

Recommendation from the Scientific Expert Group on Occupational Exposure Limits for 1,1-Dichloroethane

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8 hour TWA	:	100 ppm (412 mg/m ³)
STEL (15 mins)	:	-
Additional classification	:	"skin"

<u>Substance:</u>

1,1-Dichloroethane

CH_3 - $CHCl_2$

Synonyms	:	ethylidene	chloride;	ethylidene	dichloride;
methyldichlorometh	ane				
EINECS N°	:	200-863-5			
EEC N° :	602-0	11-00-1	Classification : F;	Xn; R22 X	Ki; R36/37
CAS N°	:	75-34-3			
MWt	:	98.97			
Conversion f	actor (2	0°C, 101 kPa)	: 4.12 mg/	m ³ = 1 ppm	

1. Occurrence/use

1,1-Dichloroethane is a colourless liquid with a strong odour. It has a MPt of -97 °C, a BPt of 57 °C and a vapour pressure of 24.3 kPa at 20°C. The vapour density is 3.4 times that of air and it is explosive in the range 5.5 - 11.4% in air.

1,1-Dichloroethane is used as a solvent and as a chemical intermediate in production of 1,1,1-trichloroethane. It was previously used as a pesticide and as an anaesthetic. The production rate is decreasing as 1,1,1-trichloroethane is being phased out.

2. Health Significance

Little is known of the toxicokinetics of 1,1-dichloroethane. The log $P_{O/W}$ of 1,2-dichloroethane, which has a skin notation (log $P_{O/W} = 1.5$; Banerjee *et al.*, 1980) and 1,1-dichloroethane (log $P_{O/W} = 1.9$) are comparatively similar. Moreover, a high skin absorption has been calculated for 1,1-dichloroethane (Fiserova-Bergerova *et al.*, 1990). Metabolism results in dechlorination and formation of conjugates that are excreted in the urine. A significant proportion of inhaled 1,1-dichloroethane is exhaled unchanged.

The acute toxicity of 1,1-dichloroethane is low, with reported 8h-LC50 values in mice and rats of 17,300 ppm (71,276 mg/m³) for 2 hours and 16,000 ppm (65,900 mg/m³) for 8 hours, respectively (Henschler, 1970).

Exposure of rats, guinea pigs, rabbits and cats to atmospheres of 500 ppm (2060 mg/m³), 6 h/d, 5 d/w for 13 weeks, resulted in no overt adverse effects (Hofmann *et al.*, 1971).

Subsequent exposure of the same groups of animals to 1000 ppm (4120 mg/m³) for an additional 13 weeks was tolerated by rats, guinea pigs and rabbits. In cats, a decrease in body weight gain and macroscopic and microscopic evidence of kidney damage were observed. This was attributed to biotransformation of dichloroethane to oxalic acid, resulting in formation of calcium oxalate crystals in the kidney tubules (Hofmann *et al.*, 1971). In a study conducted by Dow Chemical (1971) no evidence of gross or haematological or histological changes were seen in rats, guinea pigs, rabbits and dogs

exposed to 500 and 1000 ppm (2060 and 4120 mg/m³), 7 h/d, 5 d/w for 6 months.

1,1-Dichloroethane was found to be mutagenic in the Ames test modified for volatile substances (Riccio *et al.*, 1983; Milman *et al.*, 1988) whereas the standard Ames assay and tests with *Asp. nidulans* gave a negative results (Simmons *et al.*, 1977; Crebelli *et al.*, 1988). DNA-repair was induced in hepatocytes isolated from rats and mice (Milman *et al.*, 1988; Williams *et al.*, 1989). Microsomes from liver, lung and stomach of rats and mice catalyse the formation of DNA-adducts *in vitro* and after i.p. application of 1,1-dichloroethane to rats and mice DNA-adducts were detected in liver, lung and stomach (Colacci *et al.*, 1985). DNA-fragmentation was not detected in livers of BALB/c-mice after i.p. application (Taningher *et al.*, 1991).

1,1-Dichloroethane did not increase the transformation of BALB/c-3T3 cells (Tu *et al.*, 1985; Milman *et al.*, 1988) but enhanced the transformation rate induced by SA7-adenovirus in SHE cells (Hatch *et al.*, 1983). In a short-term rat liver foci assay, 1,1-dichloroethane did not induce GGT-foci but enhanced the foci initiated by diethylnitrosamine (Milman *et al.*, 1988).

Gavage carcinogenicity studies have been performed in both rats and mice (NCI, 1978; Weisburger, 1977). The data are not considered to be adequate to allow the carcinogenicity of 1,1-dichloroethane to be evaluated.

The data on mutagenicity and carcinogenicity are not considered to be adequate to draw a conclusion on these toxicological endpoints.

1,1-Dichloroethane has been shown to be embryotoxic only at exposure levels in excess of those necessary to cause maternal toxicity (Schwetz *et al.*, 1974).

There are no human data available that are relevant for establishing occupational exposure levels.

Recommendation

The study of Hofmann et al. (1971), indicating a NOAEL of 500 ppm (2060 mg/m³) for kidney damage in animals, was considered to be the best available basis for proposing occupational exposure limits. In view of the absence of human data, an uncertainty factor of 5 was considered appropriate. The recommended 8-hour TWA is 100 ppm (412 mg/m³). No STEL was considered to be necessary.

A "skin" notation was also recommended as percutaneous absorption is likely to significantly increase the total body burden.

At the levels recommended, no measurement difficulties are foreseen.

Key Bibliography

- Banerjee, S., Yalkowsky, S.H. and Valvani, S.C. (1980) Water solubility and octanol-water partition coefficient of organic: limitations of the solubility-partition coefficient correlation. Environ. Sci. Technol. <u>14</u>, 1227-1229.
- Basilico, S. and Garlanda, T. (1993). Occupational Exposure Limits Criteria Document for 1,1-Dichloroethane, EUR 15960 EN.
- Colacci, A., Arfellini, G., Mazzullo, M., Prodi, G., and Grilli, S. (1985) Genotoxicity of 1,1-Dichloroethane. Res. Comm. Chem. Pathol. Pharmacol. 2, 243-245.
- Crebelli, R., Benigni, R., Franekic, J., Conti, G., Conti, L., and Carere, A. (1988) Induction of chromosome malsegregation by halogenated organic solvents in Aspergillus nidulans: unspecific or specific mechanism? Mutat. Res. 210, 401-411.
- Dow Chemical (1971). Unpublished data: Biochemical Research Laboratory Dow Chemical Co, Michigan, as cited in American Industrial Hygiene Association Hygienic Guides 1,1-dichloroethane, Am. Ind. Hyg. Ass. J. 32, 64-70.
- Fiserova-Bergerova, V., Thomas Pierce, J. And Droz, P. O. (1990). Dermal absorption potential of industrial chemicals: criteria for skin notation. Am. J. Ind. Med. 17, 617-635.
- Hatch, G. G., Mamay, P. D., Ayer, M. L., Casto, B. C. and Nesnow, S. (1983). Chemical enhancement of viral transformation in Syrian hamster embryo cells by gaseous and volatile chlorinated methanes and ethanes. Cancer Res. 43, 1945-1950.
- Henschler, D. (1970). "Toxikologisch-Arbeitsmedizinische Bengründungen von MAK-Werten", Verlag Chemie.
- Hofmann, H., Birnstiel, H. and Jobst, P. (1971). Zur Inhalationstoxizität von 1,1- und 1,2-Dichloräthan. Arch. Toxicol. 27, 248-265.
- Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C., and Tyson, C.A. (1988) Rat liver foci and in vitro assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. Ann. NY. Acad. Sci. 534, 521-530.
- NCI (1978). National Cancer Index, Bioassay for 1,1-dichloroethane for possible carcinogenicity. Vol 66, DHEW publ. no. (NHI) 78-1316 [abstract]
- Riccio, E., Griffin, A., Mortelmans, K., Milman, HA. (1983) A comparative mutagenicity study of volatile halogenated hydrocarbons using different metabolic activation systems. Environ Mutagen 5, 472.
- Schwetz, B. A., Leong, B. K. J. and Gehring, P. J. (1974). Embryo and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in rats. Toxicol. Appl. Pharmacol. 28, 452-464.
- Simmons, V. F., Kauhanen, K and Tardiff, R. G. (1977). Mutagenic activity of chemicals identified in drinking water. In "Progress in Genetic Toxicology" (eds D. Scott, B. A. Bridges and F. H. Sobels). Elsevier/North Holland Biomedical Press, pp 249-258.

- Taningher, M., Parodi, S., Grilli, S., Colacci, A., Mazzullo, M., Bordone, R., and Santi, L. (1991) Lack of correlation between alkaline DNA fragmentation and DNA covalent binding induced by polychloroethanes after in vivo administration. Problems related to the assessment of a carcinogenic hazard. Cancer Detection and Prevention 15, 35-39.
- Tu, A.S., Murray, A., Hatch, K.M., Sivak, A., and Milman, H.A. (1985) In vitro transformation of BALB/c-3T3 cells by chlorinated ethanes and ethylenes. Cancer Lett. 28, 85-92.
- Weisburger, E. (1977). Carcinogenicity studies on halogenated hydrocarbons. Environ. Health Perspect. 21, 7-16.
- Williams, G.M., Mori, H., and McQueen, C.A. (1989) Structure- activity relationships in the rat hepatocyte DNA-Repair test for 300 chemicals. Mutat. Res. 221, 263-268.