Recommendation from the Scientific Expert Group

on Occupational Exposure Limits

for Chloroform

8 hour TWA	:	2 ppm (10 mg/m^3)
STEL (15 mins)	:	-
Additional classification	:	"skin"

Substance:

Chloroform $CHCl_3$

Synonyms	:	Trichloromethane; methyl trichloride; Freon 20		
EINECS N°	:	200-663-8		
EEC N°	:	602-006-00-4	Classification :	Xn; R22-48/20/22 Xi; R38 Carc. Cat. 3: R40
CAS N°	:	67-66-3		
MWt	:	119.38		

Conversion factor (20°C, 101kPa) : 4.97 mg/m^3 = 1 ppm

Occurrence/use:

Chloroform is a colourless, volatile, non-flammable liquid with a characteristic sweet odour. It has a MPt of -63°C, a BPt of 62°C and a vapour pressure of 21 kPa at 20°C. It has a vapour density of 4.1 times that of air. The odour threshold is about 20 ppm (about 100 mg/m^3).

Chloroform is usually supplied containing a stabiliser such as ethanol. Traces of chloroform may occur naturally and also arise from the chlorination of water supplies and sewage. It is used as a raw material in the production of chlorodifluoromethane and as an industrial process solvent and in laboratory work. The production rate in the EEC is in excess of 10,000 tonnes per annum.

Health Significance:

Chloroform is well-absorbed by inhalation, orally and percutaneously (Tsurata, 1975; Corley *et al., 1990*). The principle route of elimination is by exhalation. Carbon dioxide is the main metabolite although phosgene may also be formed.

Chloroform is of low to moderate toxicity, with death occurring immediately by respiratory depression during narcosis, or delayed due to hepatotoxicity. Liquid chloroform is highly irritant but irritancy has not been reported for the vapour.

The critical effects of chloroform occur in the liver and kidneys of experimental animals following repeated exposure. Exposure of rats, rabbits and guinea pigs to 25 ppm (124 mg/m^3) for 7h/d, 5d/w for 6 months resulted in histopathological changes in the livers and kidneys (Torkelson *et al*, 1976). These changes were not evident in rats allowed a 6-week recovery period. Exposure to 25 ppm (124 mg/m^3) for 4 h/d for 6 months did not produce such effects in the livers and kidneys of rats. The results of the 7 h/d exposure study are considered to provide a more appropriate basis for deriving an 8-hour TWA than the results of the 4 h/d exposure study.

Chloroform is carcinogenic by oral administration to rats and mice, producing liver and kidney tumours in a sex- and strain- dependent manner (Page and Saffioti, 1976; Jorgenson *et al*, 1985). Inhalation carcinogenicity studies have not been performed. The genotoxic potential has been investigated in a number of studies, both *in vitro* and *in vivo*. The results have generally been negative, although there is some indication of clastogenic activity (Fujie *et al*, 1990). In view of the site, sex and strain specificity of the tumourigenicity, and the negative responses in most genotoxicity assays, the carcinogenicity of chloroform is generally assumed to occur via a non-genotoxic mechanism dependent upon chronic tissue damage.

Reproductive studies in animals have shown that fetal abnormalities occurred in rats (acaudia, short tail, imperforate anus) and in mice (cleft palate) following inhalation exposure of the dam to 100 ppm (497 mg/m^3), and anomalies in rats (delayed ossification and wavy ribs) at 30 ppm (150 mg/m^3) for 7h/d during gestation (Schwetz, 1974). In an unpublished study, female rats were exposed to chloroform in concentrations of 3, 10 or 30 ppm (15, 50 or 150 mg/m^3) for 7h/day between day 7 and day 16 of pregnancy (Baeder and Hofmann, 1991). At 10 and 30 ppm (50 and 150 mg/m^3), slight reductions in maternal food consumption and body wieght gain were recorded. In the 30 ppm (150 mg/m^3) group, the body weight of fetuses was slightly but significantly decreased and delayed skeletal ossification of the cranial bones was observed. No exposure related effects were reported in the fetuses in the 10 ppm (50 mg/m^3) exposure group, and no effects were seen in either dams or fetuses in the 3 ppm (15 mg/m^3) exposure group.

Studies of occupational exposure to chloroform have indicated that concentrations of about 20 - 80 ppm (about 100 - 400 mg/m^3) lead to a variety of minor complaints including headache, lassitude, depression and digestive disturbances (Challen *et al*, 1958). At concentrations from 205 ppm (1019 mg/m^3), similar symptoms plus increased incidences of hepatomegaly have been reported (Bomski *et al*, 1967). Outbreaks of toxic jaundice in workers occupationally exposed to chloroform have been reported by Phoon (1975, 1983). However, due to the sampling techniques used the levels of exposure reported in these studies are not reliable for deriving a 8-hour TWA. There is no information available on the carcinogenic or genotoxic potential of chloroform in man.

Recommendation:

In view of the lack of evidence for genotoxicity and of the specificity of carcinogenicity, it is considered that the tumours observed in chloroform-treated animals are associated with chronic tissue damage. Thus chloroform is not likely to be carcinogenic under occupational exposure conditions providing protection from toxicity. The study of Torkelson *et al* (1976), establishing a LOAEL of 25 ppm (124 mg/m^3) for liver and kidney damage in animals exposed for 7 h/d, 5 d/w for 6 months, was considered to be the best available basis for proposing occupational exposure limits. An uncertainty factor of 10 was considered appropriate to allow for the absence of a NOAEL in this 7 h/d exposure study, and for the interindividual and interspecies differences in chloroform toxicity, which are due to different rates of metabolic activation. Taking into account the preferred value approach, the recommended 8-hour TWA is 2 ppm (10 mg/m^3), which is considered low enough to avoid reproductive effects. A STEL is not proposed, but good control of excursions is necessary to avoid narcotic and other effects.

A "skin" notation was recommended as dermal absorption could contribute substantially to the total body burden.

At the levels recommended, no measurement difficulties are foreseen.

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