Rijksinstituut voor Volksgezondheid
en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*

Stofdocument deel A

CAS-nr: 71-55-6

1,1,1-Trichloorethaan

CH_3CCl_3

VN-nr: 2831

GEVI: 60

Synoniemen: methylchloroform, methyltrichloormethaan (Engels: 1,1,1-Trichloroethane)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m^3)**	830	830	830	830	830	830
Alarmeringsgrenswaarden	**AGW (mg/m^3)**	4.600	3.700	3.300	2.400	2.100	1.700
Levensbedreigende waarden	**LBW (mg/m^3)**	24.000	24.000	24.000	19.000	15.000	12.000

Datum vaststelling: 16-12-2010

1 mg/m^3 = 0,180 ppm; 1 ppm = 5,55 mg/m^3

Explosiegrens: LEL = 7,5 vol% ≈ 420.000 mg/m^3

Geur: zoete, stekende geur

LOA: 34.000 mg/m^3

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: moeilijk brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,5

Molecuulmassa:	133,4 g/mol
Zuurgraad:	geen data
LogKow:	2,5
Wateroplosbaarheid:	0,05 g/100 ml (niet)
Verzadigde dampdruk:	133 mbar

Overige informatie

Publieke grenswaarde: 555 mg/m^3 (8 uur)

MAK: 1100 mg/m^3

TLV-TWA: 1900 mg/m^3

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: lichte oogirritatie

VRW → AGW: tranenvloed, duizeligheid

AGW → LBW: verminderde reflexen, ataxie, bewustzijnsdaling, vertraagde ademhaling, hartritmestoornissen

Boven LBW: coma, ademstilstand, hartstilstand, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- 1,1,1-Trichloorethaan werkt irriterend op de ogen
- 1,1,1,-Trichloorethaan heeft een depressieve werking op het CZS en de ademhaling.
- Een hoge concentratie kan de gevoeligheid van het hart voor adrenaline verhogen.

Effecten bij blootstelling aan vloeistof

Huidcontact: roodheid, droge huid.

Oogcontact: tranenvloed, roodheid en pijn.

Carcinogeniteit

IARC classificatie: 3

CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

algemeen: frisse lucht, rust en arts raadplegen.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken, spoelen en wassen met water en zeep..

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken, arts raadplegen en direct spoedeisende medische hulp inzetten.

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.

Stofdocument deel B

CAS-nr: 71-55-6 **1,1,1-Trichloroethane** **CH_3CCl_3** **UN-nr: 2831**

Basis for the Dutch Intervention Values

VRW: Same point of departure as for AEGL value but using different uncertainty factors, 2h value added

AGW: 30-minute – 8-hour AEGL values are adopted; 10 minute AGW based on different point of departure; 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 16-12-2010 AEGL document: Interim, 2000

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	830	830	830	830	830	830	Slight eye irritation and dizziness in humans
AGW	4,600	3,700	3,300	2,400	2,100	1,700	Ataxia in animals (30 min - 8h) Threshold for cardiac sensitization in animals (10 min)
LBW	24,000	24,000	24,000	19,000	15,000	12,000	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: The VRW values are developed based upon results from a controlled experiment with 6 healthy male human volunteers exposed by inhalation to 450 ppm (2500 mg/m^3) 1,1,1-trichloroethane for 2 time periods of 4 hours separated by a 1.5-hour interval. Eye irritation and slight dizziness were reported by some subjects. This exposure was used as point of departure for the VRW levels. The eye irritation and slight dizziness produced by 1,1,1-trichloroethane did not increase in severity or frequency during the second 4-hour exposure period and the complaints were sporadic. Therefore, the VRW value was held constant across time. An uncertainty factor of 3 was applied to account for intraspecies differences. The AEGL-1 values were derived using an intraspecies uncertainty factor of 2 instead of 3. Among humans the Maximum Alveolar Concentration for volatile anesthetics typically varies by about 2-3 fold. Mild CNS effects like slight dizziness would be expected to occur within a similar range of variation. The VRW values are considered conservative and should be protective of the toxic effects of 1,1,1-trichloroethane. The eye irritation experienced by humans is usually characterized as “slight” even at much higher exposure concentrations as the proposed VRW values. Several chamber exposure studies using similar exposure concentrations showed similar outcomes among human subjects. Because only mild untoward effects were observed at concentrations that were 2 times the proposed value and the severity did not increase with time, this VRW value is considered appropriate.

AGW: The AGW values are based on results from an animal study in which groups of 6 rats were exposed to 0, 1500, 3000, 6000 and 12000 ppm (0, 8300, 17000, 33000 and 67000 mg/m^3) 1,1,1-trichloroethane for 4 hours. The rat EC_{50} values for ataxia were used as point of departure for deriving the AGW values. This study establishes the loss of equilibrium with the observation of EC_{50} values for ataxia in rats at 30 minutes, 1, 2, and 4 hours from the start of exposure at 6740, 6000, 4240, and 3780 ppm (37000, 33000, 24000 and 21000 mg/m^3). These values were used for the 30 minute, 1, 2, and 4 hour AGW values with an uncertainty factor of 10 applied, 3 each for intra- and inter-species variability for a total of 10. Extrapolation was made to the 8-hour time point using the equation $C^n \times t = k$ where n = 3.3, based on least squares fit of this data. The intra-species uncertainty factor of 3 is based on the previously described argument that the Maximum Alveolar Concentration for volatile anesthetics should not vary by more than a factor of 2-3 fold. The interspecies uncertainty factor of 3 is supported by the similarity of effects manifested in rodents compared to humans produced by agents that are CNS depressants. Human exposures to concentrations of up to 955 ppm (5300 mg/m^3) for 1.3 hours are well tolerated with minimal CNS effects, which support the AGW values.

The 10 minute AGW value was based on the NOAEL for cardiac sensitization of 2500 ppm (14000 mg/m^3) in dogs exposed for 10 minutes to 1,1,1-trichloroethane. Because the dog appears to be a

good model for the human heart, an interspecies uncertainty factor of 1 was applied. Because this is a conservative test, an intraspecies uncertainty factor of 3 was applied to protect sensitive individuals. The resulting 10 minute AGW value of 4700 mg/m^3 is slightly lower than the value that would have resulted from time scaling from the 30 minute AGW value (5200 mg/m^3).

LBW: The LBW values were based upon results of an animal study in which groups of 12 rats were exposed for 6 hour to 1,1,1-trichloroethane. The concentration causing no deaths in rats after 6 hour exposure, which was estimated from an exposure-concentration graph, was used to derive the LBW. The concentration-response curve crosses the X-axis between 7000 and 8000 ppm (39000 and 44000 mg/m^3). Therefore, as a conservative estimate, a value of 7000 ppm (39.000 mg/m^3) for a duration of 6 hours was used as point of departure for the derivation of LBW values. An intraspecies uncertainty factor of 3 and an interspecies uncertainty factor of 1 were applied for a total uncertainty factor of 3. The intraspecies uncertainty factor of 3 is based on the previously described argument that the Maximum Alveolar Concentration for volatile anesthetics should not vary by more than a factor of 2-3 fold. The interspecies uncertainty factor of 1 is supported by the similarity of effects manifested in rodents compared to humans produced by agents that are CNS depressants and by the observed 2 to 5-fold greater blood:air partition coefficient for 1,1,1-trichloroethane in rodents compared to humans. This principle determines the relative blood concentration for a vapor and because it is higher for rats, a higher blood concentration is achieved at lower exposure concentrations among rodents compared to humans. Time-scaling was performed using the equation $C^n \times t = k$ where n = 3, based on the rat lethality data. The 1-hour value was also used for the 10- and 30-minute values so as not to exceed the threshold for cardiac sensitization observed in a study with dogs (LOAEL: 10 minute exposure to 5000 ppm; 28000 mg/m^3).

Additional toxicological information (including relevant results of a general literature search, if any)

Studies indicate that children and particularly infants are more resistant than adults to the effects of various volatile anesthetics. The susceptibility of individuals of different ages has been extensively studied in the anesthesia literature. Minimal Alveolar Concentrations (MAC) producing lack of movement in 50% of persons exposed to that concentration show a pattern with maximal sensitivity (lowest MAC values) in newborns, pregnant women, and the elderly. The least sensitive (highest MAC values) occur in older infants, toddlers and children as compared to normal adults. The total range is 2-3 fold.

Human deaths have been reported following exposure to high concentrations of 1,1,1-trichloroethane in occupational as well as abuse situations. These deaths typically result from respiratory failure due to CNS depression or from cardiac arrhythmias following sensitization of the heart to epinephrine. Human response to 1,1,1-trichloroethane is typically characterized by eye irritation and subtle CNS effects which become measurable at levels above 450 ppm (2500 mg/m^3) at exposure durations of about 4 hours. Observable effects range from slight behavioral changes (accompanied by eye irritation in humans) at 500 ppm (2800 mg/m^3) to unconsciousness and respiratory arrest at higher concentrations (10,000-30,000 ppm, 55,000-170,000 mg/m^3). Based on the available data, a NOAEL for the threshold of subtle CNS effects is 350 ppm (900 mg/m^3) for durations up to 8 hours, the established ACGIH-TLV. Concentrations above 900 ppm (5000 mg/m^3) for periods of 70-75 minutes appear to be the threshold for loss of equilibrium concomitant with feelings of light-headedness and eye irritation. Disturbances in equilibrium occurred at 1740 ppm (9700 mg/m^3) after 5 minutes of exposure, and at levels above 2650 ppm (15,000 mg/m^3), a definite loss of equilibrium is evident after only a few minutes exposure.

Developmental toxicity, but not teratogenicity, in the form of developmental delays has been identified in rats and rabbits at concentrations that produced maternal toxicity. No developmental effects have been identified in humans. Limited epidemiological evidence on possible reproductive effects is inconclusive.

H332: Harmful if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans).

No carcinogenic risk potency (CRP) was derived.

No adequate epidemiological data on the carcinogenic

Odour and derivation of the LOA value

Odour: sweet, pungent odour.

Odour threshold: 2160 mg/m^3 [AIHA cited in AEGL TSD]

potential of this compound in humans exists. However, a chronic inhalation study in rats and mice exposed to 1500 ppm (8000 mg/m^3) revealed no evidence of any carcinogenic effect.	LOA = 11.8 * 2160 * 1.33 = 34,000 mg/m^3 (The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value) The LOA is higher than the intervention values.

***Other standards and guidelines** (1h values in mg/m^3, unless otherwise indicated)*

VRW level **830**	*AEGL-1* 1,300	*ERPG-1* 1,900		*IDLH:* 3900 (30 minutes)
AGW level **3,300**	*AEGL-2* 3,300	*ERPG-2* 3,900		
LBW level **24,000**	*AEGL-3* 23,000	*ERPG-3* 19,000		