HALOGENATED SOLVENT INDUSTRY ALLIANCE • (914) 725-1492
1075 CENTRAL PARK AVENUE • SCARSDALE, NEW YORK 10583

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TO: APPLICATIONS COUNCIL
HEALTH DATA COMMUNICATIONS COMMITTEE
HEALTH AND SCIENCE COMMITTEE

CEFIC METHYL CHLOROFORM DOCUMENT

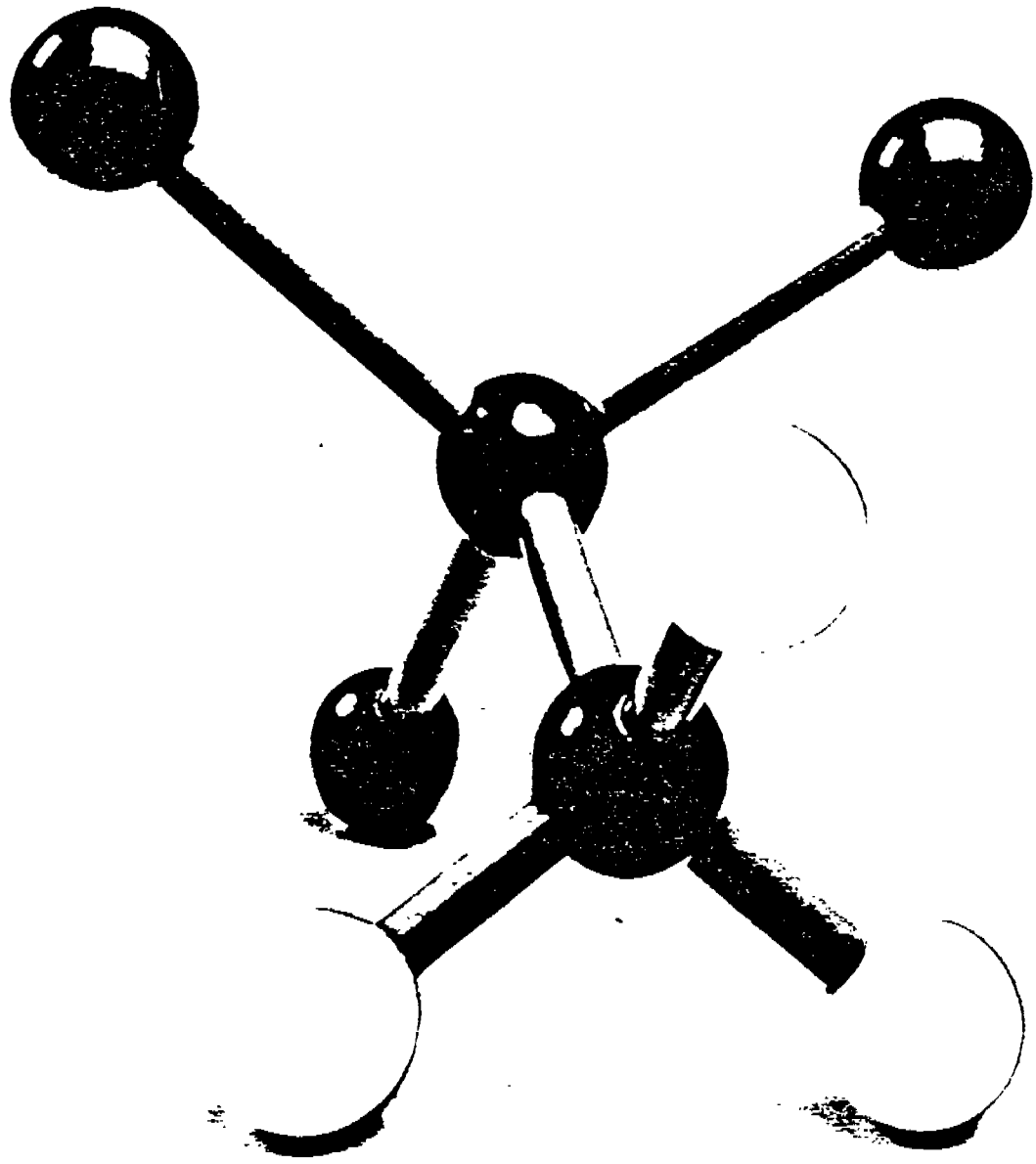
Attached is the summary of methyl chloroform information prepared by Conseil Europeen des Federations de l'Industrie Chimique (CEFIC). Please note that although the title suggests it is a use-oriented document, much health effects information is included.

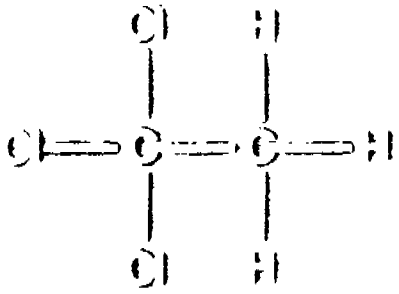
Paul A. Cammer
Executive Director

Attachment

SL 037314

CEFIC B.I.T. Solvants Chlorés





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1.1.1-Trichloroethane in metal cleaning and other industrial applications

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1,1,1 TRICHLOROETHANE

in Metal Cleaning and Other Industrial Applications

1984

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CONTENTS

This paper has been prepared by the manufacturers of 1,1,1 trichloroethane in Europe.

SUMMARY

1,1,1-trichloroethane (or methyl chloroform) is a non-flammable solvent, mainly used for metal cleaning and as a solvent or co-solvent in aerosols, adhesives, surface coatings and many similar formulations.

The West European consumption of 1,1,1-trichloroethane in 1983 was estimated at 156 kt. The high growth rate in the 60's and early 70's was largely dependent on the replacement of Tri and Per. There has been no growth since 1979 and future growth is expected to be limited to 1-2% per year maximum.

The bulk of 1,1,1-trichloroethane in the environment is to be found in the troposphere (lower atmosphere). Current concentrations are of the order of 0.1 ppb v/v. It is destroyed in the natural atmospheric oxidation cycle and thus does not accumulate in the environment. The atmospheric lifetime is around 10 years.

Approximately 10% of the emissions of 1,1,1-trichloroethane will reach the stratosphere (upper atmosphere). If current theories are correct, which is still far from certain, this could result in some contribution to ozone depletion. However, this contribution would be very small and could be quickly reversed if emissions were reduced.

1,1,1-trichloroethane has a relatively low toxicity which probably reflects the limited extent to which is is metabolised in living organisms. Its major physiological effect is acute central nervous system depression, and probably cardiosensitisation at very high exposure levels. Long term animal studies have failed to show any increase in tumour incidence and it is thus considered to be extremely unlikely that it will cause carcinogenic effects in humans.

Studies carried out on 1,1,1-trichloroethane, when viewed as a whole, do not suggest that adverse effects are likely to be encountered at or below the current OEL (Occupational Exposure Limit) of 350 ppm (UK figure).

1 USE-CONSUMPTION

Stabilised 1,1,1-trichloroethane (or methyl chloroform) has been marketed in Europe since the early sixties. Its principal use has been and remains degreasing of metallic or metaloplastic pieces. Its physical properties and toxicological characteristics make it a product well suited to the practical requirements of industrial degreasing. It is widely used in cold cleaning processes in the engineering industry.

The use of 1,1,1-trichloroethane in vapour cleaning processes is in equipment very similar to that used for trichloroethylene and perchloroethylene. Support given by the producers to the user mirrors that for these solvents and plant design at present and projected for the future is similar. Solvent recovery and waste disposal techniques for 1,1,1-trichloroethane are also similar. These factors have been described in full in BIT/CEFIC papers dealing with trichloroethylene (1) and perchloroethylene (2).

It is also used as a solvent in adhesives, paints, varnishes and various solutions of polymers where its properties of non-flammability and low toxicity are important.

In 1983, the European market for 1,1,1-trichloroethane was estimated at K156 tons*. The high growth rate in the 60's and early 70's was dependent on the replacement of Tri and Per.Replacement is now reaching saturation and there has been no growth in the total market since 1979. Future growth is expected to be limited to 1-2% per year maximum.

* Estimate : EEC + Scandinavia, Spain, Austria, Switzerland, Portugal and Greece.

2 PHYSICAL AND CHEMICAL PROPERTIES

Chemical formula	CH_3-CCl_3	
Molecular weight	133,4	g/mol
Boiling point (1013 mbar)	74,0	°C
Freezing point	-33	°C
Rel. density d_4^{20} at 20°C	1.337	g/cm^3
Refractive index n_D^{20}	1.4379	
Specific heat at 20°C	1.0	kJ/kg K
Latent heat of vapourisation at bp (1013 mbar)	240	kJ/kg
Flash point (TOC.ASTM D 13107)	none	
Solubility of water at 25°C	0.03	% by wt.
Solubility in water at 25°C	0.15	% by wt.
Vapour pressure at 20°C	133	mbar
Vapour density at bp (air = 1 1013 mbar)	4.6	kg/m^3
Viscosity at 20°C	0.86	cP

Commercial grades of 1,1,1-trichloroethane contain added stabilisers to ensure that the solvent is compatible with light metals and processing aids under the arduous conditions met in metal cleaning. The stabilisers consist of metal deactivators and acid acceptors generally in the range 3-5% by weight. This confers stability on the product in cleaning processes and in the various formulations.

1,1,1-trichloroethane is not decomposed by heat or light under normal conditions of use but some decomposition occurs in the presence of open flames and red hot surfaces, to form hydrogen chloride and traces of phosgene. Thermal decomposition of the vapour in air is likely to commence in the temperature range 150-285°C (3).

Under the influence of ultraviolet light from welding arcs, some decomposition occurs mostly to acid products but some phosgene is also produced, and therefore solvent degreasing operations should be well separated from welding.

1,1,1-trichloroethane reacts only very slowly with water at ordinary temperatures. The liquid solvent is stable to oxidation especially when suitable stabilisers are present.

3 1,1,1-TRICHLOROETHANE IN THE ENVIRONMENT

3.1 Concentrations in the Air

Information on the concentration of 1,1,1-trichloroethane and other chlorinated solvents in the atmosphere has previously been published by numerous authors, Lovelock et al (4), Wilkness et al (5), Lovelock (6, 7), Lillan et al (8) and McConnell (9). Data has also become available in reports from NAS (10) and DOE (11). The most recent data available is from NASA/WMO (14), Singh et al (12), Prinn et al (15) amd Khalil and Rasmussen (23).

The average background concentrations (ie in regions remote from industrial centres) are in the range 0.13-0.18 ppb (10, 11) with significantly higher concentrations in the northern hemisphere than in the southern hemisphere (12). Table 1 shows results of measurements made in 1972-76 in various parts of Europe (13). The concentrations exhibit the large variations typical of industrialised areas, ranging from the background levels up to several ppb for air masses originating in urban centres.

TABLE 1 - CONCENTRATIONS OF 1,1,1-TRICHLOROETHANE IN AIR (ppb v/v)

LOCATION	COUNTRY	$[CCl_3-CH_3]$
Liverpool (Childwall)	UK	0.17
Widnes (Pex Hill)		0.34
Delamere		0.03-0.20
Frodsham		0.05-1.01
Moel Famau (N Wales)		0.34-0.68
Rannoch Moor (Scotland)		0.17-0.25
Forest of Dean		0.47
Hengelo (Open Country)	NL	0.02-0.05
Hengelo (Centre)		<0.02-0.13
Weiwerd		<0.02
Munich (Centre)	D	ND
Munich 1 km fc		0.17-0.67
Munich 5 km fc		ND-0.50
Munich 10 km fc		ND-0.34
Munich 20 km fc		ND
Ranzel *		1.51-1.68
Langel *		1.51-6.55
Unkendorf *		<0.50
Bochum (ref 18)		0.33
Bruxelles	B	0.17-0.39
Uccle		<0.17
Uccle		ND
Namur		ND-0.34
Lyon (Centre)	F	<0.84-2.01
Lyon 20 km du centre		<0.84-0.84

* More recent analysis (May 81) made near to Ranzel, Langel and Unkendorf do not show values above the detection level.

ND = Not Detected

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The climatic conditions will have an influence on the concentrations in the air, although the evaporation of solvent contained in water tends to make the concentrations uniform as suggested by McConnell and Lovelock (6, 7, 9).

3.2 Concentrations in Water

Measurements have also been carried out of concentrations in the waters of rivers (13) and the sea (Table 2) as well as in potable water (Table 3). The majority of values found lie in the range 0.1 - 0.3 ppb.

These low concentrations found in the sea have been confirmed by the mass balance analysis carried out by Neely and Plonka indicating that only 2 percent of total 1,1,1-trichloroethane emissions are found in the ocean (16). It has also been reported that in aqueous media, the primary dissipative process is evaporation rather than hydrolysis (17).

TABLE 2

CONCENTRATIONS OF 1,1,1-TRICHLOROETHANE IN RIVERS AND SEAS (ppb w/w*)

LOCATION	COUNTRY	1,1,1-TRICHLOROETHANE
Liverpool Bay	UK	<0.25 - 3.3
Twente Canal, Hengelo	NL	0.07
Twente Canal, Delden		<0.1
Eems		<0.1
Oostfriese Gaatje (South)		0.3
Oostfriese Gaatje (North)		0.1
Ranselgat		0.3
Huibertgat		0.2
Marghera	I	0.6
River Durance Pont Oraison	F	ND
Ste Tulle		ND

ND - Not Detected

* 1 ppb w/w represents 1 part in 10^9 by weight.

TABLE 3

CONCENTRATIONS OF 1,1,1-TRICHLOROETHANE IN POTABLE WATERS (ppb w/w)

COUNTRY	LOCATION	DATE	KIND OF WATER	[CCl_3-CH_3]
UK	5 samples from NW England	1974	Tap water	0.4 - 1.0
NL	Hengelo	February 1975	Tap water	0.04
	Hengelo	June	" " Hengelo	0.1
	Borne	1975	" " Borne	0.3
F	Lyon	Juillet September 1976	Tap water	0.18 - 0.25
	Ourlins Lyon	Juillet September 1976	" "	0.15 - 0.34
	Fleurieux	Juillet September 1976	" "	0.05 - 0.1
B	Bruxelles	11.10.76	Tap Water	<0.4
	Schelle	11.10.76	" "	<0.4
	Wavre	11.10.76	" "	<0.4
	Bruxelles	8.10.76	Well water	<0.4
L	Lavacherie	7.10.76	Spring water	<0.5 <0.4

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3.3 Concentrations in Food and in Animal and Human Tissues

Here again, it is in the work of McConnell et al (9) that the greatest amount of information on this subject is to be found. In the common foods, amounts of 1-10 ppb 1,1,1-trichloroethane have been found, the lowest in fruits and meat, and the highest in fatty substances.

In human tissues concentrations in the range 1-5 ppb in kidneys and liver and 2-24 ppb in fatty tissues have been measured (9). More recent data is available which gives a similar concentration profile (18).

The conclusions reached from analysis of 1,1,1-trichloroethane in the UK support the view that together with trichloroethylene and perchloroethylene these substances are widely distributed at concentrations of a few parts in 10^9 in industrial and populated areas but that they do not bioaccumulate via food chains (9, 19).

4 DEGRADATION OF 1,1,1-TRICHLOROETHANE IN THE ENVIRONMENT

4.1 In the Atmosphere

The atmospheric measurements made by Lovelock (7) show that the 1,1,1-trichloroethane found in the environment comes almost entirely from industrial sources. Earlier estimates of the atmospheric burden compared with the amount produced suggested that 1,1,1-trichloroethane had a lifetime in the environment of between 5 and 10 years (20, 21, 22). A recent publication (15) suggests a global atmospheric lifetime of 10 years, whilst Khalil and Rasmussen in their latest publication (23) calculate 6 years.

The most important destruction mechanism for 1,1,1-trichloroethane in the environment is thought to be via reaction with hydroxyl radicals mostly in the troposphere. Estimates of the average hydroxyl radical concentration in the troposphere (3×10^5 to 9.5×10^5 molecules/cc (15, 16, 24), taken together with measurements of the rate of hydroxyl radical attack on 1,1,1-trichloroethane (25) suggest that this is the major route for removal of 1,1,1-trichloroethane from the environment. Current estimates (20) suggest that this tropospheric mechanism accounts for 90% of the 1,1,1-trichloroethane emissions.

Approximately 10% of the 1,1,1-trichloroethane emitted to the atmosphere is likely to be transported to, and destroyed in, the stratosphere. The chlorine content will be released to take part in the atmospheric chlorine cycle, which according to theory could lead to depletion of ozone levels. However since 1979, advances in the science have led to a significant downward trend in the predicted effect of the chlorine cycle, considered alone, on atmospheric ozone. Current theory predicts that for the five chlorofluorocarbons, 1,1,1-trichloroethane and carbon tetrachloride, the overall long term steady state calculated ozone depletion

would be 3-5%. The depletion caused by 1,1,1-trichloroethane would represent less than one tenth of this and would be less than half of that attributed to natural emissions of methyl chloride (26, 27, 28). Furthermore it is estimated that when the effect of other gases, such as CO_2, N_2O, CH_4 and NO_x are taken into account, there will be no change in total ozone, at least for several decades.

1,1,1-trichloroethane differs in its behaviour in the atmosphere from long lived compounds such as chlorofluorocarbons, in one major respect: any harmful effects, such as the postulated effect on stratospheric ozone, could be rapidly reversed by a reduction in the amount released to the atmosphere on account of its relatively short life compared with fluorocarbons.

It is very difficult to simulate atmospheric degradation processes in the laboratory, and the detailed mechanism by which CH_3-CCl_3 is broken down to stable end products, HCl, CO_2 and H_2O is not fully understood. However, in the laboratory, photo oxidation of 1,1,1-trichloroethane leads to the formation of HCl, phosgene and CO_2 as well as acetic acid and 1,1,1,2 tetrachloroethane (29, 30).

4.2 In the Hydrosphere

The rate at which 1,1,1-trichloroethane transfers to the oceans depends on the rate of transfer across the air/sea interface (19). Once in the ocean, degradation proceeds relatively slowly. Experiments have shown that under environmental conditions of temperature and pH the reaction products are acetic acid, hydrochloric acid and vinylidene chloride. Although published estimates and calculations of the half life have shown some variation (31, 32), more recent unpublished data is more consistent and a half life of 10 years (33) and 4 years (34) have been determined.

5 TOXICOLOGY

The toxicological effects of 1,1,1-trichloroethane have been reviewed by NIOSH (35), EPA (36, 37) and the UK Health and Safety Executive (38).

5.1 Human Toxicology

5.1.1 Acute case reports

A 47 year old male accidentally drank 28 cc of 1,1,1-trichloroethane, and this resulted in nausea, vomiting and diarrhoea within 1 hour. Urine tests initially indicated some kidney pathology, but symptoms eased after 6 hours and the man was asymptomatic after 12 hours. After 50 hours, serum bilirubin was elevated, but a series of kidney and liver function tests were normal, as were the heart and blood profiles (38).

A number of cases of sudden death following VSA (volatile substance abuse) incidents involving 1,1,1-trichloroethane in the US were reported by Bass (40). The author discusses the possibility that the deaths resulted from cardiac sensitisation to endogenous catecholamines.

Several case reports of acute occupational over-exposure by inhalation are reviewed by NIOSH (35). Varying degrees of anaesthesia are reported, and the cases include several with fatal outcome. In the fatal cases, lung congestion and oedema are reported, as well as varying degrees of congestion of other organs; atmospheric concentrations were estimated at in excess of several thousand ppm. The non-fatal cases involved dizziness, lightheadedness and sometimes nausea and vomiting; recovery was uneventful, with electrocardiograms and liver and kidney function tests being normal.

5.1.2 Human experimental exposures

1,1,1-trichloroethane has been used as an inhalation anaesthetic in humans (41, 42). 10 000 to 26 000 ppm is reported (42) to be required for the induction of anaesthesia, with 6000 to 22 500 ppm being required for the maintenance of light surgical anaesthesia.

Several experimental studies are reported in which various psycho-physiological tests were carried out on human subjects exposed to various levels of 1,1,1-trichloroethane by inhalation (43, 44, 45, 46). Lightheadedness was reported at 2600 ppm (43) and at 1000 ppm after 75 minutes (41). Romberg and similar tests were reported positive at these levels. Equilibrium was reported not to be disturbed by exposure at 1000 ppm for 30 minutes and neither reflexes nor equilibrium were disturbed by 500 ppm for up to 450 minutes (44). 900 ppm (43) is reported to affect Romberg performance and to induce lightheadedness in some subjects. Salvini (45) reported that a range of psychophysiological tests were normal following exposure to 350 ppm and 450 ppm for 8 hours, with the exception of decreased perceptive capability under stress at 450 ppm. Gamberale (45) exposed 12 subjects to 250, 350, 450 and 550 ppm for four continuous 30 minute periods and reported that a range of psychophysiological tests showed statistically significant differences at 350 ppm or more. These last two reports (45, 46) have been criticised by NIOSH (35) on the grounds of possible confounding factors and such studies rarely employ a double blind technique, which is fundamental to scientifically sound psychophysiological experimentation. These studies, taken together, show no convincing evidence of effects of this type at or below 350 ppm.

5.1.3 Human field studies

Binaschi (47) reported that the concentration of 1,1,1-trichloroethane in air in a work room in which workers had reported symptoms was 250 ppm. Details of symptoms and the other solvents involved are not given.

Kramer (48) measured numerous physiological parameters in a matched pair study on two adjacent textile plants. Air concentrations of 1,1,1-trichloroethane varied from 11 to 838 ppm, with a mean of 115 ppm; exposure was for up to 6 years. The authors concluded that no health impairment was suffered by workers at these concentrations.

Stewart reported (49, 50) that no injury to man followed repeated occupational exposures to 500 ppm or less and Hatfield (51) stated that 100-200 ppm with peaks to 800 ppm had prevailed in the cleaning of aeroplane tip tanks for several years without incident.

A clinical, neurophysiological and behavioural study of female workers exposed to 1,1,1-trichloroethane showed no significant differences between the exposed and control groups with respect to clinical features, maximum motor conduction velocity, conduction velocity of slow fibres and psychometric data (52).

5.1.4 Effect on skin, eyes and mucous membranes

Lung oedema has been reported in cases of fatal inhalation over exposure (35).

Slight eye irritation was reported at 900-1000 (44) and eye, nose and throat irritation at 400-450 ppm (45) and 420-612 ppm (53).

Immersion of a hand in liquid 1,1,1-trichloroethane for 30 minutes resulted in mild erythema which persisted for one hour (54). It has been reported (50) that absorption of toxic amounts through the skin in normal industrial operations is highly unlikely.

5.2 Animal Toxicology

5.2.1 Acute studies

Oral LD50's are reported (42) to range from 9470 to 12 300 mg/kg in various species. The inhalation LC50 in the rat is reported (55) at 18 000 ppm (3 hr) and 14 000 ppm (7 hr). The major effect reported is central nervous system depression. Adams et al (55) found that concentrations approaching the LC50 produced no significant pathological changes in the liver or kidneys of rats. Cardiosensitisation has been reported: Reinhard et al (56) found cardiosensitisation in 3/18 dogs at 5000 ppm and 12/12 dogs at 10 000 ppm (ventricular fibrillation occurred in one dog at the top dose level); Trochimowicz (57), on the other hand, did not find cardiosensitisation in a study of 41 dogs at 5000 ppm.

5.2.2 Subacute studies

Adams et al (55) exposed rabbits, rats, guinea pigs and a monkey to concentrations ranging from 650 ppm to 5000 ppm by inhalation for 7 hours/day for periods ranging from 4 to 12 weeks. The monkey showed no tissue histopathology at 3000 ppm, rabbits showed a slight depression in growth rate at 5000 ppm but no histopathology, rats showed temporary growth retardation at 5000 ppm but no histopathology and there were no efects at 3000 ppm while guinea pigs (the most sensitive species) showed slight centrilobular fatty infiltration of the liver (without necrosis) at 3000 ppm, no histopathological effects at 1500 ppm and depression of growth rate at 650 ppm and above.

Prendergast (58) exposed monkeys, dogs, rabbits, rats and guinea pigs to 2200 ppm, 8 hours/day, 5 days/week for 30 exposures. Monkeys, dogs and rabbits showed slight weight loss but otherwise all animals were reported normal (including histopathology). Continuous exposure at 370 ppm for 90 days showed some non-specific lung congestion.

MacEwen et al (59) exposed mice to 250 and 1000 ppm continuously for 14 weeks. 1000 ppm showed reversible fatty changes in the liver but no necrosis; 250 ppm showed no liver effects. McNutt (60) on the other hand, in a similar experiment, reported centrilobular hypertrophy at 1000 ppm with increased liver weight and elevated triglycerides, and transient elevated triglycerides at 250 ppm.

5.2.3 Chronic studies

Quast et al (61) exposed rats to 875 and 1750 ppm of a 1,1,1-trichloroethane formulation for 6 hours/day, 5 days/week for 12 months; rats were allowed to survive for up to 31 months. Female rats at 1750 ppm showed an increased incidence of focal hepatocellular alterations which were not progressive or life shortening; apart from this minimal effect, there were no changes at either dose level in either sex in body weight, mortality, haematology, urinalysis, clinical chemistry, cytogenetic studies, terminal organ weights or gross and histopathology that could be attributed to exposure.

NCI (62) exposed Osborne-Mendel rats and B6C3F1 mice to 1,1,1-trichloroethane by oral gavage 5 days/week for 78 weeks. There were two dose levels; for rats 750 and 1500 mg/kg/day and for mice the time weighted average doses were 2807 and 5615 mg/kg/day. Both species showed depression of body weight and the survival time, particularly of mice, was adversely affected. Extensive non-tumour histopathology was carried out but not analysed statistically. The non-neoplastic lesions observed are described as being of types observed previously as spontaneous occurrences in ageing laboratory mice and rats.

Groups of male and female B6C3F1 mice (80/sex/group) were exposed (63) to vapour concentrations of 0, 150, 500 or 1500 ppm of a 1,1,1-trichloro ethane formulation for 6 hours/day, 5 days/week for 2 years. Ten mice/sex from each group were predesignated for interim sacrifices after 6, 12 and 18 months exposure. Fifty mice/sex from each group were assigned to the study to be terminated after 24 months. Parameters measured during the study included mortality, in life clinical signs of toxicity, haematology, clinical chemistry, body weight, organ weights (liver, kidneys, brain, heart, testes), gross patholgy and hispathology. Inhalation exposure of male and female B6C3F1 mice to these dose levels for two years did not result in any toxic or carcinogenic effect considered due to the test chemical.

5.3 Mutagenicity/Carcinogenicity

1,1,1-trichloroethane has been tested for mutagenic activity using bacterial systems (64, 65), a mammalian cell system (66), a host mediated assay system with Saccharomyces Pombe (67) and bone marrow cytogenetics (61). All results are negative, with the exception of the cell transformation test (66) and a weak positive in one of the strains used by Simmon (65). EPA (36) cite an equivocal result in a Salmonella system obtained by Litton Bionetics. The chemical composition of the material tested must be considered when interpreting these results.

In the long term inhalation study by Quast et al (61, described in 5.2.3 above), the tumour incidence in rats exposed to 875 or 1750 ppm was not increased relative to that seen in control animals.

Similarly in the two year mouse inhalation study describ d above (63) no carcinogenic effect was seen at 1500 ppm or below.

The NCI Bioassay (62, described in 5.2.3 above), showed no increased tumour incidence compared with controls in mice or rats of either sex, although NCI believe the study to be flawed because of the reduced survival time of both rats and mice. This study is being repeated by NTP.

Bell (68) reported preliminary findings from a chronic inhalation study which exposed rats to 200, 440 and 875 ppm 1,1,1-trichloroethane for 7 hours/day, 5 days/week for 18 month. There was no indication during initial audit studies of a carcinogenic response.

5.4 Reproductive Toxicology

Schwetz et al (69) exposed pregnant rats and mice to 875 ppm 1,1,1-trichloroethane for 7 hours/day from days 6 to 15 of gestation. No teratogenic effects were seen in either species.

York et al (70) exposed female rats to 2100 ppm 1,1,1-trichloroethane by inhalation before mating and/or during pregnancy. There was no significant detrimental effect on any of the maternal or foetal toxicity parameters measured, nor was there any teratogenic effect.

Lane et al (71) carried out a reproductive study in which male and female mice and their offspring were exposed to up to 1000 mg/kg/day 1,1,1-trichloroethane in drinking water. No compound related effect was seen on fertility, gestation, viability or lactation indices, nor were dominant lethal or teratogenic effects observed in either of the two generations tested.

5.5 Metabolism

1,1,1-trichloroethane is metabolised to a very small extent, and this limited metabolism may underlie the generally low toxicity of 1,1,1-trichloroethane. Hake (72) showed that 99% of an ip injected dose is excreted unchanged via the pulmonary route by rats. Schumann et al(73, 74) showed 97% exhaled in rats to be unchanged and 92-94% in mice. Mice were also shown to exhale 1,1,1-trichloroethane more rapidly, and to biotransform approximately 5 fold more on a body weight basis than rats. Repeated exposure did not significantly affect the disposition of 1,1,1-trichloroethane compared with singly exposed rats and even after long term repeated exposure the biotransformation of 1,1,1-trichloroethane remains limited. Also, 1,1,1-trichloroethane was shown to possess little potential for significant bioaccumulation in rodents. In man (75), 44% of an inhaled dose is exhaled unchanged in the first hour.

Trichloroacetic acid and trichloroethanol have been detected as metabolites (76). It has been suggested (72, 76) that 1,1,1-trichloroethane is metabolically oxidised to trichloroethanol, which is then either excreted as the glucuronic acid conjugate or further oxidised to trichloroacetic acid and excreted as such. It is not considered that urinary metabolite measurements (77, 35) or breath analysis (35) currently provide reliable methods for evaluating exposure to 1,1,1-trichloroethane.

5.6 Review of likely effects in Humans and Conclusions

Acute over-exposure by inhalation will result in central nervous system depression and possibly cardiosensitisation. If the exposure has been severe enough such incidents can prove fatal.

1,1,1-trichloroethane is unlikely to have an adverse effect on the liver as evidenced by both acute and chronic animal studies as well as human studies and the uneventful recovery of human cases of non-fatal over-exposure.

Almost all the experimental psychophysiological studies reported suffer from a failure to follow a double blind protocol; even so, there are no indications of any such effect at levels below 350 ppm.

Human field studies must also be interpreted with caution; difficulties with controls, confounding multiple exposure, subjective symptoms and inadequate atmospheric determinations are among the problems usually encountered. The studies published on 1,1,1-trichloroethane, when viewed as a whole, do not suggest that adverse effects are likely to be encountered at levels at or below 350 ppm, which is the current OEL (Occupational Exposure Limit) in the UK (78).

1,1,1-trichloroethane has proved to be generally non-mutagenic in the various test systems employed and has failed to increase tumour incidence in any of four separate long term animal studies (three by inhalation and one by ingestion). It is thus considered to be extremely unlikely that it will cause carcinogenic effects in humans.

Reproductive and teratogenicity studies in animals have shown no evidence of adverse effect.

In conclusion there is no evidence, from any of the animal or human studies reported, to suggest that adverse effects are likely to be encountered in humans at occupational exposure levels at or below 350 ppm.

REFERENCES

1 BIT Paper - Trichloroethylene

2 BIT Paper - Perchloroethylene

3 Crummett W B and Stenger V A, Ind & Eng. Chem. Vol 48, 3, 434-436, 1956

4 Lovelock J E, Maggs R J, Wade R J, Nature 241, 194-196, 1973

5 Wilkness P E, Lamontage R A, Larson R E, Swinnerton J W, Dikson C R, and Thomson T, Nature 245, 45-47, 1973

6 Lovelock J E, Nature 252, 292, 1974

7 Lovelock J E, Nature vol 267, 32, 1977

8 Lillan D, Env. Sci. Technology 9, 12, 1042-1048, 1975

9 McConnell G, Ferguson D M, Pearson C R, Endeavour 34, 13, 1975

10 National Academy of Sciences Report: Stratospheric Ozone Depletion by Hydrocarbons: Chemistry and Transport, Washington D C, 1979

11 United Kingdom Department of the Environmental Report: "Chlorofluorocarbons and their effect on Stratospheric Ozone" Petroleum Paper No 15, 1979

12 Singh H B, Salas L J and Stiles R E
Selected Man-made Halogenated Chemicals in the Air and Oceanic Environment
J Geophys. Res, Vol 88 no 66, 3675-3683, April 1983

13 Correia Y, Martens G, Van Mensch F, Whim B P, Atmospheric Environment, Vol II, 1113, 1977

14 NASA/WMO Report No 11 "The Stratosphere 1981: Theory and Measurement May 1981

15 Prinn et al, J Geophys. Res, Vol 88, No C13, 8415-8426, Oct 1983

16 Neely W B and Plonka J H, Estimation of time-averaged Hydroxyl Radical Concentration in the Troposphere, Env. Sci. Tech., 12, 317-321, 1978

17 Lapp T, Proceedings of the Conference on Methylchloroform and other Halocarbon Pollutants, Washington D C, 27-28 February 1979. EPA-600/9-80-003, PB80-142433

18 Bauer U, Zbl. Bakt. Hyg., I Abt. Orig. B 174, 200-237 (1981)

19 Liss D S and Slater P G, Nature 247, 181, 1974

20 Derwent R G and Eggleton A E J, Quart J R Met Soc, 107, 231-242, 1981

21 McConnell J C, Schiff H I, Science 199, 174, 1978

22 Chang J S and Penner J E, Preprint entitled "Analysis of Global Budgets of Halocarbons" submitted to Atmos. Environ.

23 Khalil M A K, Rasmussen R A, Chemosphere 13, 7, 789-800, 1984

24 Fishmann J and Crutzen P J "The Distribution of the Hydroxyl Radical in the Troposphere". First years research summary EPA Grant No 5804921-01

25 NASA ref publication 1010 "Chlorofluormethanes and the Stratosphere"

26 Derwent R G, Curtis A R, Stratospheric Ozone Depletion Estimates, United Kingdom Atomic Energy Authority, Report No AERE 10168, June 1981

27 NASA (1984) Report to Congress

28 NAS (1984) Causes and Effects of Changes in Stratospheric Ozone

29 Christiansen V O, Dahlberg J A, Anderson H F, Acta. Chem. Scand., 26, 3, 319, 1972

30 Bertrand L, Exsteen-Meyers L, Franklin J A, Hygbrechts G and Olbregts J, Int J Kinetics, 3, 89, 1971

31 Pearson C R, McConnell G, Proc R Soc London - Ser B - 189, 305, 1975 - CA 83, 54 219 k, 1975

32 Walraevens R, Trouillet P et Devos A, Intern. J. Chem. Kinetics, 6, 777, 1974

33 Walraevens R, Gerkens, Private Communication

34 McConnell - Private Communication

35 NIOSH, Criteria for a Recommewnded Standard, Occupational Exposure to 1,1,1-Trichloroethane HEW (NIOSH) 76-184, July 1976.

36 An Assessment of the Need for Limitations on Trichloroethylene, Methyl Chloroform and Perchloroethylene, EPA 560/11-79-009, July 1979

37 Health Assessment Document for 1,1,1-Trichloroethane (Methyl Chloroform), EPA 600/8-82-003F, February 1984

38 Toxicity Review 9 - 1,1,1-Trichloroethane, UK Health & Safety Executive 1984

39 Stewart R D and Andrews J T, J A M A, 195, 904-906, 1966

40 Bass M, J A M A, 212, 2075-2079, 1970

41 Krantz J C et al, Anaesthesiology, 20, 635-640, 1959

42 Dornette W H L et al, Anaesth. Analg. (Cleve), 39, 249-253, 1960

43 Stewart R D et al, Am. Ind. Hyg. Assoc. J., 22, 252-262, 1961

44 Torkelson T R et al, Am. Ind. Hyg. Assoc. J., 19, 353-362, 1958

45 Salvini M et al, Br. J. Ind. Med., 28, 286-292, 1971

46 Gamberale F et al, Arbete. Och. Halsa., 1, 29-50, 1972

47 Binaschi S et al, Boll. Soc, Ital. Biol. Sper., 45, 94-96, 1969

48 Kramer C G et al, Health of Workers Exposed to 1,1,1-Trichloroethane, A Matched Pair Study, Dow Chemical Co., Midland, Michigan, 1976

49 Stewart R D, J Occup. Med., 5, 259-262, 1963

50 Stewart R D, Ann. Occup. Hyg., 11, 71-79, 1968

51 Hatfield T R and Maykoski R T, Arch. Environ. Health, 20, 279-281, 1970

52 McConnell J C and Schiff H I, Science 199, 174, 1978

53 Stewart R D et al, Arch. Environ. Health, 19, 467-446

54 Stewart R D and Dodd H C, Am. Ind. Hyg. Assoc. J., 25, 439-446, 1964

55 Adams E et al, Arch. Ind. Hyg. Occup. Med., 1, 225-236, 1950

56 Reinhardt C F et al, J Occup. Med., 15, 953-955, 1973

57 Trochimowicz H J et al, J Occup. Med., 18, 26-30, 1976

58 Prendergast J et al, Tox. Appl. Pharm., 10, 270-289, 1967

59 MacEwen J D et al, NASA Contract Report No 134-323, 1974

60 McNutt N et al, Lab. Invest., 32, 642-654, 1975

61 Quast J F et al, Toxicologic and Carcinogenic Evaluation of a 1,1,1-Trichloroethane Formulation by Chronic Inhalation in Rats, Report HET K/1716/56, Dow Chemical Co., Midland, Michigan, October 1978

62 Bioassay of 1,1,1-Trichloroethane for Possible Carcinogenicity, NCI-CG-TR-3, January 1977

63 Dow Chemical - Unpublished information (1984)

64 Henschler D, Arch. Toxicol., 37, 233-236, 1977

65 Simmon V G et al in Scott, Bridges and Sobels, Progress in Genetic Toxicology Vol II, Elsevier, Amsterdam, 249-258, 1977

66 Price P J et al, In Vitro, 14, 290-293, 1978

67 Loprieno N et al, Unpublished manuscript, cited in 36

68 Bell Z G, PPG Industries Inc, letter to Dr S C Mazalski, EPA, December 8, 1978, cited in 36

69 Schwetz B A et al, Tox. Appl. Pharm., 32, 84-96, 1975

70 York R G et al, J. Tox. Environ. Health, 9, 251-266, 1982

71 Lane R W et al, Tox. Appl. Pharm., 63, 409-421, 1982

72 Hake C L et al, Arch. Environ. Health, 1, 101, 1960

73 Schumann A M et al, Fund. Appl. Tox., 2, 27-32, 1982

74 Schumann A M et al, Tox. Appl. Pharm., 62, 390-401, 1982

75 Morgan A et al, Ann. Occup. Hyg., 13, 219-233, 1970

76 Ikeda M and Ohtsuji H, Br. J. Indust. Med., 29, 99-104, 1972

77 Prost G H et al, Arch. Mal. Prof., 33, 197-198, 1972

78 Guidance Note EH40, HSE, Occupational Exposure Limits, 1984