Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

Ethyl acrylate

EC Number: 205-438-8
CAS Number: 140-88-5

CLH-O-0000006958-55-01/F

Adopted

18 March 2020

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18 March 2021

CLH-O-0000006958-55-01/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: **Ethyl acrylate**

EC Number: **205-438-8**

CAS Number: **140-88-5**

The proposal was submitted by **Austria** and received by RAC on **19 December 2019.**

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 2020** 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	607-032-00-X	Ethyl acrylate	205-438-8	140-88-5	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 H302 H312 H332 H315 H319 H317 H335	GHS02 GHS07 Dgr	H225 H302 H312 H332 H315 H319 H317 H335		Eye Irrit. 2; H319: C => 5 % STOT SE 3; H335: C => 5 % Skin Irrit. 2; H315: C => 5 %	Note D
Dossier submitters proposal	607-032-00-X	Ethyl acrylate	205-438-8	140-88-5	**Modify** Acute Tox. 3 Acute Tox. 4 Acute Tox. 4	**Modify** H331 H312 H302	**Modify** GHS06	**Modify** H331 H312 H302		**Add** inhalation: ATE = 9 mg/L (vapours) dermal: ATE = 1800 mg/kg bw oral: ATE = 1120 mg/kg bw	
RAC opinion	607-032-00-X	Ethyl acrylate	205-438-8	140-88-5	**Modify** Acute Tox. 3 Acute Tox. 4 Acute Tox. 4	**Modify** H331 H312 H302	**Modify** GHS06	**Modify** H331 H312 H302		**Add** inhalation: ATE = 9 mg/L (vapours) dermal: ATE = 1800 mg/kg bw oral: ATE = 1120 mg/kg bw	
Resulting Annex VI entry if agreed by COM	607-032-00-X	Ethyl acrylate	205-438-8	140-88-5	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	GHS06 GHS02 Dgr	H225 H331 H312 H302 H335 H315 H319 H317		inhalation: ATE = 9 mg/L (vapours) dermal: ATE = 1800 mg/kg bw oral: ATE = 1120 mg/kg bw Eye Irrit. 2; H319: C ≥ 5 % STOT SE 3; H335: C ≥ 5 % Skin Irrit. 2; H315: C ≥ 5 %	Note D

GROUNDS FOR ADOPTION OF THE OPINION

RAC general comment

Ethyl acrylate is manufactured and/or imported in Europe in a quantity of 100000 to 1000000 tonnes per year. It is used in the manufacture of paints, textiles, non-woven fibres and in formulation or repacking.

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 (10 males per dose)	1120	710, 840, 1000, 1190, 1410, 1680, 2000, 2380 vehicle Methocel	0: 0/10 710: 1/10 840: 1/10 1000:2/10 1190: 6/10 1410: 8/10 1680: 10/10 2000: 10/10 2380: 10/10	2	1984	Comparable OECD TG 401; purity 99%
rat (5 males per dose)	554	291, 462, 732, 1162, 1881 vehicle aqueous emulsion with 0.5 or 5% Traganth	291: 0/5 462: 2/5 732: 3/5 1162: 5/5 1881: 5/5	3	1958	Similar to OECD TG 401
rat (10 males per dose)	1020	795, 1000, 1260, and 1580 Vehicle not specified	795: 0/10 1000: 4/10 1260: 10/10 1580: 10/10	3	1949	Similar to OECD TG 401
rat (1-5 per dose)	461-731	18, 73, 291, 461, 731, 1159, 4609 Vehicle 10 or 20% olive oil	18: 0/1 73: 0/1 291: 0/1 731: 0/1 291: 0/5 461: 2/5 731: 4/5 1159: 3/3 1159: 2/2 4609: 2/2	3	1958a	
rat (5 per dose/sex)	>900	55, 10, 225, 450, or 900 vehicle aqueous ethanol	900: M 1/5, F 0/5	3	1986	Similar to OECD TG 401

mouse (5 per dose/sex)	900-1800	100, 225, 450, 900 or 1800 vehicle aqueous ethanol	1800: M 4/5, F: 3/5	3	1986	Similar to OECD TG 401
mouse (5 per dose)	1800	1000, 1400, 2000,2800, 4000 vehicle peanut oil	1000: M: 0/5, F: 0/5 1400: M: 0/5,F: 0/5 2000: M: 4/5, F: 4/5 2800: M: 5/5, F: 5/5 4000: M: 5/5, F: 5/5	3	1950	
rabbit (female)	280-420	120, 180, 280, 420, 620, 940 no vehicle	120: 0/1 180: 0/3 280: 0/4 420: 2/2 620: 1/1 940: 1/1	3	1949	
rabbit (2 per dose)	>184 - ≤ 368	184, 368, 736 vehicle aqueous emulsion in traganth (10% or 20%	184: 0/2 368: 1/2 736: 2/2	3	1960	
mouse (4 per dose)	1800	4 dose levels vehicle not specified		3	1982	Similar to OECD TG 401
rat	1020			3	1975	
rat (2 per dose)	>2000	Single dose, 2000 Vehicle PEG		3	1986	
cat (1 per dose)	>736	184, 368, 736 Vehicle 10% in corn oil		3	1960	
rat	800	vehicle aqueous emulsion in traganth (10% or 20%		4	1979	
no information	2080	no information		4	1971	

All studies show deficiencies; however, the available information is considered adequate for concluding on harmonized classification and on an ATE value. The most reliable study (Klimisch score 2) is the (first) study from 1984 with an LD_{50} of 1120 mg/kg bw. The NTP studies from 1986 did not result in an LD_{50} but could support a lower bound value of about 900 mg/kg bw.

The most appropriate study (1984; LD_{50} 1120 mg/kg bw) results in category 4 (Acute Tox 4 (oral) if the LD_{50}/ATE values are > 300 and ≤ 2000 mg/kg bw). This is supported by the LD_{50} values of studies in rodents with sufficient reliability. Only two studies with limited reliability would fall into the boundaries of category 3.

The DS proposed to classify ethyl acrylate as Acute Tox. 4; H302 with an ATE value of 1120 mg/kg bw.

Comments received during consultation

One MSCA agreed with the proposal as Acute Tox. 4 but proposing an ATE value of 554 mg/kg bw based on the study from 1958. In respond to this comment the DS considered that the converted ATE value of 500 mg/kg bw for Category 4 is in the same order of magnitude as the proposed ATE value of 554 mg/kg bw. Therefore, the DS proposed an ATE of 500 mg/kg bw.

Two other MSCAs were supportive of the classification as Acute Tox. 4 and the ATE of 1120 mg/kg bw.

Assessment and comparison with the classification criteria

There are 15 studies available, none of them according to guidelines or in conformity with GLP. LD_{50} values range from 280-2080 mg/kg bw from studies performed with rat, mouse, rabbit and cat, and using several different vehicles.

The most reliable study from 1984 results in an LD_{50} of 1120 mg/kg bw. This is supported by the NTP studies from 1986, which did not result in a LD_{50}, but show a lower boundary of 900 mg/kg bw. This leads to a classification as Acute Tox. 4 ($300 < LD_{50} \leq 2000$ mg/kg bw). The LD_{50} of the most reliable study results in an ATE of 1120 mg/kg bw.

RAC concludes that ethyl acrylate meets the criteria for cat 4 ($300 < ATE \leq 2000$ mg/kg bw) and should be classified as **Acute Tox. 4; H302 (Harmful if swallowed) with an ATE of 1120 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)	Reliability (DS)	Study	Remarks
rat (6 males per dose)	3049	2000, 2514, 3162, 3976, 5000	2000: 0/6 2514: 3/6 3162: 3/6 3976: 5/6 5000: 5/6	2	1986a	Comparable OECD TG 402/GLP; purity 99%
mouse (6 males per dose)	2997	2400, 3200, 4000	2400: 1/6 3200: 3/6 4000: 6/6	2	1986	Similar to OECD TG 402; purity 99%
rabbit (10 per dose)	1800	1580, 2000, 2520	1580: 1/10 2000: 5/10 2520: 10/10	2	1949	Similar to OECD TG 402
rat (4 per dose)	>5000	5000	0/6	3	1986d	
mouse (6 males per dose)	>5000	5000	no mortalities	3	1986d	
rat (1 male, 4 females per dose)	Not determined	1840	4/5	3	1958b	
rabbit (2 per dose)	>184	184	0/2	3	1958c	
rabbit (6-10 per dose)	Not specified	0.53-1.8	no information	3	1981	Similar to OECD TG 402
rabbit	Not determined			3	1949	

rabbit (2-4 per dose)	460	0.25, 0.5, 1.0, 4.0 mL/kg	0.25: 0/4 0.5: 2/4 1.0: 4/4 4.0: 2/2	3	1989	
rabbit (4 per dose)	580	0.5, 1 mL/kg	0.5: 1/4 1.0: 4/4	3	1989	
rabbit (2 per dose)	>126 & <252	126, 252	126: 0/2 252: 2/2	3	1986	
No information	1950			4	1971	

Thirteen studies are available, reporting a range for LD_{50} values between 126 and 252 to > 5000 mg/kg bw. Some studies used non-occlusive application or other applications. The rabbit studies from 1989 (with LD_{50} values leading to category 3) used an ambiguous test substance ('taft product').

Two studies of good quality resulted in an LD_{50} of 2997 mg/kg bw (in mice, 1986) and 3049 mg/kg bw (in rats, 1986a). Another study (1949) with rabbits, of somewhat lower quality, resulted in an LD_{50} of 1800 mg/kg bw.

The DS proposed to classify ethyl acrylate as Acute Tox. 4; H312 with an ATE value of 1800 mg/kg bw.

Comments received during consultation

Three MSCAs support the classification as Acute Tox. 3 and the ATE of 1800 mg/kg bw.

Assessment and comparison with the classification criteria

The three most reliable studies (Klimisch score 2), performed on rats (1986a), mice (1986), and rabbits (1949) lead to LD_{50} values of 3049, 2997 and 1800 mg/kg bw, respectively. It is noted that rabbits seem to be more sensitive than other species, also when taking into account the less reliable studies (noticing that these Klimisch score 3 rabbit studies are more recent).

RAC concludes that ethyl acrylate meets the criteria for cat 4 ($1000 < LD_{50} \leq 2000$ mg/kg bw) and should be classified as **Acute Tox. 4; H312 (Harmful in contact with skin) with an ATE of 1800 mg/kg bw.** The classification is supported by information from other rabbit studies.

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 per dose)	9	6.3, 8.1, 9.9, 11.4, 12.3	6.3: 1/10 8.1: 6/10 9.9: 7/10 11.4: 7/10 12.3: 9/10	2	1985	Similar to OECD TG 403; purity 98-98.5%; 4h
rat (5 males per dose)	25.8 (1 h), converted 12.9	23.2, 29.5, 35.3	23.2: 2/5 29.5: 3/5 35.3: 5/5	2	1989	Equivalent to OECD TG 403/GLP; purity 99.8%; 1h

rat (6 males per dose)	> 6.1	1.2, 2.0, 3.1, 4.1 and 6.1	1.2: 0/6 2.0: 0/6 3.1: 0/6 4.1: 0/6 6.1: 1/6	3	1981	4h
rat (6 per dose)	> 4.1 & < 8.2	4.1, 8.2, 16.3	4.1: 0/6 8.2: 5/6 16.3: 6/6	3	1949	Similar to OECD TG 403; 4h
rat (5 males/females per dose)	<9.137	9.137	M 4/5, F 2/5*	3	2012	Similar to OECD TG 403/GLP; 4h
rabbit (1 male, 4 females per dose)	<4.83	4.83	all animals died	3	1949	7h
Guinea pig (2 per dose)	<4.83	4.83	all animals died	3	1949	7h
monkey (3 per dose)	-	0.31	no mortalities	3	1995	Similar to OECD TG 403; 3, 6 h
rat (3 per dose)	<165	162 - 175	4 min: 0/6 8 min: 2/6 15 min: 6/6 30 min: 6/6	3	1958d	Similar to OECD TG 403; 4-30 min
rat (6 per dose)	5.8	4.1, 16.4	4.1: 0/4 16.4: 4/4	3	1989b	4h
rat	7.4		-	4	1979	Exposure duration not specified
mouse	16		-	4	1979	Exposure duration not specified
mouse (4-15 per dose)	Not determined	0.025, 0.05, 0.1, 0.5	0.025: 2/4 0.05: 4/7 0.1: 7/10 0.5: 6/15	4	1962	Exposure duration not specified

* Discrepancy: REACH dossier and Table 12 in CLH report provide F: 2/5, text in CLH report provides F: 3/5.

One GLP conform and guideline study in rats is available for ethyl acrylate, however only one single concentration is reported. At 9.317 mg/L 4/5 male and 3/5 females died, giving a strong indication that the 4h LC_{50} < 9 mg/L. In addition, two studies with adequate reliability (1985, 1989) reported LC_{50} values after 4h of exposure of 9 and 12.9 mg/L. An additional study (1981) provided an indication of the lower boundary with 1/6 deaths at 6.1 mg/L. Several studies of lower reliability reported 4h LC_{50} values in the range of 4.1-16 mg/L.

Overall, the data indicate a classification as category 3 (LC_{50} values > 2.0 mg/L and ≤ 10.0 mg/L, 4h exposure), based on LC_{50} of 9 mg/L, supported by the GLP conform study, which determined a LC_{50} < 9.137 mg/L, and a study indicating a LC_{50} > 6.1 mg/L.

The DS proposed to classify ethyl acrylate as Acute Tox. 3; H331 with an ATE value of 9 mg/L (vapours), based on the lowest LC_{50} value.

Comments received during consultation

One MSCA agreed with the proposal as Acute Tox. 3 and proposed ATE.

The other two MSCAs were in support of Acute Tox. 3, but not with the proposed ATE. One MSCA proposed a generic ATE of 3 mg/L (as other studies showed that it must be lower than 9 mg/L and no clear ATE can be defined). The other MSCA proposed an ATE of 7 mg/L, based on the LC_{50} values expected to be higher than 6.3 mg/L (mortality 1/10) and lower than 8.1 mg/L (mortality 6/10) of the 1985 study, performed similar to OECD TG 403 with 4 hours exposure to vapour of ethyl acrylate (purity: 98-98.5 %).

The DS responded that indeed other studies indicate a lower ATE value, although due to the used dosing no final value can be derived (but it may be between 6 and 7 mg/L). The converted ATE value would be 3 mg/L, while no mortalities were seen at doses around 4 mg/L (except in the 1949 study with 7h exposure). The DS cannot support a converted ATE, but proposed a value of around 7 mg/L based on a weight of evidence approach.

Assessment and comparison with the classification criteria

Thirteen acute inhalation studies (vapour) are available. Two reliable studies (Klimisch score 2) in rats result in 4h LC_{50} values of 9 and 12.9 mg/L. The lowest LC_{50} of 9 mg/L results in a classification ($2 < LC_{50} \leq 10$ mg/l for vapours) as Acute Tox. 3.

From the studies (with Klimisch score 2) used for assessing the category 3, the lowest LC_{50} is 9 mg/L. Other studies (with Klimisch score 3) suggest that the LC_{50} might be lower. However, these studies have uncertainties and it is difficult to establish an overall LC_{50} on these studies. Therefore, RAC considers appropriate an ATE of 9 mg/L.

RAC concludes that ethyl acrylate meets the criteria ($2 < LC_{50} \leq 10$ mg/L) and should be classified as **Acute Tox. 3; H330 (Toxic if inhaled) with an ATE of 9 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).