CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation),

Annex VI, Part 2

International Chemical Identification:
Methyl acrylate

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

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

Index Number: **607-034-00-0**

Contact details for dossier submitter:

Environment Agency Austria, Spittelauer Lände 5, A-1090 Vienna

on behalf of the Austrian Competent Authority (Austrian Federal Ministry for sustainability and tourism, Stubenring 1, 1010 Vienna, Austria)

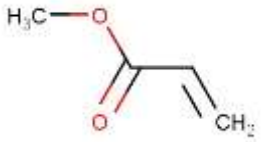
Version number: 02 Date: January 2020

CONTENTS

1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Methyl prop-2-enoate
Other names (usual name, trade name, abbreviation)	2-Propenoic acid methyl ester Propenoic acid methyl ester Methoxycarbonylethylene Acrylic acid methyl ester Methyl propenoate
ISO common name (if available and appropriate)	Not applicable
EC number (if available and appropriate)	202-500-6
EC name (if available and appropriate)	Methyl acrylate
CAS number (if available)	96-33-3
Other identity code (if available)	RTECS: AT2800000 ICSC Number: 0625 UN Number: 1919 PubChem CID: 7294
Molecular formula	$C_4H_6O_2$
Structural formula	
SMILES notation (if available)	COC(=O)C=C
Molecular weight or molecular weight range	86.09 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	≥ 80 wt %

1.2 Composition of the substance

Methyl acrylate is a mono-constituent substance.

Table 2: Constituents (non-confidential information).

Constituent **(Name and numerical identifier)**	**Concentration range (% w/w minimum and maximum in multi-constituent substances)**	**Current CLH in Annex VI Table 3.1 (CLP)**	**Current self-classification and labelling (CLP)**
Methyl acrylate EC 202-500-6 CAS 96-33-3	Not applicable	Flam. Liq. 2 (H225) Acute Tox. 4 * (H302) Acute Tox. 4 * (H312) Acute Tox. 4 * (H332) Skin Irrit. 2 (H315) Eye Irrit. 2 (H319) Skin Sen. 1 (H317) STOT SE 3 (H335) Note D	Flam. Liq. 2 (H225) Acute Tox. 4 (H302) Acute Tox. 4 (H312) Acute Tox. 3 (H331) Skin Irrit. 2 (H315) Eye Irrit. 2 (H319) Skin Sen. 1B (H317) STOT SE 3 (H335) Aquatic Chronic 3 (H412)

Table 3: Impurities (non-confidential information) if relevant for the classification of the substance.

Impurity **(Name and numerical identifier)**	**Concentration range** **(% w/w minimum and maximum)**	**Current CLH in Annex VI Table 3.1 (CLP)**	**Current self-classification and labelling (CLP)**	**The impurity contributes to the classification and labelling**
No data available				

Table 4: Additives (non-confidential information) if relevant for the classification of the substance.

Additive (Name and numerical identifier)	Function	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The additive contributes to the classification and labelling
No relevant data on additives available.					

Table 5: Test substances (non-confidential information).

Identification of test substance	Purity	Impurities and additives (identity, %, classification if available)	Other information	The study(ies) in which the test substance is used
The test substance is methyl acrylate in all reported studies. If available, the purity is given in the study records below.		The test substance frequently contains a polymerization inhibitor.	The existing harmonised classification accounts for stabilizers (Note D)	

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 6: Proposed harmonised classification

	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 H302 H312 H332 H315 H319 H317 H335	GHS02 GHS07 Dgr	H225 H302 H312 H332 H315 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. 4 Acute Tox. 4 Acute Tox. 3 **Retain**	**Modify** H302 H312 H331 **Retain**	**Modify** GHS06 **Retain** GHS02 Dgr	**Modify** H302 H312 H331 **Retain**		**Add** Oral: ATE = 500 mg/kg bw	Retain Note D

[04.01-MF-003.01]

					Flam. Liq. 2 Skin Irrit. 2 Eye Irrit. 2 Skin Sen. 1 STOT SE 3	H225 H315 H319 H317 H335		H225 H315 H319 H317 H335		Dermal: ATE = 1250 mg/kg bw Inhalation: ATE = 3 mg/L (vapour)	
Resulting Annex VI entry if agreed by RAC and COM	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. 3 Skin Irrit. 2 Eye Irrit. 2 Skin Sen. 1 STOT SE 3	H225 H302 H312 H331 H315 H319 H317 H335	GHS02 GHS06 Dgr	H225 H302 H312 H331 H315 H319 H317 H335		Oral: ATE = 500 mg/kg bw Dermal: ATE = 1250 mg/kg bw Inhalation: ATE = 3 mg/L (vapour)	Note D

Table 7: Reason for not proposing harmonised classification and status under public consultation

Hazard class	Reason for no classification	Within the scope of public consultation
Explosives	*hazard class not assessed in this dossier*	No
Flammable gases (including chemically unstable gases)	*hazard class not assessed in this dossier*	No
Oxidising gases	*hazard class not assessed in this dossier*	No
Gases under pressure	*hazard class not assessed in this dossier*	No
Flammable liquids	*hazard class not assessed in this dossier*	No
Flammable solids	*hazard class not assessed in this dossier*	No
Self-reactive substances	*hazard class not assessed in this dossier*	No
Pyrophoric liquids	*hazard class not assessed in this dossier*	No
Pyrophoric solids	*hazard class not assessed in this dossier*	No
Self-heating substances	*hazard class not assessed in this dossier*	No
Substances which in contact with water emit flammable gases	*hazard class not assessed in this dossier*	No
Oxidising liquids	*hazard class not assessed in this dossier*	No
Oxidising solids	*hazard class not assessed in this dossier*	No
Organic peroxides	*hazard class not assessed in this dossier*	No
Corrosive to metals	*hazard class not assessed in this dossier*	No
Acute toxicity via oral route	Acute Tox 4, H302	Yes
Acute toxicity via dermal route	Acute Tox 4, H312	Yes
Acute toxicity via inhalation route	Acute Tox 3, H331	Yes
Skin corrosion/irritation	*hazard class not assessed in this dossier*	No
Serious eye damage/eye irritation	*hazard class not assessed in this dossier*	No
Respiratory sensitisation	*hazard class not assessed in this dossier*	No
Skin sensitisation	*hazard class not assessed in this dossier*	No
Germ cell mutagenicity	*hazard class not assessed in this dossier*	No
Carcinogenicity	*hazard class not assessed in this dossier*	No

Hazard class	Reason for no classification	Within the scope of public consultation
Reproductive toxicity	*hazard class not assessed in this dossier*	No
Specific target organ toxicity-single exposure	*hazard class not assessed in this dossier*	No
Specific target organ toxicity-repeated exposure	*hazard class not assessed in this dossier*	No
Aspiration hazard	*hazard class not assessed in this dossier*	No
Hazardous to the aquatic environment	*hazard class not assessed in this dossier*	No
Hazardous to the ozone layer	*hazard class not assessed in this dossier*	No

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

Methyl acrylate had a harmonized classification under the Dangerous Substances Directive (67/548/EEC). This was translated to a harmonized CLP classification in Annex VI, Regulation (EC) No 1272/2008 (CLP Regulation) and the minimum classification (according to Annex VII) was applied to acute toxicity for all routes (marked as Acute Tox. 4 * for all routes).

The harmonised classification for methyl acrylate is

Flam. Liq. 2, H225
Acute Tox. 4 *, H302
Acute Tox. 4 *, H312
Acute Tox. 4 ,* H332
Skin Irrit. 2, H315
Eye Irrit. 2, H319
Skin Sen. 1, H317
STOT SE 3, H335

Note D[1]

Self-classification:

[1] Note D: Certain substances which are susceptible to spontaneous polymerisation or decomposition are generally placed on the market in a stabilised form. It is in this form that they are listed in Part 3 of Annex VI to Regulation (EC) No 1272/2008.

The frequency of hazard classifications based on all C&L notifications was retrieved from ECHA dissemination site [accessed 12/2020] and is given below. In total, 877 notifiers provided information on their hazard classifications (33 aggregated notifications). One notifier reported ethyl acrylate as not meeting GHS hazard criteria.

Hazard classifications occurring in notifications:

Hazard code	Hazard statement	% of notifications
H225	Highly Flammable liquid and vapor	100
H301	Toxic if swallowed	4.1
H302	Harmful if swallowed	96.5
H312	Harmful in contact with skin	100
H315	Causes skin irritation	100
H317	May cause an allergic skin reaction	100
H319	Causes serious eye irritation	100
H331	Toxic if inhaled	61.1
H332	Harmful if inhaled	32.3
H335	May cause respiratory irritation	100
H412	Harmful to aquatic life with long lasting effects	30.8
H411	Toxic to aquatic life with long lasting effects	0.5

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

[B.] Justification that action is needed at Community level is required.

Reason for a need for action at Community level:

- Change in existing entry due to changes in the criteria (DSD-CLP)
- Disagreement by DS with current self-classification

Further detail on need of action at Community level:

There is a harmonised classification entry in Annex VI to Regulation (EC) No 1272/2008 containing a minimum classification and it is concluded that a refinement of the classification based on available data is justified. Differences in self-classification between different notifiers in the C&L Inventory and registration dossier are discovered.

Methyl acrylate is an important industrial chemical. To minimize uncertainties in classification and ensure a high level of protection of workers, classification for acute toxicity has been evaluated.

5 IDENTIFIED USES

Methyl acrylate is manufactured and/or imported in the European Economic Area in 10 000 - 100 000 tonnes per year. Identified uses are in articles, at industrial sites and in manufacturing (Table 8).

Table 8: Registered uses of methyl acrylate (according to ECHA dissemination database, November 2020).

Manufacture	Manufacture of intermediates at production site
	Manufacture of substance (and distribution)
	Polymerization at production sites
	Polymerization at downstream user sites
	Use as laboratory reagent
Uses at industrial sites	Manufacture of Intermediates at downstream user sites
	Manufacture of Intermediates at production sites
	Polymerization at downstream user sites
	Polymerization at production sites
	Use as laboratory reagent
	Industrial application of adhesives
Article service life	Manufacture of intermediates at production sites
	Polymerization at downstream user sites
	Manufacture of intermediates at downstream user sites
	Polymerization at production sites
	Manufacture and distribution
	Use as laboratory reagent

6 DATA SOURCES

Systematic searches for publications and other relevant data were performed based on the following databases:

- U.S. National Library of Medicine, Pubmed.gov[2]

[2] https://www.ncbi.nlm.nih.gov/pubmed assessed at 7.2.2019

- TOXNET[3], ChemID*plus*[4], IPCS[5], eChemPortal[6], EPA Comptox Dashboard[7], EPA Chemview[8]
- Chemical Abstracts, Medline, Biosis, Embase, SciSearch, PQScitech (at host STN International Europe[9])

in addition to unspecific databases (e.g., *google scholar*).

The REACH registration dossier for methyl acrylate, available from ECHA's disseminated database (accessed 2019) has been analysed for study references, which then have been considered as data sources for this CLH report.

Relevant reviews and monographs with toxicological risk assessments on methyl acrylate were analysed for study references. Used reviews are Murphy and Davies (1993), IARC (IARC, 1979) and more recent IARC assessments, OECD (2005), MAK Commission (Hartwig and MAK Commission, 1986) and more recent MAK evaluations, ECETOC (1998).

Whenever relevant information in secondary sources was identified, it was attempted to retrieve the respective primary sources.

7 PHYSICOCHEMICAL PROPERTIES

Table 9: Summary of physicochemical properties

Property	Value	Reference	Comment
Physical state at 20°C and 101,3 kPa	Liquid	(ECHA Dissemination, 2019)	Visual observation
Melting/freezing point	-75.6 °C	(ECHA Dissemination, 2019)	Reported from handbook, measured at 1013.25 hPa
Boiling point	80.1 °C	(ECHA Dissemination, 2019)	Measured at 1013.25 hPa

[3] https://toxnet.nlm.nih.gov/ assessed at 7.2.2019

[4] https://chem.nlm.nih.gov/chemidplus/ assessed at 7.2.2019

[5] http://www.inchem.org/ assessed at 7.2.2019

[6] http://www.echemportal.org/echemportal/page.action?pageID=9 assessed at 7.2.2019

[7] https://comptox.epa.gov/dashboard/ assessed at 7.2.2019

[8] https://chemview.epa.gov/chemview assessed at 7.2.2019

[9] http://www.stn-international.de/index.php?id=123 assessed at 13.2.2019

Property	Value	Reference	Comment
Relative density	0.95	(ECHA Dissemination, 2019)	Reported from handbook, measured at 20 °C
Vapour pressure	90 hPa	(ECHA Dissemination, 2019)	Measured at 20 °C
Surface tension	not surface active	(ECHA Dissemination, 2019)	
Water solubility	60 g/L	(ECHA Dissemination, 2019)	Reported from handbook, measured at 20 °C
Partition coefficient n-octanol/water	0.739	(ECHA Dissemination, 2019)	Measured at 25 °C
Flash point	-2.8 °C	(ECHA Dissemination, 2019)	Reported from publication, measured at 1013.25 hPa
Flammability	Highly flammable	(ECHA Dissemination, 2019)	Reported from secondary source, measured
Explosive properties	Non-explosive	(ECHA Dissemination, 2019)	Estimated, based on chemical structure
Self-ignition temperature	468 °C	(ECHA Dissemination, 2019)	Reported from handbook, measured at 1013.25 hPa
Oxidising properties	No oxidising properties	(ECHA Dissemination, 2019)	Estimated, based on chemical structure
Granulometry	Not applicable		
Stability in organic solvents and identity of relevant degradation products	Not applicable		
Dissociation constant	Not applicable		
Viscosity	0.472 mPa*s	(ECHA Dissemination, 2019)	Reported from data base, measured at 25 °C

8 EVALUATION OF PHYSICAL HAZARDS

Not performed for this substance.

[04.01-MF-003.01]

9 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

Evaluation not performed for this substance.

10 EVALUATION OF HEALTH HAZARDS

Acute toxicity

10.1 Acute toxicity - oral route

Table 10: Summary table of animal studies on acute oral toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels, duration of exposure	Value LD50	Reference
Acute oral toxicity, Similar to OECD 401 GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rat, strain and sex not specified 5 or 10 animals per dose group (conflicting reports)	Methyl acrylate Source: no information Purity: no information	196, 303, 481, 762 and 1210 mg/kg bw (calculated with a density of 0.96 g/mL); original data were 204, 316, 501, 794 and 1260 mL/kg bw [sic!, µL/kg bw is correct]) Single application via gavage Vehicle: 0.5 or 10% aqueous Traganth (conflicting reports). Concentration in Vehicle: 2%. Maximum volume applied: 63 mL/kg bw Post exposure observation: 7 days	768 mg/kg bw, in the dossier, the original value is reported as "800 µL" [800 µL/kg bw implied] Mortalities: 1210 mg/kg bw: 5/5 762 mg/kg bw: 2/5 481 mg/kg bw: 0/5 303 mg/kg bw: 0/5 196 mg/kg bw: 0/5	BASF AG (1958a) in (OECD (2005) [Study 001 in REACH registration]
Acute oral toxicity, Similar to OECD 401 GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rat, Sherman, no information on sex 10 animals per dose group	Methyl acrylate Source: no information Purity: no information	6 dose groups, no concentrations specified, but spaced by a factor of 1.58 Single application via gavage Vehicle: No information No information on post exposure observation	300 mg/kg bw No information on mortalities	Smyth and Carpenter (1948) [Study 002 in REACH registration]
Acute oral toxicity, Similar to OECD 401	Rabbit, strain not specified, females only Different group sizes, see	Methyl acrylate Source: no information Purity: no	120, 180, 280, 420, 620 and 100 mg/kg bw Single application	280 - 420 mg/kg bw Mortalities: 120: 0/2	Treon et al. (1949) [Study 004 in

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance,**	**Dose levels, duration of exposure**	**Value** **LD50**	**Reference**
GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	mortality table for details	information	via gavage No vehicle No information on observation time	180: 0/4 280: 2/2 420: 1/1 620: 1/1 1000: 1/1	REACH registration]
Acute oral toxicity, Similar to OECD 401 GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Mouse, ddY, male only 4 animals per dose group	Methyl acrylate Source: Tokyo Kasei Co Purity: No information	No information on dose levels Single application via gavage Vehicle: no information No information on post exposure observation	826 mg/kg bw (95% CI: 594 - 1150), reported as 9.6 mmol/kg bw (6.9-13.4) No information on mortalities	Tanii and Hashimoto (1982) [Study 003 in REACH registration]
Acute oral toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rabbit, no information on species or sex 2 animals per dose group	Methyl acrylate Source: no information Purity: no information	0.4, 0.8 mg/kg bw Single application via gavage Vehicle: 10% or 20% in aqueous Traganth, not further specified No information on post exposure observation	> 0.4 & < 0.8 mL/kg bw Mortalities: 0.4 mL: 0/2 0.8 mL: 2/2	BASF AG (1960) in OECD (2005) [Study 005 in REACH registration]
Acute oral toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Cat, no information on species or sex 1 animal per dose group	Methyl acrylate Source: no information Purity: no information	0.4, 0.8 mg/kg bw Single application via gavage Vehicle: 10% or 20% in aqueous Traganth, not further specified No information on post exposure observation	> 0.4 & < 0.8 mL/kg bw Mortalities: 0.4 mL: 0/2 0.8 mL: 2/2	BASF AG (1960) in OECD (2005) [Study 006 in REACH registration]
Acute oral toxicity, Similar to OECD 401 GLP: no Reliability (REACH registration): 3	Rat, Wistar, no information on sex No information on group size	Methyl acrylate Source: no information Purity: no information	No information on dose groups Single application via gavage Vehicle: polyethylene glycol, no further information	277 mg/kg bw No information on mortalities	Paulet and Vidal (1975) [Study 009 in REACH registration]

[04.01-MF-003.01]

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels, duration of exposure	Value LD50	Reference
Reliability (this assessment): 3			7 days post observation time		
Acute oral toxicity, Similar to OECD 401 GLP: No information Reliability (this assessment): 4	Mouse, CF-1, no information on sex No information on group size	Methyl acrylate Source: No information Purity: No information	No information on dose levels Single application via gavage Vehicle: No information Post exposure observation: No information	840 mg/kg bw No information on mortalities	Latven (1993) in OECD (2005) [Study 007 in REACH registration]
Acute oral toxicity, No further information Reliability (this assessment): 4 This result is likely a mistake that is passed on within secondary references, it could not be verified.	No information	No information	No information	200 mg/kg bw No further information	Fassett (1963) in OECD (2005) [Study 008 in REACH registration]

10.1.1 Short summary and overall relevance of the provided information on acute oral toxicity

Two old studies on rats, similar to OECD Guideline 401, are available (BASF AG, 1958 the key study in the REACH registration dossier and Smyth, 1948). Both studies are limited in their reliability primarily due to the lack of characterization of the test material. These studies determined an LD_{50} of 768 mg/kg bw and 300 mg/kg bw. One further rat study lacking important experimental details, which reports a LD_{50} of 277 mg/kg bw (Paulet and Vidal, 1975), is not considered to be of sufficient reliability to be taken into account.

Several studies performed on rabbits, mice or cats, are available which have a lower value for classification because of insufficient dose groups or small group sizes. LD_{50} in these studies ranges from 280 – 826 mg/kg bw. Finally, LD_{50} values from studies only reported in secondary sources without experimental details (RL4) range from 200 – 840 mg/kg bw and are not considered relevant for the assessment.

No human studies with relevance for comparison with the criteria in Regulation (EC) No 1272/2008 are available.

[04.01-MF-003.01]

10.1.2 Comparison with the CLP criteria

According to Table 3.1.1 of Regulation (EC) No. 1272/2008 a substance shall be classified as

- Acute Tox. 4 (oral) if the LD_{50}/ATE values are > 300 and ≤ 2000 mg/kg bw.

- Acute Tox. 3 (oral) if the LD_{50}/ATE values are > 50 and ≤ 300 mg/kg bw.

All available studies have deficiencies, however, the information available is considered adequate for concluding on a harmonized classification and ATE value. Among the available studies, the studies on rats (being the preferred species for classification of oral toxicity) with several dose groups and sufficient animals per dose group are considered the most appropriate ones for classification. The lower LD_{50} from these studies (300 mg/kg bw) lies just at the boundary between category 3 and category 4, while the other LD_{50} (768 mg/kg bw) corresponds to category 4. The remaining study results, which include tests on additional species, predominantly produced results corresponding to category 4, while one study is giving a range for the LD_{50} where the lower bound is belonging to category 3. Taken together, the WoE favours a classification as Acute Oral Tox. 4, as the majority of studies in several species come to this conclusion and the much fewer studies that indicate category 3 are not considered reliable enough to deviate from the majority of study outcomes.

10.1.3 Conclusion on classification and labelling for acute oral toxicity

Based on the criteria for classification in regulation (EC) No. 1272/2008, methyl acrylate has to be classified in category 4 for acute oral toxicity (Acute Tox. 4, H302).

No single study can be identified as pivotal for classification therefore using the default ATE is most appropriate. Based on the conversion rules in Table 3.1.2 of Regulation (EC) No. 1272/2008, an ATE value of 500 mg/kg bw is indicated.

10.2 Acute toxicity - dermal route

Table 11: Summary table of animal studies on acute dermal toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels duration of exposure	Value LD50	Reference
Acute dermal toxicity, Similar to OECD 402 GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rabbit, no information on strain or sex 6 animals per dose group	Methyl acrylate No information on source No information on purity	No information on dose levels Occlusive application Vehicle: Methyl "Cellosolve" 24 h exposure No information on post exposure observation	1250 mg/kg bw (reported as 1.3 mL/kg, converted with density 0.96 g/mL) Mortalities: No information	Smyth and Carpenter (1948) [Study 001 in REACH registration]

[04.01-MF-003.01]

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels duration of exposure	Value LD50	Reference
Acute dermal toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 2 Reliability (this assessment):3	Rabbit, no information on strain or sex 3 animals per dose group	Methyl acrylate No information on source No information on purity	Only dose: 190 mg/kg bw Occlusive application 24 h exposure 21 d observation time	> 190 mg/kg bw Mortalities: all 3 animals survived	BASF AG, (1958b) in OECD (2005) [Study 002 in REACH registration]
Acute dermal toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 3 Reliability (this assessment): 3	Rat, no information on sex and strain 5 animals per dose group	Methyl acrylate No information on source No information on purity	Single dose level: 1920 mg/animal Exposed skin was submerged in test substance 4 h exposure 28 d observation	No LD50 calculated Mortalities: 1920 mg: 4/5	BASF AG, (1958b) in OECD (2005) [Study 005 in REACH registration]
Acute dermal toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 3 Reliability (this assessment): 3	Rabbit, no information on strain and sex 2 animals per dose group	Methyl acrylate No information on source No information on purity	No information on dose levels Application to ears, no vehicle, no further information on application (occlusive/non-occlusive not specified) 24 h exposure 28 d observation	No LD50 determined Mortalities: 2 mL/animal: 1/2 4 mL/animal: 2/2	BASF AG, (1958b) in OECD (2005) [Study 004 in REACH registration]
Acute dermal toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 3 Reliability (this assessment): 3	Rabbit, no information on strain or sex 1 animal per group	Methyl acrylate No information on source No information on purity	Repeated application of 1 or 5 mL, total dose 4.3, 28.4, 32.6 g/kg bw. Occlusive application 1 to 3 h total exposure (removal by washing between applications) Observation time not specified, highest dose was	> 32.6 g/kg bw No mortality observed at highest dose	Treon et al. (1949) [Study 003 in REACH registration]

[04.01-MF-003.01]

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels duration of exposure	Value LD50	Reference
			observed for 8 weeks		

10.2.1 Short summary and overall relevance of the provided information on acute dermal toxicity

Only a limited number of studies on dermal toxicity are available. Among the available studies, the study by Smyth and Carpenter (1948), which is also the key study in the REACH registration, stands out regarding reliability because it is the only one where several doses were tested (although no methodological description of the dose groups is given in the primary source) on more than 2 animals per dose. The remaining studies have considerable deficiencies, but do not contradict the LD_{50} determined in the study by Smyth and Carpenter (1948).

No human studies with relevance for comparison with the criteria in regulation (EC) No 1272/2008 are available.

10.2.2 Comparison with the CLP criteria

According to Table 3.1.1 of Regulation (EC) No. 1272/2008 a substance shall be classified as

- **Acute Tox. 4 (dermal) if the LD_{50}/ATE values are > 1000 and ≤ 2000 mg/kg bw**
- **Acute Tox. 3 (dermal) if the LD_{50}/ATE values are > 200 ≤ 1000 mg/kg bw**

A classification is proposed based on the only available study which determined an LD_{50}, although the reliability is limited. The major concern is the lacking information on purity and dose groups. This study reports a LD_{50} of 1250 mg/kg bw, which corresponds to category 4 of the CLP criteria for acute dermal.

10.2.3 Conclusion on classification and labelling for acute dermal toxicity

Based on the criteria in regulation (EC) No 1272/2008 methyl acrylate has to be classified in category 4 for acute dermal toxicity (Acute Tox. 4, H312).

Based on the LD_{50} used for classification an ATE value of 1250 mg/kg bw is indicated.

10.3 Acute toxicity - inhalation route

Table 12: Summary table of animal studies on acute inhalation toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, , form and particle size (MMAD)	Dose levels, duration of exposure	Value LC50	Reference
Acute inhalation toxicity, Equivalent to OECD 403 GLP: no Reliability (REACH registration): 1 Reliability (this assessment): 2	Rat, Sprague-Dawley, male and female 5 males and 5 females per dose group	Methyl acrylate, as vapour Purity: 99.5% Source: No information	3.1, 5.7, 6.7, 8.6 and 10.9 mg/L (analytical) 4 h exposure 14 days post exposure observation	6.5 mg/L (95% CI: 5.8 – 7.2) Mortalities: 10.9 mg/L: 20/20 8.6 mg/L: males: 4/10, females: 10/10 6.7 mg/L: males: 9/10, females: 4/10 5.7 mg/L: males: 4/10, females: 2/10 3.1 mg/L: 0/20 Same study, but with fasted animals: 5.7 mg/L (No CI given)	BASF AG (1979) in OECD (2005) [Study 002 and 006 in REACH registration]
Acute inhalation toxicity, Similar to OECD 403 GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 2	Rat, Holtzman, male only 6 males per dose group	Methyl acrylate, as vapour Purity: 99% Source: Aldrich Chemical Co., Milwaukee	200, 365, 500, 750, 1000 and 1500 ppm (analytical), corresponding to 0.71, 1.30, 1.79, 2.68, 3.57, and 5.36 mg/L 4 h exposure 72 h post exposure observation	> 2.7 & < 3.6 mg/L Mortalities: 0.71 mg/L: 0/6 1.30 mg/L: 0/6 1.79 mg/L: 0/6 2.68 mg/L: 1/6 3.57 mg/L: 4/6 5.36 mg/L: 6/6	Silver and Murphy (1981) [Study 010 in REACH registration]
Acute inhalation toxicity, Similar to OECD 403 GLP: no Reliability (this assessment): 2	Rat, Sprague Dawley, male only 10 males per dose group	Methyl acrylate, as vapour Purity: 98 – 98.5 %, Source: no information	1086, 1143, 1303, 1629, 1697, 2715 ppm (analytical) 4 h exposure No information	1350 ppm (95% CI: 1161 – 1570) corresponding to 4.8 mg/L Mortalities: 1086 ppm: 2/10	Oberly and Tansy (1985)

[04.01-MF-003.01]

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, , form and particle size (MMAD)	Dose levels, duration of exposure	Value LC50	Reference
			on post-exposure observation	1143 ppm: 3/10 1303 ppm: 5/10 1629 ppm: 7/10 1697 ppm: 8/10 2715 ppm: 10/10	
Acute inhalation toxicity, Equivalent to OECD 403 GLP: no Reliability (REACH registration): 1 Reliability (this assessment): 2	Hamster, chinese, male and female 5 males and 5 females per dose group	Methyl acrylate, as vapour Purity: 99.5% Source: No information	1.0, 2.0, 2.5, 3.1 and 5.7 mg/L (analytical) 4 h exposure 14 days post exposure observation	2.5 mg/L (No CI given) Mortalities: 5.7 mg/L: 20/20 3.1 mg/L: males 5/10, females 7/10 2.5 mg/L: males 6/10, females 9/10 2.0 mg/L: males: 1/10, females: 2/10 1.0 mg/L: 0/20 Same study, but with fasted animals: 3.2 mg/L (No CI given)	BASF AG (1979) in OECD (2005) [Study 003 and 008 in REACH registration]
Acute inhalation toxicity, Equivalent to OECD 403 GLP: no Reliability (REACH registration): 1 Reliability (this assessment): 2	Mouse, NMRI, male and female 5 males and 5 females per dose group	Methyl acrylate, as vapour Purity: 99.5% Source: No information	1.0, 3.2, 5.7, 6.7, 8.6, 10.9 mg/L (analytical) 4 h exposure 14 days post exposure observation	5.1 mg mg/L (No CI given) Mortalities: 10.9 mg/L: 20/20 8.6 mg/L: males 9/10, females 10/10 6.7 mg/L: males 9/10, females 10/10 5.7 mg/L: males 3/10, females 0/10 3.2 mg/L: males 4/10, females 1/10 1.0 mg/L: 0/20 Same study, but with fasted	BASF AG (1979) in OECD (2005) [Study 004 and 007 in REACH registration]

[04.01-MF-003.01]

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, , form and particle size (MMAD)	Dose levels, duration of exposure	Value LC50	Reference
				animals: 5.7 mg/L (No CI given)	
Acute inhalation toxicity, similar to OECD 403 GLP: yes Reliability (REACH registration): 1, key study Reliability (this assessment): 3 This study is reported as "According to OECD 403", with RL1. However, only a single exposure concentration is reported	Rat, Wistar, male and female 5 males and 5 females per dose group	Methyl acrylate, as vapour Purity: 99.95% Batch: 011063eda0 No information on source	Only concentration level: 10.8 mg/L (analytical) 4 h exposure 14 days post exposure observation	<10.8 mg/L Mortalities: 10.8 mg/L: m 5/5, f 2/5	Unnamed study report (2012) [Study 001 in REACH registration]
Acute inhalation toxicity, Similar to OECD 403 GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rat, strain and sex not specified 6 animals per dose group	Methyl acrylate, as vapour Purity: no information Source: no information	No information on dose groups No analytical determination, concentrations estimated from dilution settings 4 h exposure 14 days post-exposure observation	3.6 mg/L (no CI given) Mortalities at 3.6 mg/L: 3/6 No mortality data on other concentrations	Smyth and Carpenter (1948) [Study 011 in REACH registration]
Acute inhalation toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rat, Sprague Dawley, male and female, No information on group size	Methyl acrylate, as vapour Purity: no information Source: no information	Only single concentration (saturated vapour with analytical determination) Unclear description of exposure method (could be stationary vapour atmosphere)	males, 33000 ppm: 1/5 deaths females, 34000 ppm: 3/5 deaths (corresponding to 118 mg/L and 121 mg/L, respectively)	Vernot et al. (1977) [Study 013 in REACH registration]

[04.01-MF-003.01]

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance, , form and particle size (MMAD)**	**Dose levels, duration of exposure**	**Value** **LC50**	**Reference**
			1 h exposure 14 days post-exposure observation		
Acute inhalation toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rat, no information on strain and sex 6 animals per group	Methyl acrylate, as vapour Purity: no information Source: no information	Approximately 86.4 mg/L (9% vol) (calculation via evaporation rate, no analytical determination)2 min to 8 min exposure 14 days post-exposure observation	2 min: 0/6 deaths 4 min: 2/6 deaths 8 min: 6/6 deaths	BASF AG, (1958a) in OECD (2005) [Study 009 in REACH registration]
Acute inhalation toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rabbit, no information on strain or sex 4 animals per group	Methyl acrylate Purity: no information Source: no information	2.75 h exposure to 9.04 mg/L, 1 h exposure to 8.70 mg/L (no information on analytical determination)	8.7 mg/L, 1h: 2/4 9.04 mg/L, 2.75 h: 4/4 No further information	Treon et al, (1949) [Study 012 in REACH registration]
Acute inhalation toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 3 Reliability (this assessment): 4	Rat, No information on strain or sex No information on groups	Methyl acrylate Purity: no information Source: no information	No information	7.3 mg/L No further information	Lomonova and Klimova (1979) [Study 014 in REACH registration]
Acute inhalation toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 3	Mouse, No information on strain or sex No information on groups	Methyl acrylate Purity: no information Source: no information	No information	12.8 mg/L (reported as 3635 ppm) No further information	Lomonova and Klimova (1979) [Study 015 in REACH registration]

[04.01-MF-003.01]

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, , form and particle size (MMAD)	Dose levels, duration of exposure	Value LC50	Reference
Reliability (this assessment): 4, (publication only available in foreign language)					
Acute inhalation toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 3 Reliability (this assessment): 4, (no translation available)	No information on experimental animals No information on groups	Methyl acrylate Purity: no information Source: no information	No information	LCLo: 9.4 mg/L LC100: 20 mg/L No further information	Karpov (1955) [Study 016 in REACH registration]]
Acute inhalation toxicity, Not similar to guideline GLP: no Reliability (REACH registration): 4 Reliability (this assessment): 4	Rats, no information on strain or sex No information on groups	Methyl acrylate Purity: no information Source: no information	5 h exposure, No further information	LCLo: 5.5 mg/L Originally reported as 1540 ppm No further information	Secondary source: Velling (1978) in OECD (2005) [Study 017 in REACH registration]
Acute inhalation toxicity, Not similar to guideline GLP: no Reliability (this assessment): 4	No information on groups	Methyl acrylate Purity: no information Source: no information	No information	1600 ppm (corresponding to 5.7 mg/L) Only value reported in secondary source, no further information	Secondary source: Parod (2014)

10.3.1 Short summary and overall relevance of the provided information on acute inhalation toxicity

A GLP conform guideline study is reported as key study in the REACH dossier, however only a single concentration level has been reported (Unnamed, 2012). At 10.8 mg/L, 5/5 male and 3/5 female rats died, giving a strong indication that the LC_{50} is < 10.8 mg/L. Yet the study can't be used as a basis for classification

because of a missing lower bound of toxicity. The confidential information in the registration dossier has been checked to confirm that no information on additional concentration levels is available.

However, several other studies of acceptable quality are available. Three of them have the same study design and were performed with rats, mice or hamsters. In addition, each species was tested in non-fasted and fasted state. For comparison with the criteria in regulation (EC) No 1272/2008, the study on non-fasted rats is the most relevant. This study determined an LC_{50} of 6.5 mg/L (95% CI: 5.8 – 7.2 mg/L, BASF AG (1979) in OECD (2005)). The other studies in this series derive comparable LC_{50} values (2.5 – 5.7 mg/L). Additional studies of acceptable reliability performed on rats determined LC_{50} values of 2.7 – 4.8 mg/L (Oberly and Tansy, 1985; Silver and Murphy, 1981).

Several unreliable study results are available with the majority of results backing the results of the reported studies above and only two results, which are only known from secondary sources without experimental detail, are available which correspond to a less stringent classification of acute inhalation toxicity.

In conclusion, all available studies with acceptable reliability indicate a LC_{50} in the range of 2.7 – 6.5 mg/L.

No human studies with relevance for comparison with the criteria in Regulation (EC) No 1272/2008 are available.

10.3.2 Comparison with the CLP criteria

According to Table 3.1.1 of Regulation (EC) No. 1272/2008 a substance shall be classified as

- Acute Tox. 4 (inhalation) if the LD_{50} values are > 10.0 mg/L and ≤ 20.0 mg/L (4h exposure)
- Acute Tox. 3 (inhalation) if the LD_{50} values are > 2.0 mg/L and ≤ 10.0 mg/L (4h exposure)

No GLP-conform guideline study is available. However several non-GLP studies of acceptable reliability are available. These studies uniformly correspond to a classification as category 3 (2.0 – 10.0 mg/L). This classification is further supported by the majority of other study results and none of the studies provides a reason to deviate from category 3.

10.3.3 Conclusion on classification and labelling for acute inhalation toxicity

Based on the criteria in regulation (EC) No 1272/2008, methyl acrylate has to be classified in category 3 for acute inhalative toxicity (Acute Tox. 3, H 331).

The study with the lowest LD_{50} relevant for classification did not derive an LD_{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 Table 3.1.2 of regulation (EC) No 1272/2008. Consequently, an ATE value of 3 mg/L is indicated for vapours.

10.4 Skin corrosion/irritation

Evaluation not performed for this substance.

10.5 Serious eye damage/eye irritation

Evaluation not performed for this substance.

10.6 Respiratory sensitisation

Evaluation not performed for this substance.

10.7 Skin sensitisation

Evaluation not performed for this substance.

10.8 Germ cell mutagenicity

Evaluation not performed for this substance.

10.9 Carcinogenicity

Evaluation not performed for this substance.

10.10 Reproductive toxicity

Evaluation not performed for this substance.

10.11 Specific target organ toxicity-single exposure

Evaluation not performed for this substance.

10.12 Specific target organ toxicity-repeated exposure

Evaluation not performed for this substance.

10.13 Aspiration hazard

Evaluation not performed for this substance.

11 EVALUATION OF ENVIRONMENTAL HAZARDS

Evaluation not performed for this substance.

12 EVALUATION OF ADDITIONAL HAZARDS

Evaluation not performed for this substance.

13 ADDITIONAL LABELLING

Not applicable for this evaluation.

14 ANNEXES

All relevant information for classification is included in this document.

15 REFERENCES

BASF AG, Department of Toxicology (1958a). Report on toxicological studies with different acrylic acid esters, unpublished study. (VII/308), 9 December 1958.

BASF AG, Department of Toxicology (1958b). unpublished studies. VII/308 and 348, 21 July 1958.

BASF AG, Department of Toxicology (1960). Report on toxicological studies with acrylic acid esters in rabbits and cats, unpublished study. (VII/308), 8 November 1960.

BASF AG, Department of Toxicology (1979). unpublished study, Determination of the acute inhalation toxicity. (78/622), 14 February 1979.

ECETOC, European Centre for Ecotoxicology and Toxicology of Chemicals (1998). JACC Report No. 37. Joint Assessment of Commodity Chemicals. Methyl Acrylate. Brussels, Belgium.

ECHA Dissemination (2019). Information on Chemicals - Registered Substances. European Chemicals Agency. Online: http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

Fassett, D.W. (1963). Esters. In: Patty, F.A., Patty's Industrial Hygiene and Toxicology, Vol. II, 2nd ed., Interscience Publishers New York, 1877-1880.

Hartwig, A.; MAK Commission (1986). Methylacrylat [MAK Value Documentation in German language, 1986]. In: The MAK-Collection for Occupational Health and Safety, 1-9. https://onlinelibrary.wiley.com/doi/10.1002/3527600418.mb3527609633d3527600011.

IARC, International Agency for Research on Cancer (1979). Acrylic Acid, Methyl Acrylate, Ethyl Acrylate and Polyacrylic Acid. In: IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Vol. 19. Some Monomers, Plastics and Synthetic Elastomers, and Acrolein, WHO, World Health Organization, Geneva, Switzerland. https://monographs.iarc.fr/wp-content/uploads/2018/06/mono19.pdf, 47-71.

Karpov, B.D. (1955). Toxicological assessment of methylacrylate. *Gigiena i Sanitarija*, 20, 19-22.

Latven, A.R. (1993). Munich Research Laboratory Inc., Rohm and Haas Company, Contract Laboratory No. 50RC-1003 (1956) cited in Tyler T et al.(eds): Health Effect Assessments of the Basic Acrylates. CRC Press

Lomonova, G.V.; Klimova, E.I. (1979). [Data on the toxicology of the methyl and ethyl ethers of acrylic acid]. *Gigiena Truda i Professional'nye Zabolevaniia*, 9, 55-56.

Murphy, S.R.; Davies, J.H. (1993). Methyl acrylate health effects assessment. In: Taylor, T.B.; Murphy, S.R.; Hunt, E.K., Health Effect Assessments of the Basic Acrylates, CRC Press, Boca Raton, FL, 33-52.

Oberly, R.; Tansy, M.F. (1985). LC50 values for rats acutely exposed to vapors of acrylic and methacrylic acid esters. *Journal of Toxicology and Environmental Health*, 16, 811-822.

OECD, Organisation for Economic Co-Operation and Development (2005). SIDS Dossier. Methyl Acrylate (CAS No. 96-33-3). Paris, France.

Parod, R.J. (2014). Methyl Acrylate. In: Wexler, P., Encyclopedia of Toxicology, 2nd edition, Academic Press, 69-71.

Paulet, G.; Vidal, E. (1975). [On the toxicity of some acrylic and methacrylic esters, acrylamide and polyacrylamides]. *Archives des Maladies Professionnelles de Médecine, du Travail et de Sécurité Sociale*, 36, 58-60.

Silver, E.H.; Murphy, S.D. (1981). Potentiation of acrylate ester toxicity by prior treatment with the carboxylesterase inhibitor triorthotolyl phosphate (TOTP). *Toxicology and Applied Pharmacology*, 57, 208-219

Smyth, H.F.; Carpenter, C.P. (1948). Further experience with the range finding test in the industrial toxicology laboratory. *Journal of Industrial Hygiene and Toxicology*, 30, 63-68.

Tanii, H.; Hashimoto, K. (1982). Structure-toxicity relationship of acrylates and methacrylates

Toxicology Letters, 11, 125-129.

Treon, J.F.; Sigmon, H.; Wright, H.; Kitzmiller, K.V. (1949). The toxicity of methyl and ethyl acrylate

Journal of Industrial Hygiene and Toxicology, 31, 317-326.

Unnamed study report (2012) REACH registration data. https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15313/7/3/3

Velling, E.I. (1978). Arkhangel'skaya Materialy por Voprosu Prom. Toksikol. Klin. Prof. Boleznei Sbornik 45-53 (1957) in Chem. Abstr. 54, 14457ff (1954). as cited in: BASF AG, Department of Toxicology, unpublished study (XXVI/351), 30 May 1978.

Vernot, E.H.; MacEwen, J.D.; Haun, C.C.; Kinkead, E.R. (1977). Acute toxicity and skin corrosion data for some organic and inorganic compounds and aqueous solutions. *Toxicology and Applied Pharmacology*, 42, 417-423