Compound	Methyl methacrylate	*Data collection sheet*
N°CAS 80-62-6 1 ppm = 4.16 mg/m^3	**CLP:** Skin Irrit. 2 (H315), Skin Sens. 1 (H317), STOT SE 3 (H335)	

Organisation name	**Health Canada**	**IPCS**	**U.S. EPA**	**REACH Registrants**
Risk value name	TC	TC	RfC	DNEL
Risk value (µg/m^3)	52	200	700	74300 (systemic), 104000 (local)
Reference period	chronic	chronic	chronic	chronic
Year	1992	1996	1997	2011, update 2016
Key study	Rohm and Haas, 1977; Rohm and Haas, 1979a; Rohm and Haas, 1979b	Lomax, 1992; Lomax et al., 1997; Rohm and Haas, 1979b	Lomax, 1992; Lomax et al., 1997; Rohm and Haas, 1979b	not indicated
Study type	2 a chronic inhalation (0, 104, 416, 1664 mg/m^3)	2 a chronic inhalation (0, 104, 416, 1664 mg/m^3)	2 a chronic inhalation (0, 104, 416, 1664 mg/m^3)	not indicated
Species	rat, hamster	rat	rat	not indicated
Duration of exposure in key study	6 h/d, 5 d/week, 2 a	6 h/d, 5 d/week, 2 a	6 h/d, 5 d/week, 2 a	
Critical effect	several (reduced weight gain, nasal epithelial lesions)	degeneration/atrophy of olfactory epithelium	degeneration/atrophy of olfactory epithelium	not indicated
Critical dose value	NOEC 410 mg/m^3	NOEC 102.5 mg/m^3	$BMDL_{10}$ 146 mg/m^3	not indicated
Adjusted critical dose	52 mg/m^3 (continuous exposure, HEC-adjustment)	18.3 mg/m^3	BMC_{10} 25.6 mg/m^3 (continuous exposure); BMC_{10} (HEC) 7.2 mg/m^3	
Single assessment factors (see table R.8.6)	UF_H 10 x UF_A 10 x UF_D 10 = 1000	UF_H 10 x UF_A 10 = 100	UF_H 3 x UF_A 3 = 10	not indicated (total factor, systemic: 28; total factor, local: 2)
Other effects				

UF_L used LOAEL; UF_H intraspecies variability; UF_A interspecies variability; UF_S used subchronic study; UF_D data deficiencies, AS allometric scaling

Compound	Methyl methacrylate (MMA)		Factsheet
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	750
EU-LCI status	2	Draft/final	Final
EU-LCI year of issue	3	Year when the EU-LCI value was issued	2016
General information			
CLP Index No	4	INDEX	607-035-00-6
EC No	5	EINECS — ELINCS — NLP	201-297-1
CAS No	6	Chemical Abstracts Service number	80-62-6
Harmonised CLP classification	7	Human health risk-related classification	Skin Irrit. 2, Skin Sens. 1, STOT SE 3
Molar mass and conversion factor	8	[g/mol] and [ppm — mg/m^3]	100.12 1 ppm = 4.16 mg/m^3
Key data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	Lomax LG (1992); U.S.EPA (1998a)
Read-across compound	10	Where applicable	
Species	11	Rat etc. / human	Fisher-344 rats (50/sex/ group)
Route/type of study	12	Inhalation, oral feed, etc.	Inhalation
Study length	13	Days, subchronic, chronic	Chronic
Exposure duration	14	Hours/day, days/week	6 h/d, 5 d/w
Critical endpoint	15	Effect(s), site of	Lesions of olfactory epithelium
Point of departure (POD)	16	LOAEC*L, NOAEC*L, NOEC*L, benchmark dose, etc.	NOAEC
POD value	17	[mg/m^3] or [ppm] or [mg/kg$_{BW}$×d]	104 mg/m^3 (25 ppm)
Assessment factors (AF)	**18**		
Adjustment for exposure duration	19	Study exposure hrs/day, days/week	5.6
Study length	20	sa→ sc→ c *(R8-5)*	1
Route-to-route extrapolation factor	21		1
Dose-response	22 a	Reliability of dose-response, LOAEL → NOAEL	1
	22 b	Severity of effect *(R 8-6d)*	1
Interspecies differences	23 a	Allometric Metabolic rate *(R8-3)*	1
	23 b	Kinetic + dynamic	2.5
Intraspecies differences	24	Kinetic + dynamic Worker — general population	10
AF (sensitive population)	25	Children or other sensitive groups	1
Other adjustment factors Quality of whole database	26	Completeness and consistency Reliability of alternative data *(R8-6 d,e)*	1

Result			
Summary of assessment factors	27	Total Assessment Factor (TAF)	140
POD/TAF	28	Calculated value (µg/m³ and ppb)	743 µg/m³ and 178.6 ppb
Molar adjustment factor	29	Used in read-across	
Rounded value	30	[µg/m³]	750
Additional comments	31		
Rationale section	32		

Data compilation and evaluation for methyl methacrylate is based on a project funded by the German Environment Agency (Voss JU, 2017).

Methyl methacrylate (MMA) is a colourless liquid with an acrid fruity odour. No natural sources of MMA are known. MMA is a large-scale technical product. It is mainly used for the production of high molecular polymers, e. g. acrylic glass. In indoor air of homes, schools, nursery schools and offices, MMA is usually not detectable. However, very high concentrations of up to 13000 µg/m^3 have been measured following improper renovation works in buildings. Similarly, high concentrations of about the same level can occur in nail and beauty salons.

No human or animal data on resorption of MMA following inhalation are available. In the isolated respiratory tract of rats, an uptake of about 20 % has been determined. Distribution and metabolism of MMA parallels that of other aliphatic esters, i.e. hydrolysis in nasal epithelia with the formation of the corresponding acid and alcohol. In this case, methacrylic acid and methanol MMA taken up into the bloodstream is also rapidly hydrolysed. The metabolites are further oxidised, with no accumulation in the body. Only small amounts of MMA are excreted in urine. The main elimination is by carbon dioxide in exhaled air.

Rationale for critical effect
The derivation of the EU-LCI is based on animal toxicity studies. Epidemiological studies of workers with occupational exposure to MMA may be used as supportive evidence but are considered insufficient as basis for the derivation.

The lesions of the olfactory epithelium in the nose of rats are considered as the critical effect. In a chronic inhalation study male and female F344 rats were exposed to MMA concentrations of 0, 104, 416 or 1664 mg/m^3 for 6 h/d, 5 d/week for two years. A detailed histologic examination of animals in all exposure groups revealed a concentration-dependent increase in the incidence and severity of olfactory epithelial lesions. This study gave a NOAEC of 104 mg/m^3 (Lomax, 1992; Lomax et al., 1997; U.S.EPA, 1998).

Similar lesions of the olfactory epithelium as produced by MMA have also been observed following inhalation exposure of rats to aliphatic esters of other saturated and unsaturated carboxylic acids and alcohols, e.g., methyl and ethyl acetate (ECB, 2003; Hardisty et al., 1999). The lesion was associated with the formation of the carboxylic acid by hydrolysis of the corresponding ester, which, after exceeding the specific buffer capacity of the cells, led to acidification and consequently cytotoxic damage. Similar lesions were also caused by methyl acrylate (U.S. EPA, 1990), which, however, was more active than MMA and for which additional effects as reaction with sulfhydryl groups contribute to the toxic effect (OECD SIDS, 2003). The latter only plays a minor role in case of MMA.

The chronic inhalation toxicity study with rats (Lomax, 1992; Lomax et al., 1997; U.S.EPA, 1998) was taken as the basis for the derivation of the EU-LCI. A benchmark calculation (using BMDS version 2.6.0.1 of U.S. EPA) has been performed for the incidence of minimal to severe degeneration/atrophy of the olfactory epithelium in male rats. The best-fitted model gave a BMDL05 of 120 mg/m^3 which was only slightly above the reported NOAEC of 104 mg/m^3. Thus, the conventional NOAEC approach may be used as well.

Rationale for starting point (POD)
The NOAEC of 104 mg/m^3 for olfactory epithelial lesions in rats is used as the POD for the derivation of the EU-LCI.

Rationale for extrapolation factors
Adjustment for exposure duration: 5.6
Interspecies differences: 2.5
Intraspecies differences: 10.

Total extrapolation factor is 140, leading to a rounded value of 750 µg/m^3.

A slightly higher value of 850 µg/m^3 would be obtained by using the BMDL05 of 120 mg/m^3 as POD.
The EU-LCI is in the range of the absolute odour threshold (0.21 ppm = 0.86 mg/m^3) determined by Nagata (2003).

References

Blaszkewicz M, Kiesswetter E, Kleinbeck S, Juran S, Schäper M (2010) Abgrenzung und Differenzierung 'irritativer' und 'belästigender' Effekte von Gefahrstoffen (FF228). Endbericht zum Verbundprojekt (OJ).

ECB (2002) European Union Risk Assessment Report. Methyl methacrylate, CAS No: 80-62-6, EINECS No: 201-297-1. Institute for Health and Consumer Protection, European Chemicals Bureau. Office for Official Publications of the European Communities, Luxembourg.

Hardisty JF, Garman RH, Harkema JR, Lomax LG, Morgan KT (1999) Histopathology of nasal olfactory mucosa from selected inhalation toxicity studies conducted with volatile chemicals. Toxicol Pathol 27:618-627.

Lomax LG (1992) Histopathologic evaluation of the nasal cavities from Fisher 344 rats exposed to methyl methacrylate vapor for two years. Rohm and Haas Company SH, PA. Cited in US EPA (1998).

Lomax LG, Krivanek ND, Frame SR (1997) Chronic inhalation toxicity and oncogenicity of methyl methacrylate in rats and hamsters. Food Chem Toxicol 35:393-407.

Nagata Y (2003) Measurement of odor threshold by triangle odor bag method. Japan. Ministry of Environment. http://www.env.go.jp/en/air/odor/measure/02_3_2.pdf

Rohm and Haas (1977) Subchronic vapor inhalation study with methyl methacrylate (C50680) in F344 rats and B6C3F1 mice.

Rohm and Haas (1979a) 18-month vapor inhalation safety evaluation study in hamsters: methyl methacrylate vapor, final report. Hazleton Laboratories America IV, VA. Cited in US EPA (1998).

Rohm and Haas (1979b) A two year vapour inhalation safety evaluation study in rats: methyl methacrylate vapour, final report. Hazleton Laboratories America IV, VA. Cited in US EPA (1998).

U.S.EPA (1998) Chemical Assessment Summary: Methyl methacrylate; CASRN 80-62-6. Agency USEP Washington, D.C. http://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/1000_summary.pdf

U.S.EPA (2008) Methyl Methacrylate (CAS Reg. No 80-62-6). Interim Acute Exposure Guideline Levels (AEGLs).. United States Environmental Protection Agency (US EPA) OoPPaTO
http://www2.epa.gov/sites/production/files/2014-08/documents/methyl_methacrylate_interim_oct_2008_v1.pdf

Voss JU (2017) Toxikologische Basisdaten und Textentwurf für die Ableitung von EU-LCI-Werten für Triethylamin (CAS Nr. 121-44-8), Tributylphosphat (CAS Nr. 126-73-8), Triethylphosphat (CAS Nr. 78-40-0), Methylmethacrylat (CAS Nr. 80-62-6) und Ethylmethylketon (CAS Nr. 78-93-3). UBA Texte 42/2017. https://www.umweltbundesamt.de/publikationen/toxikologische-basisdaten-textentwurf-fuer-die