

# METHYL METHACRYLATE

**CAS number:** 80-62-6

**Synonyms:** Methacrylic acid methyl ester, methyl alpha-methyl-acrylate, methyl-2-methylpropenoate, methyl-2-methyl-2-propenoate, 2-methyl-2-propenoic acid methyl ester, MMA, methyl  $\alpha$ -methyl acrylate

**Chemical formula:**  $C_5H_8O_2$

## Workplace exposure standard (retained)

**TWA:** 50 ppm (208 mg/m<sup>3</sup>)

**STEL:** 100 ppm (416 mg/m<sup>3</sup>)

**Peak limitation:** —

**Notations:** DSEN

**IDLH:** 1,000 ppm

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

## Recommendation and basis for workplace exposure standard

A TWA of 50 ppm (208 mg/m<sup>3</sup>) is recommended to protect for irritation and potential chronic respiratory conditions in exposed workers.

A STEL of 100 ppm (416 mg/m<sup>3</sup>) is recommended to protect for acute irritation in exposed workers.

## Discussion and conclusions

Methyl methacrylate is used as monomer in the production of acrylic polymer for sheeting, dental reconstruction, medical implants and concrete impregnation.

Critical effects of exposure are irritation of the eyes and respiratory tract and impaired olfaction (smell) and respiratory function. Rats appear to be more susceptible to irritation effects than humans because of anatomical differences in the nasal cavity (ACGIH, 2018; DFG, 2010). Liver damage is reported in animals at irritational thresholds in sub-chronic studies, but not over chronic exposure periods (ACGIH, 2018). The weight of evidence from several workplace exposure studies indicates that no adverse effects occur at average air concentrations between 40 to 50 ppm (ACGIH, 2018; DFG, 2010). The onset of eye and respiratory irritation are reported above 100 ppm in acrylic plant workers (DFG, 2010). This is supported by a LOAEC of 116 ppm for fibrotic pulmonary oedema in sub-chronically exposed rats (ACGIH, 2018).

The existing TWA is based on a NOAEC of 50 ppm from workplace exposure studies. The recommended STEL of 100 ppm is considered protective of irritation effects reported in workers between 125 and 200 ppm (ACGIH, 2018).

## **Recommendation for notations**

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

Classified as a skin sensitiser and not a respiratory sensitiser according to the GHS.

A skin notation is not recommended based on the available evidence.

DRAFT

## APPENDIX

### Primary sources with reports

Source	Year set	Standard
<b>SWA</b>	<b>1995</b>	<b>TWA: 50 ppm (208 mg/m<sup>3</sup>); STEL: 100 ppm (416 mg/m<sup>3</sup>)</b>
<b>ACGIH</b>	<b>2015</b>	<b>TLV-TWA: 50 ppm (205 mg/m<sup>3</sup>); TLV-STEL: 100 ppm (410 mg/m<sup>3</sup>)</b>
<p>TLV-TWA intended to protect for eye and respiratory tract irritation, pulmonary oedema and impaired olfactory function.</p> <p>TLV-STEL intended to protect for acute eye and respiratory tract irritation reported above 100 ppm in humans.</p> <p>Reported allergic dermatitis, erythema and skin oedema in exposed workers warrant a dermal sensitiser notation.</p> <p>Not classifiable as a human carcinogen based on chronic animal exposure studies and limited epidemiological data.</p> <p>Summary of data:</p> <p>TLV-TWA and TLV-STEL expected to be sufficiently low to protect for irritation and adverse pulmonary effects reported for workers above 100 ppm and rats and a LOAEC of 116 ppm and NOAEL of 25 ppm.</p> <p>Human data:</p> <ul style="list-style-type: none"> <li>Occupational health study showed time-averaged workplace concentrations at 30–65 ppm with excursions at 170–250 ppm; irritation complaints reported above 200 ppm <ul style="list-style-type: none"> <li>cases of mucous membrane irritation at 125–200 ppm not confirmed</li> </ul> </li> <li>Transient eye irritation in surgical theatre workers exposed at up to 77 ppm</li> <li>Increased colon and rectal cancers in exposed production plant workers (n=2,524, &gt;10 mo) <ul style="list-style-type: none"> <li>not separable from mixed exposures</li> <li>increased cancer incidence not affirmed in several similar other studies (n=6,548 and 3,381) and epidemiological study (n=2,671)</li> </ul> </li> <li>Comprehensive review of workplace studies showed no adverse effects occurred after repeated average exposures at 50 ppm (8 h; presumably considered the human NOAEC) or 62–601 ppm (20 min) <ul style="list-style-type: none"> <li>equivocal evidence for pulmonary function impairment at exposures up to 93 ppm, mixed exposures and smoking habits were not separable from available data</li> <li>case control study showed increased OR for lung function impairment in workers (n=77), which decreased with cumulative exposure time suggesting the effects were transient rather than a chronic inflammatory response.</li> </ul> </li> <li>Positive skin sensitisation results reported in several patch-test studies using 5–100%; positive results generally characterised by contact dermatitis, erythema and oedema.</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>LC<sub>50</sub>: 7,093 ppm (rats, 4 h); less recent acute inhalational studies report lethal air concentrations between 41–48 ppm, dismissed due to measurement inaccuracies</li> <li>LOAEC: 116 ppm for liver necrosis and fibrotic pulmonary oedema in sub-chronic inhalation study (male rats, 7 h/d, 5 d/wk, 3 mo); no evidence for substance accumulation</li> <li>Reduced body weight at 500 and 1,000 ppm (rats, mice, 6 h/d, 5 d/wk, 14 wk) <ul style="list-style-type: none"> <li>dose-dependent mortality, cerebellar congestion, haemorrhage and nasal epithelial necrosis, sloughing and inflammation reported at 2,000–5,000 ppm</li> </ul> </li> </ul>		



Source	Year set	Standard
		<ul style="list-style-type: none"> <li>No adverse effects at 100 and 400 ppm (male beagles, 6 h/d, 5 d/wk, 3 mo)</li> <li>No evidence for carcinogenic activity at 250/500 or 500/1,000 ppm (female/male rats) and 500 or 1,000 ppm (female/male mice) in lifetime inhalational study <ul style="list-style-type: none"> <li>dose-dependent upper respiratory tract inflammation, degeneration, and epithelial hyperplasia reported;</li> <li>similar chronic inhalation study with treatment range: 25–400 ppm found comparable toxic endpoints; NOAEC of 25 ppm (rats, 6 h/d, 5 d/wk, 2 yr)</li> </ul> </li> <li>No evidence for developmental toxicity in several inhalation studies at 99–2,028 ppm (rats)</li> <li>Considered non-mutagenic <i>in vitro</i> and <i>in vivo</i>; slight increase in frequency of chromosomal aberrations at high concentrations <i>in vitro</i> in mouse lymphoma L5178Y and Chinese hamster ovarian cells, but not affirmed <i>in vivo</i> in mice at 250 mg/kg (oral).</li> </ul> <p>Insufficient data available to assign notations for skin absorption and respiratory sensitisation.</p>
DFG	2010	MAK: 50 ppm (201 mg/m <sup>3</sup> )
		<p>Summary of additional data:</p> <p>MAK derived from human exposure data in favour of rat inhalation data due to anatomical differences of the nasal cavity that increase susceptibility of rats to irritational effects.</p> <p>Exposed workers showed no signs of adverse effects at average exposures of 40 ppm over 8.8 yr; irritation is reported at acute exposures of 100 ppm, therefore MAK of 50 ppm is retained.</p> <p>A carcinogenicity notation not warranted based on lack of evidence for carcinogenic activity in chronic animal exposure studies.</p> <p>Skin notation not warranted based on low <i>in vitro</i> skin penetration rate, which would contribute minimally to overall burden relative to inhalational exposure at the MAK.</p> <p>Dermal sensitizer notation assigned based on positive results in human and animal studies.</p> <p>Human data:</p> <ul style="list-style-type: none"> <li><i>In vitro</i> skin penetration rate: 274 µg/cm<sup>2</sup>/h (occlusive) and 107 µg/cm<sup>2</sup>/h (non-occlusive)</li> <li>PBPK models indicate anatomical differences in respiratory tract result in 3–8 times lower effective exposure to nasal tissues in humans than in rats</li> <li>CNS depression and hypotension reported at 36–83 ppm in exposed workers (exposure up to 11 yr); not used to derive MAK due to insufficient documentation</li> <li>No irritation effects at 40 ppm in exposed workers at acrylic sheet production plant; irritation reported at acute exposures &gt;100 ppm</li> <li>No olfactory impairment in production plant workers chronically exposed to 50 ppm (n=175)</li> <li>Slight respiratory obstruction and chronic coughing in 8/40 workers exposed to average concentrations of 18.5–21.6 ppm over 5–10 yr; not considered in MAK derivation due to use of static monitoring devices</li> <li>Positive respiratory sensitisation in isolated cases of chronically exposed workers; these patients presented dyspnoea and wheezing when challenged with pure or diluted substance in prick- or patch-tests</li> <li>No evidence for carcinogenic activity in epidemiological studies of acrylic sheet production workers (also cited by ACGIH, 2018).</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>LD<sub>50</sub>: &gt;5,000 mg/kg (rabbits, dermal)</li> <li>Positive dermal sensitisation results in maximisation test, induction using 10% in olive oil and challenged with 1% in olive oil (guinea pigs)</li> </ul>

Source	Year set	Standard
<ul style="list-style-type: none"> <li>10–20% deposition and metabolism in lower respiratory tract following inhalational dose of 21, 104, or 538 ppm (rats)</li> <li>Negative mutagenicity results <i>in vivo</i> considered inadequate to dismiss clastogenicity observed <i>in vitro</i> (mice, also cited in ACGIH, 2018).</li> </ul> <p>Insufficient data to recommend respiratory sensitisation notation.</p>		
<b>SCOEL</b>	<b>2006</b>	<b>TWA: 50 ppm (201 mg/m<sup>3</sup>); STEL: 100 ppm (402 mg/m<sup>3</sup>);</b>
<p>Summary of additional data:</p> <p>Recommended TWA based on weight of evidence of human and animal exposure data. Several workplace studies indicate exposure at 50 ppm does not cause adverse respiratory effects, supported by a NOAEL of 25 ppm for slight degeneration of the nasal epithelium in rats with a corresponding LOAEL of 100 ppm (also cited in ACGIH, 2018). PBPK modelling suggests the human respiratory tract would be at least 3 times less sensitive to these effects than that of rats (also cited in DFG, 2010).</p> <p>The recommended STEL is based on reports of sensory irritation in workers exposed to concentrations &gt;100 ppm.</p> <p>Skin notation not warranted based on low systemic toxicity and low dermal penetration rate.</p> <p>Despite demonstrated dermal sensitisation potential, inadequate evidence for asthma induction in exposed individuals does not warrant a sensitisation notation.</p> <p>Human data:</p> <ul style="list-style-type: none"> <li>Sensory irritation threshold not established in humans; expected to be near 100 ppm</li> <li>Equivocal evidence for respiratory sensitisation, whereby expressed symptoms may be due to local irritation effects at high transient concentrations rather than asthmatic reaction</li> <li>Workplace study of polymerisation plant showed no adverse respiratory effects or pulmonary function deficiencies in workers at average concentrations of 50 ppm with brief peak exposures up to 500 ppm (also cited in ACGIH, 2018).</li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>Respiratory tract irritation caused by local enzymatic hydrolysis to methacrylic acid, which causes nasal epithelial degeneration</li> <li>Positive sensitisation results in maximisation test (guinea pigs)</li> <li>Non-mutagenic <i>in vitro</i> and <i>in vivo</i>; clastogenicity reported <i>in vitro</i> in mammalian cell cultures at cytotoxic concentrations</li> <li>Negligible toxicity to fertility expected due to absence of systemic effects in repeat dose animal studies</li> <li>No evidence for developmental toxicity at 2,028 ppm (rats, 6 h/d, GD 5–16, also cited in ACGIH, 2018).</li> </ul>		
<b>OARS/AIHA</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>HCOTN</b>	<b>NA</b>	<b>NA</b>
No report.		

## Secondary source reports relied upon



Source	Year	Additional information
NICNAS	✓ 2014	<ul style="list-style-type: none"> <li>• Skin and respiratory irritation, asthmatic reactions and local neurological symptoms (not specified) reported in exposed workers at &lt;112 ppm</li> <li>• Erythema and eczema in 18/20 volunteers with 5% topical treatment</li> <li>• Mild erythema in 1/3 volunteers exposed to saturated cotton pellets for 48 h</li> <li>• Headache, lethargy, light-headedness and sensation of heavy limbs reported in acutely exposed workers during monomer mixing</li> <li>• Not considered mutagenic; <i>in vitro</i> clastogenicity in mammalian cells not affirmed <i>in vivo</i>.</li> </ul>
IARC	✓ 1994	<ul style="list-style-type: none"> <li>• Inadequate evidence for carcinogenicity in humans; evidence suggests lack of carcinogenicity in animals.</li> </ul>
US EPA	✓ 1998	<ul style="list-style-type: none"> <li>• Chronic inhalation study with treatment range 25–400 ppm (rats, 6 h/d, 5 d/wk, 2 yr, also cited in ACGIH, 2018) used principally to derive inhalational reference concentration;               <ul style="list-style-type: none"> <li>◦ hyperplasia in mucosal membranes and nasal cavity at 400 ppm</li> <li>◦ concentration-dependent histopathological changes to nasal cavity between 100–400 ppm</li> <li>◦ NOAEC: 25 ppm.</li> </ul> </li> </ul>
OECD	✓ 2001	<ul style="list-style-type: none"> <li>• Systemic toxic effects reported &gt;1,000 ppm (rats) and &gt;500 ppm (mice); effects included degenerative and necrotic lesions in liver, kidney, brain, and atrophic changes in spleen and bone marrow, but were not observed in chronic studies up to 1,000 ppm.</li> </ul>
US NIOSH	✓ 1994	<ul style="list-style-type: none"> <li>• IDLH based on acute inhalation toxicity data in humans.</li> </ul>

## 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	NA
HCIS	Skin sensitisation – category 1
NICNAS	Skin sensitisation – category 1
EU Annex	Skin sensitisation – category 1
ECHA	NA
ACGIH	Carcinogenicity – A4, DSEN



Source	Notations
DFG	Sh (dermal sensitiser)
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 3
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:	no
Dermal LD <sub>50</sub> ≤ 1000 mg/kg:	no
Dermal repeat-dose NOAEL ≤ 200 mg/kg:	
Dermal LD <sub>50</sub> /Inhalation LD <sub>50</sub> < 10:	
<i>In vivo</i> dermal absorption rate > 10%:	
Estimated dermal exposure at WES > 10%:	
a skin notation is not warranted	

## IDLH

Is there a suitable IDLH value available? Yes

## Additional information

Molecular weight:	100.13
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m <sup>3</sup> ; 1 mg/m <sup>3</sup> = Number ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH <input type="checkbox"/> DFG <input type="checkbox"/> SCOEL

## Workplace exposure standard history

Year	Standard
Click here to enter year	

## References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7<sup>th</sup> 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) (2010) Methyl methacrylate – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2006) Recommendation from the Scientific Committee on Occupational Exposure Limits for methyl methacrylate. SCOEL/SUM/126.

International Agency for Research on Cancer (IARC) Some industrial chemicals. IARC Monographs – volume 60.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) 2-Propenoic acid, 2-methyl-, methyl ester: Human health tier II assessment – IMAP report.

Organisation for Economic Cooperation and Development (OECD) (2001) SIDS initial assessment profile – 2-Methyl-2-propenoic acid, methyl ester (Methyl methacrylate).

Tenth Adaptation to Technical Progress Commission Regulation (EU) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

US Environmental Protection Authority (US EPA) (1998) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Methyl methacrylate.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – methyl methacrylate.