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

Stofdocument deel A

CAS-nr: 79-01-6

Trichloorethyleen

$ClCH=CCl_2$

VN-nr: 1710

GEVI: 60

Synoniemen: trichlooretheen, tri, ethyleentrichloride (Engels: trichloroethylene)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarde	**VRW (mg/m^3)**	1.400	960	710	550	460	420
Alarmeringsgrenswaarde	**AGW (mg/m^3)**	5.300	3.400	2.500	1.800	1.500	1.300
Levensbedreigende	**LBW (mg/m^3)**	33.000	33.000	21.000	13.000	8.400	5.300

Datum vaststelling: 24-09-2009

1 mg/m^3 = 0,183 ppm; 1 ppm = 5,47 mg/m^3

Explosiegrens: LEL = 7,9 vol% ≈ 430.000 mg/m^3

Geur: oplosmiddelachtig, etherisch, zoet

LOA: 2400 mg/m^3

Fysisch-chemische eigenschappen

Uiterlijk: kleurloze vloeistof

Brand: niet brandbaar

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,3

Molecuulmassa:	131,4 g/mol
Zuurgraad:	geen data
LogKow:	Ca. 2,3
Wateroplosbaarheid:	Slecht
Verzadigde dampdruk:	77 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid

MAK: niet afgeleid

TLV-TWA: 273 mg/m^3

Zeer vluchtig

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie ogen en luchtwegen, hoesten

AGW → LBW: benauwdheid, hoofdpijn, duizeligheid, misselijkheid, braken, bewustzijnsdaling, lethargie

Boven LBW: coma, ademnood, hartritmestoornissen, sterfte

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Trichloorethyleen werkt irriterend op de ogen, huid en luchtwegen.
- Trichloorethyleen heeft een depressieve werking op het CZS.
- Het ontstaan van lever- en nierschade na blootstelling aan trichloorethyleen is beschreven.
- Bij blootstelling aan hoge concentraties kunnen mogelijk hartritmestoornissen ontstaan.

Effecten bij blootstelling aan vloeistof

Huidcontact: irritatie, roodheid, droge huid

Oogcontact: irritatie, roodheid, pijn

Carcinogeniteit

IARC classificatie: 1

CRP: 50.808 mg/m^3

Beknopte medische informatie

***Ontsmetting* damp**

algemeen: frisse lucht, rust, en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: verontreinigde kleding uittrekken en minimaal 20 min. spoelen met veel water of douchen.

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

inslikken: mond laten spoelen (uitspugen!), GEEN braken opwekken 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.

National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Stofdocument deel B

CAS-nr: 79-01-6 **Trichloroethylene** **ClCH=CCl$_2$** **VN-nr: 1710**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 24-09-2009 AEGL document: Interim, 2008

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	1400	960	710	550	460	420	Marginal CNS-effects in humans
AGW	5,300	3,400	2,500	1,800	1,500	1,300	CNS effects in humans
LBW	33,000	33,000	21,000	13,000	8,400	5,300	NOEL for mortality in mice

Derivation of the Dutch Intervention Values

VRW: The VRW derivation is based on the NOAEL of 300 ppm (1,600 mg/m^3) from a human volunteer study. Eight subjects exposed to 300 ppm for 2 hours showed no significant impairment of neurobehavioral function, with marginal CNS-depression present in only 1 out of 8 volunteers. For extrapolation across durations, a human PBPK model of Boyes et al. (2002) was used. The human model applied was derived from a model for rats. The peak concentration of trichloroethylene in blood after 2 hours of exposure to 300 ppm (1,600 mg/m^3) was first calculated and subsequently the external concentrations that would produce the same blood concentration for the other exposure durations were determined. The dose metric in this calculation is the peak of unchanged trichloroethylene in blood. Blood levels of trichloroethylene were found to correlate well with neurotoxic effects in rats after acute exposure and accordingly the latter are an acceptable dose metric. Following exposure to an external concentration of 300 ppm (1,600 mg/m^3) for 2 hours (the NOAEL), the model predicted a trichloroethylene concentration in blood of 4.78 mg/l. This value compares reasonably well to the peak blood concentrations of trichloroethylene as seen in various volunteer studies exposed to similar concentrations. Using the 4.78 mg/l target value external concentrations were calculated for the standard intervention value durations. For interindividual variation among humans an intraspecies factor of 3 is used. A higher factor is not necessary because the mechanism of action (general CNS depression) does not vary more than a factor of 2-3 within the human population.

AGW: Human data relevant for AGW endpoints are scant. The effects seen at 1,000 ppm (5,500 mg/m^3) are relatively mild effects for an AGW level. However, because of the lack of another reliable human NOAEL, the value of 1,000 ppm (5,500 mg/m^3) for 2 hours is considered the highest level without an AGW effect. At this concentration there was self-reported light-headedness, dizziness and lethargy and also a reduced performance in neurobehavioral tests (primarily the pegboard test). Following exposure to an external concentration of 1,000 ppm (5,500 mg/m^3) for 2 hours, the human PBPK model of Boyes et al. (2002) predicted a trichloroethylene concentration in blood of 18.3 mg/l. Although no human metabolism studies are available with appropriate exposure levels to support this calculated blood level, it should be noted that the level of 18.3 mg/l is a factor 5 lower than the blood level needed for anaesthesia (100 mg/l). Using 18.3 mg/l as the target value, the external concentrations were calculated for the standard intervention value durations. For interindividual variation among humans an intraspecies factor of 3 is used. A higher factor is not necessary because the mechanism of action (general CNS depression) does not vary more than a factor of 2-3 within the human population. In addition the severity of the effects is considered to be less than needed for AGW.

LBW: The lower 95% confidence levels of the LC_{05}-values (the Benchmark Concentration for the 5% response) derived from a rat study may be considered the most appropriate basis for deriving the LBW. The calculations with the above mentioned PBPK-model (according to the above mentioned procedure) generated values that are considered to be too low compared to the available human evidence. Therefore, an alternative approach was developed. This starts with the NOAEL for mortality observed in mice: 4,600 ppm (25,000 mg/m^3) for 4 hours. Although this concentration is probably nominal, it has been shown in many studies that actual concentrations are close to nominal levels. Therefore, the level of 4600 ppm (25000 mg/m^3) can be used. For interindividual variation among humans an intraspecies factor of 3 is used. A value of n= 1.511 is derived from the above mentioned rat study by probit analysis. Compared to rats, humans need much higher external concentrations for reaching a certain concentration in blood. Therefore, an interspecies extrapolation factor is not considered necessary.

Finally, in LBW derivation it is also taken into account that cardiac arrhythmias may occur in humans at levels of 10,000 ppm (55,000 mg/m^3) and higher and that 10,000 ppm (55,000 mg/m^3) will quickly result in complete

narcosis. Therefore, this level should not be exceeded. In addition, general anaesthesia may be associated with vomiting, which is another risk factor, especially in the absence of medical assistance. Therefore, the 10 min LBW is set equal to the 30 minute value.

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

The effects on the CNS are similar to those of other solvents. This is possibly a pure physical interaction of these solvents with the membranes of the cells in the CNS. In humans it is reasonably expected that pulmonary uptake of trichloroethylene following inhalation is rapid. Based on the effects of various volatile anaesthetics maximal sensitivity is expected in newborns (particularly prematures), pregnant women, and the elderly. The least sensitive are older infants, toddlers and children compared to normal adults. The total variation, however, is not more than 2-3 fold.

No human reproductive studies are available. Developmental toxicity was examined in several epidemiological studies (chronic exposure) in which the association between both paternal and maternal exposure to trichloroethylene and spontaneous abortions was studied. Paternal exposure to trichloroethylene was not found to be a risk factor for spontaneous abortions. The number of cases were too small to allow an analysis for the association of maternal exposure to trichloroethylene and abortions.

Trichloroethylene was formerly used on a limited scale as a medical anaesthetic and analgesic. 5,000-15,000 ppm (27,000 – 82,000 mg/m^3) for producing light anaesthesia and 3,500-5,000 ppm (19,000 – 27,000 mg/m^3) for analgesia. Simultaneous exposure to alcohol and trichloroethylene gave significant effects on performance in behavioural tests, compared to those observed with after exposure to one of these substances alone (possibly due to inhibition of metabolism of tetrachloroethylene.

H315: Causes skin irritation; H319: Causes serious eye irritation; H336: May cause drowsiness or dizziness; H341: Suspected of causing genetic effects; H350: May cause cancer.

Carcinogenicity and derivation of the CRP value

IARC classification: 1 (Carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):
10^{-4} risk level after inhalation: 0.232 mg/m^3 [AEGL]
CRP = (10^{-4} risk level * average life span in hours)/DRCF = (0.232 * 613,200) /2.8 = 50,808 mg/m^3

IARC concluded that there is sufficient evidence in humans for the carcinogenicity of trichloroethylene. Trichloroethylene causes cancer of the kidney. A positive association has been observed between exposure to trichloroethylene and non-Hodgkin lymphoma and liver cancer.
IARC reviewed a large number of occupational epidemiology studies. Two conducted meta-analyses based on a largely similar set of case–control and cohort studies of cancer of the kidney reported statistically significant meta-relative risks (meta-RR) for cancer of the kidney and exposure to trichloroethylene of 1.3 and 1.4. One meta-analysis reported a higher meta-RR of 1.6 (95% CI, 1.3–2.0) for groups with a higher exposure. A meta-analysis of cohort and case–control studies of non-hodgkin lymphoma reported statistically significant meta-RRs of 1.2 (95% CI,1.1–1.4) for non-Hodgkin lymphoma and any exposure to trichloroethylene and 1.4 (95% CI, 1.1–1.8) for higher exposure.

Odour and derivation of the LOA value

Odour: solvent like, ether-like, sweet

OT_{50}: 28 ppm (153 mg/m^3) [EPA]
LOA = 11.8 * OT_{50} * 1.33 = 2401 mg/m^3 (439 ppm)

(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 lies above the VRW and AGW, but is lower than the LBW levels at the time points 10, 30 and 60 minutes.

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

VRW level **710**	*AEGL-1* 710	*ERPG-1* 550		IDLH: 5,500 (10 minutes)
AGW level **2,500**	*AEGL-2* 2,500	*ERPG-2* 2,700		
LBW level **21,000**	*AEGL-3* 21,000	*ERPG-3* 27,300		