data provided by the registrant(s) are discussed below.
EMA was tested in two bacterial reverse mutation assay. These two studies were performed before the publication of the current version of OECD 471, therefore the strain set is incomplete according to the current guideline. Both studies gave negative results. Moreover the substance was tested in L5178Y mouse lymphoma cells for gene mutation and chromosome aberrations induction (Moore et al. 1988). In mouse lymphoma cells the substance was weakly positive for both endpoints, but in the gene mutation experiment survival was less than 20% while in the chromosome aberration assay the cytotoxicity level was not determined. The Sister chromatid exchange assay SCE in CHO gave positive results.

The information available from *in vitro* studies on EMA is not sufficient to allow a clear conclusion. The bacterial studies were performed according to an old OECD guideline. The mammalian *in vitro* studies, in particular addressing clastogenicity, gave positive results, however, it is not clear whether this positive outcome were a true indication of clastogenicity or were due at least in part to a secondary effect of cytotoxicity.

In vivo data
As reported by the registrant(s), no data for EMA *in vivo* genotoxicity are available.

Category approach

The registrant(s) proposed a category-based read-across approach to address the information needs for mutagenicity. This approach was considered not acceptable and the following points were highlighted as major drawbacks: (i) lack of analysis of structural differences and the impact of these differences for the category members and the possibility to predict their properties, (ii) lack of data on the corresponding alcohol metabolites and (iii) no endpoint specific justification for the proposed read-across.

Therefore, the registrant(s) were requested in the substance evaluation decision to perform the battery of *in vitro* studies in order to reach a conclusion on the genotoxic potential of the substance.

In November 2017 the registrant(s) updated the dossier(s) and provided a revised justification for the read-across/category approach, which follows the principles described in the RAAF document (ECHA, 2017). The registrant(s) presented a strategy based on the category of lower alkyl (C1-C8) methacrylates. The members of the category are: MMA (the substance evaluated by France), EMA (i.e., the substance under evaluation in the present SEV), n-Butyl methacrylate (nBMA), iso-Butylmethacrylate (iBMA), and 2-Ethylhexylmethacrylate (2-EHMA), which differ for an incremental change in chain length in the respective alcoholic moieties. The rationale for the category formation is identified in the common chemical reactivity and common primary metabolic pathway.

For genotoxicity endpoints, the arguments for the EMA assessment are built on the hypothesis that different compounds have the same type of effects. In particular, electrophilic binding of the intact ester to DNA or proteins is hypothesised to result in "absence of variations in the strength of the predicted effect(s)" for the category members, and thus Scenario 6 of RAAF is selected by the registrant(s) for the genotoxicity assessment of EMA.

In this category, while the bacterial studies gave consistently negative results, some indication of gene mutation and clastogenicity was found in studies conducted *in vitro* on mammalian cells. However these findings were always reported in the presence of evident (and in some case excessive) cytotoxicity, therefore their biological relevance is questionable.

The available information for *in vivo* genotoxicity studies of the category members is summarized below:

- Most available studies on the reference substance MMA were performed before the publication of the current OECD guidelines and gave ambiguous results while the dominant lethal study on MMA is negative. The concern for mutagenicity was also confirmed by France in their substance evaluation (ANSES, 2018).
- The only recent *in vivo* micronucleus study reported is on the analogue nBMA. The test gave negative results.

Although the arguments and the settings of the category as were submitted in the justification document are considered acceptable, eMSCA disagrees with the assumptions that lead to the choice of the scenario 6 for the genotoxicity assessment. The reason of the disagreement relies on the mutagenicity assessment of MMA, which has a crucial role for the assessment of the category as a whole. Being MMA the lower bound of the category and the nearest neighbour of EMA, if its mutagenicity is not clarified and the mutagenic

concern is not completely ruled out, the evaluation of EMA based on the absence of genotoxicity effects for the entire category cannot be carried out. In fact, potential clastogenic effects leading to a concern for mutagenicity were not ruled out during the MMA evaluation (SEV conclusion document; 17 December 2018), and the possibility of falling into scenario 4, implying a "variation in the strength of the predicted effect(s) according to a regular pattern", cannot be excluded.

In conclusion eMSCA is of the opinion that the read-across adaptation for filling mutagenicity data gap for EMA is not acceptable. As a consequence, there appear to be data gaps for standard information requirements for mutagenicity.

7.9.6. Carcinogenicity

As reported by the registrant(s), no data on carcinogenicity of EMA are available.
The registrant(s) proposed a category-based read-across approach for the evaluation of the carcinogenicity potential. In particular, experimental data on MMA, a substance of the OECD category of short-chain alkyl methacrylates, were used to fill data gaps of ethyl methacrylate. No carcinogenic effects were observed after oral or inhalation administration of methyl methacrylate to mice or rats. Moreover the epidemiological data on increased tumor rates in exposed cohorts were of limited reliability and cannot be related to MMA as the solely causal agent.

In conclusion, there is no relevant concern on carcinogenicity in humans and animals for MMA as also confirmed by IARC in the monograph 60, 1994 and in the substance evaluation for MMA. Therefore, based on the available information currently the concern for carcinogenicity for EMA is not confirmed. However, since there are potential data gaps related to mutagenicity, the possibility of carcinogenicity of EMA cannot be completely ruled out.

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

Not evaluated.

7.9.8. Hazard assessment of physico-chemical properties

None impacting human health.

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

Not evaluated.

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

On the basis of the study presented, the registrant(s) concluded the substance is Skin Sens. 1B and based on the available information, the eMSCA can support this conclusion.

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.11. PBT and VPVB assessment

Persistence

Based on the results of the ready biodegradability study, the registrant(s) concluded that the substance is not expected to be persistent in the environment and it does not meet the P or vP criteria. The eMSCA can support this conclusion.

Bioaccumulation

Due to the low log Kow value, the registrant(s) concluded the substance does not meet the B o vB criteria. The eMSCA can support this conclusion.

Toxicity

The substance does not meet the T criterion for PBT assessment, showing data for long-term aquatic toxicity higher than the NOEC/EC10 value of 0.01 mg/l for freshwater organisms. The eMSCA can support this conclusion.

Overall conclusion

Based on the available information the eMSCA concludes that there is no concern for PBT.

7.12. Exposure assessment

7.12.1. Human health

There are no exposure scenarios of concern for workers and consumers. However, in the CSR is reported that all consumer uses have to be considered as polymer uses. In the CSR is also reported that migration studies showing very low migration of the monomers from the polymers when they are in contact with foods, human skin or body fluids like sweat and saliva, are available. However, eMSCA recommends the registrant(s) to perform a quantitative exposure assessment for the consumer uses.

7.12.2. Environment

Following the notification of decision on substance evaluation, the registrant(s) provided an updated CSR with 7 distinct exposure scenarios to better evaluate the exposure:

Manufacture of substance (ES1)
Use in production of formulations and re-packing (ESS2)
End use as monomer in formulations (ES3)
Use as intermediate (ES4)
End use as monomer in polymerisation (wet process) (ES5)
End use as monomer in polymerisation (dry process) (ES6)
Professional end use in formulations (ES7)

As stated by the registrant(s), in the new version of CSR, all scenarios have been assessed as local generic scenarios. Substance volume of 10 kT for region has been estimated as worst case (confidential survey of TF MMA consortium). Defaults of EUSES scenarios have been mainly used. Where defaults of EUSES have been evaluated to be too conservative they have been changed respectively using collected data, described and justified in the environmental contributing scenarios.

A group of manufacturers and importers, which have developed the exposure assessment for registration, compared to their own data and data of Emission Scenario Documents (ESDs), evaluated defaults of ECETOC TRA as conservative. Realistic release factors of

manufacturing and formulating processes are typically on a much lower level than ECETOC TRA defaults for industrial scale. Where defaults have been evaluated to be too conservative they have been changed respectively using collected data and ESD documents (Emission scenario document on coating industry and on chemical industry, OECD 2009; see also TGD on risk assessment, Part IV), described and justified in the exposure scenarios.

7.13. Risk characterisation

Based on the currently available information there is no risk identified.

Environment
The registrant(s) provided the information necessary to evaluate the risk for the environment, providing appropriate justifications for each refinement.

In conclusion, all RCR values calculated in all exposure scenarios are less than 1 and the risk is considered to be controlled in each environmental compartment.

7.14. References

ANSES, 2018: Substance Evaluation Conclusion as required by REACH Article 48 and Evaluation Report for methyl methacrylate, EC No 201-297-1, CAS No 80-62-6. (https://echa.europa.eu/documents/10162/c92faa6c-7134-fc58-5266-5b373cdc9286)

Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and- read-across)

Registration dossier for ethyl methacrylate, European Chemicals Agency. http://echa.europa.eu/

7.15. Abbreviations

AF Assessment factor
CAS Chemical abstracts service
C&L Classification and labelling
CLP Classification, labelling and packaging (Regulation (EC) No 1272/2008)
CM Carcinogenicity, mutagenicity
CCH Compliance checks
DNEL Derived no effect level
EMA Ethyl MethAcrylate
eMSCA Evaluating Member State Competent Authority
MMA Methyl MethAcrylate
NOAEL No Observed Adverse Effect Level
NOEC No Observed Effect Concentration
PBT Persistent, Bioaccumulative, Toxic
PEC Predicted Environmental Concentration
PNEC Predicted No Effect Concentration
RAAF Read-Across Assessment Framework
RCR Risk characterization ratio
vPvB Very Persistent and very Bioaccumulative