Chlorotrimethylsilane

Health-based recommended occupational exposure limit

Gezondheidsraad **Voorzitter**
Health Council of the Netherlands

Aan de Staatssecretaris van Sociale Zaken en Werkgelegenheid

Onderwerp : Aanbieding adviezen over Chloortrimethylsilaan en Butylacetaten
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Mijnheer de Staatssecretaris,

Bij brief van 3 december 1993, nr. DGV/BMO-U-932542, verzocht de Staatssecretaris van Welzijn, Volksgezondheid en Cultuur namens de Minister van Sociale Zaken en Werkgelegenheid om gezondheidskundige advieswaarden af te leiden ten behoeve van de bescherming van beroepsmatig aan stoffen blootgestelde personen.

Per 1 januari 1994 heeft mijn voorganger daartoe een commissie ingesteld die de werkzaamheden voortzet van de Werkgroep van Deskundigen (WGD). De WGD was een door de genoemde Minister ingestelde adviescommissie.

Hierbij bied ik u - gehoord de Beraadsgroep Gezondheid en Omgeving - twee publicaties aan van de commissie over chloortrimethylsilaan en butylacetaten.
Deze publicaties heb ik heden ter kennisname aan de Minister van Volksgezondheid, Welzijn en Sport en aan de Minister van Volkshuisvesting, Ruimtelijke Ordening en Milieubeheer gestuurd.

Hoogachtend,
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Health-based recommended occupational exposure limit

report of the Dutch Expert Committee on Occupational Standards,
a committee of the Health Council of The Netherlands

to

the Minister and State Secretary of Social Affairs and Employment

No. 2001/05OSH, The Hague, 15 November 2001

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is "to advise the government and Parliament on the current level of knowledge with respect to public health issues..." (Section 21, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport, Housing, Spatial Planning & the Environment, Social Affairs & Employment, and Agriculture, Nature Preservation & Fisheries. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

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Samenvatting en advieswaarde

1 Vraagstelling

Op verzoek van de Minister van Sociale Zaken en Werkgelegenheid leidt de Commissie WGD van de Gezondheidsraad gezondheidskundige advieswaarden af voor beroepsmatige blootstelling aan toxische stoffen in de lucht. Die afleiding is de eerste fase van een drietrapsprocedure die moet leiden tot wettelijke grenswaarden. Dit rapport is tot stand gekomen in samenwerking met de 'Nordic Expert Group', die de regeringen van de scandinavische landen en IJsland van advies dient.

In het voorliggende rapport bespreekt de commissie de gevolgen van blootstelling aan chloortrimethylsilaan in de lucht op de werkplek. De conclusies van de commissie zijn gebaseerd op wetenschappelijke publicaties die vóór maart 1998 zijn verschenen.

2 Vóórkomen; fysische en chemische eigenschappen

Chloortrimethylsilaan is een kleurloze vloeistof met een stekende, zoutzuur-achtige geur. De damp is zwaarder dan lucht en verspreidt zich over de grond. Bij verwarming of ontbranding ontleedt de stof, waarbij corrosieve en giftige dampen ontstaan. Het reageert heftig met water tot zoutzuur. Vorming van zoutzuur vindt ook plaats, indien de stof in aanraking komt met vochtige oppervlakken.

Chloortrimethylsilaan wordt gebruikt voor het vervaardigen van vloeibare siliconen, als silylerend agens en bij de produktie van propyleenoxide.

Vanwege de hoge reactiviteit wordt chloortrimethylsilaan gemaakt en gebruikt in gesloten systemen.

3 Monitoring

Er zijn geen methoden gevonden waarin de bemonstering en analyse van chloortrimethylsilaan in lucht of biologische media worden beschreven.

4 Huidige grenswaarden

Er is geen grenswaarde voor chloortrimethylsilaan vastgesteld of aanbevolen in Nederland, Duitsland,de Scandinavische landen, IJsland, Finland, het Verenigd Koninkrijk en de VS.

5 Kinetiek

De commissie heeft geen gegevens gevonden over de toxicokinetiek van chloortrimethylsilaan.

6 Effecten

De commissie heeft geen gedocumenteerde gegevens gevonden over toxische effecten van blootstelling aan chloortrimethylsilaan bij mensen. In het algemeen wordt gesteld, dat dampvormig en vloeibaar chloortrimethylsilaan ernstig irriterend is voor de ogen, de huid en de slijmvliezen. Orale opname kan ernstige verbranding van de mond en de maag veroorzaken.

In dierproeven was chloortrimethylsilaan corrosief voor ogen en huid. In acute inhalatieproeven bleek chloortrimethylsilaan zeer toxisch bij muizen maar niet bij ratten.

Chloortrimethylsilaan was niet mutageen in testen met bacteriën en gist. Het veroorzaakte geen genmutaties, zusterchromatidenuitwisselingen en DNA-schade in testen met zoogdiercellen (lymfomacellen van de muis), maar gaf wel een zwakke toename in chromosoomafwijkingen in dezelfde cellen. De stof induceerde geen chromosoomafwijkingen in het beenmerg van ratten na een eenmalige intraperitoneale injectie van doses tot 74 mg/kg lichaamsgewicht. Hexamethyldisiloxane, het hydrolyseproduct van chloortrimethylsilaan liet hetzelfde beeld zien in deze testen (hoogste doses *in vivo* beenmergtest: 1030 mg/kg lichaamsgewicht). Zoutzuur, het andere hydrolyseproduct dat ook was meegenomen in alle hierboven genoemde *in vitro* testen, scoorde in al deze testen negatief (*in vivo* niet onderzocht).

Er zijn geen gegevens uit dierproeven waarin de toxiciteit (met inbegrip van reproductietoxiciteit en carcinogeniteit) van chloortrimethylsilaan na herhaalde toediening is onderzocht. In een diermodel voor de inductie van longtumoren met de daarvoor zeer gevoelige A/He muizen, veroorzaakte chloortrimethylsilaan een toename van de incidentie en multipliciteit van longtumoren. De interpretatie van dit gegeven wordt bemoeilijkt door het feit dat de relevantie van dit model niet duidelijk is, en door het feit dat genoemde toename slechts plaats vond bij de “maximum tolerated dose” (MTD).

7 Evaluatie

Chloortrimethylsilaan is een zeer irriterende stof, waarschijnlijk als gevolg van de zeer snelle hydrolyse tot zoutzuur. De commissie heeft geen studies gevonden naar de effecten van herhaalde blootstelling (inbegrepen carcinogeniteit en effecten op de reproductie). Op basis van de gegevens over genotoxiciteit is de commissie van mening, dat chloortrimethylsilaan geen genotoxische eigenschappen heeft.

8 Gezondheidskundige advieswaarde

De Commissie WGD van de Gezondheidsraad concludeert, dat de beschikbare toxicologische gegevens over chloortrimethylsilaan onvoldoende zijn voor het vaststellen van een gezondheidskundige advieswaarde.

Executive summary

Health Council of the Netherlands: Dutch Expert Committee on Occupational Standards. Chlorotrimethylsilane; Health-based recommended occupational exposure limit. The Hague: Health Council of the Netherlands, 2001; publication no. 2001/05OSH

1 Scope

At the request of the Minister of Social Affairs and Employment, the Health Council of the Netherlands recommends health-based occupational exposure limits for the concentration of toxic substances in air at the workplace. These recommendations are made by the Council's Dutch Expert Committee on Occupational Standards. They constitute the first step in a three-step procedure that leads to legally-binding limit values. The present report on chlorotrimethylsilane was prepared in co-operation with the Nordic Expert Group, wich advises the Nordic Governments.

The joint report, the committee discusses the consequences of occupational exposure to chlorotrimethylsilane and, if appropriate, recommends a health-based occupational exposure limit. The committee's conclusions are based on scientific publications prior to March 1998.

2 Occurrence, physical and chemical properties

Chlorotrimethylsilane is a colourless liquid with a sharp hydrogen chloride-like odour. Its vapour is heavier than air, travels along surfaces. At elevated temperatures or combustion, it decomposes producing corrosive and toxic vapours. It violently reacts with water producing hydrogen chloride. Also upon contact with surface moisture, it releases hydrogen chloride.

Chlorotrimethylsilane is used as an intermediate for silicone fluids, as a silylating agent, and as a component of a catalyst for propylene oxide production.

Because of the high reactivity, chlorotrimethylsilane must be manufactured, stored, and used in airtight, highly specialized installations.

3 Monitoring

No methods for monitoring chlorotrimethylsilane in air or biological samples were found.

4 Current limit values

No occupational exposure limits/standards for chlorotrimethylsilane are established or recommended in The Netherlands, Germany, the Nordic countries, the UK, and the USA (ACGIH).

5 Kinetics

There were no data available on the toxicokinetics of chlorotrimethylsilane.

6 Effects

No toxicological data in humans were found in the literature. Severe irritation of skin, eyes (from exposure to the liquid), and mucous membranes (by vapours), and severe burns of mouth and stomach following ingestion were mentioned.

In animals, chlorotrimethylsilane caused severe corrosion (burns and blisters) of eyes (cornea, eyelids) and skin. It was highly toxic in mice but not in rats upon single inhalation exposure.

Chlorotrimethylsilane had no genotoxic properties in bacteria and yeast *in vitro*. In mouse lymphoma cells, it did not cause gene mutations, SCEs, or DNA damage, but showed some weak potential for inducing chromosome aberrations. An *in vivo* chromosome aberration test in bone marrow of rats was negative at single ip doses up to 74 mg/kg bw. Hexamethyldisiloxane, a hydrolysis product of chlorotrimethylsilane, showed similar results in these tests (highest ip dose tested in rat bone marrow assay: 1030 mg/kg bw). Hydrogen chloride, the other hydrolysis product and included in the *in vitro* tests as well, was negative in all these tests.

There are no data from repeated dose toxicity studies (including reproduction toxicity and carcinogenicity). In a very sensitive model of unclear significance (i.e., lung tumour response in A/He mice), chlorotrimethylsilane increased both the incidence and the multiplicity of lung tumours, but at the maximum tolerated dose only.

7 Hazard assessment

Chlorotrimethylsilane is a very irritative compound, probably due to its very fast hydrolysis to hydrogen chloride. There is no information from repeated dose (including reproduction toxicity and carcinogenicity) studies. Based on the genotoxicity data, the committee does not consider chlorotrimethysilane to be genotoxic.

8 Recommended occupational exposure limit

The Dutch Expert Committee on Occupational Standards considers the toxicological data base too poor to justify the recommendation of a health-based occupational exposure limit for chlorotrimethylsilane.

Chapter 1

Scope

1.1 Background

In the Netherlands, occupational exposure limits for chemical substances are set using a three-step procedure. In the first step, a scientific evaluation of the data on the toxicity of the substance is made by the Dutch Expert Committee on Occupational Standards (DECOS), a committee of the Health Council of the Netherlands, on request of the Minister of Social Affairs and Employment (Annex A). This evaluation should lead to a health-based recommended exposure limit for the concentration of the substance in air. Such an exposure limit cannot be derived, if sufficient data are not available or if the toxic action cannot be evaluated using a threshold model. In the latter case, an exposure-response relationship is recommended for use in regulatory standard setting.

In the next phase of the three-step procedure, the Social and Economic Council advises the Minister on feasibility of using the health based value as a regulatory Occupational Exposure Limit (OEL), or recommends a different OEL. In the final step of the procedure, the Minister of Social Affairs and Employment sets the official Occupational Exposure Limit.

1.2 Committee and method of work

This document is a co-production of DECOS and the Nordic Expert Group for Documentation of Occupational Exposure Limits (NEG). It is a result of an agreement between both groups to prepare jointly criteria documents which can be used by the

regulatory authorities in the Netherlands and in the Nordic countries. The draft document has been prepared by H. Stouten, A.A.J.J.L. Rutten, I.A. van de Gevel, and F. de Vrijer from the Toxicology Division of the TNO Nutrition and Food Research Institute, Zeist, The Netherlands, and was first reviewed by DECOS and thereafter by NEG.

In 1999 the DECOS released a draft of the report for public review. The individuals and organisations that commented on the draft are listed in Annex C. The DECOS has taken these comments into account in deciding on the final version of the report.

1.3 Data

This document deals with a critical review of the chemistry, use, and toxicology of chlorotrimethylsilane. Furthermore, it contains an occupational health risk assessment of chlorotrimethylsilane.

For the preparation of this document, literature has been retrieved from several data bases using online and CD-ROM systems (last update: May 1998).

Chapter 2

Identity, properties, and monitoring

2.1 Identity

2.1.1 Structure

2.1.2 *Chemical names and synonyms/registry numbers*

Chemical name	:	chlorotrimethylsilane
CAS registry no	:	75-77-4
Synonyms	:	trimethylchlorosilane; monochlorotrimethylsilicone; silane, chlorotrimethyl-; silane, trimethylchloro-; silicane, chlorotrimethyl; silylium, trimethyl-; trimethylsilyl chloride
EINECS no	:	200-900-5
RTECS no	:	VV2710000

2.2 Physical and chemical properties (EPA85, Stu96, EC96)

Molecular formula	:	C_3H_9SCl
Molecular weight	:	108.66
Boiling point (101.3 kPa)	:	58.0 ºC
Melting point (101.3 kPa)	:	-57.7 ºC
Relative density 0.9	:	0.9
Vapour density (air=1)	:	3.75
Vapour pressure (20 C; 101.3 kPa)	:	25.3 kPa
Relative density of saturated vapour/air mixture (air=1; 20 C)	:	1.7
Flashpoint	:	-18.0 ºC
Auto-ignition temperature	:	417.0 ºC
Explosive limits (%, in air)	:	1.8-6.0
Solubility in water	:	*vigorous hydrolysis*
Solubility in organic solvents	:	soluble in benzene, ether, perchloroethylene
Log $P_{octanol/water}$	:	3
Physical form colourless liquid	:	colourless liquid
Odour	:	sharp hydrogen chloride-like odour
Conversion factors 1 ppm = 4.5 mg/m^3 (20 C; 101.3 kPa)	:	1 ppm = 4.5 mg/m^3 1 mg/m^3 = 0.22 ppm

The chlorotrimethylsilane vapour is heavier than air, travels along surfaces, and can be ignited from distance. It violently reacts with water producing hydrogen chloride and causing a fire and explosion hazard. Upon contact with surface moisture, it releases hydrogen chloride which will corrode most metals and form flammable hydrogen gas.

Generally, it hydrolyzes very rapidly to hydrogen chloride and trimethylsilanol which condenses rapidly to form hexadimethyldisiloxane and water. The committee is of the opinion that the presence of hydrogen chloride in air might idicate the presence of accidently released chlorotrimethylsilane.

At elevated temperatures or combustion, it decomposes producing corrosive and toxic vapours (silicium dioxide, phosgene, hydrogen chloride). It violently reacts with acids, amines, alcohols, and oxidizing agents.

2.3 Validated analytical methods

No validated method was found which can be used for the direct determination of chlorotrimethylsilane in air or biological samples. The rapid hydrolysis of chlorotrimethylsilane will complicate its determination.

Chapter 3

Sources

3.1 Natural occurrence

Chlorotrimethylsilane does not occur naturally.

3.2 Man-made sources

3.2.1 Production

Chlorotrimethylsilane is produced by a Grignard reaction of silicon tetrachloride with methyl-magnesium chloride. Furthermore, chlorotrimethylsilane can be formed in a reaction of silicon metal with methyl chloride at elevated temperature using copper as a catalyst. Thereafter, chlorotrimethylsilane is separated from mixed methylchlorosilanes by fractional crystallization (NLM98).

According to the IUCLID Data Sheet (see also Section 7.3), there are five production sites in Europe (excluding the former Soviet Union), three in the USA, and three in Japan. The annual production per European facility through the years 1990-1994 was stated to be in the range of 1-5 kilotonnes, the worldwide production in the range of 15-40 kilotonnes (EC96).

3.2.2 Uses

Chlorotrimethylsilane is used as an intermediate by the production of silicone fluids (as a chain terminating agent), as a silylating agent, and as a catalyst for the production of propylene oxide (EPA85, NLM98). According to the IUCLID Data Sheet, the entire European production is used for the manufacture of organosilicic derivatives, mainly polysiloxanes (EC96).

Because of the high reactivity, chlorotrimethylsilane must be manufactured, stored, and used in airtight, highly specialized installations (EC96).

Chapter 4

Exposure

4.1 General population

No quantitative data were found.

However, environmental levels may be neglectable. Chlorotrimethylsilane is not a naturally occurring compound, and is produced and used in closed systems at the same facility. When it is accidently released into the environment, it will hydrolyze very rapidly to hydrogen chloride and trimethylsilanol which condenses rapidly to form hexamethyldisiloxane and water (EC96, NLM98).

4.2 Working population

No quantitative data were found. As stated before, because of its high reactivity, chlorotrimethylsilane is used in closed systems, and exposure levels may therefore be neglectable. Moreover, because of this high reactivity, in case of exposure, this may be to hydrogen chloride and hexamethyldisiloxane.

No serious industrial hygiene hazards were stated to exist at a US chlorosilane production plant (NLM98).

Chapter 5

Toxicokinetics

5.1 Introduction

There is no information found with respect to the toxicokinetics of chlorotrimethylsilane.

Chlorotrimethylsilane will be rapidly hydrolyzed upon contact with tissue fluid releasing hydrogen chloride and trimethylsilanol which condenses to form hexamethyldisiloxane and water (NLM98).

The committees considers trimethylsilanol to be a stable compound that will not be metabolized to a great extent.

In view of the rapid hydrolysis in aqueous environments, it is obvious that toxicokinetic studies, even at low concentrations, are difficult to carry out.

5.2 Absorption

No data available.

Based on physico-chemical properties (ie. a molecular weight of 109 and a Log $P_{o/w}$ of 3) absorption through the skin can be expected. This view is supported by the findings from an acute dermal toxicity study (see Section 6.2.2), although the corrosive nature of chlorotrimethylsilane may have enhanced dermal penetration by breaking down normal barriers.

5.3 Distribution

No data available.

5.4 Biotransformation

No data available.

5.5 Excretion

No data available.

5.6 Biological monitoring

No data available.

5.7 Summary

Upon contact with tissue fluids, chlorotrimethylsilane will be hydrolyzed releasing hydrogen chloride.

There is no information available on uptake, distribution, biotransformation, and biologicalmonitoring of chlorotrimethylsilane.

Chapter 6

Effects

6.1 Observations in man

6.1.1 Irritation and sensitization

Direct contact of chlorotrimethylsilane as a liquid causes severe skin or eye burns (EPA85). Exposure to the vapour irritates mucous membranes. Ingestion causes severe burns of mouth and stomach (EPA85).

6.1.2 Toxicity due to experimental or occupational exposure

No data available.

6.2 Animal experiments

6.2.1 Irritation and sensitization

Chlorotrimethylsilane causes severe eye irritation in rabbits (grade 9 on a scale of 1 to 10). In addition, severe burns of the cornea and eyelids were observed (NLM98). When 0.005 ml undiluted chlorotrimethylsilane was placed directly on the cornea of one eye of New Zealand white rabbits (n=6), the maximum mean Draize score was 31.5/110 at 6 h. Immediate discomfort, moderate corneal injury, iritis, and moderate to

severe conjunctivitis (with necrosis) were reported, most eyes healing by seven days (i.e., the observation/recording period) (BRRC92, Mye93a).

When exposed to vapours, corneal opacity was observed in rats at concentrations of 12,850 mg/m^3 (2855 ppm) and higher, but not at 10,415 mg/m^3 (2314 ppm) (exposure duration: 1h) (see also Section 6.2.2) (BRR92, Mye93a). No data on eye irritation were available from a two-week inhalation study using rats (see Section 6.2.3) (EC96).

Chlorotrimethylsilane blanches the skin after direct contact, followed by blisters (NLM98). When 0.5 ml undiluted chlorotrimethylsilane was applied under occlusion (for 4 h) to the clipped, intact dorsal skin of New Zealand white rabbits (n=6), the modified primary irritation index for erythema and oedema (estimated from Draize readings) was 2.2/8.0. Necrosis was observed on each animal within one hour after contact, accompanied by severe erythema, moderate oedema, and desquamation. The effects persisted through seven days (i.e., the observation/recording period (BRRC92, Mye93a).

No data on sensitization were found.

Conclusion

Chlorotrimethylsilane causes severe skin and eye irritation. Since the skin effects persisted throughout the observation period, the compound should be considered as corrosive to the skin.

6.2.2 Acute toxicity

The acute toxicity of chlorotrimethylsilane is high after exposure by inhalation, because the vapour strongly irritates mucous membranes. In rats, a 1-h LC_{50} of approximately 13,175 mg/m^3 (2928 ppm) has been determined after exposing male and female rats (n=5/sex/group) nose-only to vapour concentrations of approximately 10,415, 12,850, 14,790, and 16,840 mg/m^3 (2314, 2855, 3289, 3742 ppm). The mortality observed in a fourteen-day observation period was 1/10 (female), 3/10 (all females), 10/10, and 10/10 for the 2314-, 2855-, 3289-, and 3742-ppm group, respectively. The animals exposed to the two highest concentration groups died on the first observation day. Because of this early dying, recording of clinical signs and body weights was limited to the two lower concentration groups showing nasal crust, rough coat as the main signs, and initial body weight loss and decreased total mean body weight gain. At necropsy, major findings included corneal opacity (in the three higher concentration groups) and diffuse or focal dark coloured areas of the lungs (in all treated groups) (Kol87). When exposed to

nearly satured vapours*, all exposed female Sprague-Dawley rats (n=5) died within twelve minutes. Toxic signs reported included lachrymation, hyperactivity, ataxia, and gasping. At necropsy, red patchy lungs and gas-filled stomachs and intestines were seen (BRRC92, Mye93a). In mice, mortality was observed at much lower levels. An 'absolute lethal concentration' (LC_{100}) of 100 mg/m^3 was reported (Vor69). However, this only figure was presented in a table and not any experimental detail was given. The committees can not assess the significance of this finding and therefore can not draw conclusions about possible differences in susceptibility between rats and mice.

Following oral (gavage) administration of 0.25 ml undiluted chlorotrimethylsilane/kg to fasted male Sprague-Dawley rats, 5/5 animals died within two to six days without preceding signs. At necropsy, dark red lungs, liver, kidneys, and adrenals, and ulcerated stomachs were observed. When given samples diluted in Silicone L-45 oil (dose range: 2.0-8.0 ml/kg; n=5/sex/group; observation period: 14 d), the LD_{50} (95% confidential limits), as contained sample, was 5.66 (4.11-7.79) and 6.63 (5.67-7.74) ml/kg for male and female animals, respectively. The lowest lethal dose was 2.0 ml/kg. Sluggishness, dyspnea, rales, salivation, and prostration were observed, and death followed within 30 minutes to two days. At necropsy (descendents), red to black stomachs and intestines, white gas in stomachs and thoracic cavities, black stomach contents, blanched livers, and red fluid in thoracic cavities were seen, while survivors did not show gross lesions (BRRC92, Mye93a). The difference in results when testing the undiluted or diluted test compound is not uncommon when testing corrosive compounds.

When chlorotrimethylsilane was applied under occlusion (for 24 h) to the clipped, intact dorsal skin of New Zealand white rabbits (dose range: 1.0-4.0 ml/kg; n=5/sex/group; observation period: 14 d), LD_{50}s were 2.83 (95% c.l.: 1.56-3.63) and 1.78 (95% c.l.: 0.84-3.79) ml/kg for male and female animals, respectively. The lowest lethal dose was 1.0 ml/kg. Local effects included erythema, oedema, necrosis, and scabs, systemic effects immediate discomfort, sluggishness, unsteady gait, diarrhea, and persistent weight loss. Death occurred at 30 minutes to eight days. At necropsy, livers with pink to dark red areas were seen (BRRC92, Mye93a).

An ip LD_{Lo} of 750 mg/kg bw has been reported in mice (NIO98; details not presented).

Conclusion

Based on acute lethality data, the committees consider the toxicity of chlorotrimethylsilane after inhalation to be low in rats.

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* estimated to be ca 250,000 ppm from: (compound's vapour pressure in Pa/10^5) * 10^6 Pa (result in ppm)

Based on EC criteria, chlorotrimethylsilane would be classified as toxic if swallowed and as harmful in contact with skin.

6.2.3 *Repeated dose and carcinogenicity studies*

The IUCLID Data Sheet includes one repeated inhalation study in which an unknown number of male and female Sprague-Dawley rats were exposed to approximately 150 mg/m^3 (34 ppm) chlorotrimethylsilane or to approximately 45 mg/m^3 (30 ppm) HCl, 6 h/d, 5 d/w, for two weeks. No treatment-related clinical signs were observed, and the study did not show differences between the two exposure groups (EC96). No more data were presented.

In A/He male and female mice, chlorotrimethylsilane increased both the incidence (ca 2 fold: 79% vs 37% and 48% in untreated and vehicle-treated controls, resp) and the multiplicity of lung tumours at the maximum tolerated dose (MTD) level (1,000 mg/kg bw, total dose; two ip injections; vehicle: tricaprylin). No such effects were noted after injection of a total dose of 200 or 500 mg/kg bw (time of sacrifice: 24 w after first injection; point of time of second injection not indicated) (Sto75). Remarkably, these high ip doses of chlorotrimethylsilane - which may be very toxic in mice upon acute exposure by inhalation - did not cause immediate death.

No other repeated dose (including reproduction toxicity and carcinogenicity) studies were found.

Conclusion

The toxicity (including reproduction toxicity and carcinogenicity) following repeated dosing of chlorotrimethylsilane cannot be evaluated because of lack of data. Although chlorotrimethylsilane showed some carcinogenic potential in the A/He mouse lung tumour model, the significance of this finding is questionable since this occurred at the maximum tolerated dose only. Furthermore, this model is very sensitive, and a large number of false positives have been found in this model.

6.2.4 *Mutagenic and genotoxic activity*

A summary of *in vitro* and *in vivo* genotoxicity studies is presented in Table 1.

Table 1 Summary of *in vitro* and *in vivo* genotoxicity assays for chlorotrimethylsilane.

test system	concentration	+/- activation	response	reference
S . typhimurium (TA1535, TA1537, TA1538, TA98, TA100)	0.001-5 µl/plate 0.001-5 µl/plate	- S9 + S9	negative negative	Isq88a
S. typhimurium TA1535, TA1537, TA98	0-1666 µg/plate 0-1666 µg/plate	- S9 + S9	negative negative	Mor86
S. typhimurium TA100	0-1666 µg/plate 0-3333 µg/plate	- S9 + S9	weakly positive[a] weakly positive[a]	
S. typhimurium TA1535, TA1537, TA97, TA98, TA100	1.0-100 µg/plate 98-6666 µg/plate	-S9[b] +S9[c]	negative negative	Zei92
E. coli (W3110)	0.001-5 µl/plate 0.001-5 µl/plate	- S9 + S9	negative negative	Isq88a
S. cerevisiae (D4)	0.001-5 µl/plate 0.001-5 µl/plate	- S9 + S9	negative negative	Isq88a
Sister chromatid exchange (SCE) (mouse L5178Y lymphoma cells)	0.02-0.64 µg/ml 0.02-0.64 µg/ml	- S9 + S9	negative negative	Isq88a
gene mutation (mouse L5178Y lymphoma cells)	0.02-0.64 µl/ml 0.02-0.64 µl/ml	- S9 + S9	negative negative	Isq88a
chromosome aberrations (mouse L5178Y lymphoma cells)	0.02-0.64 µg/ml 0.02-0.64 µg/ml	- S9 + S9	positive negative	Isq88a
chromosome aberrations (*in vivo*; rat bone marrow cells)	0-74 mg/kg bw (single; ip)	not relevant	negative	Isq88b

[a] see text Mor86

[b] TA1537 not tested without S9;

[c] from Arochlor-induced rat and hamster liver (at 10 and or 30%)

As to prokaryotic testsystems, Mortelmans et al reported a weak positive response in *S. typhimurium* strain TA100 both in the presence and in the absence of a metabolic activation system (liver S9 of rats and hamsters). Maximum responses of approximately 1.5 times the control values were obtained in two out of three trials without metabolic activation, in three out of three trials with induced hamster liver S9, and in one out of two trials with induced rat liver S9. In half of these positive trials (one nonactivated, one hamster-liver activated, one rat-liver activated), these results were seen at the highest noncytotoxic level only. Results in strains TA1535, TA1537, and TA98 were negative (Mor86). In a separate test, chlorotrimethylsilane was not mutagenic in *S. typhimurium* strain TA100.

Tests with other strains (TA1535, TA1537, TA1538, TA98) and with *E. coli* (strain W3110) were negative as well. Hydrogen chloride, trimethylsilanol and hexamethyldisiloxane, hydrolysis products, were not mutagenic in these assays either. All these tests were performed with and without an S9 metabolic activation system

(Isq88a). Furthermore, chlorotrimethylsilane as well as hydrogen chloride, trimethylsilanol and hexamethyldisiloxane were not mutagenic in *S. cerevisiae* (Isq88a).

When tested in mouse L5178Y lymphoma cells both in the presence and in the absence of a metabolic activating system, chlorotrimethylsilane did not induce gene mutations or sister chromatid exchanges, but it did induce a significant increase in the percentage of cells with chromosome aberrations in the absence of the S-9 mix. Although in the table in which the chromosome aberration results were presented a dose-related response was indicated, it was stated in the text, that "non-linear, erratic patters were associated with cellular response to treatment with trimethylchlorosilane, ..." making the significance of this finding difficult to interpret (Isq88a).

The negative results in gene mutation tests in bacteria (*S. typhimurium*) and mammalian cells (mouse L5178Y lymphoma cells) were confirmed by similar findings in unpublished studies performed by Bayer AG and the US National Cancer Institute (DE Thomas, letter to DECOS).

Hydrogen chloride did not induce gene mutations, Sister Chromatid Exchanges (SCEs), and chromosome aberrations. Trimethylsilanol did neither induce gene mutations nor sister chromatid exchanges in the presence of the S-9 mix. Howver, in the absence of the S-9 mix, trimethylsilanol induced SCE's and chromosome abberations in mouse lymphoma cells. Hexamethyldisiloxane was negative when tested for gene mutations and SCEs, but produced in the absence of the S-9 mix a significant increase in the percentage of aberrant cells at one single dose in the middle of the dose range. Neither chlorotrimethylsilane, nor hydrogen chloride nor hexamethyldisiloxane induced a positive responses in the alkaline elution assay in mouse lymphoma cells (Isq88a).

Chlorotrimethylsilane did not cause significant increases in chromosome aberrations in bone marrow of rats following single ip injections of 0, 19, 37, 74 mg/kg bw (sampling times at 6, 24, and 48 h). Hexamethyldisiloxane and trimethylsilanol, injected ip, were negative as well. Although dose levels were stated to be based on a preliminary MTD-finding study (MTD: maximum tolerated dose), no data were presented on general or bone marrow toxicity in the bone marrow assay (Isq88b).

Conclusion

Chlorotrimethylsilane is not mutagenic in bacteria and yeast *in vitro*. It did not induce gene mutations, SCEs, or DNA damage in mouse lymphoma cells, but it showed some weak potential for inducing chromosome aberrations in these cells.

In vivo, it was negative in a bone marrow chromosome aberration assay in rats at single ip doses up to 74 mg/kg bw.

Hexamethyldisiloxane showed a similar picture: negative in the aforementioned *in vitro* tests, apart from a weakly positive result in the chromosome aberration test, and negative *in vivo* in bone marrow of rats given a single ip injection of up to 1030 mg/kg bw.

Hydrogen chloride was negative in the aforementioned *in vitro* tests (not tested *in vivo*).

6.2.5 Effects on reproduction

No data available.

6.3 Summary

No toxicological data in humans were found in the literature. Severe irritation of skin, eyes (from exposure to the liquid), and mucous membranes (by vapours), and severe burns of mouth and stomach following ingestion were mentioned.

In animals, chlorotrimethylsilane caused severe corrosion (burns and blisters) of eyes (cornea, eyelids) and skin. It was highly toxic in mice, but not in rats after single inhalation exposure.

Chlorotrimethylsilane and hexamethylsiloxane had no genotoxic properties in bacteria and yeast *in vitro*. In mouse lymphoma cells, they did not cause gene mutations, SCEs, or DNA damage, but showed only some weak potential for inducing chromosome aberrations. Hydrogen chloride was negative when concomitantly tested in all these assays. An *in vivo* chromosome aberration test in bone marrow of rats was negative at single ip doses up to 74 and 1030 mg/kg bw of chlorotrimethylsilane and hexamethyldisiloxane, respectively.

There are no data from repeated dose toxicity (including reproduction toxicity and carcinogenicity) studies. In a very sensitive model of unclear significance (i.e., lung tumourresponse in A/He mice), chlorotrimethylsilane increases both the incidence and the multiplicity of lung tumours, but at the maximum tolerated dose only.

Chapter 7

Existing guidelines, standards, and evaluations

7.1 General population

No guidelines for the general population were found.

7.2 Working population

No occupational standards set by regulatory bodies were available.

In European industrial practice, the limit value of hydrogen chloride (7 mg/m^3) is used (EC96).

7.3 Evaluations

Following “Council Regulation (EEC) 793/93 on the Evaluation and Control of the Risks of Existing Substances” the European chemical industry by means of a lead company is requested to submit data to the International Uniform Chemical Information Data base (IUCLID) to allow a risk assessment of these chemicals by the member states of the EC. The data base contained a data sheet on chlorotrimethylsilane (last update: December 18, 1995; lead company: Dow Corning Europe). However, these data were not yet evaluated by a EC member state (EC96).

Chapter **8**

Hazard assessment

8.1 Assessment of health hazard

It is noticed that clorotrimethylsilane is a very reactive compound and, therefore, manufactured, stored, and handled in closed systems, and that in case of exposure, if any, this may be to its hydrolysis products, hydrogen chloride, trimethylsilanol and hexamethyldisiloxane*.

The available data on chlorotrimethylsilane do not allow a proper health hazard evaluation. In acute experiments, severe irritation has been observed probably as a consequence of rapid hydrolysis to hydrogen chloride. There were no data from repeated dose toxicity (including reproduction toxicity and carcinogenicity) experiments. Based on the genotoxicity data available, the committees do not consider chlorotrimethylsilane (or its hydrolysis products) to be genotoxic (nearly all experiments were negative).

8.2 Groups at extra risk

No specific groups at extra risk are identified in the literature.

* In Annex D, an impression of the toxicity of both hydrolysis products is given.

8.3 Health-based recommended occupational exposure limit

The toxicological data base is too poor to justify the recommendation of a health-based occupational exposure limit for chlorotrimethylsilane.

8.4 Additional considerations

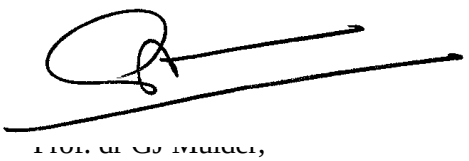
The committee is of the opinion that it is not possible to use the available data on the toxicity of hydrogen chloride, and hexamethyldisiloxane for the evaluation of the toxicity of chorotrimethylsilane, because no data are available on the other (reactive) intermediate trimethylsilanol. The latter compound might cause irritation as well.

Chapter **9**

Recommendations for research

- Evaluation of the toxicity of hexamethyldisiloxane (the major condensation product of chlorotrimethylsilane).
- Data on the metabolic fate of chlorotrimethylsilane at low concentrations.
- 28-day or 90-day inhalation toxicity study.
- Analytical method for determining occupational air levels.

The Hague, 15 November 2001,
for the committee,



dr ASAM van der Burght,
scientific secretary

Prof. dr GJ Mulder,
chairman

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NLM98 US National Library of Medicine (NLM). Hazardous Substances Databank (HSDB) [CD-ROM], issue January 1998. SilverPlatter International, 1998 (last update chlorotrimethylsilane file: February 1997).

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Annexes

Annex **A**

Request for advice

In a letter dated October 11, 1993, ref DGA/G/TOS/93/07732A, to, the State Secretary of Welfare, Health and Cultural Affairs, the Minister of Social Affairs and Employment wrote:

Some time ago a policy proposal has been formulated, as part of the simplification of the governmental advisory structure, to improve the integration of the development of recommendations for health based occupation standards and the development of comparable standards for the general population. A consequence of this policy proposal is the initiative to transfer the activities of the Dutch Expert Committee on Occupational Standards (DECOS) to the Health Council. DECOS has been established by ministerial decree of 2 June 1976. Its primary task is to recommend health based occupational exposure limits as the first step in the process of establishing Maximal Accepted Concentrations (MAC-values) for substances at the work place.

In an addendum, the Minister detailed his request to the Health Council as follows:

The Health Council should advice the Minister of Social Affairs and Employment on the hygienic aspects of his policy to protect workers against exposure to chemicals. Primarily, the Council should report on health based recommended exposure limits as a basis for (regulatory) exposure limits for air quality at the work place. This implies:

- A scientific evaluation of all relevant data on the health effects of exposure to substances using a criteria-document that will be made available to the Health Council as part of a specific request for advice. If possible this evaluation should lead to a health based recommended exposure limit, or, in the

case of genotoxic carcinogens, a ‘exposure versus tumour incidence range’ and a calculated concentration in air corresponding with reference tumour incidences of 10^{-4} and 10^{-6} per year.

- The evaluation of documents review the basis of occupational exposure limits that have been recently established in other countries.
- Recommending classifications for substances as part of the occupational hygiene policy of the government. In any case this regards the list of carcinogenic substances, for which the classification criteria of the Directive of the European Communities of 27 June 1967 (67/548/EEG) are used.
- Reporting on other subjects that will be specified at a later date.

In his letter of 14 December 1993, ref U 6102/WP/MK/459, to the Minister of Social Affairs and Employment the President of the Health Council agreed to establish DECOS as a Committee of the Health Council. The membership of the Committee is given in annex B.

Annex **B**

The committee

- GJ Mulder, *chairman*
  professor of toxicology; Leiden University, Leiden
- RB Beems
  toxicological pathologist; National Institute of Public Health and the Environment, Bilthoven
- PJ Borm
  toxicologist, Heinrich Heine Universität, Düsseldorf, Germany
- JJAM Brokamp, *advisor*
  Social and Economic Council, The Hague
- VJ Feron,
  professor of toxicology; TNO Nutrition and Food Research Institute, Zeist
- DJJ Heederik
  epidemiologist; IRAS, Utrecht University, Utrecht
- LCMP Hontelez, *advisor*
  Ministry of Social Affairs and Employment, The Hague
- G de Jong
  occupational physician; Shell International Petroleum Maatschappij, The Hague
- TM Pal
  occupational physician; Netherlands Centre for Occupational Diseases, Amsterdam
- IM Rietjens
  professor in toxicology, Wageningen University, Wageningen

- H Roelfzema, *advisor*
  Ministry of Health, Welfare and Sport, The Hague
- T Smid
  occupational hygienist; KLM Health Safety & Environment, Schiphol and professor of working conditions, Free University, Amsterdam
- GMH Swaen
  epidemiologist; Maastricht University, Maastricht
- HG Verschuuren
  toxicologist; DOW Europe, Horgen (Switzerland)
- F de Wit
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- JM Rijnkels, *scientific secretary*
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- ASAM van der Burght, *scientific secretary*
  Health Council of the Netherlands, The Hague

Nordic Expert Group

- G Johanson *chairman*
  toxicologist; National Institute for Working Life, Solna (Sweden)
- V Kristjansson
  occupational hygienist; Administration of Occupational Safety and Health, Reykjavik (Iceland)
- K Savolainen
  Finnish Institute of Occupational Health, Helsinki (Finland)
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  National Institute of Occupational Health, Oslo, Norway
- J Jarnberg, *scientific secretary*
  National Institute for Working Life, Solna (Sweden)

The first draft of the present advisory report was prepared by H Stouten, MSc, from the Department of Occupational Toxicology of the TNO Nutritionand Food Research Institute, by contract with the Ministry of Social Affairs and Employment.

Secretarial assistance: T van der Klugt
Lay-out: J van Kan.

Annex **C**

Comments on the public draft

A draft of this repport was released in 1999 for public review. The following persons or organisation commented on the draft document:

- DE Thomas, Centre European Des Silicones (CEFIC)
  Bruxelles
- E Ball, Health and Safety Executive (HSE)
  Great Brittain

Annex **D**

Toxicity data on hydrogen chloride and hexamethyldisiloxane

The next paragraphs are not the result of an extensive literature search but merely meant to give some impression of the toxicity of hydrogen chloride and hexamethyldisiloxane. The data on hexamethyldisiloxane are mainly from abstracts from records of the US EPA's database TSCATS (referred to as TSCA) and were retrieved via Toxline on CD-ROM and via the Right-to-Know Network on the Internet (http://www.rtk.net).

Hydrogen chloride

As to hydrogen chloride, data on effects on humans are from very old reports. Levels above 15 mg/m^3 (10 ppm) were considered to lead to work impairment and above 75 mg/m^3 (50 ppm) to work hindrance; above 150 mg/m^3 (100 ppm), work would be impossible (Kam92).

In experimental animal studies, the principle effects following acute inhalation exposure to hydrogen chloride (occurring at several thousands of ppm) are irritation of the eyes, respiratory tract, and exposed areas of skin. When rabbits and guinea pigs were exposed to 152 mg/m^3 (100 ppm) hydrogen chloride, 6 h/d, for five days, only slight respiratory difficulties, eye and nasal irritation, and slightly reduced haemoglobin levels were observed. No adverse effects or morphological changes occurred in a monkey, rabbits, and guinea pigs exposed to 46 mg/m^3 (30 ppm), 6 h/d, for four weeks. In a life-time inhalation carcinogenicity study, laryngeal hyperplasia, but no serious nasal

epithelial irritation or preneoplastic or neoplastic lesions were seen in rats exposed to 15 mg/m^3 (10 ppm), 6 h/d, 5 d/w (Kam92, SEG93).

Hexamethyldisiloxane

Hexamethyldisiloxane did not demonstrate any evidence of sensitization in a repeated insult patch test with 87 caucasian females, 2 hispanic females, and 11 caucasian males (TSCA).

In experimental animals, no irritation was observed in two separate studies following single application of hexamethyldisiloxane to the skin of rabbits (Mye93b, TSCA), conforming the negative results of an older study (Row48). Following repeated application (10 over a 14-day period) to the skin of rabbits, slight irritation was found (TSCA). When instilled into both eyes of rabbits, the compound was concluded to be minimal irritating to unwashed eyes and minimal irritating to eyes washed after one minute of contact. Severe irritation of the iris and mild to no irritation of the conjunctiva were observed after 1 hour in both eyes, but not at 24 hours and later time points (TSCA). In another study, hexamethylsisiloxane produced a maximum mean score of 1.8/110 at 1 hour. Iritis (in 1/6 rabbits) and minor conjunctivitis were seen but healed by 1-2 days (Mye93b). These results concur with those from an older report in which instillation of the test substance produced immediate irritation which was healed by one hour (Row48)

Hexamethyldisiloxane was not very toxic following single exposures by inhalation, gavage, or dermal application. In rats exposed to “substantially” saturated atmospheres (according to Row48, a saturated atmosphere should be at the order of 39,000-40,000 ppm at 21-22 C), the median time for death in 50% of the animals was fifteen and twenty minutes for males and females, respectively. The minimum time needed to induce mortality was 13 minutes. Signs observed were hyperactivity followed by hypoactivity, laboured breathing, convulsions, and red discharge from eyes and nose; at necropsy, there were dark red lungs and liver (Mye93b). In other experiments, exposure to “substantially” saturated vapours did not induce mortality or toxic signs in animals exposed for one hour but caused the death of 2/6 rats after 6 and 7 hours of exposure, respectively, in one study while all rats survived a six-hour exposure in a second study (TSCA). Dermal LD_{50}s of 16.0 and >16.0 ml/kg bw were reported for male and female rabbits, respectively (Mye93b). No mortality or behavioural effects were seen in rabbits following a single dermal dose of 2000 mg/kg bw (TSCA). An oral LD_{50} of >16.0 ml/kg bw was found in rats (Mye93b). Furthermore, it was reported that doses up to 34,600 mg/kg bw did not induce mortality, behavioural effects, or gross pathological changes (TSCA).

Following repeated exposure, in rats exposed to 499 or 1004 ppm, 6 h/d, 5 d/w, for two weeks, only effects were seen in the male animals including a dose-related trend toward increased mean kidney weights, a statistically significantly increased relative kidney weight in the high exposure group, corresponding with an increased severity of hyaline droplets in the proximal tubules (TSCA). In an older experiment in which female rats and guinea pigs exposed to 4400 ppm, 7 h/d, for fifteen days over an eighteen-day period (rats) or for twenty days over a 26-day period (guinea pigs), slightly increased absolute liver and kidney weights and slightly decreased body weight gains were seen in rats and guinea pigs, respectively. No effects were observed upon gross or microscopic examination (Row48). In guinea pigs exposed to 12,000-15,000 ppm, 30-40 min/day, for 20 days, no mortality was found (Bad52). In a 28-day dermal toxicity study using rats, nonocclusive application, 6 h/d, 5 d/w, of doses up to 1000 mg/kg bw/d only induced decreases in body weight gain and food consumption in weeks 3 and 4 and in absolute liver weights in the male animals given 1000 mg/kg bw/d (TSCA).

Trimethylsilanol

Trimethylsilanol was negative is a dominant lethaal assay in rats after oral treatment for 5 days per week for 8 week (Isq88B).

No additional toxicity data was found for trimethylsilanol.

Annex **E**

Abbreviations

bp	boiling point
EC_{50}	concentration at which a described effect is found in 50% of the exposed animals or at which the effect is decreased up to 50% of the control value
HBR-OEL	health based recommended occupational exposure limit
h	hour
IC_{50}	concentration at wAbbreviationshich inhibition of a certain function is found up to 50% of the control value
LC_{50}	lethal concentration for 50% of the exposed animals
LC_{lo}	lowest lethal concentration
LD_{50}	lethal dose for 50% of the exposed animals
LD_{lo}	lowest lethal dose
LOAEL	lowest observed adverse effect level
MAC	maximaal aanvaarde concentratie (maximal accepted concentration)
MAEL	minimal adverse effect level
MAK	Maximale Arbeitsplatz Konzentration
MOAEL	minimal observed adverse effect level
MTD	maximum tolerated dose
NAEL	no adverse effect level
NEL	no effect level
NOAEL	no observed adverse effect level
OEL	occupational exposure limit
PEL	permissible exposure limit
ppb	parts per billion $(v/v)10^{-9}$
ppm	parts per million $(v/v)10^{-6}$
RD_{50}	concentration at which a 50% decrease of respiratory rate is observed
REL	recommended exposure limit

STEL	short term exposure limit
tgg	tijd gewogen gemiddelde
TLV	threshold limit value
TWA	time weighted average
V_{max}	maximal reaction velocity of an enzyme

Organisations

ACGIH	American Conference of Governmental Industrial Hygienists
CEC	Commission of the European Communities
DECOS	Dutch Expert Committee on Occupational Standards
DFG	Deutsche Forschungsgemeinschaft
EPA	Environmental Protection Agency (USA)
FDA	Food and Drug Administration (USA)
HSE	Health and Safety Executive (UK)
IARC	International Agency for Research on Cancer (WHO)
INRS	Institut National de Recherche et de Sécurité (France)
NIOSH	National Institute for Occupational Safety and Health (USA)
NTP	National Toxicology Programme (USA)
OECD	Organisation for Economic Cooperation and Development
OSHA	Occupational Safety and Health Association (USA)
RTECS	Registry of Toxic Effects of Chemical Substances
SER	Social and Economic Council (Sociaal-Economische Raad NL)
WATCH	Working Group on the Assessment of Toxic Chemicals (UK)
WHO	World Health Organisation

Toxicological terms

bid	*bis in diem* (twice per day)
bw	body weight
CARA	chronic non-specific respiratory diseases
CHD	coronary heart disease
CNS	central nervous system
ECG	electrocardiogram
EEG	electro encephalogram
FCA	Freunds Complete Adjuvans
FEV	forced expiratory volume
FSH	follicle stimulating hormone
GD	gestation day(s)
GPMT	guinea pig maximisation test
GSH	glutathione
HLiA	hamster liver activated
IHD	ischaemic heart disease
im	intramuscular
ip	intraperitoneal
ipl	intrapleural
it	intratracheal
iv	intravenous
LH	lutheinising hormone
MAC	minimal alveolar concentration

MFO	mixed function oxidase
NA	not activated
PNS	peripheral nervous system
po	*per os* (= oral)
RBC	red blood cells
RLiA	rat liver activated
SCE	sister chromatid exchange
sc	subcutaneous
UDS	unscheduled DNA-synthesis

Statistical terms

GM	geometric mean
OR	Odds Ratio
RR	relative risk
SD	standard deviation
SEM	standard error of mean
SMR	standard mortality ratio

Analytical methods

AAS	atomic absorption spectroscopy
BEEL	biological equivalent exposure limit
BEI	biological exposure index
BEM	biological effect monitoring
BM	biological monitoring
ECD	electron capture detector
EM	environmental monitoring
FID	flame ionisation detector
GC	gas chromatography
GLC	gas liquid chromatography
GSC	gas solid chromatography
HPLC	high performance liquid chromatography
IR	infrared
MS	mass spectrometry
NMR	nuclear magnetic resonance
PAS	personal air sampling
TLC	thin layer chromatography
UV	ultraviolet

Annex **F**

DECOS-documents

DECOS has produced documents on the following substances.

To be ordered from the Health Council of the Netherlands:

Acetone cyanohydrin	1995/05WGD
p-Aramid fibres	1997/07WGD
Azathioprine	1999/04OSH
Aziridine (ethyl imine)	2000/13OSH
1,2,3-Benzotriazole	2000/14OSH
Bisphenol A and its diglycidylether	1996/02WGD
Bromoethane	1998/10WGD
1,2-and t-Butanol	1994/10
β-Butyrolactone	1999/05OSH
Cadmium and inorganic cadmium compounds	1995/04WGD
Calculating cancer risk	1995/06WGD
Carbadox	1999/06OSH
Carbon disulphide	1994/08
Chlorine dioxide	1995/07WGD
p-Chloroaniline	1998/09WGD
4-Chloro-o-toluidine	1998/08WGD
Chromium and its inorganic compounds	1998/01WGD
Cresols	1998/15WGD
Copper sulphate	1999/01OSH
1996-1997 WGD-rapporten/1996-1997 DECOS reports	1999/01WGD
1,2-Dibromoethane	1999/07OSH
1,2-Dichloroethane	1997/01WGD
Diethylsulphate	1999/08/OSH

Diglycidyl resorcinol ether	1999/09OSH
Diphenylamine	1997/05WGD
Endotoxins	1998/03WGD
Epichlorohydrin (1-Chloro-2,3-epoxypropane)	2000/10OSH
1,2-Epoxybutane	1998/11WGD
1,2-Ethanediamine	1996/03WGD
Ethyleneglycol ethers	1996/01WGD
Ethylene thiourea	1999/03OSH
Formamide and dimethylformamide	1995/08WGD
Hydrazinoethanol, phenylhydrazine, isoniazid, maleic hydrazide	1997/03WGD
Isopropyl acetate	1997/04WGD
Man made mineral fibers	1995/02WGD
2-Meathylaziridine (propylene imine)	1999/10OSH
Methyl Methacrylate	1994/09
Methacrylates. Ethyl methacrylate, n-butyl methacrylate and isobutyl methacrylate	1994/11
Methyl-t-butylether	1994/23
Methyl chloride	1995/01WGD
4,4'-Methylene bis (2-Chloroaniline)	2000/09OSH
4,4'-Methylene dianiline	2000/11OSH
Metronidazole	1999/11OSH
2-Nitropropane	1999/13OSH
N-Nitrosodimethylamine (NDMA)	1999/12OSH
2-Nitrotoluene	1998/12WGD
Pentaerythritol	1997/06WGD
Phenol	1996/04WGD
o-Phenylenediamine	1998/06WGD
Piperidine	1997/08WGD
Procarbazine hydrochloride	1999/14OSH
1- and 2-Propanol	1994/24
Propylene oxide	1997/02WGD
Ronidazole	1998/05WGD
Styrene	1998/07WGD
Quartz	1998/02WGD
1,1,1-Thrichloroethane	1995/03WGD
1,2,3-Trichloropropane	1994/25
1,2,3-Trichloropropane	1998/14WGD
Urethane (ethyl carbamate)	200012OSH
Vinylbromide	1999/15OSH
Wood dust	1998/13WGD