2-Methylcyclohexanone

(CAS No: 583-60-8)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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1 Introduction

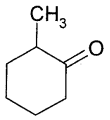
The present document contains the assessment of the health hazard of 2-methylcyclohexanone by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by AAE Wibowo, Ph.D. (Coronel Institute of the Academic Medical Centre, Amsterdam, the Netherlands).

The evaluation of the toxicity of 2-methylcyclohexanone has been based on the review the American Conference of Governmental Occupational Hygienists (ACGIH) (ACG96). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, literature was retrieved from the databases Medline, Chemical Abstracts, Embase (starting from 1966, 1970 and 1988, respectively), and HSEline, NIOSHTIC, Cisdoc, and Mhidas (backwards from 1997) and Poltox (Toxline, Cambr Sc Abstr, FSTA) (backwards from 1994), using the following key words: 2-methylcyclohexanone and 583-60-8. The final search was carried out in October 1997.

In February 1999, the President of the Health Council released a draft of the document for public review. Comments were received by the following individuals and organisations: P Wardenbach Ph.D. (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, Dortmund, Germany). These comments were taken into account in deciding on the final version of the document.

An additional literature search in May 2002 did not result in information changing the committee's conclusions.

2 Identity

name	:	2-methylcyclohexanone
synonyms	:	*o*-methylcyclohexanone; 1-methylcyclohexan-2-one
molecular formula	:	$CH_3C_5H_9CO$
structural formular	:	
CAS number	:	583 - 60 - 8

3 Physical and chemical properties

molecular weight	:	112,2
boiling point	:	165°C
melting point	:	-13.9°C
flash point	:	48°C (closed cup)
vapour pressure	:	at 55°C: 1.33 kPa
solubility in water	:	insoluble
log $P_{octanol/water}$	:	1.54 (estimated)
conversion factors	:	1 mg/m^3 = 0.21 ppm
(20°C, 101.3 kPa)		1 ppm = 4.67 mg/m^3

Data from ACG96, http://esc.syrres.com

2-Methylcyclohexanone is a somewhat viscous colourless liquid with an odour similar to that of acetone. The compound is chemically stable, but may darken when exposed to light. Although methylcyclohexanones are available as pure compounds, they are usually found as isomeric mixtures (*ortho*-, *meta*- and *para*-) (ACG96). The odour threshold is not known.

4 Uses

Methylcyclohexanone is used as a solvent in making lacquers, varnishes, and plastics; in the leather industry; and as a rust remover. The commercial product is a mixture of isomers (ACG96).

5 Biotransformation and kinetics

The committeere did not find data on the absorption and distribution of methylcyclohexanones. Topping et al. reported that methylcyclohexanones are reduced to methylcyclohexanols and excreted in urine as sulphuric and glucuronic acid conjugates (Top94).

6 Effects

Human data

The committee did not find human data on effects due to exposure to 2-methylcyclohexanone.

Animal data

Following application of 0.01 mL of undiluted ester to the uncovered clipped abdomen of 5 albino rabbits, 2-methylcyclohexanone scored an injury grade of 3 (i.e., giving rise to 'a strong capillary injection') on a scale from 1 to 10 (Smy69; see also Smy49).

The committee did not find data from studies on skin sensitisation in experimental animals.

When instilled into the eyes of rabbits, 2-methylcyclohexanone scored an injury grade of 5 on a scale of 1 to 10, which was defined as producing an injury of up to 5.0 points (out of a maximum of 20) 18 to 24 hours after instillation of 0.005 mL of undiluted test substance (0.02 mL gives over 5.0 points) (Smy69; see also Car46)*.

A 4-hour exposure to a concentration of 2-methylhexanone of 13,090 mg/m^3 (2800 ppm) caused mortality in 3/6 rats (Smy69). Topping et al. cited a study from 1938 in which mice, guinea pigs, and rats exposed to 16,345 mg/m^3 (3500 ppm) methylcyclohexanone vapour for 30 minutes showed irritation of the mucous membranes and effects on the central nervous system. Rabbits and cats became somnolent after a 1-hour exposure to 11,675 mg/m^3 (2500 ppm). A concentration of 2100 mg/m^3 (450 ppm) produced irritation in mice (Top94).

The oral LD_{50} for rats was 1980 (range: 1369-2868) mg/kg bw and the dermal LD_{50} for rabbits was 1637 mg/kg bw (Smy69). This suggests absorption of the compound through the skin.

Treon et al. performed a number of acute and repeated-dose experiments (Tre43a, Tre43b) with 'methylcyclohexanone' but since this was a mixture of chiefly 3- and 4-methylcyclohexanone (Tre43b), this studies are not discussed here.

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* Grade 5 was also characterised as a 'severe burn from 0.005 mL' (Smy54).

The committee did not find data on studies on repeated-dose toxicity, including carcinogenicity and reproduction toxicity, or on mutagenicity and genotoxicity of 2-methylcyclohexanone.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) of 2-methylcyclohexanone in the Netherlands is 230 mg/m^3 (50 ppm), with a skin notation.

Existing occupational exposure limits for 2-methylcyclohexanone in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

The committee did not find human data on effects due to exposure to 2-methylcyclohexanone or data from studies on repeated-dose toxicity, including carcinogenicity and reproduction toxicity, and on mutagenicity or genotoxicity were not found.

In experimental animals, 2-methylhexanone was a skin- and eye-irritating compound. Based on acute lethality data, 2-methylhexanone was of low toxicity following inhalation (4-hour LC_{50} rat: 13,090 mg/m^3 or 2800 ppm), dermal (LD_{50} rabbit: 1637 mg/kg bw), and oral (LD_{50} rat: 1980 mg/kg bw) exposure.

The committtee considers the toxicological database on 2-methylcyclohexanone too poor to justify recommendation of a health-based occupational exposure limit.

The committee concludes that there is insufficient information to comment on the level of the present MAC-value.

References

ACG96 American Conference of Governmental Industrial Hygienists (ACGIH). o-Methylcyclohexanone. In: TLVs and other occupational exposure values - 1996 [CD ROM], version 1.7 - s4 02/01/95. Cincinnati OH, USA: ACGIH, 1996.

ACG02a American Conference of Governmental Industrial Hygienists (ACGIH). Guide to occupational exposure values -2002. Cincinnati OH, USA: ACGIH®, Inc, 2002: 83.

ACG02b American Conference of Governmental Industrial Hygienists (ACGIH). 2002 TLVs® and BEIs®. Threshold Limit Values for chemical substances and fysical agents. Biological Exposure Indices. Cincinnati OH, USA: ACGIH®, Inc, 2002: 41.

Arb00a Arbejdstilsynet. Grænseværdier for stoffer og materialer. Copenhagen, Denmark: Arbejdstilsynet, 2000; At-vejledning C.0.1.

Arb00b Arbetarskyddsstyrelsen. Hygieniska gränsvärden och åtgärder mot luftföroreningar. Solna, Sweden: Arbetarskyddsstyrelsen, 2000; Ordinance AFS 2000:3.

Car46 Carpenter CP, Smyth HF Jr. Chemical burns of the rabbit cornea. Am J Ophthalmol 1946; 29: 1363-72.

CEC00 Commission of the European Communities (CEC). Commission Directive 2000/39/EC of 8 June 2000 establishing a first list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work. Official Journal of the European Communities 2000; L142 (16/06/2000): 47-50.

DFG02 Deutsche Forschungsgemeinschaft (DFG): Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe. MAK- und BAT-Werte-Liste 2002. Maximale Arbeitsplatzkonzentrationen und Biologische Arbeitsstofftoleranzwerte. Weinheim, FRG: Wiley-VCH, 2002: 79 (rep no 38).

HSE02 Health and Safety Executive (HSE). EH40/2002. Occupational exposure limits 2002. Sudbury (Suffolk), England: HSE Books, 2002: 21.

Smy49 Smyth HF Jr, Carpenter CP, Weil CS, et al. Range-finding toxicity data, List III. J Ind Hyg Toxicol 1949; 31: 60-2.

Smy54 Smyth HF Jr, Carpenter CP, Weil CS, et al. Range-finding toxicity data. List V. AMA Arch Ind Hyg Occup Med 1954; 10: 61-8.

Smy69 Smyth HF Jr, Carpenter CP, Weil CS, et al. Range finding toxicity data: List VII. Am Ind Hyg Ass J 1969; 30: 470-6.

SZW02 Ministerie van Sociale Zaken en Werkgelegenheid (SZW). Nationale MAC-lijst 2002. The Hague, the Netherlands: Sdu, Servicecentrum Uitgevers, 2002: 34.

Tre43a Treon JF, Crutchfield WE Jr, Kitzmiller KV. The physiogical response of rabbits to cyclohexane, methylcyclohexane, and certain derivatives of these compounds. I. oral administration and cutaneous application. J Ind Hyg Toxcicol 1943; 25: 199-214.

Tre43b Treon JF, Crutchfield WE Jr, Kitzmiller KV. The physiogical response of rabbits to cyclohexane, methylcyclohexane, and certain derivatives of these compounds. II. Inhalation. J Ind Hyg Toxicol 1943; 25: 323-7.

Top94 Topping DC, Morgott DA, David RM, et al. Methylcyclohexanones. In: Clayton GD, Clayton FE, eds. Toxicology. 4th ed. New York, USA: John Wiley & Sons, Inc, 1994: 1842-3.(Patty's industrial hygiene and toxicology; Vol II, Pt C.

TRG00 TRGS 900. Grenzwerte in der Luft am Arbeitsplatz; Technische Regeln für Gefahrstoffe. BArbBl 2000; 2.

Annex

Occupational exposure limits for 2-methylcyclohexanone in various countries.

country -organisation	occupational exposure limit		time-weighted average	type of exposure limit	note[a]	reference[b]
	ppm	mg/m^3				
the Netherlands						
-Ministry of Social Affairs and Employment	50	230	8 h	administrative	S	SZW02
Germany						
-AGS	50	230	8 h		S	TRG00
	200	920	15 min			
-DFG MAK-Kommission	-[c]	-		MAK	S	DFG02
Great-Britain						
-HSE	50	233	8 h	OES		HSE02
	75	350	15 min	STEL		
Sweden	-	-				Arb00b
Denmark	50	230	8 h	OEL	S	Arb00a
USA						
-ACGIH	50	-	8 h	TLV	S	ACG02b
	75	-	15 min	STEL		
-OSHA	100	460	8 h	PEL	S	ACG02a
-NIOSH	50	230	10 h	REL	S	ACG02a
	75	345	15 min	STEL		
European Union						
-SCOEL	-	-				CEC00

[a] S = skin notation; which mean that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation.

[b] Reference to the most recent official publication of occupational exposure limits.

[c] Listed among substances for which studies of the effects in man or experimental animals have yielded insufficient information for the establishment of MAK values.