METHACRYLIC ACID

CAS number: 79-41-4

Synonyms: 2-Methylpropenoic acid, 2-propenoic acid, 2-methyl

Chemical formula: $C_4H_6O_2$

Structural formula: —

Workplace exposure standard (retained)

TWA: **20 ppm (70 mg/m^3)**

STEL: **—**

Peak limitation: **—**

Notations: **—**

IDLH: **—**

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 20 ppm (70 mg/m^3) is recommended to protect eye and upper respiratory tract irritation in exposed workers.

Discussion and conclusions

Methacrylic acid is used as a monomer in polymer production.

Critical effects of exposure are irritation of the upper respiratory tract, eyes and skin. Human exposure data are limited. Poorly documented reports indicate skin toxicity and corneal damage are associated with occupational exposures at 113 ppm (ACGIH, 2018). A NOAEC of 100 ppm for slight hyperplasia of the nasal epithelium with a corresponding LOAEC of 350 ppm is reported in a 90-day inhalation study in rats (DFG, 2016). A comparable endpoint is reported in mice with a NOAEC of 20 ppm. However, mice and rats are considered more susceptible to the effects of inhalational exposure than humans due to anatomical differences of the nasal cavity (DFG, 2016).

The TWA of 20 ppm is recommended to be retained and is expected to be protective of local irritation reported in workers exposed at 113 ppm (ACGIH, 2018) and is supported by a NOAEC of 100 ppm for this endpoint in rats (DFG, 2016). The TWA is also expected to be protective of potential systemic effects, which were observed as reduced body weight gain in animals at inhalational doses above 200 ppm (DFG, 2016).

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

There are insufficient data to recommend a skin notation.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 20 ppm (70 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 20 ppm (70 mg/m^3)***

TLV-TWA intended to minimise potential for eye and skin irritation.

Summary of data:

Human and animal exposure data are limited and indicate 20 ppm is protective of reported acute irritation effects and is supported by analogy to more toxic acrylic acid, which has a TLV-TWA of 2 ppm.

Human data:

- Contact sensitisation reported in small number of workers (not specified) in 37 studied cases
- No respiratory symptoms, skin toxicity and severe corneal burns reported in medical examinations of acutely exposed plant workers:
  - air concentrations ≤113 ppm (no further information provided).

Animal data:

- LD_{50}: 1,020–5,080 mg/kg (guinea pigs, dermal occlusive, 24 h)
- Causes severe eye and skin irritation (guinea pigs):
  - eye contact causes blindness
- Oral LD_{50}: 1,600 mg/kg (mice), 2,260 mg/kg (rats)
- Eye irritation and body weight loss at 1,300 ppm (rats, 5 h/d, 5 d):
  - no abnormal findings in urinary or haematological parameters, clinical chemistry or gross examination at necropsy reported in 2 separate studies with this dose regimen
- Slight renal congestion at 300 ppm reported in sub-chronic inhalation study (rats, 6 h/d, 20 d)
- Given these acute and sub-chronic inhalation data, cited article recommends a provisional OEL of 20 ppm following application of an UF (no further information on derivation of OEL or UF provided)
- Slight alveolar haemorrhaging and granularity in liver cytoplasm, no adverse haematological or gross pathological effects at 5 or 10 mg/kg/d in repeat oral dose study (rats, 10 doses):
  - histopathological lesions attributed to corrosivity of the compound
- Major metabolite of methyl acrylate, considered responsible for degeneration of nasal mucosa in exposed rodents (no further details provided)
- No mutagenicity or ADME data presented.

Insufficient data available to recommend a TLV-STEL or notations for carcinogenicity, skin absorption or sensitisation.

DFG	***2015***	***MAK: 50 ppm (180 mg/m^3)***

Summary of additional data:

MAK based on NOAEC of 100 ppm and corresponding LOAEC of 350 ppm for slight hyperplasia in respiratory epithelia in rats exposed by inhalation for 90 d. MAK of 50 ppm derived by applying a

Source	Year set	Standard
factor of 2 to the NOAEC of 100 ppm and is considered sufficient based on the minimal effects observed at the LOAEC. The MAK is higher than that of acrylic acid (10 ppm), which is supported by the higher median RD_{50} in mice for methacrylic acid (22,000 ppm) compared with that of acrylic acid (685 ppm). Carcinogenicity notation not assigned by analogy to methacrylic acid methyl ester, of which methacrylic acid is the major metabolite and demonstrates no carcinogenicity in animals or genotoxicity *in vivo*. Dermal exposure route considered negligible in relation to MAK based on analogy to dermal absorption data of acrylic acid. No sensitiser notation assigned based on negative results in animals and inconclusive results in humans. Human data: • Modelled retention of 78% of inhaled dose at 10–80 ppm: ○ simulated blood half-life ≈2.5 min • Dermal absorption rate of 4% aqueous acrylic acid 28.9 µg/cm²/h used as analogy to assess skin notation. Animal data: • 95% of inhaled doses deposit in the upper respiratory tract and causes irritation • Blood half-life of 10 or 20 mg/kg ip injection ≈1.7 min • LC_{50}: 1988 ppm (rats, 4 h) • RD_{50}: 22,000 ppm (mice, 30 min); mild sensory irritation at 4,900 ppm, moderate to severe at 9,400 ppm • Available dermal application/penetration studies used undiluted or concentrated substance, unsuitable for assessment of occupational exposure due to high corrosive nature • NOAEL: 100 ppm for nasal epithelium hyperplasia and body weight loss in sub-chronic inhalation study (rats, 6 h/d, 5 d/wk, 90 d): ○ LOAEL of 350 ppm ○ another study with NOAEL: 20 ppm degeneration of the nasal epithelium (mice, 6 h/d, 5 d/wk, 90 d) not used in assessment due to anatomical differences in nasal cavity of mice compared with humans, which increased severity of reported effects • No substance-specific fertility studies available, no adverse effects in genitals or effects on sperm motility/morphology observed in 90 d inhalation studies with rats: ○ no effects on fertility or development at 50–400 mg/kg in 2 gen repeat gavage study with methacrylic acid methyl ester (rats) • NOAEL: 300 ppm, highest tested dose, for developmental toxicity (rats, 6 h/d, gestation 6–20 d); ○ maternal NOAEL: 200 ppm for reduced body weight gain • Non-mutagenic *in vitro* in bacteria; methacrylic acid methyl ester is clastogenic *in vitro* at cytotoxic concentrations, ○ non-mutagenic *in vivo* in dominant lethal and micronucleus tests.		
SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***NA***	***NA***
No report.		

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	2018	• No systemic toxicity, ○ irritational effects reported for 9.6% solution in acetone at 150–600 mg/kg in repeat dermal application study (mice, 9 exposures, 3 wk) • No evidence for carcinogenicity in chronic inhalation study with methyl methacrylate, metabolised to methacrylic acid, ≤1,000 ppm (rats, n=50/sex/group, 6 h/d, 5 d/wk, 2 yr).

ECHA	✓	2019	• Upper respiratory tract irritation is most sensitive end point:
			  ○ occurs before systemic toxicity manifested as reduced body weight gain in 2 yr chronic inhalation study with methyl methacrylate (rats)
			• Long-term inhalation DNEL calculated from NOAEL of 100 ppm for nasal epithelium hyperplasia (rats, 90 d, also cited in DFG, 2016)
			• Overall assessment factor of 11.9 applied to account for scaling exposure duration, inter- and intraspecies differences and exposure duration:
			  ○ DNEL: 8.4 ppm.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? No

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	—
HCIS	—
NICNAS	—
EU Annex	NA
ECHA	—
ACGIH	—
DFG	—
SCOEL	NA
HCOTN	NA
IARC	NA
US NIOSH	NA

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

Skin notation assessment

Calculation		
Adverse effects in human case study:		
Dermal LD_{50} ≤1000 mg/kg:	no	
Dermal repeat-dose NOAEL ≤200 mg/kg:		
Dermal LD_{50}/Inhalation LD_{50} <10:		
In vivo dermal absorption rate >10%:		
Estimated dermal exposure at WES >10%:	yes	
		insufficient data to assign a skin notation

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	86.06
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 3.52 mg/m^3; 1 mg/m^3 = 0.284 ppm
This chemical is used as a pesticide:	☐
This chemical is a biological product:	☐
This chemical is a by-product of a process:	☐
A biological exposure index has been recommended by these agencies:	☐ ACGIH ☐ DFG ☐ SCOEL

Workplace exposure standard history

Year	Standard
Click here to enter year	

References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the *TLVs® and BEIs® Guidelines section* on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2016) Methacrylic acid – MAK value documentation.

European Chemicals Agency Regulation (ECHA) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018) 2-Propenoic acid, 2-methyl: Human health tier II assessment – IMAP report.