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.

Bezoekadres
Parnassusplein 5
2511 VX Den Haag
Telefoon (070) 340 75 20
email: GR@gr.nl

Postadres
Postbus 16052
2500 BB Den Haag
Telefax (070) 340 75 23

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

Bezoekadres
Parnassusplein 5
2511 VX Den Haag
Telefoon (070) 340 75 20
email: GR@gr.nl

Postadres
Postbus 16052
2500 BB Den Haag
Telefax (070) 340 75 23

Methanethiol

(CAS reg. nr 74-93-1)

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/008, The Hague, 14 December 2000

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1 Introduction

The present document contains the assessment of the health hazard of methanethiol 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 February 1998, 1981 until October 1997 and 1937 until December 1997, respectively, and using the following key words: methanethiol (and isotopic compounds), methyl mercaptan or 74-93-1. Data considered to be critical were evaluated by reviewing the original publications. The final literature search has been carried out in February 1998, followed by an additional search in May 1999.

In December 1998, 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	:	methanethiol
synonyms	:	mercaptomethane methylmercaptan methyl mercaptan methyl sulfhydrate thiomethanol thiomethyl alcohol
CAS reg nr	:	74-93-1
molecular formula	:	CH_3SH

Data from ACG91, How92.

3 Physical and chemical properties

molecular weight	:	48.11
melting point	:	-123°C
boiling point	:	5.9°C
vapour pressure	:	20°C: > 1 kPa
odour threshold	:	0.0032 mg/m^3 0.00004 - 0.082 mg/m^3
flash point (open cup)	:	-17.8 °C
explosive limits	:	3.9 - 21.8 vol% in air
solubility in water	:	20°C: 23.3 g/l
log $P_{oct/water}$	:	not found
conversion factors (20 °C, 101.3 kPa)	:	1 mg/m^3 = 0.50 ppm 1 ppm = 2.00 mg/m^3

Data from Amo83, Lid96, Rut86.

Methanethiol is a colourless gas with a very disagreeable odour, described as that of rotten cabbage. The gas is heavier than air and spreads over the floor with a chance of ignition from a distance. Combustion of the product results in toxic gases. It reacts vigorously with oxidants, with a chance of fire and explosion. It reacts with acids, forming toxic and flammable gas (hydrogen sulphide). It reacts with light metals (NIA98).

4 Uses

Methanethiol is used to give odour to natural gas and in the synthesis of methionine. It is also employed as an intermediate in the production of pesticides, fungicides, jet fuel, and plastics. In addition, it may be encountered as a by-product in the operations of paper and pulp mills (ACG86, ACG91).

5 Biotransformation and kinetics

Metabolic studies have been performed with radiolabeled methanethiol intraperitoneally injected in the rat. Both the carbon (^{14}C) and the sulphur (^{35}S) of the methanethiol were rapidly oxidized to carbon dioxide and sulphate, respectively. In the first hour after the injection 29.2% of the dose was exhaled

as CO_2. In the first eight hours after the injection 32% of the dose was found in the urine as sulphur compounds. Further the methyl moiety was incorporated in the methyl groups of methionine, choline and creatine. The sulphur moiety was not incorporated in methionine or cysteine (Can53).

Other investigators established the half-life time for the metabolism of methanethiol into sulphate. After a single intra peritoneal injection into rats the $t_{½}$ was 1.21 hour. The $t_{½}$ for the elimination of sulphate in the urine was 8.47 hour (Der84).

Methanethiol could be detected in exhaled air (0.04 to 0.10 mg/m^3) of persons exposed to high concentrations of methanethiol (concentration is not reported; probably more than 20 mg/m^3). After exposure to lower concentrations of a combination of methanethiol, hydrogen sulphide and dimethylsulphide, dimethylsulphide is detected in exhaled air. After exposure to 11.3 ppm sulphides the concentration of dimethylsulphide in exhaled air was 0.62 ppm. The authors suggest that the method can be used to assess recent exposure to a mixture of sulphide compounds (Jäp93).

6 Effects and mechanism of action

Human data

Low level symptoms of exposure to methanethiol are eye and mucous membrane irritation, dizziness, staggering gait, nausea, and vomiting. Respiratory tract irritation may lead to pulmonary oedema and hepatic and renal damage (ACG91).

Workers (n=29) in the digest area of a pulpmill, where woodchips are 'digested' into carbohydrates, had a higher incidence of chest illness than a control group of 310 railroad workers (missed work at least 1 week during the past three years, 36.3% vs. 14.8% in the control group, $p < 0.05$). The exposure was mainly to methanethiol, with a maximum concentration of 15.0 ppm (30 mg/m^3) and a mean of 1.4 ppm (2.8 mg/m^3), calculated as an 8 h time weighted average (TWA). Lower concentrations of SO_2 were present (mean 0.5 ppm) in less sites than methanethiol. The measuring time is not given. Spirometric values of these workers were not different from those of the control group, nor after correction for smoking (Ena84). However, the committee considers that the parameter studied (absenteeism because of alleged disease) did not really reflect chest illness, further chest illness was not well defined, and thirdly, the effects cannot be unequivocally ascribed to methanethiol.

Another group of workers (n=17) in a pulpmill was exposed to a mixture of methanethiol (0.07 - 2.0 ppm, 0.14 - 4.0 mg/m^3), hydrogen sulphide (0.05 - 5.2 ppm), and dimethylsulphide (0.03 - 3.2 ppm, calculated as a 8 h TWA). There are no further data as to how the measurements were performed. The number of complaints (subjective symptoms) among the workers was comparable to that of a control group (n=50). However, the average annual number of days on sick leave of the workers tended to be higher (12.9 against 7.1 days, no statistical calculation). The activity of delta-aminolaevulinic acid synthase and haem synthase in blood was decreased in 8 and 6 cases, respectively (in the table the investigators presented only 5 cases instead of 6, who are below the range of the control values). No statistical calculation was performed (Ten83). Since the workers were exposed to a mixture of compounds, the committee concludes that the effects found cannot be ascribed to methanethiol alone.

A 53-year old Negro labourer was hospitalized because of coma appearing shortly after exposure to methanethiol. There are no data on the exposure concentration and duration. Acute, severe haemolytic anaemia and methaemoglobinaemia developed: both were brief in duration. The likely mechanism of the haemolysis was an oxidant effect of methanethiol in a person deficient in erythrocyte glucose-6-phosphate dehydrogenase. Deep coma persisted until death 28 days after exposure to the chemical agents. The immediate cause of death was pulmonary embolism (Shu70).

Inhabitants of areas in the neighbourhood of paper mills were studied for respiratory and other symptoms. The highly polluted areas had concentrations of 2 - 5 µg/m^3 methanethiol as an annual mean; the highest daily average concentration was 50 µg/m^3. The concentrations were estimated from a computer simulation model, no measurement data were reported. The residents were also exposed to hydrogen sulphide (respectively 8 and 100 µg/m^3) and to low concentrations of sulphur dioxide. The complaints of the residents from severely polluted areas were compared with those from moderately polluted and nonpolluted areas. The Odds Ratio for eye and nasal symptoms and for cough during the previous 12 months were significantly increased in the severely polluted areas, compared with the control group. For these symptoms and for breathlessness or wheezing and for headache, there was a dose-related increase in Odds Ratio for having experienced symptoms often or constantly. Only for eye symptoms in residents from moderately polluted areas the increase was statstically significant (Jaa90). It can be concluded that adverse health effects occur after exposure to malodorous sulphur compounds at levels considerably lower than reported previously by other authors, and also at levels lower than

the current Dutch MAC values (for methanethiol 1 mg/m^3, for hydrogen sulphide 15 mg/m^3). The observed exposure to hydrogen sulphide was considerably lower than the current WHO standard (150 µg/m^3 for 24 h mean). However, the committee considers it questionable to ascribe the effects to methanethiol, because it is not the only compound to which the inhabitants were exposed.

Animal data

The acute toxicity of methanethiol in animals after short-term exposure is moderate: the LC_{50} for rats is 1350 mg/m^3, for mice the LC_{50} is 6.53 mg/m^3 (Lew92).*

Observations from one rat, exposed to 20,000 mg/m^3 methanethiol, indicate that it affected the respiration, and stopped it altogether after 14 min of exposure. Autopsy revealed small bleedings in the lungs and alveoli filled with erythrocytes (Lju43).

Groups of 31 male Sprague Dawley rats were exposed to 0, 2, 17 and 57 ppm (4, 34, and 114 mg/m^3), for 7 hours/day, 5 days/week for 3 months. After three months there was a concentration-related decrease of the body weight, which was significant in the high-dose group. No effects were observed in organ weights and clinical chemistry parameters (Tan81). It can be concluded that the NOAEL for subchronic exposure in rats is 34 mg/m^3. However, the nose was not examined for possible local effects.

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 methanethiol in the Netherlands is 0.5 ppm (1 mg/m^3), 8 h TWA.

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

* There must be an error in one of these data, then it is not expected that there is a 200-fold species difference between rats and mice.

8 Assessment of health hazard

At high concentrations methanethiol affects respiration both in humans and animals, leading ultimately to death (Shu70, Lju43). At lower concentrations respiratory irritation is observed, together with eye and skin irritation (ACG91). Local irritation of the respiratory tract seems to be the critical effect. However, the human studies available describe effects after exposure to a mixture of compounds, and the animal study did not include the local effects. The no observed adverse effect level (NOAEL) found in the subchronic animal study was 34 mg/m^3 and concerned a decrease in body weight (Tan81).

It is expected that after inhalation of methanethiol the compound is totally resorbed and to a large extent metabolized. A small fraction is exhaled unchanged (Jäp93).

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

The committee considers the toxicological data base on methanethiol too poor to justify recommendation of a health-based occupational exposure limit.

Regarding the available animal data the committee has no reason to suspect that the current MAC value of 1 mg/m^3 (0.5 ppm), 8 hour time weighted average (TWA) is too high. This concentration is also well above the reported odour thresholds.

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Annex

Occupational exposure standards for methanethiol 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	0.5	1	8 h	administrative		SZW00
Germany						
-AGS	0.5	1	8 h	administrative		TRG00
-DFG MAK-Kom.	0.5	1	8 h	MAK		DFG99
Great-Britain						
-HSE	0.5	1	8 h	OES		HSE99
Sweden	1[c]		8 h	level limit value		NBO96
Denmark	0.5	1	8 h			Arb96
USA						
-ACGIH	0.5	0.98	8 h	TLV		ACG00
-OSHA	10	20	-	ceiling		
-NIOSH	0.5	1	15 min	ceiling; STEL		
European Union						
-SCOEL	-	-				Hun97

[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] the limit value 1 ppm applies to the sum total of concentrations of dimethyl disulfide, dimethyl sulfide and methyl mercaptan