Methylcyclohexane

(CAS No: 108-87-2)

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/154 The Hague, October 27, 2005

Preferred citation:
Health Council of the Netherlands: Committee on Updating of Occupational Exposure Limits. Methylcyclohexane; Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands, 2005; 2000/15OSH/154.

1 Introduction

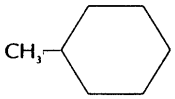
The present document contains the assessment of the health hazard of methylcyclohexane by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by AAE Wibowo, Ph.D. and M Verberk, Ph.D. (Coronel Institute,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

In January 1998, literature was searched in the databases Medline, Chemical Abstracts, and Embase, starting from 1966, 1970, and 1988, respectively, and using the following keywords: methylcyclohexane, cyclohexylmethane, and 108-87-2. HSELINE, CISDOC, MHIDAS, NIOSHTIC (from 1985/1987-January 1998) and Poltox (Toxline, Cambridge Scient Abstr, FSTA; from 1990-January 1995), databases available from CD-ROM, were consulted as well.

In February 1999, the President of the Health Council released a draft of the document for public review. Comments were received from 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 search in Toxline and Medline in February 2005 did not result in information changing the committee's conclusions.

2 Identity

name	: methylcyclohexane
synonyms	: hexahydrotoluene; cyclohexylmethane; toluene hexahydride
molecular formula	: $C_6H_{11}C_3$
structural formula	
CAS number	: 108-87-2

3 Physical and chemical properties

molecular weight	: 98.21
boiling point	: 101°C
melting point	: -127°C
flash point	: -4°C (closed cup)
vapour pressure	: at 25°C: 5.7 kPa
solubility in water	: not soluble (at 20°C: 1.4 mg/100 mL)
log $P_{octanol/water}$	: 3.61 (experimental); 3.59 (estimated)
conversion factors	: at 20°C, 101.3 kPa: 1 mg/m^3 = 0.24 ppm 1 ppm = 4.09 mg/m^3

Data from ACG96, NLM03, http://www.syrres.com/esc/est_kowdemo.htm.

Methylcyclohexane is a colourless liquid with a faint benzene-like odour (ACG96). Odour thresholds of 480 (2000 mg/m^3) (Rut86) and 630 ppm (2580 mg/m^3) (Amo83) have been reported.

4 Uses

Methylcyclohexane is used in organic synthesis and as a solvent for cellulose ethers. It is a component of jet fuel (ACG96).

5 Biotransformation and kinetics

The committee did not find human data on the biotransformation and kinetics of methylcyclohexane in humans.

Zahlsen et al. studied the inhalation kinetics of C6 to C10 aliphatic, aromatic and naphthenic hydrocarbons in rats after repeated exposure, using methylcyclohexane as a model compound for C7 naphthenic hydrocarbons. Rats were exposed to a methylcyclohexane concentration of 100 ppm (409 mg/m^3), 12 hours/day, for 3 consecutive days. The hydrocarbon concentrations were measured in blood, brain, liver, kidney, and perirenal fat immediately after each exposure and 12 hours after the final exposure. During the exposure period, the highest methylcyclohexane concentrations were found in the perirenal fat tissue (356-550 μmol/kg), followed by the kidney (94.7-127.7 μmol/kg), brain (44.4-47.2 μmol/kg), liver (30.1-32.7 μmol/kg), and blood (5.8-6.4 μmol/kg). The distribution pattern of hydrocarbons in the brain was totally different from that in blood. The concentrations of C6 to C9 naphthenes (including

methylcyclohexane) were roughly twice that of the aliphatic and aromatic compounds (Zah92). This study demonstrated clearly that comparable groups of aliphatic, aromatic, and naphthenic hydrocarbons possess distinctly different toxicokinetic properties when inhaled. Absorption, distribution, and accumulation are strongly related to molecular structure, but also to the number of carbon atoms and possibly to differences in metabolism and enzyme induction potential. Zahlsen et al. did not determine the elimination half-lives of the compounds.

Parnell et al. analysed the urine of male Fischer rats collected during 48 hours after oral administration of methylcyclohexane doses of 800 mg/kg bw. After hydrolyses with glucuronidase/sulphatase, metabolites identified included cyclohexylmethanol, *trans*-3-methylcyclohexanol, *trans*-4-methylcyclohexanol, *cis*-2-hydroxy-*cis*-4-methylcyclohexanol, *cis*-2-hydroxy-*trans*-4-methyl-cyclohexanol, and *trans*-2-hydroxy-*cis*-4-methylcyclohexanol at a relative ratio of 10.1:2.0:1.0:2.1:15.7:22.4. Not any cyclcohexanecarboxylic acid was found. Analysis of urine not treated with glucuronidase/sulphatase showed no traces of methylcyclohexane metabolites (Par88). Elliott et al. studied the kinetics of methylcyclohexane in rabbits given single oral doses of ^{14}C-labelled compound of ca. 200-235 mg/kg bw. Sixty hours after administration, 65% of the dose was excreted in the urine, 15% in expired air (10% as parent compound, 5% as CO_2), 0.5% in the faeces; 4-5% remained in the carcass. Forty-two and 2% of the dose were excreted as glucuronide and sulphate conjugates, respectively. The major metabolites were the glucuronide conjugates of *trans*-4-methylcyclohexanol (ca. 15% of the dose), *cis*-3-methylcyclohexanol (11.5%), and *trans*-3-methyl-cyclohexanol (10.5%). Minor metabolites (accounting for 0.5-2.5%) included glucuronides of *cis*-4-methylcyclohexanol and of *cis*- and *trans*-2-methyl-cyclohexanol. No cyclohexanediols were found. The small urinary amounts of cyclohexylmethanol (0.3%) and free and glycine-conjugated benzoic acid (ca. 0.5 and 1.5%, (respectively) suggested some minor aromatisation of the cyclohexane ring via hydroxylation and carboxylation of the methyl group (Ell65).

6 Effects and mechanism of action

Human data

The committee did not find data on the irritation and sensitisation properties of methylcyclohexane in humans.

Soleo et al. reported subclinical neuropathy in a group of workers employed in a rubber shoe factory and exposed to a mixture of solvents containing 38-40% heptane, 8-10% 3-methylhexane, 27-30% 2-methylhexane, 17-21% methylcyclohexane, 0.2% hexane, and a little amount of various other solvents (Sol87). Valentini et al. reported a case of a 32-year-old woman who complained of vertigo, leg and arm paraesthesia, and leg pain about 3 months after she started working at home as a shoemaker. At that time, an EEG revealed mild and aspecific signs of brainstem involvement. Motor conduction velocity studies revealed mild reduction in the sciatic nerve, and electromyography indicated moderate signs of bilateral denervation in the leg muscles. The diagnosis was peripheral neuropathy due to solvents. During a representative working day (8-10 hours), she manufactured about 20 pairs of shoe uppers, using an estimated amount of glue of 130 g. The glue contained several solvents, especially ethyl acetate, cyclohexane, and heptane, and also methylcyclohexane, which could have been present at a concentration of ca. 37 mg/m^3 (9 ppm) as was found in an experimental exposure reconstruction in this particular workroom (Val94).

Mason et al. studied the effects of long-term exposure to a mixture of organic solvents on liver functions of 3 groups of workers (2 non-exposed groups and one exposed group). The mixture of solvents consisted mainly of toluene, heptane, and methylcyclohexane. The results showed significant differences in urinary 6β-hydroxycortisol/free cortisol ratios and 6β-hydroxycortisol and bile acid concentrations between the exposed and control groups. No differences were found in serum alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and γ-glutamyltransferase activities, as well as in the urinary concentrations of bilirubin and D-glucaric acid (Mas94).

In a case control-study, Agnesi et al. studied the relationship between maternal exposure to organic solvents in shoe industry and the risk of spontaneous abortion. Cases, 108 subjects with clinically recognised spontaneous abortion (ICD codes 632-634-636), and controls, 108 age-, year- and residence-matched females with normal delivery, were traced in discharge registry files of a regional Italian hospital. Measurements in ca. 30 shoe factories showed the presence of various organic solvents, among which methylcyclohexane. The mean concentrations of methylcyclohexane were 30 mg/m^3 (7 ppm) (n=30 samples) in 1989 and 120 mg/m^3 (29 ppm) (n=10 samples) in 1992. Cases and controls were divided into 3 exposure categories, based on time and kind of glueing: not exposed (78 cases, 88 controls), exposed to low levels (12 cases, 12 controls), and exposed to higher levels (18 cases, 8 controls). The relative risk (RR) of spontaneous abortion in women exposed to higher concentrations of organic solvents during pregnancy was 3.85 (95% CI: 1.24-

11.9; $p<0.05$), after adjustment for confounding factors. The RR was 1.58 (95% CI: 0.62-4.06) in women exposed to low organic solvent concentrations (Agn97).

Because of concomitant exposure to other hydrocarbons solvents, the committee cannot assess the aetiological role of methylcyclohexane concerning the effects described above.

Animal data

Irritation and sensitisation

Without providing details, methylcyclohexane was stated to be slightly, transiently irritating to the eyes of rabbits (Sut69). Instillation of 0.1 mL undiluted methylcyclohexane (technical; purity: not given) into the eyes of male and female rabbits, using an unwashed procedure, only induced conjunctival redness in 4/6 and 1/6 rabbits at 1 hour and 24 hours post-treatment, respectively; mean Draize scores were 1.3 and 0.3, respectively. At all other time points thereafter (up to 7 days), scores were 0.0 (maximum score possible: 8.0) (Pen82a).

Without providing details, methylcyclohexane was stated to be moderately irritating to the skin when held in contact for 24 hours (Sut69). Twenty-four hour occluded application of 0.5 mL of undiluted methylcyclohexane to one intact and one abraded site of the skin of rabbits (n=3/sex) caused only very slight erythema in all 5 abraded sites and 4/5 intact sites, 24 hours post-application, and in 1/5 abraded and 1/5 intact sites, 72 hours post-application (one male animal was found dead prior to the 24-hour observation); the mean primary irritation score was 0.55 (maximum: 8.0) (Pen82b). Methylcyclohexane was applied to the clipped skin of a rabbit in 12 portions of 5 mL of methylcyclohexane at 5-minute intervals on 6 successive days. After 1 hour, the test compound was washed off. Irritation appeared on the 2nd day and increased somewhat with successive treatments. Hardening, thickening, and ulceration appeared later, and the experiment was terminated after the 6th day (Tre43a).

Acute toxicity

When rats were exposed to vapour concentrations of 82,000-260,000 mg/m^3 (ca. 20,000-62,000 ppm), mortality occurred within 13-70 minutes, animals showing anaesthesia, lethargy, ataxia, and terminal convulsion. Exposure to 11,000 mg/m^3 (ca. 2600 ppm), for 6 hours, induced only minor symptoms (lethargy in 3 hours) (Sut69). In mice, a 2-hour LC_{50} of 41,500 mg/m^3 (ca. 10,000

ppm) has been reported (Izm82). Exposure to ca. 31,000-41,000 mg/m^3 (7500-10,000 ppm), for 2 hours, produced prostration in mice; concentrations of ca. 41,000-51,000 mg/m^3 (10,000-12,500 ppm) mortality (ACG96). All 4 rabbits died within 70 minutes when exposed to 59,900 mg/m^3 (ca. 15,000 ppm). Signs of toxicity included severe convulsions, narcosis, laboured breathing, salivation, and conjunctival congestion (Tre43b).

Oral LD_{50} values of 3200 and 2250 mg/kg bw were reported for rats and mice, respectively (Izm82, Sut69). Treon et al. found that the range of the minimum oral lethal dose of methylcyclohexane (containing 3% toluene) in rabbits was between 4000 and 4500 mg/kg bw. All animals (n=4/dose) survived doses of 1000 to 4000 mg/kg bw, while doses of 4500 to 10,000 mg/kg bw were lethal to all animals within 84 to 5.5 hours, respectively. Animals showed severe diarrhoea, weight loss, and laboured breathing, but no convulsions. The results of blood examinations were within normal limits (Tre43a).

An intraperitoneal LD_{50} of approximately 3200 mg/kg bw has been reported in rats (Sut69).

Repeated-dose toxicity

Treon et al. exposed rabbits (n=4/group), 6 hours/day, 5 days/week, to concentrations of 39,550 (ca. 9500 ppm) (for 2 weeks), 28,750 (ca. 6900 ppm) (for 2 weeks), 21,900 (ca. 5260 ppm) (for 4 weeks), 11,350 (ca. 2720 ppm) (for 3 weeks), 4570 (ca. 1100 ppm) (for 10 weeks), or 948 mg/m^3 (ca. 230 ppm) (for 10 weeks). At 39,550 and 28,750 mg/m^3, mortality occurred in 4/4 and 1/4 rabbits, respectively. The animals exposed to 39,550 mg/m^3 showed convulsions, light narcosis, laboured breathing, salivation, and conjunctival congestion; those exposed to 28,750 mg/m^3 lethargy and impaired coordination of legs. Apart from slight lethargy in animals exposed to 21,900 mg/m^3, no mortality or signs of intoxication were observed in the other exposure groups. Only for the animals exposed to 11,350 mg/m^3, results from microscopic examination, viz., barely demonstrable evidence of cellular liver and kidney injury (not further specified) were presented. In addition, Treon et al. reported that no microscopic lesions were observed in tissues of one monkey exposed to 1460 mg/m^3 (ca. 350 ppm) for 10 weeks (6 hours/day, 5 days/week) (Tre43b).

MacEwen and Vernot exposed rats (F344; n=65/sex/group), mice (C57BL/6; n=200 females/group), hamsters (Golden Syrian; n=100 males/group), and dogs (beagle; n=4/sex/group) to methylcyclohexane concentrations of 0, 400, or 2000 ppm (i.e., 1636 or 8180 mg/m^3), 6 hours/day, 5 days/week, for 1 year. At the end of the 1-year exposure period, 10 rats/sex, 20 mice, and 10 hamsters were killed

and necropsied to investigate the primary tissues. The remaining animals were held for an additional observation period of one year (Mac80, Mac81, Mac84).

In rats, body weights of females sacrificed at the end of the exposure period were unaffected during the exposure period while decreased body weights were observed in males exposed to 400 (by 6%; $p<0.05$) and 2000 ppm (by 8%; $p<0.01$). Statistically significant organ weight changes were found in the 2000-ppm groups only and included decreases in absolute lung weights in males and in absolute and relative liver weights in females and in increases in relative liver and heart weights in males. Evaluation of haematology and clinical chemistry data* showed dose-related decreases in leukocyte counts in male and female animals, being statistically significant from control values in both male groups ($p<0.05$) and in the 2000-ppm female group ($p<0.01$), a statistically significant ($p<0.01$) decrease in haemoglobin level in 2000-ppm males, and a dose-related decrease in sodium levels in males, being statistically significantly different from controls in both groups ($p<0.01$). No differences between controls and female exposure groups were seen upon macroscopic and microscopic examinations. In male rats, there was a significant increase in the incidence of testicular tumours in the animals of the 400-ppm group (incidence: 5/10; controls: 0/11; 2000 ppm: 2/11; $p<0.05$) as well as increases in the incidence of renal tubular dilation (controls: 1/11; 400 ppm: 2/10; 2000 ppm: 4/11; not significant). Upon macroscopic and microscopic examination of animals sacrificed following the 12-month post-exposure period, no statistically significant differences in the incidences of neoplastic and non-neoplastic lesions were seen between control and female rat exposure groups. In male rats, there were only statistically significant increases in the incidences of medullary mineralisation (controls: 1/53; 400 ppm: 2/55; 2000 ppm: 19/52) and epithelial hyperplasia of the renal papilla (controls: 1/53; 400 ppm: 1/55; 2000 ppm: 23/52). The severity of these lesions was not reported (Mac80, Mac81, Mac84).

For mice, no data on survival or body weight were given. Exposure did not result statistically significant tissue changes in animals sacrificed at the end of the exposure period (these data concerned 29 to 39 animals where only 20/group should have been killed). In mice killed after the 12-month exposure-free observation period, there were no statistically significant differences in the incidences of neoplastic and non-neoplastic lesions between control and exposure groups, although increased incidences in uterine multiple cysts were

* For female rats, only data on red and white blood cell counts, haemotocrit, and haemoglobin were presented. Because of haemolysis of female rat blood samples, no clinical chemistry comparisons could be made.

reported (controls: 10/164; 400 ppm: 22/158; 2000 ppm: 23/152 (Mac80, Mac81, Mac84).

Body weights of the male hamsters of both exposure groups were lower than those of controls throughout the exposure period, with a maximum decrease of roughly 20% for both exposure groups. There was no clear dose response. For both exposure and control groups, body weights increased until about month 2, but decreased gradually from month 4 onwards. After ending exposure, body weights of the exposed animals increased rapidly reaching control values at month 14. Thereafter, body weights decreased again, those of the animals having been exposed to 2000 ppm more than those of the 400-ppm group. Post-mortem examination of the animals sacrificed at the end of the exposure period (17-24 animals/group instead of 10/group that were scheduled) did not reveal exposure-related tissue changes. In hamsters killed after the 12-month exposure-free observation period, there were no statistically significant differences in the incidences of neoplastic and non-neoplastic lesions between control and exposure groups, although increased incidences in renal cortical fibrosis were observed (controls: 4/75; 400 ppm: 12/76; 2000 ppm: 10/81) (Mac80, Mac81, Mac84).

For dogs, no data were presented apart from a transient dose-related increase in serum alanine aminotransferase levels, which was attributed to a single dog per group exhibiting high levels where the others were normal and the accidental death of one male animal of the 400-ppm group (Mac80, Mac81, Mac84).

Besides irritation (see ‘Irritation and sensitisation’), slight hypothermia and transient body weight loss was observed following repeated applications of 12 portions of 5 mL of methylcyclohexane at 5-minute intervals on 6 successive days to the clipped skin of a rabbit (Tre43a).

Parnell et al. reported very slight renal tissue damage in male Fischer rats (n=8; controls: n=6) after administration of oral doses of methylcyclohexane of 800 mg/kg bw on every other day for 2 weeks. No further details of the tissue damage were given, but tissues of exposed animals were compared with those of controls for ‘characteristic lesions of hydrocarbon-induced nephropathy, including hyaline droplet formation, tubular cysts, and papillary calcification’. No other organs were examined (Par88).

The committee did not find data from mutagenicity/genotoxicity or reproduction toxicity studies on methylcyclohexane.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for methylcyclohexane in the Netherlands is 1600 mg/m^3 (400 ppm), 8-hour TWA.

Existing occupational exposure limits for this substance in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

The committee did not find data on the biotransformation and kinetics of methylcyclohexane in humans. In rats, exposed to 409 mg/m^3 (100 ppm), 12 hours/day, for 3 days, highest methylcyclohexane concentrations were found in perirenal fat tissue followed by kidney, brain, liver, and blood (ratio roughly 75:20:8:5:1). Analysis of urine of rats, given single oral doses of 800 mg/kg bw, showed metabolism of methylcyclohexane to proceed through hydroxylation of, especially, the cyclohexane ring followed by conjugation, *trans*-2-hydroxy-*cis*-4-methylcyclohexanol, *cis*-2-hydroxy-*trans*-4-methylcyclohexanol, and cyclohexylmethanol being the main metabolites. Sixty hours after administration of oral doses of about 200 mg/kg bw to rabbits, 65% of the dose was excreted in the urine, 15% in expired air (10% as parent compound, 5% as CO_2), 0.5% in the faeces; 4-5% remained in the carcass. The major metabolites were the glucuronide conjugates of *trans*-4-methylcyclohexanol (ca. 15% of the dose), *cis*-3-methylcyclohexanol (11.5%), and *trans*-3-methylcyclohexanol, accounting for ca. 15-11% of the dose, while no diols and only very little cyclohexylmethanol (0.3%) were found.

The committee did not find data on the irritation and sensitisation properties of methylcylcohexane in humans. Because of concomitant exposure to other hydrocarbons solvents, the committee cannot assess the aetiological role of methylcyclohexane concerning liver, nervous system, and reproduction effects reported in exposed people.

In experimental animals, methylcyclohexane appeared only very slightly irritating to the eyes and skin of rabbits. Rats survived 6-hour exposures to 11,000 mg/m^3 (ca. 2600 ppm), showing lethargy, but died within 13-70 minutes when exposed to concentrations of 82,000-260,000 mg/m^3 (ca. 20,000-62,000 ppm). For mice, the 2-hour LC_{50} was 41,500 mg/m^3 (ca. 10,000 ppm), lower levels producing prostration. All (4) rabbits died within 70 minutes when exposed to 59,900 mg/m^3 (ca. 15,000 ppm). Oral LD_{50} values were 3200 and

2250 mg/kg bw for rats and mice, respectively. Rabbits survived single oral doses of 4000 mg/kg bw, but all died at doses of 4500 mg/kg bw and higher.

Repeated (6 hours/day, 5 days/week, 2 weeks) exposure to concentrations of 39,550 and 28,750 mg/m^3 (ca. 9500 and 6900 ppm, respectively) caused mortality in 4/4 and 1/4 rabbits, respectively, animals showing dose-related clinical signs indicative of nervous system effects. Exposure to 21,900 mg/m^3 (ca. 5250 ppm) for 4 weeks only caused slight lethargy while no signs of toxicity were observed at 11,350 mg/m^3 (ca. 2720 ppm), for 3 weeks. In the rabbits of the latter group, there were microscopic liver and kidney lesions. Exposure to 4570 mg/m^3 (ca. 1100 ppm), for 10 weeks, was found to be 'innocuous' to rabbits. When male and female rats, female mice, male hamsters, and male and female dogs were exposed to 8180 mg/m^3 (2000 ppm) for 1 year, there were decreases in body weights in male rats (by 8%) and in male hamsters (by roughly 20%) and changes in relative organ weights (females: decreased liver weights; males: increased liver and heart weights) and in haematology and clinical chemistry values (males and females: decreased leukocyte counts; males: decreased haemoglobin and sodium levels) in rats. No statistically significant differences between controls and any of the animal exposure groups were seen upon macroscopic and microscopic pathological examinations. Macroscopic and microscopic examination of animals sacrificed following a 12-month post-exposure period did not reveal statistically significant differences in incidences of neoplastic and non-neoplastic lesions between female rats, female mice, and male hamsters and their respective control groups; in male rats, almost all control and exposed animals showed nephropathy while there were statistically significantly increased incidences of medullary mineralisation and epithelial hyperplasia of the renal papilla in the 2000-ppm animals. Following exposure of these groups of species to 1636 mg/m^3 (400 ppm), for 1 year, only decreased body weights in male rats (by 6%) and hamsters (by roughly 20%) and an increased incidence of testicular tumours (probably interstitial cell tumours; 5/10 vs. 0/11 in controls; $p<0.05$; at 2000 ppm: 2/11) were found upon haematology, clinical chemistry, macroscopic and microscopic evaluation. Macroscopic and microscopic examination of animals sacrificed following a 12-month post-exposure period did not reveal statistically significant differences in incidences of neoplastic and non-neoplastic lesions between exposed animals and their respective control groups.

The committee takes 1636 mg/m^3 (400 ppm) (Mac80, Mac81, Mac84), a NOAEL for kidney effects in rats and a MOAEL for body weight effects, as a starting point for deriving a health-based recommended occupational exposure limit (HBROEL). For the extrapolation to a HBROEL, an overall assessment

factor of 9 is used. This factor covers the following aspects: intraspecies variation and confidence in the database. The committee considered a factor for interspecies variation not appropriate since the rat appeared the most sensitive species out of 4 species tested. Thus, applying this factor and using the preferred value system, a health-based recommended occupational exposure limit of 200 mg/m^3 (48 ppm), is recommended for methylcyclohexane.

The committee recommends a health-based occupational exposure limit (HBROEL) of 200 mg/m^3 (48 ppm) for methylcyclohexane, as an 8-hour time-weighted average (TWA).

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Annex

Occupational exposure limits for methylcyclohexane 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	400	1600	8 h	administrative		SZW05
Germany						
- AGS	200	810	8 h			TRG04
	800	3240	15 min			
- DFG MAK-Kommission	200	810	8 h		[d]	DFG05
	400	1620	15 min[c]			
Great-Britain						
- HSE	-	-				HSE02
Sweden	-	-				Swe00
Denmark	200	805	8 h	OEL		Arb02
USA						
- ACGIH	400	-	8 h	TLV		ACG05
- OSHA	500	2000	8 h	PEL		ACG04
- NIOSH	400	1600	10 h	REL		ACG04
European Union						
- SCOEL	-	-				EC05

[a] S = skin notation; which means 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] Maximum number per shift: 4, with a minimum interval between peaks of 1 hour.

[d] Listed among substances with MAK values but no pregnancy risk classification.