Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

methyl acrylate; methyl propenoate

EC Number: 202-500-6
CAS Number: 96-33-3

CLH-O-0000006956-59-01/F

Adopted

18 March 2021

18 March 2021

CLH-O-0000006956-59-01/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **methyl acrylate; methyl propenoate**

EC Number: **202-500-6**

CAS Number: **96-33-3**

The proposal was submitted by **Austria** and received by RAC on **3 February 2020.**

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

Austria has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **24 February 2020**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **24 April 2020**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Gerlienke Schuur**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **18 March 2021** by **consensus**.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	607-034-00-0	methyl acrylate; methyl propenoate	202-500-6	96-33-3	Flam. Liq. 2 Acute Tox. 4 * Acute Tox. 4 * Acute Tox. 4 * Skin Irrit. 2 Eye Irrit. 2 Skin Sen. 1 STOT SE 3	H225 H332 H312 H302 H315 H319 H317 H335	GHS02 GHS07 Dgr	H225 H332 H312 H302H315 H319 H317 H335			Note D
Dossier submitters proposal	607-034-00-0	methyl acrylate; methyl propenoate	202-500-6	96-33-3	**Modify** Acute Tox. 3 Acute Tox. 4 Acute Tox. 4	**Modify** H331 H312 H302	**Modify** GHS06	**Modify** H331 H312 H302		**Add** inhalation: ATE = 3 mg/L (vapour) dermal: ATE = 1250 mg/kg bw oral: ATE = 500 mg/kg bw	
RAC opinion	607-034-00-0	methyl acrylate; methyl propenoate	202-500-6	96-33-3	**Modify** Acute Tox. 3 Acute Tox. 4 Acute Tox. 4	**Modify** H331 H312 H302	**Modify** GHS06	**Modify** H331 H312 H302		**Add** inhalation: ATE = 3 mg/L (vapour) dermal: ATE = 1100 mg/kg bw oral: ATE = 500 mg/kg bw	
Resulting Annex VI entry if agreed by COM	607-034-00-0	methyl acrylate; methyl propenoate	202-500-6	96-33-3	Flam. Liq. 2 Acute Tox. 3 Acute Tox. 4 Acute Tox. 4 STOT SE 3 Skin Irrit. 2 Eye Irrit. 2 Skin Sen. 1	H225 H331 H312 H302 H335 H315 H319 H317	GHS02 GHS06 Dgr	H225 H331 H312 H302 H335 H315 H319 H317		inhalation: ATE = 3 mg/L (vapour) dermal: ATE = 1100 mg/kg bw oral: ATE = 500 mg/kg bw	Note D

GROUNDS FOR ADOPTION OF THE OPINION

RAC general comment

Methyl acrylate is used in articles, at industrial sites and in manufacturing. It is manufactured and imported in Europe in 10000 – 100000 tonnes per year.

HUMAN HEALTH HAZARD EVALUATION

RAC evaluation of acute toxicity

ACUTE TOXICITY – ORAL ROUTE

Summary of the Dossier Submitter's proposal

The table below shows the available acute oral studies.

Species	LD_{50} (mg/kg bw)	Dosing (mg/kg bw)	Results (mortality)	Reliability (DS)	Study	Remarks
rat (5 or 10 males per dose)	768	196, 303, 481, 762, 1210	196: 0/5 303: 0/5 481: 0/5 762: 2/5 1210: 5/5	3	1958a	Comparable OECD TG 401
rat (10 per dose)	300	6 doses	No information	3	1948	Similar to OECD TG 401
rabbit (1 to 4 females per dose)	280-420 [1]	120, 180, 280, 420, 620, 1000	120: 0/2 180: 0/4 280: 2/2 420: 1/1 620: 1/1 1000: 1/1	3	1949	Similar to OECD TG 401
mouse (4 per dose)	826	No information	No information	3	1982	
rabbit (2 per dose)	Ca 380-765	0.4, 0.8 (corresponding to 384, 768 mg/kg bw)	0.4 mL: 0/2 0.8 mL: 2/2	3	1960	
cat (1 per dose)	> 0.8 mL/kg bw	0.2, 0.4, 0.8	no mortalities[2]	3	1960	
rat	277	No information	No information	3	1975	Similar to OECD TG 401
mouse	840	No information	No information	4	1993	Similar to OECD TG 401
-	200	No information	No information	4	1960	

1. *Inconsistency between the REACH dossier (LD50 > 180 - < 280 mg/kg bw) and the CLH report Table 10.*
2. *Inconsistency between the REACH dossier (no mortalities) and the CLH report Table 10 (2 death at 0.8 mL)*

All available studies have some limitations. Two rat studies (1985a, 1948) result in LD_{50} values of 768 and 300 mg/kg bw (with no information on the test material). Other studies with rabbits,

mice or cats result in a range of LD_{50} values between 280 – 826 mg/kg bw but are less relevant because of insufficient information on dosing or small group sizes.

The lower LD_{50} of 300 mg/kg bw is just on the boundary between category 4 ($300 < LD_{50} \leq 2000$ mg/kg bw) and category 3 ($50 < LD_{50} \leq 300$ mg/kg bw). The other studies predominantly result in LD_{50} values belonging to category 4. Taken together, the majority of the studies indicate category 4, the few studies for category 3 are not considered reliable enough to consider this category.

No single study can be identified as the key study for classification, therefore the default ATE of 500 mg/kg bw was selected.

The DS proposed to classify methyl acrylate as Acute Tox. 4; H302 with a default ATE value of 500 mg/kg bw.

Comments received during consultation

One MSCA disagreed with the proposal as Acute Tox. 4. All studies reported in the CLH dossier have reliability 3 or 4. Three studies concluded on LD_{50} values resulting in category 4. One study reported an LD_{50} between 280 – 420 mg/kg bw and three studies concluded on LD_{50} resulting in category 3. The MSCA proposed Acute Tox. 3 and an ATE of 277 mg/kg bw (based on the lowest LD_{50}).

Two MSCAs can agree with a classification of Acute Tox. 4 and an ATE value of 500 mg/kg bw. One of these MSCAs remarked that the four relevant studies indicate category 4 or 3, but the study (1948) pointing to category 3 is based on a very small group size. Overall, the studies mainly indicate classification in category 4.

DS responded that category 4 is based on the most reliable study (1958) and supporting evidence.

Assessment and comparison with the classification criteria

There are nine studies available, none of them a GLP conform or guideline study. LD_{50} values range from 280 – 826 mg/kg bw from studies performed with rat, mouse, rabbit and cat, and using several different vehicles.

The most reliable studies point to a classification as Acute Tox. 4 ($300 < LD_{50} \leq 2000$ mg/kg bw), with LD_{50} values of 768 and 826 mg/kg bw. However, one study (1948) results in an LD_{50} of 300, which is exactly on the boundary between category 3 and 4. Another study results in an $180 < LD_{50} < 280$ (REACH registration dossier), different from the information in the Table of the CLH report. This would lead to a category 3, but the study has small group sizes. All in all, the studies mainly indicate a classification as category 4.

No study can be selected as key study for the ATE, furthermore, all studies have a Klimisch score 3 or 4. Therefore the default value is selected: ATE 500 mg/kg bw.

RAC concludes that methyl acrylate meets the criteria ($300 < ATE \leq 2\,000$ mg/kg bw) and should be classified as **Acute Tox. 4; H302 (Harmful if swallowed) with an ATE of 500 mg/kg bw**.

ACUTE TOXICITY – DERMAL ROUTE

Summary of the Dossier Submitter's proposal

The table below shows the available acute dermal studies.

Species	LD_{50} (mg/kg bw)	Dosing (mg/kg bw)	Results (mortality)	Rel. (DS)	Study	Remarks
rabbit (6 per dose)	1250	-	No information	3	1948	Similar to OECD TG 402
rabbit (3 per dose)	> 190	190	0/3	3	1958b	
rat (5 per dose)	Not calculated	1920	4/5	3	1958b	
rabbit (2 per dose)	Not determined	No information	2 mL/animal: 1/2 4 mL/animal: 2/2	3	1958b	
Rabbit (1 per dose)	> 32600	4300, 2840, 32600	No mortalities	3	1949	

Five studies are available. The key study in this case is the study from 1948 in which several doses were tested on more than 2 animals per dose. Other studies have (also) limitations and do not contradict the key study LD_{50}.

This study (1948) reports an LD_{50} of 1250 mg/kg bw which leads to classification as Acute Tox. 4 ($1000 < LD_{50} \leq 2000$ mg/kg bw). This study is also used for establishing an ATE of 1250 mg/kg bw.

The DS proposed to classify methyl acrylate as Acute Tox. 4; H312 with an ATE value of 1250 mg/kg bw.

Comments received during consultation

Three MSCAs support the classification as Acute Tox 4. However, two of these MSCAs prefer a generic ATE value of 1100 mg/kg bw given that in the key study no information is available on purity, mortalities or dose levels and the key study has a reliability score of 3 as all other studies.

The DS responded that based on the limited reliability of the available studies also a converted ATE of 1100 mg/kg bw can be supported.

Assessment and comparison with the classification criteria

The most reliable study from 1948 lacks information on purity, dose groups and information on mortality. However, the other four available studies also have their limitations (e.g. small group size, one dosing, no information on purity). This study reports an LD_{50} of 1250 mg/kg bw which leads to classification in category 4. Because of the limited reliability of all studies a default ATE of 1100 mg/kg bw is proposed.

RAC concludes that methyl acrylate meets the criteria for cat 4 ($1000 < LD_{50} \leq 2\,000$ mg/kg bw) and should be classified as **Acute Tox. 4; H312 (Harmful in contact with skin) with an ATE of 1100 mg/kg bw.**

ACUTE TOXICITY – INHALATION ROUTE

Summary of the Dossier Submitter's proposal

The table below shows the available acute inhalation studies.

Species	LC_{50} (mg/L)	Concentrations (mg/L)	Results (mortality)	Rel. (DS)	Study	Remarks
rat (10 males/ females per dose)	6.5	3.1, 5.7, 6.7, 8.6, 10.9	3.1: 0/20 5.7: M: 4/10, F: 2/10 6.7: M: 9/10, F: 4/10 8.6: M: 4/10, F: 10/10 10.9: 20/20	2	1979	Equivalent to OECD TG 403; purity 99.5%; 4h Same study, but with fasted animals: 5.7 mg/L
rat (6 males per dose)	> 2.7 & < 3.6	0.71, 1.30, 1.79, 2.68, 3.57, 5.36	0.71: 0/6 1.30: 0/6 1.79: 0/6 2.68: 1/6 3.57: 4/6 5.36: 6/6	2	1981	Similar to OECD TG 403, GLP; purity 99%; 4h
rat (10 males per dose)	4.8	1086, 1143, 1303, 1629, 1697, 2715 ppm	1086: 2/10 1143: 3/10 1303: 5/10 1629: 7/10 1697: 8/10 2715: 10/10	2	1985	Similar to OECD TG 403; 4h Same study, but with fasted animals: 3.2 mg/L
hamster (5 males/females per dose)	2.5	1.0, 2.0, 2.5, 3.1, 5.7	1.0: 0/20 2.0: 3/20 M: 1/10, F: 2/10 2.5: 15/20 M: 6/10, F: 9/10 3.1: 12/20 M: 5/10; F: 7/10 5.7: 20/20	2	1979	Similar to OECD TG 403; 4h Same study, but with fasted animals: 3.2 mg/L
mouse (10 males/females per dose)	5.1	1.0, 3.2, 5.7, 6.7, 8.6, 10.9	1.0: 0/20 3.2: M: 4/10, F: 1/10 5.7: M: 3/10, F: 0/10 6.7: M: 9/10, F: 10/10 8.6: M: 9/10, F: 10/10 10.9: 20/20	2	1979	Equivalent to OECD TG 403; 4h Same study, but with fasted animals: 5.7 mg/L
rat (5 males/5 females per dose)	< 10.8	10.8	M: 5/5 F: 2/5	3	2012	Similar to OECD TG 403 (but single dose); 4h
Rat (6 per dose)	3.6	3.6	3/6 at 3.6 mg/L	3	1948	Similar to OECD TG 403; 4h
rat (male/female)			M: 117 mg/L: 1/5 F: 121 mg/L: 3/5	3	1977	1h
Rat (6 per dose)		86.4	2 min: 0/6 4 min: 2/6 8 min: 6/6	3	1958a	2-8 min
Rabbit (4 per dose)	-		8.7, 1h: 2/4 9.04, 2.75 h: 4/4	3	1949	2.75h; 1h
rat	7.3			4	1979	Exposure period not specified
mouse	12.8			4	1979	Exposure period not specified

mouse	LC_{Lo} 9.3			4	1955	Exposure period not specified
Rat	LC_{Lo} 5.5			4	1978 1954	5h
No information	5.7			4	2014	Secondary source

One GLP conform guideline study (2012) in rats is available for methyl acrylate, however only one single concentration is reported. At 10.8 mg/L, 5/5 male and 3/5 female rats died, indicating that the 4h LC_{50} < 10.8 mg/L. Several other reliable studies with rats, mice and hamsters report LC_{50} values in the range of 2.5 - 6.5 mg/L. Overall, the data indicate a classification as category 3 (2.0 mg/L < 4h LC_{50} ≤ 10.0 mg/L).

The study with the lowest 4h-LC_{50} relevant for classification did not derive an LC_{50}, but only a range of possible values (> 2.7 & < 3.6 mg/L), therefore it is most appropriate to base the ATE value on the conversion rules (CLP Regulation, Table 3.1.2). Consequently, an ATE value of 3 mg/L is indicated for vapours.

The DS proposed to classify methyl acrylate as Acute Tox. 3; H331 with an ATE value of 3 mg/L (vapours).

Comments received during consultation

Three MSCAs agreed with the proposal as Acute Tox. 3 and proposed ATE of 3 mg/L.

Assessment and comparison with the classification criteria

Fifteen acute inhalation studies are available. No GLP conform guideline study is available, however several reliable studies in rats result in a range of LC_{50} values of 2.0 - 10.0 mg/L. This leads to a classification (2 < 4h LC_{50} ≤ 10 mg/L) as Acute Tox. 3.

The study with the lowest LC_{50} provided a range of > 2.7 & < 3.6 mg/L. Therefore, RAC proposes the default ATE of 3 mg/L for vapours.

RAC concludes that methyl acrylate meets the criteria for ca 3 (2 < 4h LC_{50} ≤ 10 mg/L) and should be classified as **Acute Tox. 3; H331 (Toxic if inhaled) with an ATE of 3 mg/L**.

ANNEXES:

Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).