Recommendation from Scientific Expert Group

on Occupational Exposure Limits

for 1,1,1-Trichloroethane

8 hour TWA	:	100 ppm (555 mg/m^3)
STEL (15 mins)	:	200 ppm (1110 mg/m^3)
Additional classification	:	-

Substance:

1,1,1-Trichloroethane CH_3CCl_3

Synonyms	:	Methyl chloroform, methyl trichloromethane
EINECS N°	:	200-756-3
EEC N°	:	602-013-00-2 Classification : Xn; R20
CAS N°	:	71-55-6
MWt	:	133.40

Conversion factor (20°C, 101 kPa) : 5.55 mg/m^3 = 1 ppm

Occurrence/use:

1,1,1-Trichloroethane is a colourless volatile liquid, with a chloroform-like odour. It has a MPt of -30°C, a BPt of 74°C and a vapour pressure of 13.3 kPa at 20°C. It has a vapour density of 4.6 times that of air and is explosive in the range of 8.0-10.5% in air. The odour threshold is about 100 ppm (555 mg/m^3).

1,1,1-Trichloroethane is a very efficient solvent and is used predominantly for cold cleaning and vapour degreasing of metal and machine parts. It is also frequently used as a solvent or thinner in many different formulations. The production rate in the EEC was in excess of 100,000 tonnes per annum in the 1980's but, as it is an ozone-depleting agent covered by international agreements, its production is scheduled to cease in the near future. Commercially available technical and solvent grades of 1,1,1-trichloroethane contain 3-8% stabilisers to prevent generation of hydrochloric acid.

Health Significance:

1,1,1-Trichloroethane is rapidly absorbed through the lungs and gastrointestinal tract and to a lesser extent through the skin (Stewart, 1968). Metabolism to trichloroacetic acid is limited and 95% or more of trichloroethane is exhaled unchanged (Hake *et al*, 1960).

Trichloroethane is less hepatotoxic than most other organochlorine solvents, and the critical effect in humans is adverse effects on the CNS. In an early study, exposure of six volunteers to mean trichloroethane levels of 450 ppm (2498 mg/m^3) for two periods of 4h, resulted in dizziness and excitability during the first 30 mins, and mild eye irritation was noted (Salvini *et al.,* 1971). No significant effect was seen in performance of behavioural tests. In contrast, exposure of 12 males to levels of trichloroethane increasing from 250 ppm (1388 mg/m^3) to 550 ppm (2775 mg/m^3) for subsequent periods of 30 mins, resulted in reduced perceptual speed and reduced reaction time at 350 ppm (1394 mg/m^3) (Gamberale and Hultengren, 1973). A NOEL of 250 ppm (1388 mg/m^3) was determined. More recently, studies with volunteers exposed to concentrations of 175 ppm (971 mg/m^3) or 350 ppm (1943 mg/m^3) for 3.5h demonstrated minor behavioural effects, these effects being observed after 30 minutes of exposure (MacKay *et al*, 1987). A NOAEL has not been determined.

A study indicating neurotoxicity in gerbils exposed to 70 ppm (389 mg/m^3) for 3 months (Karlsson *et al*, 1987) was not considered to be reliable as a basis for proposing limit values, because gerbils may be extremely sensitive to this effect. In a recent study, male and female Fischer 344 rats were exposed to 1,1,1-trichloroethane at 200, 630 and 2000 ppm (1110, 3497 and 11100 mg/m^3), 6h/d, 5d/w for 13 weeks. Tests for the functional integrity of the nervous system and histopathological examination revealed no treatment-related effects except for a slightly lower forelimb grip performance in the high exposure group (Mattson *et al.*, 1993).

In a developmental neurotoxicity study, rats were administered 1,1,1-trichloroethane by gavage at 0, 75, 250 and 750 mg/kg/day from day 6 of gestation to day 10 of lactation, and the offspring were observed until 2-3 months of age. No treatment related effects were seen in motor activity, a functional observational battery (FOB), neuropathology, brain measurements, or short-term memory, learning or performance (Maurissen *et al.*, 1993).

Trichloroethane appears to be negative in mutagenicity assays (de Serres and Ashby, 1981; Quast *et al*, 1978; Salamone *et al*, 1981) and gave no evidence for carcinogenicity in rats or mice exposed at 1,500 ppm (8325 mg/m^3) for 2 years (Quast *et al*, 1988).

Recommendation:

The study of MacKay *et al* (1987), indicating behavioural effects in human volunteers exposed to trichloroethane at 175 ppm (971 mg/m^3), was considered to be the best available basis for proposing occupational exposure limits. An uncertainty factor of 2 was considered to be sufficient in view of the extremely mild nature of the CNS effects. The recommended 8-hour TWA is 100 ppm (555 mg/m^3). A STEL (15 mins) of 200 ppm (1110 mg/m^3) was proposed to limit peaks in exposure that could result in eye irritation and to prevent accumulation of 1,1,1-trichloroethane in the blood to neurotoxic levels.

No "skin" notation was considered to be necessary.

At the levels recommended, no measurement difficulties are foreseen.

Key Bibliography:

Gamberale, F. and Hultengren, (1973). Methylchloroform exposure II. Psychophysiological functions. Scand. J. Work. Environ. Health, 10, 82-92.

Hake, C. L., Waggoner, T.B., Robertson, D.N. and Rowe, V.K. (1960). The metabolism of 1,1,1-trichloroethane by the rat. Arch. Environ. health 1, 183-194.

Jensen, A.A. (1991). Criteria document for occupational exposure limit values: 1,1,1- trichloroethane.

Karlsson, J.E., Rosengren, L.E., Kjellstrand, P. and Hagild, K.G. (1987). Effect of low dose inhalation of three chlorinated aliphatic solvents on DNA in gerbil brain. Scand. J. Work. Environ. Health 13, 453-458.

MacKay, C.J., Campbell, L., Samuel, A.M., Alderman, K.J., Idzikowski, C., Wilson, H.K. and Gompertz, D. (1987). Behavioural changes during exposure to 1,1,1-trichloroethane: time course and relationship to blood solvent levels. Am. J. Ind. Med. 11, 223-239.

Mattson, J.L., Albee, R.R., Lomax, L.G., Beckman, M.J. and Spencer, P.J. (1993). Neurotoxicologic examination of rats exposed to 1,1,1-trichloroethane vapor for 13 weeks. Neurotoxicology and Teratology 15, 313-326.

Maurissen, J. P. J., Shankar, M. R., Zielke, G. J., Spencer, P. J., Breslin, W. J., Crissman, J. W. and Kirk, H. D. (1993). Examination of rats for developmental neurotoxicological effects from maternal exposure to 1,1,1-trichloroethane. Report, Dow Chemical Co., Midland, Michigan.

Quast, J.F., Rampy, L.W., Balmer, M.F., Leong, B.D.J. and Gehring, P.J. (1978). Toxicological and carcinogenic evaluation of a 1,1,1-trichloroethane formulation by chronic inhalation in rats. Report, Dow Chemical Co., Midland, Michigan.

Quast, J.F., Calhoun, L.L. and Frauson, L.E. (1988). 1,1,1-Trichloroethane formulation: a chronic inhalation toxicity and oncogenicity study in Fischer 344 rats and B6C3F1 mice. Fund. Appl. Tox. 11, 611-625.

Salamone, M.F., Heddle, J.A. and Katz, M. (1981). Mutagenic activity of 41 compound in the *in vivo* micronucleus assay. Prog. Mutat. Res. 1, 686-697.

Salvini, M., Binaschi, S. and Riva, M. (1971). Evaluation of the psychophysiological functions in humans exposed to the "threshold limit value" of 1,1,1-trichloroethane. Br. J. Ind. Med. 28, 286-292.

de Serres, F.J. and Ashby, J. (1981) eds. Evaluation of short term test for carcinogens. Report of the international collaborative study. Prog. Mutat. Res. 1.

Stewart, R.D. (1968). The toxicology of 1,1,1-trichloroethane. Ann. Occup. Hyg. 11, 71-79.