Gezondheidsraad **Voorzitter**
Health Council of the Netherlands

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 gezondheidskundige 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.

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Gezondheidsraad
Health Council of the Netherlands

Onderwerp : Herevaluatie uit het buitenland overgenomen grenswaarden
Ons kenmerk : U
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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

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Cyclopentane

(CAS reg. nr: 287-92-3)

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/002, The Hague, 14 December 2000

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1 Introduction

The present document contains the assessment of the health hazard of cyclopentane 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 and Chemical Abstracts, starting from 1966 and 1970, respectively, and using the following key words: cyclopentane, pentamethylene or 287-92-3. Also the CD-roms Poltox (from 1994 backwards), HSEline, Cisdoc, Mhidas and NIOSHtic (from 1997 backwards) were consulted. Data considered to be critical were evaluated by reviewing the original publications. The final literature search has been carried out in December 1997.

In March 2000, the President of the Health Council released a draft of the document for public review. The committee received no comments.

2 Identity

name	:	cyclopentane
synonyms	:	pentamethylene
molecular/structural formula	:	C_5H_{10}
CAS reg nr	:	287 - 92 - 3

3 Physical and chemical properties

molecular weight	:	70.2
boiling point	:	49^0C
melting point	:	-94^0C
vapour pressure	:	45 kPa
solubility in water	:	none
log $P_{oct/water}$	:	7 (calculated)
conversion factors (20^oC, 101.3 kPa)	:	1 ppm = 2.92 mg/m^3 1 mg/m^3 = 0.34 ppm

Data from IPC91.

Cyclopentane is a flammable colourless liquid with a mild sweet odour. The odour threshold is not known. The vapour is heavier than air and may travel along the ground, distant ignation is possible. As a result from flow, agitation, etc. electrostatic charges can be generated (IPC91).

4 Uses

Cyclopentane is used mainly as a reagent in the laboratory. It is found in petroleum ether and other commercial solvents that are used as a fuel, in fat and wax extraction, in paints and in the shoe industry.

5 Biotransformation and kinetics

Cyclopentane vapour can be absorbed into the body by inhalation (IPC91, Hat91, NIO94) and the fluid can be taken up by ingestion (NIO94). No quantitative data on the uptake is available. There is no information on the distribution, biotransformation, excretion and biological monitoring of cyclopentane.

Pan *et al*. (Pan91) determined the levels of aliphatic hydrocarbons in blood of 85 chemically sensitive patients in the Department of Allergy in the Peking Union Medical College Hospital in Beijin, China, by using a purging trap method with gas chromatography/mass spectrometry. Thirteen patients had levels below the detection limit of less than 1 ppb and 72 were above the detection limit. The average level of cyclopentane was 9.0 ppb (0.026 mg/m^3).

6 Effects and mechanism of action

Human data

There is no human data available on effects induced by exposure to cyclopentane exclusively. Most exposure incidents usually involved a mixture of hydrocarbons.

Animal data

There are very few animal data available. Brown *et al*. (Bro71) studied the influence of some alicyclic hydrocarbons on guinea pig skin. Applications were done on both flanks of each guinea pig with a volume of 2 ml per animal. After

exposure to cyclopentane the skin showed slight erythema and dry appearance by gross observation. The epidermis/dermis dry weight ratio between treated skin and control skin was 2.1. There were no changes in the activity of arginase on the skin. From this experiment the authors concluded that the effect on the skin due to cyclopentane exposure was minor relative to other alicyclic hydrocarbons with a higher number of C atoms.

Cavender (Cav94) reported that inhalation exposure to 110 mg/m^3 (38 ppm) cyclopentane vapour induced minimal narcosis, loss of reflexes and lethality in mice. He cited this data from a study from Von Oetingen from 1940 and commented on the low safety margin. On the other hand, Lazarew and Kremnewa in 1930 reported that cyclopentane vapour caused immediate anaesthesia in a concentration of 110,000 mg/m^3, and mortality due to respiratory paralysis occurred much later (Laz30). Fang *et al*. (Fan96) recently studied the anaesthetic and convulsant properties of some compounds, including cyclopentane, in rats after inhalation. They reported that cyclopentane induced excitation (twitching, jerking and hyperactivity) at the level of 0.0026 atm blood partial pressure of the test compound. The MIC (the minimum inspired concentration required to suppress movement in response to stimulation) for cyclopentane was found to be 0.058 atm, and the MAC (the minimum alveolar anaesthetic concentration) was 0.053 atm. This study showed that the effects after inhalation exposure were excitation followed by anaesthesia.

When ingested, cyclopentane presented a low to moderate aspiration hazard in mice (Ger63). It should be noted that the tendency of a substance to constitute an aspiration hazard to the lung depends primarily on its physical properties. The combination of two physical properties, low viscosity and low surface tension, increases the aspiration hazard of light hydrocarbons.

Effects on the kidneys in rats have been reported by Bernard *et al*. (Ber89). They exposed female SD rats to cyclopentane by giving the animals 5 intraperitoneal injections of 500 mg/kg bw per week for two weeks. The results showed an increase of ß$_2$-microglobulin (geom. mean of 6.67 compared to 2.69 g/24 h in the control group) and albumin concentrations (geom. mean of 556 compared to 363 g/24 h in the control group) in the urine.

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

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for cyclopentane in the Netherlands is 1720 mg/m^3 (600 ppm), 8 h TWA.

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

8 Assessment of health hazard

From the available data the committee concludes that the target organs in the toxicity of cyclopentane are the central nervous system (CNS) and the kidneys.

Different concentrations of exposure were reported in animal experiments with effects on the CNS. One study reported minimal narcosis, loss of reflexes and lethality in mice at a concentration of 110 mg/m^3 (Cav94 cited from a study in 1940), on the other hand a study from 1930 reported anaesthesia and mortality in mice occurring at a level of 110,000 mg cyclopentane per m^3 (Laz30). Intraperitoneal injections of cyclopentane in rats at a dose of 1500 mg/kg bw induced aberrations of the kidney function (Ber89). From these studies a no observed adverse effect level (NOAEL) can not be determined.

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

The committee considers the toxicological data base on cyclopentane 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

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Bro71 Brown VKH, Box VL. The influence of some alicyclic hydrocarbons on the arginase activity of guinea pig skin. Br J Dermatol 1971; 85: 432-6.

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Fan96 Fang Z, Sonner J, Laster MJ, Ionescu P, Kandel L, Koblin DD *et al*. Anesthetic and properties of aromatic compounds and cycloalkanes: implications for mechanisms of narcosis. Anest Analg 1996; 83: 1097-104.

Ger63 Gerarde HW. Toxicological studies on hydrocarbons. Arch Environ Health 1963; 6: 329-41.

Hat91 Hathaway GJ, Proctor NH, Hughes JP, Fischman ML, editors, In: Proctor and Hughes's Chemical hazards of the workplace, third edition, 1991, New York: Van Nostrand Reinhold, 1991: 202.

HSE99 Health and Safety Executive (HSE). EH40/99 Occupational Exposure Limits 1999. Sudbury (Suffolk), England: HSE Books, 1999.

IPC91 International Programme on Chemical Safety (IPCS)-European Communities. International Chemical Safety Cards. Cyclopentane. 1991: ICSC0353.

Laz30 Lazarew NW, Kremnewa SN. Bemerkungen uber die Giftigkeit der Dampfe des Zyklopentans und seiner Homologen. Arch Exp Pathol Pharmakol 1930; 149: 116-118.

NBO96 National Board of Occupational Safety and Health. Occupational exposure limit values. Solna, Sweden: NBOSH, 1996; Ordinance AFS1996/2.

NIO94 National Institute of Occupational Safety and Health (NIOSH). NIOSH Pocket Guide to Chemical Hazards 1994. US Dept Health & Human Services, Washington, 1994.

Pan91 Pan Y, Johnson AR, Rea WJ. Aliphatic hydrocarbon solvents in chemically sensitive patients. Bol Asoc Med P R. 1991; 83: 316-320 (abstract, cited from OSH CD-rom).

SZW00 Ministerie van Sociale zaken en Werkgelegenheid (SZW). Nationale MAC-lijst 2000. The Hague, the Netherlands: Servicecentrum SDU Uitgevers, 2000.

TRG00 TRGS 900: Grenzwerte in der Luft am Arbeitsplatz; Technische Regeln fur Gefahrstoffe; B Arb Bl 2000; 2..

Annex

Occupational exposure limits for cyclopentane 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	600	1720	8 h	administrative		SZW00
Germany						
-AGS	-	-				TRG00
-DFG MAK-Kom.	-	-				DFG99
Great-Britain						
-HSE	-	-				HSE99
Sweden	-	-				NBO96
Denmark	300	850	8 h			Arb96
USA						
-ACGIH	600	1720	8 h	TLV		ACG00
-OSHA	-	-	-			
-NIOSH	600	1720	10 h	REL		
European Union						
-SCOEL						

[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