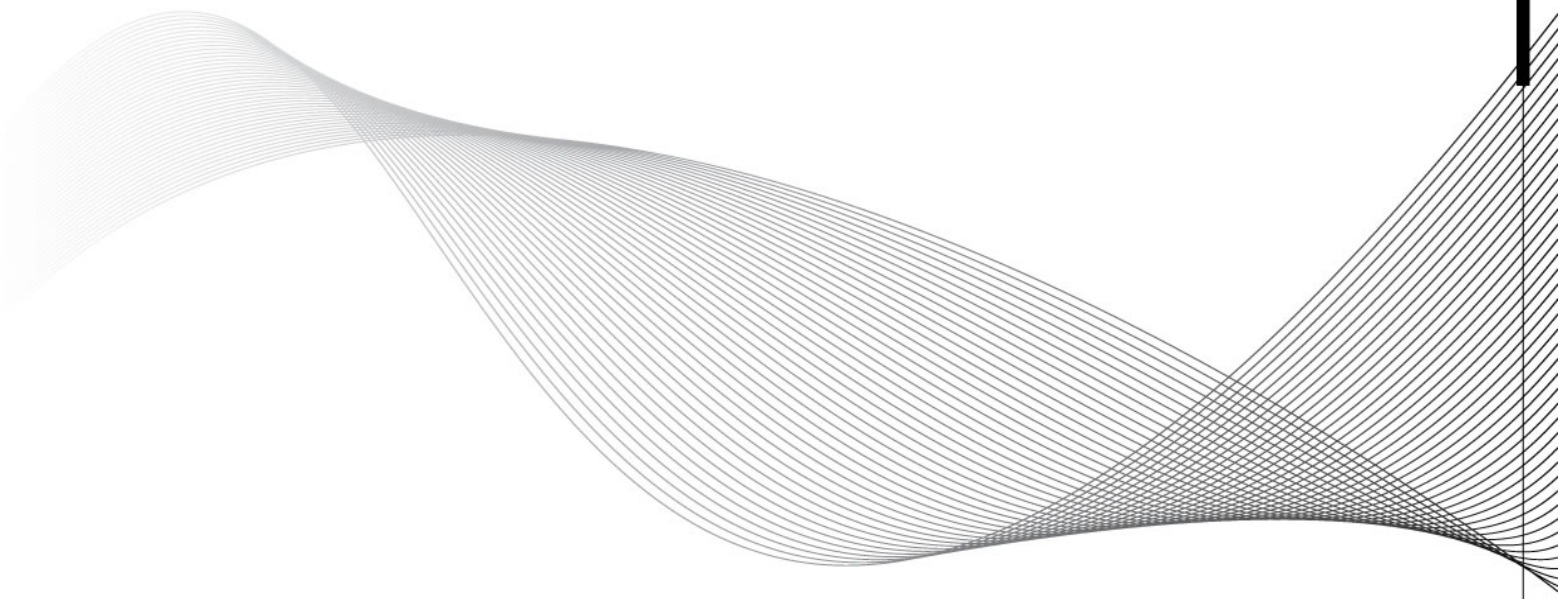
Social Europe



Recommendation from the Scientific Committee on Occupational Exposure Limits for trichloroacetic acid

SCOEL/SUM/77

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European Commission

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8 hour TWA:	no recommendation made
STEL (15 mins):	-
Additional classification:	-

The SCOEL considered that there is no adequate basis for deriving limit values.

Substance:

Trichloroacetic acid $Cl_3C\text{-}COOH$

Synonyms : TCA; trichloracetic acid; aceto-caustin; 1,1,1-trichloroethanoic acid; Amchem Grass Killer; Konesta
EINECS N° : 200-927-2
EEC N° : 607-004-00-7 Classification : C; R35
CAS N° : 76-03-9
MWt : 163.38
Conversion factor (20°C, 101 kPa) : 6.80 mg/m^3 = 1 ppm

1. Occurrence/use

TCA is a white deliquescent crystalline substance, with a slight characteristic odour. It has a MPt of 58°C, a BPt of 198°C and a vapour pressure of 0.13 kPa at 51°C. The vapour density is 5.6 times that of air.

TCA as its sodium salt is used as a herbicide, a chemical intermediate, a colour reagent in thinlayer and paper chromatography and as a laboratory reagent The production rate in the EU is in the region 5000 to 10000 tonnes per annum. TCA also occurs as a by-product of chlorination of drinking water (IARC, Monograph, 1995)

Trichloroacetic acid is a world-wide environmental polluntant (Ahlers et al. 2003).

2. Health Significance

TCA is absorbed after oral administration; no data are available on absorption following inhalation. Significant absorption through the skin does not appear to occur (Resnik and Lewis, 1973). TCA is known to undergo appreciable biotransformation but the metabolic pathways have not been elucidated. Metabolites identified in animal studies include chloroform, CO_2 and TCA glucuronide. The major route of excretion (60-70% of the administered dose, about 60% of which was unchanged TCA) is via the urine (Muller *et al.,* 1974). The major urinary products in mice and rats after administration of TCA by gavage are TCA itself and oxalic and thiodiacetic acids (Larson & Bull, 1992).TCA is moderately toxic to experimental animals on acute oral administration and results in lethality due to the acid load (Davis, 1986). Repeated administration by gavage or in the drinking water induced peroxisome proliferation in rats and mice (Elcombe, 1985). Induction was more marked in mice than in rats (De Angelo *et al*., 1989). Chronic administration of TCA in the drinking water (about 400 mg/kg body weight per day for 61 weeks) was found to result in hepatocarcinomas in B6C3F1 mice (Herren-Freund *et al.,* 1987; De Angelo and McMillan, 1988). TCA (500 mg/kg bw) in 10 daily oral doses induced in mice a small but significant elevation in hepatocyte cytoplasmic peroxisomal volume. Slight the liver hyperplasia measured as incorporation of [3H}thymidine in hepatic DNA and as the frequency of hepatocytes in S-phase was also seen (Styles et al. 1991). However, as rodents are known to be particularly sensitive to induction of hepatocarcinoma by peroxisome proliferating agents, the relevance of these observations for establishing occupational exposure limits are not clear. Male Fischer 344/N rats exposed for 104 weeks to 0.05, 0.5, or 5 g/L TCA in drinking water did not show evidence of hepatic neoplasia and, moreover, the incidence of tumours at other sites was not increased in comparison with controls. The NOEL in this study was 364 mg/kg/d (DeAngelo et al., 1997).

The developmental effects of TCA were evaluated in the pregnant Long-Evans rat. Animals were dosed by gavage on gestation days 6-15 with 0, 330, 800, 1,200, or 1,800 mg/kg/day. Soft tissue malformations were mainly observed in the cardiovascular system ranging from 9% at the low dose to 97% at the high dose. TCA was considered to be developmentally toxic (a specific cardiac teratogen) in the pregnant rat at doses of 330 mg/kg and above (Smith et al., 1989; Johnson et al., 1998).

TCA was not mutagenic in bacterial assays (Andersen *et al.,* 1972). High concentrations produced a small, but significant, increase in sister chromatid exchanges in Chinese hamster ovary cells (De Angelo and McMillan, 1988). TCA has been shown to induce single strand breaks in hepatic DNA 4 h after oral administration of 0.98 mg/kg in mice and 98 mg/kg in rats (Nelson and Bull, 1988). Increases in chromosomal aberrations and

micronuclei in bone marrow cells, and in sperm-head abnormalities were seen in mice administered TCA at 125, 250 and 500 mg/kg (Bhunya and Behera, 1987). It is considered that the *in vivo* cytogenetic effects of TCA at high doses may be due to cytotoxic effects rather than to direct action on DNA.

There are no available data relating to inhalation of TCA in animals or humans.

Information on the toxic effects of TCA in humans is extremely limited. TCA has been used as a peeling agent for exfoliation in dermatology. Bacause it is strongly corrosive, TCA has been used in medicine to remove warts, to treat extensive actinic keratosis of the face and scalp (Brodland & Roenigh, 1988; Boothby et al., 1990; Kling, 1992; Wang et al., 1992). The degree of the reaction is dependent upon the concentration: 20% provokes a mild stinging or light burning sensation, concentrations of 50 - 85 % have been used therapeutically (Resnik and Lewis, 1973). TCA has also been used for treatment of corneal diseases and, although data on eye irritation are not available, it would be expected to be corrosive or irritant on eye contact. Data relating to skin or eye irritation of TCA vapour or aerosol are not available.

Recommendation

TCA is corrosive by direct skin or eye contact with concentrated aqueous solutions. There is no reliable dose-response information for sensory irritation. Moreover, the available data do not permit identification of the critical effect likely to result from exposure to atmospheric TCA. In essence, there are only very limited animal data available, , from which a NOAEL can be derived. Therefore it is not possible to establish a health based OEL.

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