

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, hexachlooraфтаleen, methaanthiol, methylcyclohexanol, methylisopropylketon, mica, natriumhydroxide, octachlooraфтаleen, silaan, tetrachlooraфтаleen, 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
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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

Dimethoxymethane

(CAS reg. nr: 109-87-5)

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/004, The Hague, 14 December 2000

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1 Introduction

The present document contains the assessment of the health hazard of dimethoxymethane (methylal) 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 Mrs MA Maclaine Pont, M.Sc. (Wageningen University, the Netherlands).

Literature was retrieved from the data bases Medline, Toxline and Chemical Abstracts, covering the periods 1966 until November 1997, 1981 until July 1997 and 1937 until November 1997, respectively, and using the following key words: dimethoxymethane, methylal or 109-87-5. Data considered to be critical were evaluated by reviewing the original publications. The final literature search has been carried out in November 1997, followed by an additional search in May 2000.

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	:	dimethoxymethane
synonyms:	:	methylal anesthenyl dimethylformal formal methylene dimethyl ether
molecular formula	:	C ₃ H ₈ O ₂
structural formula	:	H ₃ C - O - CH ₂ - O - CH ₃
CAS reg nr	:	109-87-5

Data from How92.

3 Physical and chemical properties

molecular weight	:	76.1
melting point	:	-104.8°C
boiling point:	:	42 - 43°C
flash point:	:	-18°C
explosive limits:	:	1.6 - 17.6 vol%
vapour pressure:	:	20°C: 44 kPa; 25°C: 53 kPa
solubility in water:	:	33 g/100 ml
log $P_{\text{oct/water}}$:	0
conversion factors: (20°C, 101.3 kPa)	:	1 mg/m ³ = 0.316 ppm 1 ppm = 3.16 mg/m ³

Data from Bra93, Lid99 and NIA00.

Dimethoxymethane is a colourless liquid with a typical odour. Its vapour is heavier than air, it can spread over the floor and be ignited from a distance. It reacts vigorously with oxidants (NIA00).

4 Uses

Dimethoxymethane is used as a special purposes fuel, a solvent for perfumes, adhesives and coatings and as an agent in organic syntheses (ACG92).

5 Biotransformation and kinetics

After an intravenous injection of dimethoxymethane into dogs, the compound was mainly excreted by exhalation. Approximately 87% was exhaled in 7 hours. No dimethoxymethane was found in the exhaled air after 24 hours. Assays for the possible metabolite formaldehyde in exhaled air were negative (Vir51).

On the basis of physical properties of dimethoxymethane the dermal penetration rate through human skin is calculated to be 1.24 mg/cm² per hour, when a saturated aqueous solution is applied on 2000 cm² of skin (Fis90).

6 Effects and mechanism of action

Human data

No data on human (occupational) exposure to dimethoxymethane have been found.

Animal data

The following acute toxicity data have been found (Lew00, Wea51):

- LC₅₀ inhalatory rat: 47,400 mg/m³;
- LC₅₀ inhalatory 7 hours mouse: 57,000 mg/m³;
- LD₅₀ oral rabbit: 5708 mg/kg.

Anaesthesia was induced in dogs by intravenous injection of approximately 5 ml of 25% dimethoxymethane per kg body weight. The average concentration of dimethoxymethane in blood during surgical anaesthesia was 194 mg/100 ml. This increased to 350 mg/100 ml at respiratory arrest, and returned to 194 mg/100 ml after 1 hour. In rats, a state of surgical anaesthesia was reached with a concentration of dimethoxymethane in blood at 151 mg/100 ml; respiratory arrest occurred at 347 mg/100 ml. When dimethoxymethane was given to mice by inhalation, the concentration necessary for surgical anaesthesia was 6.5% (= 65,000 ppm = 205.4 g/m³), while that for respiratory arrest was 17% (= 170,000 ppm = 537.2 g/m³) (Vir51).

Autopsy in dogs and mice who were anaesthetized with dimethoxymethane 8 or 7 times learned that the liver, heart, brain and kidneys were grossly and microscopically normal (Vir51).

At lower concentrations (88 - 122 g/m³), fatty changes in liver and kidneys and pulmonary oedema were observed in mice (Wea51).

No signs of toxicity were observed in rats after exposure to 12,640 mg/m³, 6 hours/day, 5 days/week for two weeks. Upon autopsy the appearance of the organs was normal (Gag70).

Mutagenicity and genotoxicity

Dimethoxymethane did not induce mutations in:

- the Ames assay, using *Salmonella typhimurium* strains TA1535, TA1537 and TA1538, with and without rat liver metabolic activation (EPA89).

Dimethoxymethane induced mutations in:

- the Ames assay, using *Salmonella typhimurium* strains TA98 and TA100, without metabolic activation (EPA89).

Carcinogenicity

No data have been found on carcinogenicity of dimethoxymethane.

Reproduction toxicity

No data have been found on reproduction toxicity of dimethoxymethane.

7 Existing guidelines

The current administrative exposure occupational limit (MAC) for dimethoxymethane in the Netherlands is 3100 mg/m³ (1000 ppm), 8 h TWA.

Existing occupational exposure limits for dimethoxymethane 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 dimethoxymethane.

In animals, high concentrations induced anaesthesia, both by inhalation and by intravenous injection (Vir51, Gag70). At lower concentrations (88-122 g/m³) toxic effects were observed in liver, kidneys and lungs of exposed mice (Wea51).

After intravenous injection the compound is mainly excreted unchanged by exhalation. In dogs, approximately 87% was exhaled in 7 hours (Vir51).

Due to the limited data available the committee cannot indicate a target organ or critical effect for toxicity of dimethoxymethane.

The committee considers the toxicological data base on dimethoxymethane too poor to recommend a health-based occupational exposure limit.

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

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Annex

Occupational exposure standards for dimethoxymethane 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	1000	3100	8 h	administrative		SZW00
Germany -AGS	1000	3100	8 h	administrative		TRG00
-DFG MAK-Kom.	1000	3200	8 h	MAK		DFG99
Great Britain -HSE	1000 1250	3160 3950	8 h 15 min	OES STEL		HSE99
Sweden	-	-				NBO96
Denmark	1000	3 100	8 h			Arb96
USA -ACGIH	1000	3110	8 h	TLV		ACG00
-OSHA	1000	3100	8 h	PEL		
-NIOSH	1000	3100	10 h	REL		
European Union -SCOEL	-	-				Hun97

^a S = skin notation; which means that skin absorption may contribute considerably to the body burden; sens = substance can cause sensitization

^b reference to the most recent official publication of occupational exposure limits

