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
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

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Silane

(CAS Reg. nr: 7803-62-5)

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/014, The Hague, 14 December 2000

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1 Introduction

The present document contains the assessment of the health hazard of silane 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 S Bosman-Hoefakker, Ph.D. and H Stouten, M.Sc. (TNO Nutrition and Food Research Institute, Zeist, the Netherlands).

The evaluation of the toxicity of silane has been based on the review by the American Conference of Governmental Industrial Hygienists (ACG91). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, literature was retrieved from the online data bases Medline, Toxline, and Chemical Abstracts covering the period 1966 to 2 June 1997 (19970602/UP), 1965 to 21 March 1997 (970321/ED), and 1967 to 29 April 1997 (970429/ED; vol 126, iss 18), respectively. Medline was searched with the CAS Registry Number 7803-62-5 and the names monosilane, SiH4, silicon hydride, silicon tetrahydride, silanes/CT(L)(AE OR PO OR TO)/CT, silanes/CT(L)(ME OR PK)/CT, and silanes/CT(L)(PD/CT AND (CI OR DE)/CT, Toxline with the CAS Registry Number 7803-62-5, and Chemical Abstracts with 7803-62-5 in the Sections “Toxicology” and “Air Pollution and Industrial Hygiene”. HSDB and RTECS, data bases available from CD-ROM, were consulted as well (NIO97, NLM97). The final literature search has been carried out in June 1997.

In February 1999, the President of the Health Council released a draft of the document for public review. The committee received no comments.

2 Identity

name	:	silane
synonyms	:	monosilane silicane silicon hydride silicon tetrahydride
molecular formula	:	SiH_4
CAS reg nr	:	7803-62-5

Data from ACG91a, NLM97.

3 Physical and chemical properties

molecular weight	:	32.12
boiling point	:	-111.5°C
melting poin	:	-185°C
flash point	:	extremely flammable; may ignite spontaneously in air
vapour pressure	:	-
solubility	:	decomposes slowly in water decomposes in potassium hydroxide solutions practically insoluble in alcohol, ether, benzene, chloroform, silicochloroform and silicon tetrachloride
log $P_{oct/water}$	:	-
conversion factors (20°C, 101.3 kPa)	:	1 ppm = 1.3 mg/m^3 1 mg/m^3 = 0.75 ppm

Data from ACG91a, NLM97.

Silane is a colourless gas with a repulsive odour. At temperatures above 400°C, it decomposes into silicon and hydrogen.

4 Uses

Silane finds use in the doping of solid-state devices and as a source of hyperpure silicon for semiconductors (ACG91a).

5 Biotransformation and kinetics

No data on the biotransformation and kinetics of silane were found.

6 Effects and mechanism of action

Human data

The concentration of silane causing toxic effects in humans has not been determined. It will be mildly toxic by inhalation and silanes are irritating to the skin, eyes, and mucous membranes (ACG91a). It was stated that its vapours may cause dizziness and suffocation (NLM97).

Animal data

In rats, the 4-hour LC_{50} is 9600 ppm (approximately 13,345 mg/m^3). No effects were seen in rats exposed up to 126 ppm (approx. 175 mg/m^3) for 1 hour. In mice, 4 out of 10 animals died following exposure to 9600 ppm (approx. 13,345 mg/m^3) for 4 hours (ACG91a).

When male ICR mice were exposed to 2500, 5000, 7500, or 10,000 ppm (approx. 3475, 6950, 10,425, 13,900 mg/m^3) for 30 minutes, 1 hour, or 4 hours*, only in the animals exposed to 10,000 ppm for 4 hours, mortality (i.e., 9/12; all within 24 h) was observed. At autopsy of these animals, increased relative kidney weights, renal tubular necrosis, splenic atrophy, appearance of macrophages with debris of degenerated cells in bone marrow and thymus, and inflammatory changes of the nasal mucosa was seen. In the groups exposed for 30 minutes or 1 hour and sacrificed at week 2, mainly effects on the kidneys were found (tubular interstitial nephrosis in 6/8 and 7/8 animals, respectively). Following exposure to 7500 ppm (only 30-min exposure), tubular nephrosis was seen in 4/8 animals. The 1- and 4-hour exposures to 5000 ppm caused tubular interstitial nephritis in 1/8 and 2/8 animals sacrificed at week 2, respectively, and acute renal tubular necrosis in 0/4 and 1/4 animals sacrificed after 2 days, respectively. Concerning the 2500 ppm groups, the only effect observed was acute renal tubular necrosis in 1/4 animals exposed for 4 hours (Tak93).

In a separate (earlier conducted) study, male ICR mice (n=10/group) were exposed to approximately 1000 ppm (approx. 1390 mg/m^3) of silane for 1 hour or 2, 4, or 8 hours. After sacrifice 3 days postexposure, the organs were examined grossly, and histoogically (all exposed and non-exposed mice: nasal cavity, lung, liver, kidney, spleen, thymus, bone marrow, and testis; some of the mice: cornea, trachea, thyroid, salivary glands, and oesophagus). Biochemical and haematological parameters examined included alkaline phosphatase, aspartate and alanine aminotransferase, cholinesterase, blood urea nitrogen, sodium, potassium, red blood cell count, and total and differential white blood cell counts. Neither mortality nor exposure-related changes in any of the organs were observed. Biochemical or haematological parameters affected included an increase in red blood cell counts in mice exposed for 8 hours, an increase in blood urea nitrogen in mice exposed for 1 hour and a

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* Number of animals exposed: 8 per concentration when exposed for 30 min, all sacrificed 2 weeks postexposure; 12 per concentration when exposed for 1 or 4 h, 4 sacrificed 2 days and 8 animals 2 weeks postexposure.

decrease in the 8-hour exposure group, and a decreased white blood cell count after 1-hour exposure (Oma92).

The latter mentioned study included a subacute experiment in which mice (n=10/group) were exposed to 6 hours/day, 5 day/week 1000 ppm (approx. 1390 mg/m^3), for 2 or 4 weeks (parameters examined: see above; time of sacrifice: on the day after the final exposure). These treatments did not induce mortality, nor exposure-related haematological, biochemical, or histological changes in the mice exposed for 2 weeks. In mice exposed for 4 weeks, mild irritation, manifested in the form of a small amount of exudate (in 8/10 animals), and inflammatory cells and/or necrotic cells of the nasal mucosa (in 6/10) was observed. As to haematology/biochemical parameters, there was a statistically significant increase in white blood cell counts (lymphocytes and neutrophils) only (Oma92).

Mutagenicity and genotoxicity

Mutagenicity tests with silane showed positive results in the *S. typhimurium* strains TA98, TA100, TA1535, and TA1537, and in *E. Coli* WP2 *uvrA* when tested with and without metabolic activation (Ara94).

No data on carcinogenicity or reproduction toxicity of silane have been found.

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for silane in the Netherlands is 0.7 mg/m^3 (5 ppm), 8 h TWA.

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

8 Assessment of health hazard

The toxicological data base of silane is poor. No human data were available. Animal data were limited to acute mortality studies in rats and mice, one acute study in mice, and one (sub)acute study in mice with only one exposure level.

From mortality data in rats and mice (4-h LC_{50}s of 9600 and between 5000 and 10,000 ppm, respectively), it can be seen that silane is not toxic, i.e. no classification or labelling is warranted. Acute inhalation experiments in mice with relatively high exposure concentrations have shown that the target organ

is the kidney. Exposure to silane causes acute renal tubular necrosis and tubular interstitial nephritis. No observed effect levels (NOEL) of 2500 and 5000 ppm (approx. 3475, 6950 mg/m^3) can be established for 1-hour and 30-minutes exposures, respectively. After exposure for 4 hours to 2500 ppm (approx. 3475 mg/m^3), the lowest level tested, acute renal tubular necrosis was found in one out of four animals. No effects on histological, biochemical, and haematological parameters were seen in mice exposed to 1000 ppm (approx. 1390 mg/m^3) for up to 8 hours.

In a well conducted, subacute inhalation experiment in mice, the target organ was the nasal cavity. Exposure to 1000 ppm (approx. 1390 mg/m^3), the only level tested, for 4 weeks (6 hours/day, 5 days/week), resulted in inflammation of the nasal cavity as indicated by histological and haematological changes; these effects were not observed in mice exposed for 2 weeks. These treatment regimes did not cause other histological, biochemical, or haematological changes.

Silane was mutagenic in *in vitro* bacterial test systems. No other tests were available. Considering the positive results, the committee recommends to have more mutagenicity testing.

The current occupational exposure limit of silicon tetrahydride has been based on the acute toxicity of germanium tetrahydride (which was based on comparisons with antimony hydride and arsenic hydride), viz, haemolyse in guinea pigs following 1-hour exposure (ACG91a, ACG91b). However, no such effects were found in mice singly or repeatedly exposed to silane vapours which makes the use of and comparison with the toxicity data of germanium tetrahydride questionable.

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

The committee concludes that the (sub)acute animal data indicate that the present MAC-value of 0.7 mg/m^3 (5 ppm), as an 8 h time weighted average (TWA), may be too low.

References

ACG91a American Conference of Governmental Industrial Hygienists (ACGIH). Silicon tetrahydride. In: Documentation of the threshold limit values and biological exposure indices. 6th ed. Cincinnati OH, USA: ACGIH, 1991; 1394-5.

ACG91b American Conference of Governmental Industrial Hygienists (ACGIH). Germanium tetrahydride In: Documentation of the threshold limit values and biological exposure indices. 6th ed. Cincinnati OH, USA: ACGIH, 1991; 702.

ACG00 American Conference of Governmental Industrial Hygienists (ACGIH). 2000 TLVs® and BEIs®. Threshold Limit Values for chemical substances and physical agents. Biological Exposure Indices. Cincinnati OH, USA: ACGIH, 2000.

Ara94 Araki A, Noguchi T, Kato F, *et al*. Improved method for mutagenicity testing of gaseous compounds by using a gas sampling bag. Mutat Res 1994; 307: 335-44.

Arb96 Arbejdstilsynet. Exposure limit values for substances and materials. Copenhagen, Denmark: The Working Environment Service; Instruction no. 3.1.0.2. 1996.

DFG99 Deutsche Forschungsgemeinschaft (DFG): Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe. MAK- und BAT-Werte-Liste 1999. Maximale Arbeitsplatzkonzentrationen und biologische Arbeitsstofftoleranzwerte. Weinheim, FRG: VCH Verlagsgesellschaft mbH, 1999; Mitteilung 35.

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

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

NIO97 National Institute of Occupational Safety and Health (NIOSH). Registry of Toxic Effects of Chemical Substances (RTECS) [CD-ROM], issue April 1997. SilverPlatter International, 1997 (last update silane file: January 1997).

NLM97 US National Library of Medicine (NLM). Hazardous Substances Data Bank (HSDB) [CD-ROM], issue April 1997. SilverPlatter International, 1997 (last update silane file: February 1997).

Oma92 Omae K, Sakai T, Sakurai H, *et al*. Acute and subacute inhalation toxicity of silane 1000 ppm in mice. Arch Toxicol 1992; 66: 750-3.

SZW00 Ministerie van Sociale Zaken en Werkgelegenheid (SZW). De nationale MAC-lijst 2000. The Hague, The Netherlands: Servicecentrum Sdu Uitgevers, 2000.

Tak93 Takebayashi T. Acute inhalation of high concentrations of silane in male ICR mice. Arch Toxicol 1993; 67: 55-60.

TRG00 TRGS 900. [Grenzwerte in der Luft am Arbeitsplatz; Technische Regeln für Gefahrstoffe]. German. B A rb Bl. 2000; 2.

Annex

Occupational exposure standards for silane 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	0.7	8 h	administrative		SZW00
Germany						
-AGS	-	-				TRG00
-DFG MAK-Kom.	-	-				DFG99
Great-Britain						
-HSE	0.5	0.7	8 h	OES		HSE99
	1	1.5	15 min	STEL		
Sweden	-	-				NBO96
Denmark	0.5	0.7	8 h			Arb96
USA						
-ACGIH	5	6.6	8 h	TLV		ACG00
-OSHA	5		8 h	PEL		
-NIOSH	5	7	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