Trichloronaphthalene

(CAS reg no: 1321-65-9)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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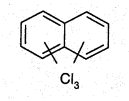
1 Introduction

The present document contains the assessment of the health hazard of trichloronaphthalene 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 Ir M Busschers and H Stouten, M.Sc. (TNO Nutrition and Food Research, Zeist, the Netherlands).

The evaluation of the toxicity of trichloronaphthalene has been based on the review by the American Conference of Governmental Industrial Hygienists (ACG99). 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 26 April 1999 (19990416/UP), 1965 to 29 January 1999 (19990129/ED), 1967 to 24 April 1999 (19990424/ED; vol 130, iss 18), respectively, using the following key words: trichloronaphthalene, the CAS registry number 1321-65-9, and a number of other CAS registry numbers related to positional isomers*. HSDB and RTECS, data bases available from CD-ROM, were consulted as well (NIO99, NLM99). The final literature search has been carried out in April 1999.

In April 2001, the President of the Health Council released a draft of the document for public review. The committee received no comments.

2 Identity

name	:	trichloronaphthalene
synonyms	:	-
molecular formula	:	$C_{10}H_5Cl_3$
structural formula	:	
CAS reg no	:	1321-65-9

Data from ACG99, Ada44

The technical products of chloronaphthalenes are often called Halowaxes. These Halowaxes are graded according to their chlorine content and all are therefore

* 55720-40-6, 55720-39-3, 55720-38-2, 55720-37-1, 55720-36-0, 55720-35-9, 55720-34-8, 55720-33-7, 51570-44-6, 51570-43-5, 50402-52-3, 50402-51-2, 2437-55-0, and 2437-54-9

mixtures of various isomers with one or two main derivatives predominating (Ben94, Cro70). Halowax 1012 is reported to be 'apparently' a trichloronaphthalene (Ada44) and Halowax 1001 a mixture of tri- and tetrachloronaphthalene (She57) or a mixture of tri- to hexachloronaphthalene, predominantly containing tetra- and pentachloronaphthalene (Cro70).

3 Physical and chemical properties

molecular weight	:	231.5
boiling point	:	304-354°C
melting point	:	93°C
flash point:	:	200°C (open cup)
vapour pressure	:	at 20°C: <0.133 kPa
solubility in water	:	insoluble in water
log $P_{octanol/water}$	:	5.43
conversion factors (20°C, 101.3 kPa)	:	not applicable

Data from ACG99, Ano86, Gre98, NIO81

Trichloronaphthalene is a colourless to pale yellow solid with an aromatic odour.

4 Uses

Trichloronaphthalene is used in lubricants and in the manufacture of insulation for electrical wire (ACG99). It was also reported to be used as a paper capacitor impregnant and in timber preservatives (Cro70).

5 Biotransformation and kinetics

The committee did not find data on uptake, distribution, biotransformation, and excretion of trichloronaphthalene.

6 Effects and mechanism of action

Human data

Mayers *et al.* (May38) described several cases of chloracne among the workers in 2 plants employing a mixture of tri- and tetrachloronaphthalene. However, according to Crow (Cro70), the evidence for the acnegenic effects of tri- and tetrachloronaphthalenes is confusing and most of the studies on this issue are incomplete and lacking a full description of all the chemicals the workers were exposed to. Therefore, other factors were probably responsible for the acne, for example, the use of pitch in these plants. Crow (Cro70) investigated a paper capacitor plant where no chloracne was observed between 1956 and 1963 in an area where a mixture of tri- and tetrachloronaphthalene was used. In another area of this plant, exposure to penta- and hexachlonaphthalenes produced chloracne in several workers. When this mixture was abandoned and replaced by a tri- and tetrachloronaphthalene mixture with polysterene, chloracne ceased. Moreover, daily experimental exposure of the ear (auricle) of 3 men to a mixture of tri- and tetrachloronaphthalene (Halowax 1001) in a 50% mineral oil suspension for 30 days did not result in acne or any other skin effects (She57).

There are several reports of hepatic injury, chloracne and/or mortality among humans working in manufacturing plants using chlorinated naphthalenes (Dri37, Pop97, Str44, War96). Although it was claimed that the main exposure was to chlorinated naphthalenes ('Halowax'), no details about specific types of chlorinated naphthalenes or exposure to other chemicals were given. Therefore, the committee could not establish the causal role of trichloronaphthalene.

Animal data

Irritation

In a study performed in 1938-40, solutions of trichloronaphthalene (Halowax 1012; chlorine content: 48%) in olive oil were applied to the ear and abdomen of unkown experimental animals (n=1/solution/area). No experimental details were presented; no (vehicle) controls were included. Application to the ear of a 10 or 20% solution, once daily, 5 days/week, for 20 or 17 times, respectively, was reported to produce some slight irritation (very slight to slight erythema, exfoliation, hair loss, follicle prominence and enlargement, slight hair loss). Upon

microscopic examination, there were no effects in the animal treated with the 10% solution while very slight epithelial hyperplasia and pitting and slight exfoliation were seen in the animal treated with the 20% solution. Application (bandaged) of the same solutions to the abdomen, for 11 or 12 times (over a 15- or 16-day period), produced moderate to severe erythema, respectively (Ada44).

Single exposure

The 100% survival dose and the 100% fatal dose after a single oral administration of trichloronaphthalene (Halowax 1012) to guinea pigs were 400 mg/kg bw and 1800 mg/kg bw, respectively (Ada44).

Repeated exposure

Two groups of rats (n=80/group) were exposed to a mixture of trichloronaphthalene with traces of tetrachloronaphthalene (chlorine content: 49.4%; ratio not given) at an average concentration of either 1.31 mg/m^3 (range; 0.10-2.60 mg/m^3), 16 hours/day, 6 days/week, for up to 134 days (total exposure: 1896 hours), or 10.97 mg/m^3 (range: 5.78-16.49 mg/m^3), 16 hours/day, 6 days/week, for up to 102 days (total exposure: 1232 hours). The animals of the low-concentration group revealed only very slight liver injury, which consisted of an occasional paler appearance and, microscopically, of low incidences of slightly enlarged cells, increased granularity of cytoplasm, vacuolisation, and, occasionally, the presence of mitotic figures, whereas the findings in the animals of the high-concentration group were similar but increased in severity. Additionally, fat vacuoles and hyaline droplets were occasionally observed (Ben38, Dri37). The committtee noticed the absence of data on a control group. Further, in view of the chlorine contents of pure tri- and tetrachloronaphthalene (46.0 and 53.4%, resp), the mixture (with a chlorine content of 49.4%) may have contained more than 'traces' of tetrachloronaphthalene.

When rats (n=10) were given oral (diet) doses of 3000 mg/day/rat (n=10) of a mixture of tri- and tetrachloronaphthalene (see above) for up to 182 days, no treatment-related mortality, effects on body weight or signs of toxicity were observed. After 2 months of exposure, slight swelling of the hepatic cells, accompanied by vacuolisation due to accumulation of large amounts of fat was seen. These changes only slightly increased with longer exposure (Ben38, Dri37). The committee noticed the absence of a control group.

Daily subcutaneous injection of doses of 15 mg/kg/bw of a mixture of tri- and tetrachloronaphthalene in paraffin oil, for 2 months, did not affect survival, behaviour, body weight, red or white blood cells, or histology (Fli36).

The committee did not find data on the potential mutagenicity/genotoxicity, carcinogenicity, or reproduction toxicity of trichloronaphthalene.

7 Existing guidelines

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

Existing occupational exposure limits for trichloronaphthalene in some European countries and in the USA are summarised in the annex.

8 Assessment of health hazard

Occupational exposure to a mixture of tri- and tetrachloronaphthalenes was associated with several cases of chloracne (May38). However, it is more likely that other factors were responsible for the acne, for example the use of pitch in these plants (Cro70). Moreover, daily experimental dermal exposure of humans to a mixture of tri- and tetrachloronaphthalenes did not result in acne or any other skin effects (She57) and Halowax 1012 (reported to be 'apparently' a trichloronaphthalene) produced irritation but no acnegenic effects after dermal exposure in an unknown animal species (Ada44). Liver injury and mortality have been associated with exposure to chlorinated naphthalenes as well (Dri37, Pop97, Str44, War96), but since no details about specific types of chlorinated naphthalenes or exposure to other chemicals were given, the committee cannot draw a conclusion with respect to a causal role of trichloronaphthalene *per se*.

Single oral dosing of guinea pigs at 1800 mg/kg bw resulted in 100% mortality, whereas all guinea pigs survived a dose of 400 mg/kg bw (Ada44).

Following repeated exposure, the liver was shown to be the target organ.

Inhalation studies in rats with trichloronaphthalene including unkown amounts of tetrachloronaphthalene resulted in very slight liver injury (1.31 mg/m^3, 16 h/day, for up to 134 days) or more severe liver injury with some fatty degeneration (10.97 mg/m^3, 16 h/day, for 102 days) (Ben38, Dri37). Due to the mentioned shortcomings (no control group, wide range in exposure concentration, uncertainties in the composition of the exposure mixture), this

study is considered not suitable as a starting point for deriving an occupational exposure limit.

Dietary administration (3000 mg/day/rat, up to 136 days) of a similar mixture of tri- and tetrachloronaphthalene resulted in fatty infiltration of the liver (Ben38, Dri37).

No effects were observed after subcutaneous injection of high doses (15 mg/kg bw, for 2 months) of a mixture of tri- and tetrachloronaphthalene to rabbits (Fli36).

No data were found on the potential mutagenicity/genotoxicity, carcinogenicity, or reproduction toxicity of trichloronaphthalene.

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

The committee concludes that, based on the slight liver injury observed in a subchronic inhalation study in rats with average exposure concentrations of approximately 1 and 11 mg/m^3, the present MAC value of 5 mg/m^3 is at least one order of magnitude too high.

References

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ACG00 American Conference of Governmental Industrial Hygienists (ACGIH). Guide to occupational exposure values - 2000. Cincinnati OH, USA: ACGIH®, Inc, 2000: 123.

ACG01 American Conference of Governmental Industrial Hygienists (ACGIH). 2001 TLVs® and BEIs®. Threshold Limit Values for chemical substances and fysical agents. Biological Exposure Indices. Cincinnati OH, USA: ACGIH®, Inc, 2001: 57.

Ada44 Adams EM. The toxicity of chlorinated naphthalenes. Midland MI, USA: Dow Chem Co, Biochem Res Lab, 1944 (available from NTIS, Springfield VA, USA; order no NTIS/OTS0206141).

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Arb00a Arbejdstilsynet. Grænseværdier for stoffer og materialer. Copenhagen, Denmark: Arbejdstilsynet, 2000; At-vejledning C.0.1.

Arb00b Arbetarskyddstyrelsen. Hygieniska gränsvärden och åtgärder mot luftföroreningar. Solna, Sweden: National Board of Occupational Safety and Health, 2000; Ordinance AFS 2000/3.

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Ben94 Benya TJ, Leber AP. Halogenated cyclic hydrocarbons. In: Clayton GD, Clayton FE, eds. Toxicology. 4th ed. New York: John Wiley & Sons, 1994: 2507-13. (Patty's industrial hygiene and toxicology; Vol II, Pt D).

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Cro70 Crow KD. Chloracne. Trans St John's Hosp Dermatol Soc 1970; 56(2): 79-99.

DFG01 Deutsche Forschungsgemeinschaft (DFG): Commission for the Investigaton of Health Hazards of Chemical compounds in the Work Area. List of MAK and BAT values 2001. Weinheim, FRG: Wiley-VCH, 2001: 35, 112 (rep no 37).

Dri37 Drinker CK, Warren MF, Bennett GA. The problem of possible systemic effects from certain chlorinated hydrocarbons. J Ind Hyg Toxicol 1937; 19: 283-311.

Fli36 Flinn FB, Jarvik NE. Action of certain chlorinated naphthalenes on the liver. Proc Soc Biol Med 1936; 35: 118-20.

Gre98 Greim H, ed. Chlorierte Naphthaline. In: Gesundheidsschädliche Arbeitsstoffe. Toxikologisch-arbeitsmedizinische Begründungen von MAK-Werte (Maximale Arbeitsplatz-Konzentrationen). 1st-27th ed. Weinheim, FRG: Wiley-VCH, 1998.

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May38 Mayers MR, Silverberg MG. Skin conditions resulting from exposure to certain chlorinated hydrocarbons. J Ind Hyg Toxicol 1938; 20: 244-58.

NIO81 National Institute of Occupational Safety and Health (NIOSH). Occupational health guideline for trichloronaphthalene. In: Occupational health guidelines for chemical hazards. Washington DC, USA:NIOSH, 1981; DHHS (NIOSH) pub no 81-123.

NIO99 National Institute of Occupational Safety and Health (NIOSH). Naphthalene, trichloro-. In: Registry of Toxic Effects of Chemical Substances (RTECS). [CD-ROM], issue July 1999. SilverPlatter International, 1999 (last update trichloronaphthalene file: July 1999).

NLM99 US National Library of Medicine (NLM). Trichloronaphthalene. In: Hazardous Substances Data Bank (HSDB). [CD-ROM], issue July 1999. SilverPlatter International, 1999 (last update trichloronaphthalene file: January 1999).

She57 Shelley WB, Kligman AM. The experimental production of acne by penta- and hexachloronaphthalenes. AMA Arch Dermatol 1957; 75: 689-95.

SZW01 Ministerie van Sociale Zaken en Werkgelegenheid (SZW). Nationale MAC-lijst 2001. The Hague, The Netherlands: Sdu, Servicecentrum Uitgevers, 2001: 42.

TRG00 TRGS 900. Grenzwerte in der Luft am Arbeitsplatz; Technische Regeln für Gefahrstoffe. BArbBl 2000; 2.

Annex

Occupational exposure limits for trichloronaphthalene 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	-	5	8 h	administrative		SZW01
Germany						
-AGS	-	5[c]	8 h		S	TRG00
-DFG MAK-Kom.	-	-[d]			S	DFG01
Great-Britain						
-HSE	-	-				HSE01
Sweden	-	-				Arb00b
Denmark	-	5				Arb00a
USA						
-ACGIH	-	5	8 h	TLV	S	ACG01
-OSHA	-	5	8 h	PEL	S	ACG00
-NIOSH	-	5	10 h	REL	S	ACG00
European Union						
-SCOEL	-	-				CEC00

[a] S = skin notation; which means that skin absorbtion may contribute considerably to the body burden; sens = substance can cause sensitisation

[b] Reference to the most recent official publication of occupational exposure limits

[c] Inhalable fraction

[d] As chlorinated naphthalenes, these compounds are listed among substances for which studies of the effects in man or in experimental animals have yielded insufficient information for the establishment of MAK values