

Aan de Staatssecretaris van Sociale Zaken en Werkgelegenheid

Onderwerp : Aanbieding adviezen herevaluatie bestuurlijke MAC-waarden
Uw kenmerk : ARBO/AMIL/97/00648
Ons kenmerk : U 2706/CB/MP/563-O3
Bijlagen : 18
Datum : 14 december 2000

Mijnheer de staatssecretaris,

Op verzoek van uw ambtsvoorganger bied ik u hierbij de eerste adviezen aan van een reeks over de gezondheidkundige basis van uit het buitenland overgenomen grenswaarden voor beroepsmatige blootstelling aan stoffen. Het verzoek om deze adviezen is in algemene zin vervat in brief nr ARBO/AMIL/97/00648 en in latere stadia door uw departement toegespitst op afzonderlijke stoffen. De adviezen zijn opgesteld door een daartoe door mij geformeerde internationale commissie van de Gezondheidsraad en beoordeeld door de Beraadsgroep Gezondheid en Omgeving.

De beoogde reeks van in het Engels gestelde adviezen zal losbladig worden gepubliceerd onder ons publicatienummer 2000/15OSH en, conform de aan de Gezondheidsraad voorgelegde toespitsingen van de adviesaanvraag, betrekking hebben op 168 stoffen. Het u thans aangeboden eerste pakket bestaat uit een Algemene Inleiding (publicatienummer 2000/15OSH/000) en uit de adviezen genummerd 2000/15OSH/001 tot en met 2000/15OSH/017, respectievelijk betrekking hebbend op:

cesiumhydroxide, cyclopentaan, diboraan, dimethoxymethaan, dipropylketon, fenylfosfine, germaniumtetrahydride, hexachloornaftaleen, methaanthiol, methylcyclohexanol, methylisopropylketon, mica, natriumhydroxide, octachloornaftaleen, silaan, tetrachloornaftaleen, en yttrium en yttriumverbindingen.

Bij afronding van de werkzaamheden van de hierboven bedoelde commissie ontvangt u een Nederlandstalige samenvatting van de in de gehele reeks van adviezen neergelegde bevindingen.

Gezondheidsraad

Health Council of the Netherlands

Onderwerp : Herevaluatie uit het buitenland overgenomen grenswaarden
Ons kenmerk : U
Pagina : 2
Datum : 14 december 2000

De u thans aangeboden adviezen heb ik vandaag ter informatie doen toekomen aan de Minister van Volksgezondheid, Welzijn en Sport en aan de Minister van Volkshuisvesting, Ruimtelijke Ordening en Milieubeheer.

Hoogachtend,

prof. dr JJ Sixma

Methylcyclohexanol (mixed isomers)

(CAS Reg. nr: 25639-42-3)

Health-based Reassessment of Administrative
Occupational Exposure Limits

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

No. 2000/15OSH/010, The Hague, 14 December 2000

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1 Introduction

The present document contains the assessment of the health hazard of methylcyclohexanol (mixed isomers) 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).

Literature was retrieved from the data bases Medline, Toxline, Chemical Abstracts and Embase, starting from 1966, 1967, 1970 and 1988, respectively, and using the substance name as a keyword. Also the CD roms HSEline, Cisdoc, Mhidas and NIOSHtic were consulted (from 1997 backwards). Data considered to be critical were evaluated by reviewing the original publications. The final literature search has been 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 organizations: dr P Wardenbach (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, Dortmund, Germany). These comments were taken into account in deciding on the final version of the document.

2 Identity

name	:	methylcyclohexanol (mixed isomers)
synonyms	:	hexahydrocresol hexahydromethylphenol methylhexalin
molecular formula	:	C ₇ H ₁₄ O
structural formula	:	
CAS reg nr	:	25639 - 42 - 3

3 Physical and chemical properties

molecular weight	:	114.2
boiling point	:	155 - 180°C
melting point	:	< -21°C
vapour Pressure	:	0.2 kPa
solubility in water	:	3.4 g/100 ml
log P _{oct/water}	:	not known
conversion factors (20 °C, 101.3 kPa)	:	1 mg/m ³ = 0.21 ppm 1 ppm = 4.75 mg/m ³

Data from IPC91

Methylcyclohexanol is a straw-coloured liquid with a weak odour like coconut oil (NIO94). The vapour can be detected by its odour at 2375 mg/m³ (500 ppm) (Hat91).

4 Uses

Methylcyclohexanol is used as a solvent for cellulose esters and ethers, a lubricant antioxidant, a blending agent of soaps and detergents, in textile and artificial silk industry, and as a degreasing agent (ACG96).

5 Biotransformation and kinetics

Methylcyclohexanol can be absorbed into the body by inhalation of its vapour, through the skin, and by ingestion of its liquid (IPC91). There are no quantitative data on absorption. Neither is there any information on distribution, biotransformation, excretion and biological monitoring methods for this compound.

Methylcyclohexanol is one of the metabolites of methylcyclohexane. Parnell *et al.* (Par88) reported among others trans-3-methylcyclohexanol and trans-4-methylcyclohexanol as urinary metabolites after oral administration of methylcyclohexane to male Fischer rats.

6 Effects and mechanism of action

Human data

According to Hathaway *et al.* (Hat91), a concentration of methylcyclohexanol equivalent to its odour threshold of 2375 mg/m³ (500 ppm) can cause upper respiratory irritation. This information was given without further details. There are no human data available on possible systemic effects induced by exposure to this compound.

Animal data

No recent animal data on methylcyclohexanol have been found.

Treon *et al.* (Tre43a) exposed young healthy rabbits to methylcyclohexanol by inhalation. One or two rabbits from each lot of 12 were set aside as controls. Three experiments were carried out, in each of which methylcyclohexanol was employed in a concentration of 560, 1060 or 2300 mg/m³ for 6 hours daily, 5 days per week over a period of 10 weeks. No deaths occurred at any concentration. Signs of intoxication, consisting of salivation, conjunctival irritation and slight lethargy, were seen only after exposure to the highest concentration of 2300 mg/m³. Concentration-related microscopic pathological changes in liver and kidneys were observed in all animals. In the lowest exposure group, however, these were 'barely discernible', according to the authors. All rabbits gained weight during the experiment. During the daily exposure periods no significant changes in body temperature between exposed and control animals were observed. According to the authors, methylcyclohexanol does not cause narcosis within the limits of the concentrations that can be obtained at ordinary temperatures. They concluded that the 'maximum safe concentration for the prolonged exposure of rabbits' would be 'very slightly below 560 mg/m³'.

The same authors (Tre43b) also exposed rabbits to methylcyclohexanol by oral administration and cutaneous application. The minimum lethal dose of methylcyclohexanol for rabbits by oral administration was between 1750 and 2000 mg/kg bw. Rapid narcosis and convulsive movements resulted. There was a decrease in the percentage of inorganic sulphates and an increase in the glucuronic acid content of the urine. Rabbits given doses ranging from 1000 to 1750 mg/kg bw lost body weight in the first 2 to 4 days and regained weight

during the following 2 to 4 days. The authors concluded that rabbits when given sublethal oral doses of methylcyclohexanol, suffered from rapidly developing anaesthesia together with spasmodic jerking of the head and rhythmic 'running' movements of the forelegs. In some cases there was slight salivation, lacrimation and distension of the ear veins.

The minimum lethal dose of methylcyclohexanol for rabbits by cutaneous administration was between 6800 and 9400 mg/kg bw. On one rabbit 10 ml methylcyclohexanol was applied to the clipped abdominal skin in two-5 ml portions at half-hour intervals, for 6 days (a total dose of 21,000 mg/kg bw). The residual material was removed after one hour by washing. During the first two days general weakness and scattered local petechiae were observed. On subsequent days deep anaesthesia, lasting for several hours, developed accompanied by convulsive movements and tremors of the forelegs. Thickening of the skin and hemorrhagic areas were noted at the site of application. The animal died 18.5 hours after the final application.

No data on long-term toxicity, mutagenicity, genotoxicity, carcinogenicity and reproduction toxicity of methylcyclohexanol have been found.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) of methylcyclohexanol in the Netherlands is 235 mg/m³ (50 ppm), 8 h TWA.

Existing occupational exposure limits for methylcyclohexanol in some European countries and in the USA are summarized in the annex.

8 Assessment of health hazard

There are no human data available on exposure to methylcyclohexanol. Studies in experimental animals indicated the central nervous system and probably also the liver and kidneys as target organs of methylcyclohexanol exposure. This is substantiated by the fact that experimental animals exposed to methylcyclohexane also showed effects of the central nervous system. Methylcyclohexanol is a metabolite of methylcyclohexane*.

Although the study by Treon *et al.* (Tre43b) is dated, the committee concludes that it has been well performed and sufficiently documented to be used as a starting point for the hazard assessment of methylcyclohexanol. The

* The committee will also reassess the current administrative OEL of methylcyclohexane.

committee considers the concentration of 560 mg/m³ (118 ppm) methylcyclohexanol in rabbits to be the lowest observed adverse effect level (LOAEL). After applying an overall assessment factor of 18 to account for starting from a LOAEL instead of a NOAEL and for inter- and intraspecies variation, the committee recommends a health-based occupational exposure limit of 31 mg/m³ which results in a preferred value of 50 mg/m³ (10.5 ppm), 8 h TWA for methylcyclohexanol (mixed isomers).

The committee recommends a health-based occupational exposure limit of 50 mg/m³ (10.5 ppm) for methylcyclohexanol (mixed isomers), as an 8 hour time weighted average (TWA).

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Annex

Occupational exposure standards for methylcyclohexanol (mixed isomers) in various countries.

country -organisation	occupational exposure limit		time-weighted average	type of exposure limit	note ^a	lit ref ^b
	ppm	mg/m ³				
The Netherlands -Ministry	50	235	8 h	administrative		SZW00
Germany -AGS	50	235	8 h			TRG00
-DFG MAK-Kom.	50	240	8 h	MAK		DFG99
Great-Britain -HSE	50	237	8 h	OES		HSE99
	75	356	15 min	STEL		
Sweden	-	-				NBO96
Denmark	50	235	8 h			Arb96
USA -ACGIH	50	234	8 h	TLV		ACG00
-OSHA	100	470	8 h	PEL		
-NIOSH	50	235	10 h	REL		
European Union -SCOEL	-	-				

^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

