Committee for Risk Assessment

RAC

Annex 1
Background document
to the Opinion proposing harmonised classification and labelling at EU level of

allyl methacrylate; 2-methyl-2-propenoic acid 2-propenyl ester

EC Number: 202-473-0
CAS Number: 96-05-9

CLH-O-0000006957-57-01/F

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It includes the proposal of the dossier submitter and the conclusion of RAC. It is based on the official CLH report submitted to public consultation. RAC has not changed the text of this CLH report but inserted text which is specifically marked as 'RAC evaluation'. Only the RAC text reflects the view of RAC.

Adopted

18 March 2021

CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2

International Chemical Identification:

Allyl methacrylate

EC Number: **202-473-0**

CAS Number: **96-05-9**

Index Number: **607-246-00-3**

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ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON ALLYL METHACRYLATE; 2-METHYL-2-PROPENOIC ACID 2-PROPENYL ESTER

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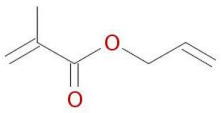
ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON ALLYL METHACRYLATE; 2-METHYL-2-PROPENOIC ACID 2-PROPENYL ESTER

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)	Prop-2-en-1-yl 2-methylprop-2-enoate
Other names (usual name, trade name, abbreviation)	2-Methyl-2-propenoic acid 2-propenyl ester 2-Methyl-acrylic acid allyl ester 2-Propenoic acid, 2-methyl-, 2-propenyl ester 2-Propenyl 2-methyl-2-propenoate 2-Propenyl ester of 2-Methyl, 2-propenoic acid ACRYESTER A Ageflex AMA Allyl alcohol, methacrylate Allyl Methacrylat AMA Methacrylic acid, allyl ester Prop-2-enoate, 2-methyl, 2-propenyl Visomer AMA
ISO common name (if available and appropriate)	Not applicable
EC number (if available and appropriate)	202-473-0
EC name (if available and appropriate)	Allyl methacrylate
CAS number (if available)	96-05-9
Other identity code (if available)	RTECS: UD3483000 PubChem CID: 7274
Molecular formula	$C_7H_{10}O_2$
Structural formula	
SMILES notation (if available)	CC(=C)C(=O)OCC=C
Molecular weight or molecular weight range	126.153 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

Allyl methacrylate 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)
Allyl methacrylate EC 202-473-0 CAS 96-05-9	Not applicable	Flam. Liq. 3 (H226) Acute Tox. 4 * (H302) Acute Tox. 4 * (H312) Acute Tox. 3 * (H331) Aquatic Acute 1 (H400)	Flam. Liq. 3 (H226) Acute Tox. 4 (H302) Acute Tox. 3 (H311) Acute Tox. 2 (H330) STOT RE 2 (H373) Aquatic Acute 1 (H400) Aquatic Chronic 3 (H412) Note D[1]

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 data 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 allyl methacrylate in all reported studies. If available, the purity is given in the study records below.				

[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.

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 6: Proposed harmonised classification and labelling

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	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	607-246-00-3	allyl methacrylate 2-methyl-2-propenoic acid 2-propenyl ester	202-473-0	96-05-9	Flam. Liq. 3 Acute Tox. 4 * Acute Tox. 4 * Acute Tox. 3 * Aquatic Acute 1	H226 H302 H312 H331 H400	GHS02 GHS09 GHS06 Dgr	H226 H302 H312 H331 H400			
Dossier submitters proposal	607-246-00-3	allyl methacrylate 2-methyl-2-propenoic acid 2-propenyl ester	202-473-0	96-05-9	**Modify** Acute Tox. 4 Acute Tox. 3 Acute Tox. 2 **Retain** Flam. Liq. 3 Aquatic Acute 1	**Modify** H302 H311 H330 **Retain** H226 H400	**Retain** GHS02 GHS09 GHS06 Dgr	**Modify** H302 H311 H330 **Retain** H226 H400		**Add** Oral: ATE = 401 mg/kg Dermal: ATE = 467 mg/kg Inhalation: ATE = 1.47 mg/L (vapours)	
Resulting Annex VI entry if agreed by RAC and COM	607-246-00-3	allyl methacrylate 2-methyl-2-propenoic acid 2-propenyl ester	202-473-0	96-05-9	Flam. Liq. 3 Acute Tox. 4 Acute Tox. 3 Acute Tox. 2 Aquatic Acute 1	H226 H302 H311 H330 H400	GHS02 GHS09 GHS06 Dgr	H226 H302 H311 H330 H400		Oral: ATE = 401 mg/kg Dermal: ATE = 467 mg/kg Inhalation: ATE = 1.47 mg/L (vapours)	

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 3, H311	Yes
Acute toxicity via inhalation route	Acute Tox 2, H330	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
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

Allyl methacrylate 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. 3 * for inhalation route and Acute Tox. 4 * for oral and dermal route).

The current harmonized classification (CLP, Annex VI Table 3.1) for allyl methacrylate is:

Flam. Liq. 3; H226

Acute Tox. 4 *; H302

Acute Tox. 4 *, H312

Acute Tox. 3 *, H331

Aquatic Acute 1, H400

Self-classification:

The frequency of hazard classifications among all C&L notifications (occurring in at least 10% of notifications) was retrieved from ECHA dissemination site [accessed 12/2020] and is given below. In total, 304 notifiers provided information on their hazard classifications (13 aggregated notifications):

Hazard code	Hazard statement	% of notifications
H226	Flammable liquid and vapor	99.7
H302	Harmful if swallowed	99.7
H311	Toxic in contact with skin	28.9
H312	Harmful in contact with skin	70.7
H330	Fatal if inhaled	28.9
H331	Toxic if inhaled	67.1
H373	Causes damage to organs through prolonged or repeated exposure	28.9
H400	Very toxic to aquatic life	99.7
H412	Harmful to aquatic life with long lasting effects	27.6

RAC general comment

Allyl methacrylate is manufactured and/or imported in 1000 to 10000 tonnes per year. It is used as monomer in dry or bead polymerisation and as an intermediate.

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.

Allyl methacrylate 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

Allyl methacrylate is manufactured and/or imported in the European Economic Area in 1 000 - 10 000 tonnes per year. Identified uses are by professional workers (widespread uses), in formulation or re-packing, at industrial sites and in manufacturing (Table 8).

Table 8: Registered uses of allyl methacrylate (according to ECHA dissemination site, November 2020)

Manufacture	Manufacturing of substance
Formulation	Formulation of preparations and re-packing
Uses at industrial sites	Industrial use for inclusion in matrix
	Industrial use of monomers
	Industrial use of monomers (dry polymerisation)
	Industrial use of monomers (bead polymerisation)
	Industrial use of monomers (emulsion polymerisation)
	Industrial use as intermediate
Uses by professional workers	Professional use for inclusion in matrix

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]
- 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 allyl methacrylate, 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 allyl methacrylate were analysed for study references. Used reviews are OECD (2009) and Régnier (2007).

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 °C	(ECHA Dissemination, 2019)	Measured at 1021 hPa
Boiling point	141 °C	(ECHA Dissemination, 2019)	Measured at 1021 hPa, extrapolated value
Relative density	0.934	(ECHA Dissemination, 2019)	Measured at 20 °C
Vapour pressure	5.18 hPa	(ECHA Dissemination, 2019)	Measured at 20 °C, extrapolated value
Surface tension	no surface active expected or can be predicted	(ECHA Dissemination, 2019)	study does not need to be conducted based on structure

[2] https://www.ncbi.nlm.nih.gov/pubmed assessed 22.1.2019
[3] https://toxnet.nlm.nih.gov/ assessed 22.1.2019
[4] https://chem.nlm.nih.gov/chemidplus/ assessed 22.1.2019
[5] http://www.inchem.org/ assessed 22.1.2019
[6] http://www.echemportal.org/echemportal/page.action?pageID=9 assessed 22.1.2019
[7] https://comptox.epa.gov/dashboard/ assessed 22.1.2019
[8] https://chemview.epa.gov/chemview assessed 22.1.2019
[9] http://www.stn-international.de/index.php?id=123 assessed 22.1.2019

Property	Value	Reference	Comment
Water solubility	2.2 g/L	(ECHA Dissemination, 2019)	Measured at 20 °C and pH 4.6 - 5.9
Partition coefficient n-octanol/water	2.15 - 2.3	(ECHA Dissemination, 2019)	Measured at 25 °C and pH 6.2
Flash point	34.5 °C	(ECHA Dissemination, 2019)	Measured at 1013.25 hPa
Flammability	Not applicable		
Explosive properties	No explosive properties	(ECHA Dissemination, 2019)	Estimated, based on chemical structure
Self-ignition temperature	265 °C	(ECHA Dissemination, 2019)	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	0.78 mPa*s	(ECHA Dissemination, 2019)	Measured at 20 °C

8 EVALUATION OF PHYSICAL HAZARDS

Not performed for this substance.

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 LD_{50}	Reference
Acute oral toxicity, Similar to OECD 401 GLP: no	Rat, CF Nelson (albino), male only 10 males per dose group	Allyl methacrylate Source: no information Purity: no	157, 313, 625 and 1250 mg/kg bw Administration not specified,	470 mg/kg bw (95% CI: 350-640 mg/kg bw) Mortalities:	Rohm and Haas Company (1975) in (OECD, 2009) [Study 001 in REACH

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance,**	**Dose levels, duration of exposure**	**Value LD_{50}**	**Reference**
Reliability (REACH registration): 2 Reliability (this assessment): 3		information	gavage implied Vehicle: 10% in corn oil (w/v) Observation time: 14 d	157 mg/kg bw: 0/10 313 mg/kg bw: 2/10 625 mg/kg bw: 7/10 1250 mg/kg bw: 10/10	registration]
Acute oral toxicity, Similar to OECD 401 GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rat, Carworth-Wistar 5 males per dose group	Allyl methacrylate Source: not specified Purity: not specified	Doses not explicitly specified, logarithmic series differing by a factor of 2 Single application via gavage No explicit information on vehicle Observation time: 14 d	401 mg/kg bw (95% CI: 289 – 560 mg/kg bw), reported as 0.43 mL/kg bw (95%CI; 0.31 – 0.60 mL/kg bw), density used for conversion not explicitly stated No information on mortalities	Smyth et al. (1969) [Study 002 in REACH registration]
Acute oral toxicity, No information on guideline GLP: no information Reliability (REACH registration): 4 Reliability (this assessment): 4	Rat, strain and sex not specified Group size snot specified	Allyl methacrylate Source: no information Purity: no information	No information on doses No information on application No information on vehicle No information on application	421 mg/kg bw No information on mortalities	Anonymous (1981) [Study 003 in REACH registration]
Acute oral toxicity, No information on guideline GLP: not specified Reliability (REACH registration): 3 Reliability (this assessment): 4 (no translation available)	Rat, strain not specified, males and females No information on group size	Allyl methacrylate Source: no information Purity: no information	No information on dose levels No information on application No information on vehicle	males: 70 mg/kg bw females: 148 mg/kg bw No information on mortalities	Smirnova et al. (1990) [Study details according to Study 004 REACH registration]

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance,**	**Dose levels, duration of exposure**	**Value LD_{50}**	**Reference**
Acute oral toxicity, No information on guideline GLP: not specified Reliability (REACH registration): 3 Reliability (this assessment): 4 (no translation available)	Mouse, strain not specified, males and females No information on group size	Allyl methacrylate Source: no information Purity: no information	No information on dose levels No information on application No information on vehicle	Males: 57 mg/kg bw Females: 184 mg/kg bw No information on mortalities	Smirnova et al. (1990) [Study details according to Study 005 REACH registration]

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

Two studies on rats are available which generally adhere to guideline principles, but have limited reliability due to lacking information on purity of the test substance (Rohm and Haas Company, 1975 in OECD, 2009; Smyth et al., 1969). These studies determined LD_{50} values of 470 mg/kg bw (95% CI: 350-640 mg/kg bw) and 401 mg/kg bw (95% CI: 289 – 560 mg/kg bw). Study results only available without experimental details from secondary references further report a LD_{50} range of 57 – 421 mg/kg bw.

No human studies with relevance for comparison with the classification criteria are available.

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 studies show deficiencies, however, the available information is considered adequate for concluding on harmonized classification and ATE value. Among the available data, the two most reliable results (LD_{50} of 470 and 401 mg/kg bw) correspond to category 4. Two study results only known from secondary literature correspond to category 3, however due to the lack of information on experimental details, they are not considered a reason to deviate from category 4.

10.1.3 Conclusion on classification and labelling for acute oral toxicity

According to the criteria for classification in Regulation (EC) No. 1272/2008, allyl methacrylate has to be classified in category 4 for acute oral toxicity (Acute Tox. 4, H302).

Based on the lowest LD_{50} used for classification an ATE value of 401 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 LD_{50}**	**Reference**
Acute dermal toxicity, Similar to OECD 402 GLP: no Reliability (REACH registration): 2 Reliability (this assessment): 3	Rabbit, Albino New Zealand 4 males per dose group	Allyl methacrylate No information on source No information on purity	No information on dose levels Occlusive application No information on vehicle 24 h exposure 14 d observation	467 mg/kg bw (95% CI: 345 - 635 mg/kg bw), reported as 0.5 mL/kg (0.37 – 0.68 mL/kg), density used for conversion not explicitly stated No information on mortalities	Smyth et al. (1969) [Study 001 in REACH registration]
Acute dermal toxicity, No information on Guideline GLP: no Reliability (REACH registration): 4 Reliability (this assessment): 4	Rabbit, strain not specified, sex not specified No information on group sizes	Allyl methacrylate No information on source No information on purity	No information on dose levels No further information	210 mg/kg bw No further information	Secondary source: Siddiqui and Hobbs (1982) [Study 002 in REACH registration]

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

Overall, two studies have been identified which are of limited reliability due to missing information on purity and study design.. The study by Smyth et al (1969) determined a LD_{50} of 467 mg/kg bw (95% CI: 345 – 635 mg/kg bw) but lacks information on the purity of the substance, on dose levels and observed mortality rates. Although no information on dose groups is given in the primary source, the study belongs to a well-known series of toxicity studies and together with the reported confidence interval, it can be assumed that several doses were tested. A second study result (210 mg/kg bw in rabbits) is only known from a secondary source without experimental details (Siddiqui and Hobbs, 1982).

No human studies with relevance for comparison with the classification criteria 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**

All available studies have deficiencies, however, the information available is considerd adequate for concluding on a harmonized classification and ATE value. The classification is based on the study by Smyth (1969) and a LD_{50} of 467 mg/kg which corresponds to category 3 according to the criteria in Regulation (EC) No 1272/2008 for acute dermal toxicity (200 – 1000 mg/kg bw). This is supported by a LD_{50} of 210 mg/kg bw reported by Siddiqui and Hobbs (1982).

10.2.3 Conclusion on classification and labelling for acute dermal toxicity

According to the criteria for classification in Regulation (EC) No. 1272/2008, allyl methacrylate has to be classified in category 3 for acute dermal toxicity (Acute Tox. 3, H311).

Based on the available LD_{50} value, an ATE = 467 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** **LC_{50}**	**Reference**
Acute inhalation toxicity, According to OECD 403 GLP: yes Reliability (REACH registration): 1, key study Reliability (this assessment): 1	Rat, Sprague-Dawley 5 males and 5 females per dose group	Allyl methacrylate, as vapour Purity: 99.6% Source: No information	0, 1.02 and 2.13 mg/L (analytical) 4 h exposure, nose only 14 days post exposure observation	1.47 mg/L (95% CI: 1.02 – 2.13 mg/L) mortalities C: m 0/5, f 0/5 1.02 mg/L: m 0/5, f 0/5 2.13 mg/L: m 5/5, f 5/5	Degussa-Hüls Corp (1999) [Also included in (OECD, 2009) as Paul, G., 2000 (Reference 33)] [Study 001 in REACH registration]
Acute inhalation toxicity, Equivalent to OECD 403 GLP: yes Reliability (REACH registration): 4 Reliability (this assessment): 2	Rat, Sprague-Dawley 5 males and 5 females per dose group	Allyl methacrylate, as vapour Purity: 99.5 % Source: No information	0, 210, 300, 350 ppm (analytical) 4 h exposure 14 days post exposure observation	1.6 mg/L (95% CI: 1.46-1.75 mg/L), reported as 310 ppm (95% CI: 283-339 ppm) mortalities C: m 0/5, f 0/5 210 ppm: m 0/5, f 0/5 300 ppm: m 2/5, f 2/5 350 ppm: m 5/5, f	Huntingdon Life Sciences (1997) (in OECD, 2009) [Study 002 in REACH registration]

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance, , form and particle size (MMAD)**	**Dose levels, duration of exposure**	**Value** LC_{50}	**Reference**
				3/5	
Acute inhalation toxicity, Guideline unknown GLP: no Reliability (REACH registration): 3 Reliability (this assessment): 4 (no translation available)	Rat, strain not specified, males and females Dose groups not specified	Allyl methacrylate, as vapour Purity: No information Source: No information	Dose levels: No information Exposure duration: No information Post exposure observation: No information	Male: 1.8 mg/L Female: 2.65 mg/L Mortalities: no information	Smirnova et al. (1990) [Study details according to Study 003 in REACH registration]
Acute inhalation toxicity, Guideline unknown GLP: no Reliability (REACH registration): 3 Reliability (this assessment): 4 (no translation available)	Mouse, strain not specified, males and females Dose groups not specified	Allyl methacrylate, as vapour Purity: No information Source: No information	Dose levels: No information Exposure duration: No information Post exposure observation: No information	Male: 5.5 mg/L Female: 10.0 mg/L Mortalities: no information	Smirnova et al. (1990) [Study details according to Study 003 in REACH registration]

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

A GLP-conform guideline study in rats is available for allyl methacrylate. The characterization of the test item purity is not given in the secondary sources OECD (2009) and ECHA (2019), therefore the study report was consulted, which is publically disseminated by US regulatory bodies as a TSCA submission (Degussa-Hüls Corp, 1999). This study is considered fully reliable and adequate to serve as basis for classification and determined a LC_{50} of 1.47 mg/L. This is supported by Huntingdon Life Sciences (1997) in (OECD, 2009), which is of nearly equal quality and determined a LC_{50} of 1.6 mg/L. The other documented, less reliable, LC_{50} values are in the range 1.8 – 10.0 mg/L.

No human studies with relevance for comparison with the classification criteria 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 (inhal) if the LC50 values are > 10.0 mg/L and ≤ 20.0 mg/L (4h exposure)
- Acute Tox 3 (inhal) if the LC50 values are > 2.0 mg/L and ≤ 10.0 mg/L (4h exposure)
- Acute Tox 2 (inhal) if the LC_{50} values are > 0.5 and ≤ 2 mg/L (4h exposure)

The LC_{50} determined in the guideline and GLP conform study corresponds to a classification in category 2 (0.5 – 2 mg/L), which is supported by a second study of nearly equal quality. The remaining study results, which are all of significantly lower reliability, are not providing arguments against this classification.

10.3.3 Conclusion on classification and labelling for acute inhalation toxicity

According to the criteria for classification in Regulation (EC) No. 1272/2008, allyl methacrylate has to be classified in category 2 for acute inhalative toxicity (Acute Tox. 2, H330). Based on the most adequate study, which is also the lowest LC_{50}, an ATE = 1.47 mg/L (vapours) is indicated.

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)	Reliability (DS)	Study	Remark
rat (=10 per dose)	470 (males)	3	1975	Similar to OECD TG 401 Dosing 157, 313, 625, 1250 mg/kg bw; Mortalities: 0/10, 2/10, 7/10, 10/10
rat (=5 per dose)	401 (males)	3	1969	Similar to OECD TG 401
rat	421 (sex not specified)	4	1981	
rat	70 (males) 148 (females)	4	1990	
mouse	57 (males) 184 (females)	4	1990	

All studies show deficiencies (no information on doses, application, vehicle), however, the available information is considered adequate for concluding on harmonized classification and on ATE value. Amongst the available data, the two most reliable results (LD_{50} of 470 and 401 mg/kg bw) correspond to category 4. These two studies in rats were performed in a manner similar to current guidelines, but without information on the purity of the substance and administration (both studies 1975, 1969), dosing or vehicle (1969).

The DS proposed to classify allyl methacrylate as Acute Tox. 4; H302 with an ATE value of 401 mg/kg bw.

Comments received during consultation

One MSCA agreed with the proposal as Acute Tox. 4. If the study from 1975 is indeed of better quality, then this MSCA considered that the ATE could be set at 470 mg/kg bw.

Another MSCA was surprised that the two most recent studies (1990) are the least detailed. If no more information is provided by the registrant, then the preference is to use the lowest LD_{50} available and classify as Acute Tox. 3, with an ATE value of 57 mg/kg bw.

The third MSCA supported classification as Acute Tox. 4 with an ATE value of 401 mg/kg bw.

IND agreed with the proposed classification.

The DS responded that the ATE of 401 mg/kg bw is preferred as this lower value is supported by study results from secondary sources with LD_{50} values ranging from 57-421 mg/kg bw. The DS disagreed on using the LD_{50} of 57 mg/kg bw as this study is only available in a two page translation of several studies (the study original language is Russian). Information on strain, number of animals and dosing is missing.

Assessment and comparison with the classification criteria

Among the five studies available, three studies (1981, 1990, 1990) contain no information regarding guideline, GLP, purity, strain, sex, group size, dose levels, application or vehicle. Resulting LD_{50}s range from 57 to 421 mg/kg bw. The other two studies (1975, 1969; Klimisch score 3) are performed similar to OECD TG 401, though are also somewhat limited; no GLP, purity not known, dose levels and vehicle (1969 study), application (1975) not specified. Nevertheless, the 1975 and 1969 studies are considered the most reliable. The two most reliable studies result in LD_{50} values of 401 and 470 mg/kg bw leading to a classification as Acute Tox. 4 ($300 < LD_{50} \leq 2000$ mg/kg bw).

The lowest LD_{50} value of 401 mg/kg bw results in a (rounded off) ATE of 400 mg/kg bw.

RAC concludes that allyl methacrylate meets the criteria for cat 4 ($300 < ATE \leq 2\,000$ mg/kg bw) and should be classified as **Acute Tox. 4; H302 (Harmful if swallowed) with an ATE of 400 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)	Reliability (DS)	Study	Remarks
rabbit (=4 males per dose)	467	3	1969	Similar to OECD TG 402; occlusive application
rabbit (sex and group size not specified)	210	4	1982	

Both studies show deficiencies, however, the available information is considered adequate for concluding on harmonized classification and ATE value. There are no experimental details on

the study from 1982. The 1969 study results in an LD_{50} value, which corresponds to category 3 according to the criteria for acute dermal toxicity (200 – 1000 mg/kg bw).

The DS proposed to classify allyl methacrylate as Acute Tox. 3; H311 with an ATE value of 467 mg/kg bw.

Comments received during consultation

Three MSCAs agreed with the classification as Acute Tox. 3.

One MSCA agreed with the proposed ATE of 467 mg/kg bw. A second MSCA proposed to use the lowest LD_{50} of 210 mg/kg bw (derived from the study with a reliability score of 4). A third MSCA proposed to choose the generic ATE of 300 mg/kg bw.

In response to this latter comment, the DS considered the generic ATE as more appropriate based on the limited reliability of both studies and the evidence from the second study.

IND agreed with the proposed classification.

Assessment and comparison with the classification criteria

With regard to the study from 1982, no experimental details are available. Classification is based on the study from 1969, performed similar to OECD TG 402, but without information on purity, dose levels and vehicle. The resulting LD_{50} of 467 mg/kg bw results in a classification ($200 < LD_{50} \leq 1000$ mg/kg bw) as Acute Tox. 3.

The generic ATE value of 300 mg/kg bw is selected because of the limited reliability of both studies.

RAC concludes that allyl methacrylate meets the criteria for cat 3 ($200 < LD_{50} \leq 1000$ mg/kg bw) and should be classified as **Acute Tox. 3; H311 (Toxic in contact with skin) with an ATE of 300 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)	Reliability (DS)	Study	Remarks
rat (= 5 per dose and sex)	1.47 (sexes combined)	1	1999	OECD TG 403/GLP; 0, 1.02, 2.13 mg/L
rat (=5 per dose and sex)	1.6 (sexes combined)	2	1997	Equivalent to OECD TG 403; 0, 210, 300, 350 ppm (converted according CLP guidance 0 - 1.08 – 1.55 – 1.70 mg/L)
rat	1.8 (males) 2.65 (females)	4	1990	Exposure duration not specified
mouse	5.5 (males) 10.0 (females)	4	1990	Exposure duration not specified

A GLP conform and guideline study in rats is available for allyl methacrylate. This study is considered fully reliable and adequate to serve as basis for classification and determined a 4h

LC_{50} of 1.47 mg/L (1999). This is supported by the 1997 study, which is of nearly equal quality and determined a 4h-LC_{50} of 1.6 mg/L. These 4h LC_{50} values correspond to a category 2 according to the criteria for acute inhalation toxicity, i.e. > 0.5 and ≤ 2 mg/L (4h exposure). The ATE is based on the most reliable study which also corresponds to the lowest LC_{50} value of 1.47 mg/L.

The DS proposed to classify allyl methacrylate as Acute Tox. 2; H330 with an ATE value of 1.47 mg/L (vapours).

Comments received during consultation

One MSCA agreed with the proposal as Acute Tox. 2. It was noted that in the 1999 study, the tested concentrations induce either no mortality or full mortality. However, the LC_{50} is supported by the 1997 study. ATE is supported. The other two MSCAs are in support of Acute Tox. 2 and the ATE of 1.47 mg/L.

IND agreed with the proposed classification.

Assessment and comparison with the classification criteria

Two reliable studies in rats result in 4h LC_{50} values of 1.47 and 1.6 mg/L. The LC_{50} values result in a classification (0.5 < 4h LC_{50} ≤ 2 mg/L) as Acute Tox. 2. The ATE value is based on the lowest 4h LC_{50} of 1.47 mg/L, and rounded off to 1.5 mg/L. It is however noted that in this 1999 study only 0% and 100% responses were obtained. The LC_{50} is considered equivalent to 1.47 mg/L, the geometric mean of the two concentrations. Nevertheless, the LC_{50} is supported by the 1997 study.

RAC concludes that allyl methacrylate meets the criteria for cat 2 (0.5 < 4h LC_{50} ≤ 2 mg/L) and should be classified as **Acute Tox. 2; H330 (Fatal if inhaled) with an ATE of 1.5 mg/L**.

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.

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