Chlorine trifluoride

(CAS reg no: 7790-91-2)

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/019, The Hague, 13 November 2001

Preferred citation:
Health Council of the Netherlands: Committee on Updating of Occupational Exposure Limits. Chlorine trifluoride; Health-based Reassessment of Administrative Occupational Exposure Limits. The Hague: Health Council of the Netherlands, 2001; 2000/15OSH/019.

1 Introduction

The present document contains the assessment of the health hazard of chlorine trifluoride 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 A. Wientjes, M.Sc. and H. Stouten, M.Sc. (TNO Nutrition and Food Research, Zeist, the Netherlands).

The evaluation of the toxicity of chlorine trifluoride 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 (19990426/UP), 1965 to 29 January 1999 (19990129/ED), and 1967 to April 24 1999 (19990424/ED), respectively, using the following key words: chlorine trifluoride, chlorine fluoride, chlorotrifluoride, trifluorochlorine, ClF_3, Cl_2F_6, and 7790-91-2. 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	:	chlorine trifluoride
synonyms	:	chlorotrifluoride
molecular formula	:	ClF_3
structural formula	:	-
CAS reg no	:	7790-91-2

Data from ACG99.

3 Physical and chemical properties

molecular weight	:	92.46
boiling point	:	11.3°C
melting point	:	- 76.3°C
flash point	:	-
vapour pressure	:	at 20°C: > 101.3 kPa
solubility in water	:	violent hydrolysis
Log $P_{octanol/water}$	:	0.53 (estimated)
conversion factors (20°C, 101.3 kPa)	:	1 ppm = 3.8 mg/m^3 1 mg/m^3 = 0.3 ppm

Data from ACG98, Per94, http://esc.syres.com.

Chlorine trifluoride, as a gas, is nonflammable, corrosive, and nearly colourless with a sweet, suffocating odour; as a liquid, it is pale green; as a solid, it is white. The gas has a density more than three times that of air. Chlorine trifluoride is extremely reactive. Explosions results on contact with organic materials and from reactions with compounds such as ammonia, carbon monoxide, hydrogen sulphide, sulphur dioxide, or hydrogen gas. It is violently hydrolysed by water, and reacts vigorously with metals. In the vapour phase, chlorine trifluoride decomposes by hydrolysis to form chlorine, chlorine monofluoride, chlorine oxyfluorides, chlorine dioxide, and hydrofluoric acid (ACG98, Per94).

4 Uses

The extreme reactivity of chlorine trifluoride constrains its use to within special plants, *e.g.*, steel apparatus. It is used as a fluorinating agent for the preparation of iron(III)fluoride, as an igniter and propellant for rockets, in nuclear reactor fuel processing, as a pyrolysis inhibitor for fluorocarbon polymers, and in etching silicon (ACG99, HSE99, Per94, Ric93).

5 Biotransformation and kinetics

Apart from a study on the distribution of fluorine in male rats following exposure to 400 ppm (1520 mg/m^3) of chlorine trifluoride, for 15 minutes, the committee did not find data on the kinetics of chlorine trifluoride. In view of the considerably

variable fluorine tissue levels found in control animals, the results of the measurements at t=0, 2, 6, and 24 h after ending exposure are difficult to interpret. Except for bone, average tissue levels ranged from 0.7 to 6.5 µg F per gram tissue wet weight (in liver at t=6 h and spleen at t=0 h, respectively). Generally there was a uniform distribution with relative high levels in the spleen, heart, (parts of) the gastrointestinal tract, and the testes. After 24 hours, the bone seemed to act as a depository for fluorine (Dos70).

6 Effects and mechanism of action

Human data

Apart from one report, cited in Per94, in which a worker exposed for 1 to 2 minutes to an unknown concentration of chlorine trifluoride emanating from a chlorine trifluoride-charcoal reactor, the committee did not find data on effects in humans due to exposure to chlorine trifluoride. The worker exposed during lunchtime for 1-2 minutes complained of a headache, abdominal pain, and dyspnea. Except some fatigue, there were no persistent effects (Per94).

Animal data

Single exposure

All rats (n=4-10) exposed to 800 ppm (3040 mg/m^3) of chlorine trifluoride gas, for periods ranging from 15 to 30 minutes, were killed in every instance while exposures for 10 or 13 minutes resulted in mortality in 0/10 and 1/8 animals, respectively. Exposure to 400 ppm (1520 mg/m^3) was lethal to 0/8, 0/4, 4/6, 7/8, and 8/8 animals when exposed for 20, 25, 30, 35, or 40 minutes, respectively. The general effect was severe inflammation of all exposed mucosal surfaces, accompanied by lacrimation. Prolonged exposure or high concentration of the gas caused burning of exposed skin areas, especially feet, and the hair became brittle and yellow. Corneal ulceration was a frequent consequence of even moderate contact. Pulmonary impairment was concluded from decreases in pulmonary release of $^{14}CO_2$ from injected [^{14}C]bicarbonate and from decreases in blood pH (Dos74).

Twenty rats exposed by inhalation to 480 ppm (1824 mg/m^3) of chlorine trifluoride exhibited increased activity immediately and showed signs of respiratory difficulty within a few minutes. All were in acute respiratory distress

within 20 minutes, and all died within 70 minutes. At a concentration of 96 ppm (365 mg/m3), the same signs developed but at a slower rate. Fourteen out of 20 animals died within 4.5 hours and 2 more died very shortly after being removed from the inhalation chamber. Histological examination of rats exposed to either concentration revealed emphysema, pulmonary oedema, vascular congestion, and fusion of the cells lining the bronchi (Hor55).

Given intraperitoneously, undiluted chlorine trifluoride gas was not lethal at doses up to 37 mg/kg bw, but extensive damage at the injection sites was observed. Larger doses were not given because of the violent reactivity of chlorine trifluoride and the extreme local discomfort of the animals (Dos74).

Repeated exposure

When rats (n=20/strain and sex not reported) and dogs (n=2/strain and sex not reported) were exposed to 21 ppm (80 mg/m^3), 6 hours/day, for 2 days, both rats and dogs showed signs of respiratory irritation and conjunctivitis during the first day. Except for eye inflammation in the dogs, animals appeared normal the morning after the first day of exposure. Signs seen during exposure on the second day were essentially the same as on the first day, except for the development of severe bilateral corneal ulcers in one dog, which persisted for a period of slightly over one month. All other animals appeared normal within a few days after the second exposure. The authors acknowledged difficulties in maintaining the exposure concentration which resulted in termination of the experiment approximately 4.5 hours after starting exposure on day 2 (Hor55).
When male dogs (n=2/group) and rats (n=20/group) were exposed to 0 and an actual concentration of *ca*. 5 ppm (20 mg/m^3), 6 hours/day, 5 days/week, for 6 weeks, signs observed (mainly in the dogs) included salivation, lacrimation, and rhinorrhea. Both dogs died within 26 days, while no mortality was found in the rats. In rats, slightly less body weight gain was seen in exposed animals when compared with controls. There were no effects on haematology and biochemistry parameters (obviously examined in dogs only). Upon macroscopic and microscopic examination, only effects on the lungs were found. They included pneumonia in dogs as well as severe lung pathology in rats (Hor55).

Exposure of dogs (n=2/group) and rats (n=20/group) to 0 and *ca*. 1.2 ppm (4.5 mg/m^3), 6 hours/day, 5 days/week, for 6 months, resulted in coughing, sneezing, rhinorrhea, salivation, panting respiration, occasional explosion of frothy fluid from the mouth and nose, and recurrent bouts of pneumonia (after 2 months) in dogs, and in less pronounced signs (depressed and unthrifty appearance,

blood-tinged discharge around nares and nose) observed as late as after several days or weeks in rats. Exposure did not affect body weight (gain) in rats, but weight gain was not as consistent or in amounts equivalent to controls in dogs. There was a treatment-related mortality in 1/2 dogs and 5/20 rats. Routine blood and urine analysis performed in dogs only showed high leucocyte counts and sedimentation rates (coinciding with pneumonia) and, in the dog that died, high blood urea nitrogen and low chloride values (indicative of renal shut-down and disturbed electrolyte balance). Upon postmortem examination, pulmonary oedema and bronchopneumonia (rats) and purulent bronchitis, pulmonary abscesses, distended gall and urinary bladder, discoloured oesophagus, and rectum void of fecal material (dog) were seen in the animals dying from exposure. Examination of the surviving animals showed effects on the lungs indicative of pulmonary irritation only. As in their other study (see Hor55), the authors acknowledged some occasional difficulties in maintaining the exposure concentration (Hor56).

7 Existing guidelines

The current administrative occupational exposure limit (MAC) for chlorine trifluoride in the Netherlands is 0.4 mg/m^3 (0.1 ppm), as a ceiling value.

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

8 Assessment of health hazard

There are no valid human studies in which well characterised exposure by inhalation of chlorine trifluoride was related to systemic effects.

Chlorine trifluoride is highly irritating to skin, eyes, and mucous membranes.

Data from inhalation experiments in rats and dogs indicate that the eyes and the respiratory tract are the target organs following acute and repeated exposure to chlorine trifluoride. Exposure of rats and dogs to approximately 1.2 ppm (4.5 mg/m^3), 6 hours/day, 5 days/week, for 6 months, caused mortality in one out of two dogs and 5 out of 20 rats. During exposure, signs of respiratory tract and eye irritation were seen in dogs and, less pronounced, in rats. Postmortem examinations showed lesions of the lungs only. Since only one concentration, at which mortality occurred, was tested and since there were difficulties in maintaining exposure concentrations, the committee concludes that this study is not suitable for deriving a health-based occupational exposure limit.

The committee did not find valid data on the reproduction toxicology, carcinogenicity, or mutagenicity/genotoxicity of chlorine trifluoride.

The committee concludes that the toxicological data base on chlorine trifluoride is too poor to justify recommendation of a health-based occupational exposure limit.

In view of the results of a 6-month inhalation study in rats and dogs in which mortality, respiratory tract and eye irritation were seen following exposure to 4.5 mg/m^3 (1.2 ppm), the committee concludes that the current MAC-value of 0.4 mg/m^3 (0.1 ppm), as a ceiling value, for chlorine trifluoride is too high.

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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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Dos74 Dost FN, Reed DJ, Smith VN, *et al.* Toxic properties of chlorine trifluoride. Toxicol Appl Pharmacol 1974; 27: 527-36.

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Annex

Occupational exposure limits for chlorine trifluoride 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	0.1	0.4	ceiling	administrative		SZW01
Germany						
- AGS	0.1	0.4	8 h			TRG00
	0.1	0.4	15 min			
- DFG MAK-Kom.	-	-[dc]				DFG01
Great Britain						
- HSE	0.1	0.38	15 min	OES		HSE01
Sweden	-	-				Arb00b
Denmark	0.1	0.4	ceiling			Arb00a
USA						
- ACGIH	0.1	-	ceiling	TLV		ACG01
- OSHA	0.1	0.4	ceiling	PEL		ACG00
- NIOSH	0.1	0.4	ceiling	REL		ACG00
European Union						
- SCOEL	-	-				CEC00

[a] S = skin notation, which means 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] 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