



IPCS

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

Environmental Health Criteria 136 1,1,1-Trichloroethane



Under the joint sponsorship of the United Nations Environment Programme,
International Labour Organisation, and the World Health Organization.



WORLD HEALTH ORGANIZATION

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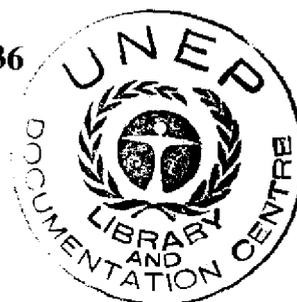
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Environmental Health Criteria 136



1,1,1-TRICHLOROETHANE

First draft prepared by Dr S. Dobson,
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World Health Organization
Geneva, 1992

The **International Programme on Chemical Safety (IPCS)** is a joint venture of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. The main objective of the IPCS is to carry out and disseminate evaluations of the effects of chemicals on human health and the quality of the environment. Supporting activities include the development of epidemiological, experimental laboratory, and risk-assessment methods that could produce internationally comparable results, and the development of manpower in the field of toxicology. Other activities carried out by the IPCS include the development of know-how for coping with chemical accidents, coordination of laboratory testing and epidemiological studies, and promotion of research on the mechanisms of the biological action of chemicals.

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CRITERIA FOR 1,1,1-TRICHLOROETHANE**

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NOTE TO READERS OF THE CRITERIA DOCUMENTS

Every effort has been made to present information in the criteria documents as accurately as possible without unduly delaying their publication. In the interest of all users of the Environmental Health Criteria documents, readers are kindly requested to communicate any errors that may have occurred to the Director of the International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda.

* * *

A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Palais des Nations, 1211 Geneva 10, Switzerland (Telephone No. 7988400 or 7985850).

**ENVIRONMENTAL HEALTH CRITERIA FOR
1,1,1-TRICHLOROETHANE**

A WHO Task Group on Environmental Health Criteria for 1,1,1-Trichloroethane met at the Institute of Terrestrial Ecology (ITE), Monks Wood, United Kingdom, from 20 to 24 May 1991. Dr M. Roberts, Director, ITE, welcomed the participants on behalf of the host institution and Dr M. Gilbert opened the meeting on behalf of the three cooperating organizations of the IPCS (UNEP/ILO/WHO). The Task Group reviewed and revised the draft criteria document and made an evaluation of the risks for human health and the environment from exposure to 1,1,1-trichloroethane.

The first draft of this document was prepared by Dr S. Dobson (ITE) and Dr A.A. Jensen (Danish Technological Institute). Dr M. Gilbert and Dr P.G. Jenkins, both members of the IPCS Central Unit, were responsible for the technical development and editing, respectively.

The efforts of all who helped in the preparation and finalization of the document are gratefully acknowledged.

ABBREVIATIONS

cAMP	cyclic adenosine monophosphate
cGMP	cyclic guanosine monophosphate
CNS	central nervous system
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
OECD	Organization for Economic Cooperation and Development
ppt	parts per trillion

1. SUMMARY

1,1,1-Trichloroethane is a chlorinated hydrocarbon which is manufactured from vinyl chloride or vinylidene chloride by chlorination. The world production was approximately 680 000 tonnes in 1988. It is a colourless, volatile liquid with a characteristic odour, and its vapour is more dense than air. It is mainly used in metal degreasing and as a solvent in many industrial and consumer products, including adhesives, spot removers, and aerosol cans. It is also a chemical intermediate. Technical trichloroethane usually contains 3-8% stabilizers to prevent degradation and the formation of hydrochloric acid; this protects metal parts from corrosion. It is non-flammable under normal conditions, but the vapour burns at high temperatures and, during welding operations, its degradation products include the poisonous gas phosgene. Contact with aluminium, magnesium, and their alloys may result in very violent reactions.

1,1,1-Trichloroethane reaches the environment readily. Owing to its long residence time in the troposphere (about 6 years) and low biodegradability, it is now ubiquitous in the environment, even far from industrial areas. Concentrations of up to $86 \mu\text{g}/\text{m}^3$ (16 ppb, w/w) have been determined in air sampled near industries producing or handling the compound.

Trichloroethane is mobile in soils and reaches the ground water. Concentrations of up to $1600 \mu\text{g}/\text{litre}$ have been found in ground or surface waters. This may be a source of contamination for drinking-water supplies.

It is estimated that 15% of the annual release of 1,1,1-trichloroethane is transported to the stratosphere where it causes ozone depletion by liberating chlorine atoms.

Acute toxic effects have been observed in bioassays with crustaceans and fish at concentrations above 7 mg/litre. Limited information suggests that bioaccumulation in aquatic organisms is low. The small amount of data makes it difficult to evaluate any effects on terrestrial organisms.

Humans are exposed to 1,1,1-trichloroethane principally by inhalation, and the substance is then rapidly absorbed into the body. Exposure by skin contact or ingestion may also occur. Trichloroethane is distributed widely in body tissues and crosses

the blood-brain and placental barriers. It has also been found in human breast milk, but is not thought to be bioaccumulated. The main route of elimination is exhalation of unchanged compound.

The acute and chronic toxicities of 1,1,1-trichloroethane are relatively low, but, under conditions of high exposure, there is a risk of toxic effects. Such conditions may occur in cases of occupational exposures, solvent abuse or accidents. Since the solvent is volatile and the vapour is much more dense than air, unexpectedly high and dangerous concentrations may occur in confined spaces such as "empty" storage tanks. This has caused several fatal and near-fatal poisonings at workplaces and elsewhere.

The critical effect in humans is on the central nervous system. Observable effects range from slight behavioural changes (accompanied by mild eye irritation) at 1.9 g/m³ (350 ppm) to unconsciousness and respiratory arrest at higher concentrations. However, fatal cardiac anomalies may also occur. Trichloroethane is less toxic to the liver than are most other organochlorine solvents. The no-observed-effect level (NOEL) for humans appears to be in the region of 1.35 g/m³ (250 ppm).

No adequate study of human carcinogenic effects has been published. However, a long-term inhalation study on rats and mice exposed to 8.1 g/m³ (1500 ppm) gave no evidence of any carcinogenic effect. 1,1,1-Trichloroethane does not have significant genotoxic potential.

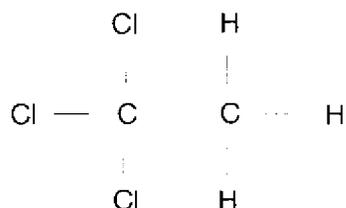
Developmental toxicity, but not teratogenicity, has been observed in rats and rabbits at concentrations that were toxic to the mother animals. The limited epidemiological evidence on reproductive effects is inconclusive.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, AND ANALYTICAL METHODS

2.1 Identity

1,1,1-Trichloroethane is an organochlorine solvent belonging to the family of chlorinated alkanes.

Chemical structure:



Empirical formula: $\text{C}_2\text{H}_3\text{Cl}_3$

Relative molecular mass: 133.4

IUPAC name: 1,1,1-trichloroethane

CAS name: ethane, 1,1,1-trichloro-

Some common synonyms: methylchloroform, MC, 1,1,1-TCE

Some common trade names: Chlorothene, Aerothene TT, Alpha-T, Genklene, Inhibisol

CAS registry number: 71-55-6

EEC identity number: 602-013-00-2

RTECS number: KJ2975000

2.2 Physical and chemical properties

2.2.1 Physical characteristics

In its pure state, 1,1,1-trichloroethane is a colourless, volatile liquid with a characteristic chloroform-like odour. The odour threshold is reported to be around 540 mg/m³ (100 ppm) (Stewart, 1968).

Trichloroethane has two structural isomers. The 1,1,2-trichloroethane isomer can be an impurity in the manufacture of 1,1,1-trichloroethane and it is known to have a different spectrum of reactivity.

Some physical and chemical properties of pure 1,1,1-trichloroethane are listed in Table 1.

2.2.2 Chemical reactivity

1,1,1-Trichloroethane has no recorded flash point and is therefore sometimes considered as non-flammable. However, it decomposes and/or oxidizes at high temperatures (> 300 °C) to hydrochloric acid and dichloroethene, together with some phosgene (Hardie, 1964). When catalysed by metal salts, especially aluminium compounds, degradation occurs at lower temperatures (Dreher, 1989) and decomposition in air to hydrogen chloride, carbon dioxide, and traces of chlorine occurs slowly at ambient temperatures (Pearson & McConnell, 1975). The formation of phosgene by the photooxidation of 1,1,1-trichloroethane during welding operations may be considerable (Dahlberg et al., 1973). 1,1,1-Trichloroethane can burn in the vapour state (de Nevers, 1986) and in admixture with air forms explosive mixtures (Wrightson & Santon, 1988; Bretherick, 1989). Contact with aluminium, magnesium, and their alloys may result in very violent reactions (Bretherick, 1981). Trichloroethane reacts slowly with water, but more rapidly with alkaline solutions such as an aqueous suspension of calcium hydroxide, forming 1,1-dichloroethene (vinylidene chloride) (Hardie, 1964). Hydrolysis, which is very slow at 20 °C but rapid at 80 °C (see Table 7), occurs in the presence of water or aqueous acids, yielding hydrochloric and acetic acids (Gerken & Franklin, 1989).

2.2.3 Commercial products

Analytical grade 1,1,1-trichloroethane has a purity of > 99.0% and contains no added stabilizers (Fluka, 1988).

Table 1. Physical and chemical properties of 1,1,1-trichloroethane

Melting point	-30.4 °C	Weast (1986)
Boiling point (at 760 mmHg)	74.1 °C	Weast (1986)
Density	1.3390	Weast (1986)
Vapour density (air = 1)	4.6	US EPA (1984)
Vapour pressure (at 20 °C)	13.3 kPa (100 mmHg)	Weast (1986)
Refractive index (at 20 °C)	1.4379	Weast (1986)
Concentration in saturated air	16.7%	Clayton & Clayton (1981)
Solubility in water	0.3 g/litre at 25 °C ^a 0.95 g/litre at 20 °C 0.480 g/litre at 20 °C	IARC (1979) Archer (1979) Pearson (1982)
Soluble in	acetone, benzene, chloroform, methanol, ether, ethanol, carbon disulfide, carbon tetrachloride	Windholz (1983) Weast (1986) CEC (1986)
Partition coefficients		Veith et al. (1980)
octanol/water (log P _{ow})	2.47 (measured)	(1980)
water/air (at 20 °C)	0.71	Pearson (1982)
blood/air (at 37 °C)	3.3	US EPA (1984)
Flammability	nonflammable under normal conditions, vapour burns at high temperature	CEC (1986)
Auto-ignition temperature	537 °C	Archer (1979)
Explosive limits in air at 25 °C	8.0-10.5 vol %	Archer (1979)

^a US EPA (1984) reported a water solubility of 4.4 g/litre at 25 °C.

Commercially available technical and solvent grade products have a purity of 90-95% and usually contain 3-8% stabilizers, mainly to prevent the generation of hydrochloric acid and to avoid corrosion of metal parts (Fluka, 1988). The stabilizers used are chemical compounds, such as nitromethane, *N*-methyl pyrrole, 1,4-dioxane, butylene oxide, 1,3-dioxolane, nitroethane, toluene,

diisopropylamine, methyl ethyl ketone, isobutyl alcohol, and 2-butanol (IARC, 1979; Clayton & Clayton, 1981; US EPA, 1984; CEC, 1986).

Twenty-two samples of stabilized technical 1,1,1-trichloroethane were shown to contain potential mutagens or carcinogens such as vinylidene chloride, dichloroethane, and 1,2-epoxybutane (Henschler et al., 1980).

2.3 Conversion factors

$$1 \text{ ppm} = 5.40 \text{ mg/m}^3$$

$$1 \text{ mg/m}^3 = 0.185 \text{ ppm}$$

2.4 Analytical methods

The first step of an analytical method for routine measurements of trichloroethane in air is sampling either on activated charcoal (tubes or diffusion samplers) filters and extraction by a solvent (e.g., carbon disulfide) or on a polymer trap and desorption by heating. This is followed by determination by gas chromatography (GC) combined with either electron capture detector (ECD), flame ionization detector (FID) or mass spectrometry (MS). GC is also used for the determination of trichloroethane in other types of samples (water, sediment, blood, etc.) by, for example, headspace analysis.

Indicator tubes may be used for preliminary surveys of air levels. The detection limit is about 270 mg/m³ (50 ppm) (Drägerwerk, 1986).

Some examples of analytical methods are summarized in Table 2.

Table 2. Analytical methods

Medium	Specification	Sampling method	Analytical method	Detection limit	Reference
Air		trap on charcoal extract with carbon disulfide	GC-FID	300 ng/sample	Niosh (1977) Olson & Chan (1987)
Air			GC-ECD	125 mg/m ³ (10 litres air)	Henschler (1978)
Air		trap on Porapak-N, desorb at 200 °C, dry over MgSO ₄	GC-ECD GC-MS	160 mg/m ³ (30 ppt)	Russell & Shadoff (1977)
Water		sparge with helium, trap on Tenax GC, desorb by heat	GC-MS		Coleman et al. (1976)
Water		direct injection of headspace gas	GC-ECD	0.05 µg/litre	Piet et al. (1978)
Water		headspace air, trap on Tenax	GC		Pereira & Hughes (1980)
Water	drinking-water	trap on XAD-2	GC-MS	0.1 µg/litre	Olson (1987)
Blood	rat arterial	headspace gas collected over 75-150 µl at 75 °C, direct injection	GC-FID	0.5 µg (6.4 µg/g blood)	Westerberg & Larsson (1982)
Blood	human		GC-ECD	0.05 mg/litre	Henschler (1978)
Blood	human	extraction with hexane	GC-ECD	≤ 0.07 µmol/litre	Pekari & Aitio (1985)
Brain	rat	headspace gas collected		0.5 µg (2.5 µg/g tissue)	Westerberg & Larsson (1982)

3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

Appraisal

1,1,1-Trichloroethane is a man-made chemical; there are no natural sources. In 1988, world-wide production was approximately 680 000 tonnes per year. However, the annual production level is expected to decline progressively due to international agreements on the control of ozone-depleting substances. It is used mainly in metal degreasing and as a solvent in many consumer products, but also finds use as an intermediate in the production of other chemicals.

3.1 Production processes

All 1,1,1-trichloroethane in the environment is anthropogenic in origin, since it does not occur naturally. It is usually produced by the hydrochlorination of vinyl chloride to 1,1-dichloroethane, followed by thermal chlorination to 1,1,1-trichloroethane (Fishbein, 1979). 1,1-Dichloroethene (vinylidene chloride) can also be directly hydrochlorinated to 1,1,1-trichloroethane, and direct chlorination of ethane or chloroethane can be used. However, the latter methods may generate other halogenated hydrocarbons as by-products (Fishbein, 1979).

3.2 Production levels

The estimated world production capacity of 1,1,1-trichloroethane was 480 000 tonnes/year in 1973 (McConnell et al., 1975) and 680 000 tonnes/year in 1988 (Midgley, 1989). About half the production is in the USA and 100 000 tonnes is produced in Japan annually. The production of 1,1,1-trichloroethane in Japan more than doubled in the period from 1979 to 1989. The production in the European Economic Community in 1979 was estimated to be 140 000 tonnes/year (Torslov, 1988). Production capacity is about 100 000 tonnes in Germany, while in 1973 the United Kingdom and France produced 20 000 and 11 000 tonnes, respectively. The annual production in eastern Europe is estimated to be less than 1000 tonnes.

The western European consumption of 1,1,1-trichloroethane in 1985 was estimated to be 173 000 tonnes, the worldwide value being about 500 000 tonnes.

Information prepared by the European Chemical Industry Federation (CEFIC, 1986) suggested that consumption of 1,1,1-trichloroethane in western Europe increased during the 1970s but stabilized during the 1980s.

The estimated annual worldwide production of 1,1,1-trichloroethane is shown in Table 3.

Table 3. Production and sales of 1,1,1-trichloroethane (tonnes/year)

Year	Worldwide production ^a	W. European production ^b	W. European sales ^c	USA production ^d	Japanese production ^e
1970	155				
1971	175				
1972	227				
1973	279			245	
1974	314		92		
1975	307		86		
1976	407		99		
1977	480		109	289	
1978	524		120	292	
1979	506		147		77
1980	552		144	315	86
1981	549		146	274	88
1982	514		142		89
1983	541		140	226	96
1984	600		144		111
1985	588		150	394	120
1986	609	205	138	291	128
1987	627	203	130	314	131
1988	678	218	129	340	139
1989		222	130		164
1990		229	122	338	

^a Midgley (1989)

^b CEFIC (1991)

^c CEFIC (1986)

^d NIOSH (1979); Midgley (1989); CMR (1991)

^e MITI (1990)

Midgley (1989) examined the annual sales of 1,1,1-trichloroethane and grouped uses into three categories: those that result in emissions for less than 6 months, for 1 year, and for more than one year. He found that applications, such as solvent cleaning, that lead to rapid emission, account for 95 to 97% of the annual reported production of 1,1,1-trichloroethane. A geographical breakdown of the emission data into global regions revealed that during the period 1980-1988 between 90% and 94% of the total production of 1,1,1-trichloroethane was sold to the industrial north, i.e. above latitude 30°N.

Under the agreement of the London Conference of the Montreal Protocol (June, 1990), use of 1,1,1-trichloroethane will be discontinued.

3.3 Uses

1,1,1-Trichloroethane is used mainly in metal cleaning/degreasing and as a solvent in various formulations, including adhesives, paints, varnishes, inks, dry cleaning agents, and typewriter correction fluids. It is also utilized as a solvent in aerosols, and it can be used as an additive to raise the flash point of many flammable solvents. 1,1,1-Trichloroethane also finds uses as a coolant and lubricant in metal cutting oils, as a solvent in textile dyeing, for cleaning plastic moulds, and as a developer for printed circuit boards.

Formerly, 1,1,1-trichloroethane was used as a solvent for various insecticides, and, together with ethylene gas, for degreasing citrus fruits and post-harvest fumigation of strawberries.

1,1,1-Trichloroethane is also a chemical intermediate in the production of vinylidene chloride. In the USA, this accounts for 23% of the total consumption of 1,1,1-trichloroethane, but this use appears to represent only 5-10% of the production elsewhere.

4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

Appraisal

1,1,1-Trichloroethane has a residence time of about 6 years in the troposphere, where it is oxidized to trichloroacetaldehyde and trichloroacetic acid. It reaches the stratosphere in significant amounts, which results in ozone depletion through the liberation of reactive chlorine atoms. The ozone-depleting potential of 1,1,1-trichloroethane is ten times lower than that of trichlorofluoromethane (CFC-11), and the global-warming potential is about 40 times lower.

In water, 1,1,1-trichloroethane is slowly dehydrochlorinated to 1,1-dichloroethene and hydrolysed to ethanoic acid, the former process being favoured by alkalinity. 1,1,1-Trichloroethane does not bind to soil particles and thus leaches readily into ground water.

Biodegradation to 1,1-dichloroethane and chloroethane has been reported to occur under anaerobic conditions.

1,1,1-Trichloroethane does not appear to bioaccumulate.

4.1 Distribution and transport between media

1,1,1-Trichloroethane enters the environment primarily via evaporation to the atmosphere, although some is discharged in industrial effluents. McConnell et al. (1975) reported rapid transfer of 1,1,1-trichloroethane from water to air and concluded that, irrespective of whether 1,1,1-trichloroethane enters the environment via water or air, a wide distribution of the chemical is likely.

Neely (1982) used the vapour pressure, water solubility, and relative molecular mass of 1,1,1-trichloroethane to assess its partitioning between major environmental compartments. The partitioning pattern was estimated to be 99.92% in air, 0.08% in water, and zero in either benthic sediments or ground. Torslov (1988) obtained similar results using a computer model based on the principles of the "fugacity" model of Mackay and predicted an environmental distribution of 99.29% in air, 0.7% in water, 0.01% in soil, sediment and aquatic biota, and zero in suspended aquatic material.

In 1978 it was estimated that 97.3% of the 1,1,1-trichloroethane used in the USA was released to the environment. Of this, 86% was released to the air, 1% to water, and about 10% was disposed of as waste (Fischer et al., 1982). It was also estimated that only about 6% of the 1,1,1-trichloroethane produced is emitted to the air or waste water during production, the remainder being released during use. The global-warming potential of 1,1,1-trichloroethane, an effect which results from its accumulation in the atmosphere, is about 40 times lower than that of trichlorofluoromethane (CFC-11) and 14 times lower than that of carbon tetrachloride.

4.1.1 Atmospheric transport

Atmospheric transport is the major route by which 1,1,1-trichloroethane is transported in the environment. Hence, it has been measured in air at remote locations (see section 5.1.1) and in rainfall (see section 5.1.2).

The ratio between concentrations of 1,1,1-trichloroethane in the northern and southern hemispheres is decreasing (Khalil & Rasmussen, 1984). Lower levels are found at mid latitudes during the summer because of greater removal by hydroxyl radicals (see section 4.2).

In a study of a whole range of halocarbons, Edwards et al. (1982) estimated that, of the chlorine in the troposphere, 45% originated from industry and 55% from natural or non-industrial sources of methyl chloride. Of the anthropogenic chlorine, 13% derived from the release of 1,1,1-trichloroethane.

In the troposphere, 1,1,1-trichloroethane is predominantly degraded by oxidation, but some is rained out and some is transferred to the stratosphere. Prior to 1977 the residence time in the troposphere was estimated to be 1 to 2 years (NRC, 1976), but the use of more reliable estimates of globally averaged levels has led to a calculated residence time of 5-7 years (Khalil & Rasmussen, 1984; Prinn et al., 1987; Midgley, 1989).

1,1,1-Trichloroethane has a long enough atmospheric lifetime for a certain portion to reach the stratosphere. In the early 1970s, it was calculated that approximately 12% of 1,1,1-trichloroethane reaching the troposphere would be transferred to the stratosphere. Revised figures have calculated that nearer to 15% is transferred (McConnell & Schiff, 1978; Singh et al., 1982).

In the stratosphere, 1,1,1-trichloroethane is degraded by photochemical processes, forming chlorine atoms and thence chlorine radicals that have the potential to deplete stratospheric ozone (see section 4.2.1).

4.1.2 Transport in water

In aquatic systems, volatilization is the major route for 1,1,1-trichloroethane removal. Oxidation and hydrolysis do not appear to play an important part in the aquatic fate of 1,1,1-trichloroethane (Dilling et al., 1975). Dilling et al. (1975) found 1,1,1-trichloroethane to be rapidly evaporated from water. At 25 °C, 90% evaporation occurred within 60-80 min from an aqueous solution containing 1 mg 1,1,1-trichloroethane/litre, the half-life being 20 min. The rate of disappearance was examined in the presence of various natural and added "contaminants", such as clays, limestone, peat, and other chemicals. None of these contaminants affected the disappearance rate by more than a factor of 2. It was concluded that no adsorption onto sediment or solids had taken place.

4.1.3 Transport in soil

The adsorption of 1,1,1-trichloroethane to soil is proportional to the organic carbon content of the soil (Urano, 1985). It has a low adsorption to silt loam (Chiou et al., 1979). These authors presented data which show that adsorption by soil organic matter occurs via a partitioning process rather than by physical adsorption.

In a dissertation report, Drake (1987) studied the fate in aerobic unsaturated soils. 1,1,1-Trichloroethane was applied to columns containing sandy or sandy loam soils (organic carbon contents of 0.69% and 3.76%, respectively), and mass balances were carried out to determine the fate of the compound. The processes studied were volatilization, transport, biodegradation, and sorption. There was no indication of biodegradation, but volatilization appeared to play a major role in the mass balance. Approximately 90% and 45% of the 1,1,1-trichloroethane applied to the sandy and sandy loam soils, respectively, were estimated to be lost via volatilization. Breakthrough of 1,1,1-trichloroethane was documented in both soils, and effluent levels of up to 10% of the 1 mg/litre influent level were observed after 25 days (Drake, 1987).

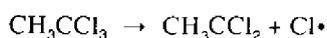
4.2 Degradation and transformation

4.2.1 Abiotic degradation

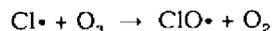
4.2.1.1 In the atmosphere

Using a concentration of 0.44 % (w/v) 1,1,1-trichloroethane in air in an enclosed flask exposed to external solar diurnal and climatic variations of incident radiation and temperature, Pearson & McConnell (1975) estimated the half-life to be 26 weeks. This is similar to the values found for dichloromethane and chloroform, and is much slower than most other chlorohydrocarbons. The authors also exposed 1,1,1-trichloroethane in the flasks to air in the presence of xenon arc radiation above 290 nm (which resembles sunlight) and monitored the degradation products. They identified carbon dioxide, hydrochloric acid, and a trace amount of chlorine. Traces of ozone, chlorine or nitrogen dioxide, gases that are known to occur in the atmosphere, were found to influence the product composition. Thus, if a minor amount of chlorine was initially present during the photo-oxidation of 1,1,1-trichloroethane, then rather more chlorine was found at the end of the experiment.

When 1,1,1-trichloroethane enters the troposphere, it is oxidized by reaction with the free hydroxyl radicals produced by the action of solar UV light to form trichloroacetaldehyde, which is further oxidized to trichloroacetic acid. The half-life for oxidation of 1,1,1-trichloroethane has been estimated to range from 2 to 5.5 years, corresponding to residence times of 5 to 7 years (Yung et al., 1975; McConnell & Schiff, 1978; Pearson, 1982). Slightly wider ranges of residence times have been recorded by other authors (Prinn et al., 1987; Fisher et al., 1990a), but the global average value generally used is around 6 years. As suggested in section 4.1.1, calculations indicate that 15% of 1,1,1-trichloroethane is transported to the stratosphere. There it is degraded by photochemical processes, induced by shorter wavelength higher energy solar radiation which does not occur at the tropospheric level, liberating chlorine atoms:



Free radical chlorine atoms (Cl•) destroy ozone and are regenerated to repeat the process.



The ozone-depleting effect of 1,1,1-trichloroethane is estimated to be 0.11 that of the chlorofluorocarbon CFC-11 (US EPA, 1980a; UNEP, 1989).

1.2.1.2 In water

Two parallel reactions result in the degradation of 1,1,1-trichloroethane in water: (a) dehydrochlorination to hydrochloric acid and 1,1-dichloroethene; (b) hydrolysis to hydrochloric and ethanoic acids (see section 2.2.2) (Gerken & Franklin, 1989). These reactions are influenced to a different degree by temperature and alkalinity (Pearson, 1982; CEFIC, 1986; Gerken & Franklin, 1989). Thus the calculated half-life at 10 °C in initially neutral demineralized water is 9.3 years and the observed half-life at 20 °C is 1.7 years (Gerken & Franklin, 1989). The half-life of 1,1,1-trichloroethane in water at varying temperatures is summarized in Table 4. Pearson & McConnell (1975) determined a half-life of 39 weeks at 10 °C in sea water at pH 8. These authors stated that it is the dehydrochlorination reaction which is very pH dependent. In artificial sea water containing salts at a concentration of 33 g/litre, the degradation rate was identical to that in demineralized water. At 25 °C, hydrolysis under neutral conditions was approximately 2.7 times faster than dehydrochlorination. Half-lives at higher temperatures have been reported by Haag & Mill (1988) and Gerken & Franklin (1989).

Since the chemical degradation rates are so slow, evaporation turns out to be the most important mechanism of loss from water (Dilling et al., 1975). These authors found a chemical degradation half-life in water containing 8.3 ppm oxygen at 25 °C of 6.9 months in natural sunlight. The same half-life was found in the dark, showing that photodegradation is negligible at the earth's surface.

4.2.2 Biodegradation

4.2.2.1 Anaerobic

In batch bacterial cultures, under methanogenic conditions at 35 °C in the dark, 1,1,1-trichloroethane at an initial concentration

Table 4. Half-life of 1,1,1-trichloroethane in water at varying temperatures^a

Temperature (°C)	Half-life	Reference
10	0.75 years 9.3 years ^b	Pearson & McConnell (1975) Gerkens & Franklin (1989)
20	1.7 years > 2.8 years	Gerkens & Franklin (1989) Vogel & McCarty (1987)
25	0.5 years 0.8 years 1 year	Dilling et al. (1975) Gerkens & Franklin (1989) Haag & Mill (1988)
40	24 days 28 days	Haag et al. (1986) Gerkens & Franklin (1989)
55	3.6 days 4.1 days	Gerkens & Franklin (1989) Mabey et al. (1983)
60	1.9 days 1.9 days 2.2 days	Walraevens et al. (1974) Gerkens & Franklin (1989) Haag et al. (1986)
65	0.9 days 1 day	Walraevens et al. (1974) Gerkens & Franklin (1989)
80	2.8 h 4.1 h 5.1 h 5.3 h	Archer & Stevens (1977) Gerkens & Franklin (1989) Haag & Mill (1988) Mabey et al. (1983)

^a From: Gerkens & Franklin (1989)

^b Extrapolation outside the temperature range investigated

of 100 µg/litre was almost completely degraded within 8 weeks, the final concentration being 0.3 µg/litre. No degradation occurred in the sterile controls. In a separate experiment, 1,1,1-trichloroethane (160 µg/litre) was added to a continuous-flow methanogenic fixed-film laboratory-scale column containing a bacterial inoculum. As with the batch experiment, 1,1,1-trichloroethane was almost completely degraded within 10 weeks (Bouwer & McCarty, 1983a). The degradation products of 1,1,1-trichloroethane were not identified.

In a study by Gossett (1985), 1,1,1-trichloroethane (initial concentration, 1.13 mg/litre) was degraded to 1,1-dichloroethane,

without a lag phase, in a bath inoculated with activated sludge under methanogenic conditions. All had been degraded within 6 days and 40% was degraded to 1,1-dichloroethane. The fate of the other 60% is unknown; some leakage occurred but not enough to account for the rest of the loss.

Bouwer & McCarty (1983b) found no degradation of 1,1,1-trichloroethane, at an initial nominal concentration of 60 $\mu\text{g}/\text{litre}$, after 8 weeks of incubation under anaerobic conditions in the presence of batch cultures of denitrifying bacteria.

Klecka et al. (1990) reported that 1,1,1-trichloroethane was readily degraded in both methanogenic and sulfate-reducing microbial cultures and that there was no lag period before the onset of degradation. Transformation products included 1,1-dichloroethane, chloroethane, and 1,1-dichloroethene. The latter was shown to be the product of abiotic breakdown, since it also occurred in microbial cultures poisoned by mercuric chloride.

Parsons & Lage (1985) found that 1,1,1-trichloroethane was biodegraded under anaerobic conditions in sediment. All of the added 1,1,1-trichloroethane (4-5 $\mu\text{g}/\text{ml}$) had disappeared within 4 to 5 months, the major degradation product being 1,1-dichloroethane. Parsons et al. (1985) reported that 16 weeks after the addition of 1,1,1-trichloroethane at a concentration of 3.6 mg/litre, 880 $\mu\text{g}/\text{litre}$ of dichloroethane had been formed.

Wilson & White (1986) found no degradation of 1,1,1-trichloroethane (added at a concentration of 765 $\mu\text{g}/\text{litre}$) in sand columns that were continuously supplied with propane for 21 days.

Boyer et al. (1987) demonstrated microbial degradation of 1,1,1-trichloroethane, added at a level of 5 or 20 mg/litre, in a packed bed (soil and activated carbon) laboratory reactor, which simulated an *in situ* decontamination system. The authors stated that biodegradation occurs under anaerobic conditions if a preferred substrate such as ethanol is present. After 43 days, no 1,1,1-trichloroethane was detectable in the reactor effluent (< 20 $\mu\text{g}/\text{litre}$). No chlorinated metabolic intermediates were observed.

4.2.2.2 *Aerobic*

Wilson et al. (1983) found no aerobic degradation of 1,1,1-trichloroethane, at a concentration of 1 mg/litre, in soil samples

collected from just above and below the groundwater table. The samples were incubated in the dark for 9 or 27 weeks.

4.3 Bioaccumulation

A bioconcentration factor of 9, comparable to that of other chlorinated solvents, has been reported for the bluegill sunfish (Veith et al., 1980). This is much lower than that predicted from the measured octanol/water partition coefficient of 2.47. The same authors also measured the loss of 1,1,1-trichloroethane from the bluegill sunfish following exposure for 28 days to a mean water concentration of 73 µg/litre. The half-life of 1,1,1-trichloroethane, as measured by the loss from the tissues of half the residue concentration attained at equilibrium, was found to be less than 24 h.

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Appraisal

As a consequence of release during its production and use, 1,1,1-trichloroethane is found in water, soil, biota, and, especially, in air. The background levels of 1,1,1-trichloroethane in air have increased over recent decades, although the rate of increase seems to be declining. Levels in industrial and urban areas tend to be higher than those in rural areas.

For the general population, air is the major source of exposure. In some cases, indoor air may contain higher levels than outdoor air. Under normal conditions, food and drinking-water are minor sources. 1,1,1-Trichloroethane has been found in breast milk. The use and abuse of consumer products and cosmetics containing 1,1,1-trichloroethane as a solvent may lead to considerable exposure.

Workers who use 1,1,1-trichloroethane, especially for degreasing or dry-cleaning operations, are particularly exposed to this solvent, although some exposure is likely in its manufacture. In the workplace, air is the major source of exposure but dermal exposure may also occur.

5.1 Environmental levels

5.1.1 Air

Rasmussen et al. (1981) monitored atmospheric concentrations of 1,1,1-trichloroethane in the Antarctic and the north Pacific coastal region of the USA between 1975 and 1980. They found that trichloroethane levels increased annually by over 20% during the period 1975-1978, then dropped below 10% during the period 1978-1980 in the Antarctic and reaching $0.55 \mu\text{g}/\text{m}^3$ (102 ppt) by 1980. In the Pacific north-west, a level of $0.84 \mu\text{g}/\text{m}^3$ (156 ppt) was reached by 1980.

It has been estimated that the annual global increase in the rate of emission of trichloroethane was 17% between the years 1956 and 1973 but only 8% per annum between 1975 and 1980 (Khalil & Rasmussen, 1981). This decline in turn resulted in a diminution of the differences in atmospheric levels between the northern and southern hemispheres (Khalil & Rasmussen, 1984).

Grimsrud & Rasmussen (1975) measured mean 1,1,1-trichloroethane concentrations of $0.54 \mu\text{g}/\text{m}^3$ (100 ppt) in the atmosphere over the rural north-west of the USA (Washington State) between December 1974 and February 1975, and Rasmussen & Khalil (1983) found $0.947 \mu\text{g}/\text{m}^3$ (175 ppt) in the lower troposphere over the Arctic in 1982. Average concentrations of 1,1,1-trichloroethane in air over Hokkaido, Japan, increased slightly between 1979 and 1988 and were of the order of $0.54\text{--}0.65 \mu\text{g}/\text{m}^3$ (100–120 ppt) (personal communication by T. Tominaga & Y. Makiide to the IPCS, 1990).

Pearson & McConnell (1975) analysed air samples from various locations in the United Kingdom. The highest levels of 1,1,1-trichloroethane, approximately $86 \mu\text{g}/\text{m}^3$ (16 ppb by mass), were found near an organochlorine manufacturing plant at Runcorn, Cheshire, and levels of $33.5\text{--}59.4 \mu\text{g}/\text{m}^3$ (6.2–11 ppb by mass) were found at Runcorn Heath. In suburban areas of the cities of Liverpool and Manchester, the concentrations ranged from 0.54 to $32.4 \mu\text{g}/\text{m}^3$ (< 0.1 to 6 ppb by mass).

Levels of 1,1,1-trichloroethane in air are summarized in Table 5.

Fischer et al. (1982) stated that, in relatively non-polluted areas, average concentrations of 1,1,1-trichloroethane could be assumed to be $0.54 \mu\text{g}/\text{m}^3$ (100 ppt) and in polluted areas levels of $2.7\text{--}5.4 \mu\text{g}/\text{m}^3$ (500–1000 ppt) could be expected. They also reported that near to large manufacturers or consumers concentrations could be as high as $540 \mu\text{g}/\text{m}^3$ (100 000 ppt). Lillian et al. (1975) monitored air samples for 1,1,1-trichloroethane at various locations in the USA and found mean levels ranging from $0.52 \mu\text{g}/\text{m}^3$ (0.097 ppb) at a rural site in Wilmington, Ohio, to $8.6 \mu\text{g}/\text{m}^3$ (1.59 ppb) in an urban area of Bayonne, New Jersey.

Air samples collected in the North Atlantic between 1982 and 1985, in the region of the Westerlies and the North-East trade winds, contained $1.08 \mu\text{g}/\text{m}^3$ (200 ppt). Above the trade winds (at 1800 m above sea level) a lower concentration of $0.84 \mu\text{g}/\text{m}^3$ (155 ppt) was found. An equivalent concentration was found at sea level in the region of the intertropical convergence. Baseline levels of 1,1,1-trichloroethane in 1985 in the South Atlantic were about $0.76 \mu\text{g}/\text{m}^3$ (140 ppt) (Class & Ballschmiter, 1986). Rasmussen & Khalil (1982) calculated that average concentrations of 1,1,1-trichloroethane in 1978 were $0.632 \mu\text{g}/\text{m}^3$ (117 ppt) in the northern hemisphere and $0.486 \mu\text{g}/\text{m}^3$ (90 ppt) in the southern hemisphere.

Table 5. 1,1,1-Trichloroethane concentrations in air

Type of location	Locality	Year	Concentration (ppt)	Reference
Industrial	Runcorn, UK	1973	≈ 16 000	Pearson & McConnell (1975)
	Bayonne, NJ, USA	1973	75-14 400	
Urban	Los Angeles, USA	1972	130-2300	Simmonds et al. (1974)
	Liverpool-Manchester, UK	1973	< 100-6000	Pearson & McConnell (1975)
	New York, USA	1974	100-1600	Lillian et al. (1975)
	Bochum, Germany	1978	18-1610 ^a	Bauer (1981)
	Lyon, France		< 840-2010	Correia et al. (1977)
	Denver, USA	1980	171-2699	Singh et al. (1982)
	Various sites, Japan	1982-1985	20-340	Magata & Furnichi (1986)
Rural	California, USA	1972	10-50	Simmonds et al. (1974)
	Various sites, UK	1973	1000-4000	Pearson & McConnell (1975)
	Various sites, USA	1974	30-350	Lillian et al. (1975)
	Hengelo, Netherlands		20-50	Correia et al. (1977)
	Oregon, USA	1975-1985	121 (1975) - 158 (1985) ^b	Prinn et al. (1987)

Table 5 (contd).

Type of location	Locality	Year	Concentration (ppt)	Reference
Rural (contd):				
	Tasmania, Australia Hokkaido, Japan	1978-1985 1979-1980	66 (1978) - 116 (1985) ^b 100-120	Prinn et al. (1987) Personal communication by T. Tomimaga & Y. Makitide to the IPCC (1990)
Oceanic	Hawaii, Pacific Samoa, Pacific Various sites, Atlantic Barbados, Atlantic	1980-1982 1978-1982 1982 1978-1985	111 (1980) - 125 (1982) 75 (1978) - 104 (1982) 132-214 ^c 93 (1978) - 144 (1985)	Khalil & Rasmussen (1984) Khalil & Rasmussen (1984) Class & Ballschmiter (1986) Prinn et al. (1987)
Polar	Near Barrow, Arctic South Pole, Antarctic	1979-1982 1975-1980	117 (1979) - 143 (1982) 45 (1975) - 102 (1980)	Khalil & Rasmussen (1984) Khalil & Rasmussen (1984)

^a The concentrations varied with wind direction and increased in the afternoon.

^b These are minimum and maximum monthly mean mixing ratios and differ slightly from the original data published by Khalil & Rasmussen (1984).

^c Northern hemisphere levels were consistently higher than southern hemisphere values.

5.1.2 Water

1,1,1-Trichloroethane has been reported to occur in ground water in many countries. Background levels tend to be low, but high levels of contamination are possible as a result of industrial activity and waste disposal.

Levels of 1,1,1-trichloroethane in water are summarized in Table 6.

Relatively high levels observed in rain water at Runcorn, United Kingdom (Pearson & McConnell, 1975), in the river Rhine, Germany (Fischer et al., 1982), in a canal in Modena, Italy (Aggazzotti & Predieri, 1986), in rivers that flow through industrial or large cities in Japan (Goto, 1979), in the inshore waters of Liverpool bay, United Kingdom (Correira et al., 1977), in ground water in Birmingham, United Kingdom (Rivett et al., 1990), and in Maryland, USA (Dever, 1986) all appear to be derived from nearby industrial activities where 1,1,1-trichloroethane is either manufactured or used.

Background levels in snow (Pearson, 1982) and in the open ocean (Pearson, 1982; Fischer et al., 1982) are usually very low, although levels up to $0.97 \mu\text{g}/\text{m}^3$ (0.18 ppb) have been found by Fischer et al. (1982) in the eastern Atlantic ocean.

5.1.3 Sediment and soil

Gossett et al. (1983) found 1,1,1-trichloroethane levels of $< 0.5 \mu\text{g}/\text{kg}$ (dry weight) in marine sediment collected from the vicinity of a Los Angeles waste water treatment plant, the effluent from which contained $31 \mu\text{g}/\text{litre}$.

Fischer et al. (1982) analysed soil samples from an industrial area of West Germany and found that 1,1,1-trichloroethane concentrations in soil interstitial water and soil particles were near to or less than the detection limits ($0.1 \mu\text{g}/\text{litre}$ and $0.1 \mu\text{g}/\text{kg}$, respectively). Samples of soil air contained 1,1,1-trichloroethane levels ranging from 0.2 to $10 \mu\text{g}/\text{m}^3$. In the same study, soil air samples from over 1000 bore holes in various locations were analysed. 1,1,1-Trichloroethane concentrations ranged from $1 \mu\text{g}/\text{m}^3$ in a rural area to over $2.2 \mu\text{g}/\text{m}^3$ in agricultural and forest soils near industrial sources and to $9 \mu\text{g}/\text{m}^3$ in urban areas.

Table 6. 1,1,1-Trichloroethane levels in water

Type of water	Locality	Characteristics	Year	Concentration (ppb)	Reference
Rain water	Runcorn, UK	near manufacturing site	1975	0.09	Pearson & McConnell (1975)
	Japan	urban		none detected	Goto (1979)
	Various sites	rain		0.005-0.09	Pearson (1982)
	Various sites	snow		0.001-0.03	Pearson (1982)
Rivers & canals	Rhine, Germany	river	1972-1976	0.01-3300	Fischer et al. (1982)
	Netherlands	canals		0.07-0.3 w/w	Correia et al. (1977)
	R. Durance, France	river	1972-1976	none detected	Correia et al. (1977)
	Modena, Italy	canal		10-40	Aggazzotti & Predieri (1986)
	Japan	river, industrial	1975	≈ 5.1	Goto (1979)
	Japan	river, large city	1975	≈ 2.5	Goto (1979)
	Japan	river, smaller cities	1975	≈ 0.1-0.81	Goto (1979)
Sea	Not defined	inshore waters	1972-1976	0.15	Pearson (1982)
	Liverpool Bay, UK	inshore water		≤ 0.25-3.3	Correia et al. (1977)
	East Atlantic	open ocean		0.05-0.18	Fischer et al. (1982)
	"Typical sites"	open ocean		0.01-0.03	Pearson (1982); Fischer et al. (1982)

Table 6 (contd).

Type of water	Locality	Characteristics	Year	Concentration (ppb)	Reference
Wells & ground waters in general					
	Zurich, Switzerland	ground water	1977	0.02-2.8	Giger et al. (1978)
	Japan	urban, shallow	1982	0.2-1600	Magara & Furuichi (1986)
		urban, deep	1982	0.2-70	
	Emilia-Romagna, Italy	"ground water"		< 1	Aggazzotti & Predieri (1986)
	Various sites	underground water	1983	0.2 (typical), 5 (high)	Pearson (1982)
	Various sites, UK			0.48 (average)	Kenrick (1983)
	Birmingham, UK	industrial; ground water	1985-1988	> 0.2-780 (46% of sample)	Rivett et al. (1990)
	Maryland, USA	near electronic plant		up to 1600	Dever (1986)
Water chlorination plant					
	Emilia-Romagna, Italy	chlorinated water		0.1-0.5	Aggazzotti & Predieri (1986)

Pearson & McConnell (1975) measured a combined concentration of 1,1,1-trichloroethane and carbon tetrachloride in sediments of Liverpool Bay, United Kingdom, of 5.5 $\mu\text{g}/\text{kg}$ (5.5 ppb).

5.1.4 Biota

Table 7 gives the ranges of 1,1,1-trichloroethane concentrations found in various marine biota collected in United Kingdom estuaries (Liverpool Bay, Firth of Forth, and Thames Estuary) by Pearson (1982) and Pearson & McConnell (1975).

Table 7. Concentration of 1,1,1-trichloroethane in various marine organisms^a

Organism	Concentration ($\mu\text{g}/\text{kg}$)
Plankton	0.03-10.7
Marine algae	10-25
Molluscs	0.05-10
Crustaceans	0.7-34
Fish, flesh	0.7-5
Fish, liver	1-15
Sea-birds, eggs	3-30
Sea-birds, liver	1-4
Seal, liver	0.2-4
Seal, blubber	8-24

^a From: Pearson (1982)

Dickson & Riley (1976) analysed various fish species and a mollusc species from Port Erin, Isle of Man, United Kingdom, and found trichloroethane (isomer not stated) concentrations of 2 and 9 $\mu\text{g}/\text{kg}$ dry weight, respectively, in gill and brain tissue of the eel *Conger conger*. Analysis of cod (*Gadus morhua*) revealed trichloroethane levels ranging from 5 $\mu\text{g}/\text{kg}$ in muscle and liver tissue to 16 $\mu\text{g}/\text{kg}$ in brain tissue. Muscle tissue of coalfish (*Pollachius birens*) contained 6 $\mu\text{g}/\text{kg}$, and a level of 4 $\mu\text{g}/\text{kg}$ was found in the digestive tissue of the mollusc *Modiolus modiolus*.

Gossett et al. (1983) collected various marine biota from the vicinity of the Los Angeles County, USA, waste water treatment

plant. 1,1,1-Trichloroethane concentrations of 4 µg/kg wet weight were found in whole invertebrate samples and < 0.3 µg/kg wet weight in shrimp muscle. Levels ranged from < 0.3 to 7 µg/kg wet weight in the liver of various fish species.

5.2 General population exposure

5.2.1 Food

A study of the average daily intake of trichloroethane in Germany showed that 10%, i.e. 3.6 µg/day, originated from foodstuffs (Duszeln et al., 1982). Uhler & Diachenko (1987) found levels of 1,1,1-trichloroethane in nine foodstuffs (mainly cheeses and ice cream), sampled in the USA, at levels of between 1 and 37 µg/kg. These levels were thought to arise from contamination either by air contact with fugitive emission of cleaning solvent or by contact with packaging materials containing 1,1,1-trichloroethane.

Entz & Diachenko (1988) surveyed 52 margarines and spread products from supermarkets in the Washington, D.C. metropolitan area between 1980 and 1982 and a further 18 products in 1984. In addition, 19 margarines were examined at manufacturing plants in 1982. The following levels were found:

	Number of store shelf samples	Number of manufacturing plant samples
Not detected ^a	11	1
Trace levels ^a	12	1
< 50 µg/kg	35	15
50-100 µg/kg	7	2
> 100-500 µg/kg	5	-

^a Trace levels of 1,1,1-trichloroethane represented < 5 µg/kg; the detection limit was about a third of the trace level.

Miller & Uhler (1988) similarly studied 46 butter samples and reported levels of from 10 µg/kg to more than 100 µg/kg. In one sample containing 7500 µg/kg, the source was traced to a packing adhesive.

Pfannhauser et al. (1988) found that levels of 1,1,1-trichloroethane were mostly below 10 µg/kg in samples of Austrian olive oil, cheese, and chocolate; only one sample of olive oil contained over 100 µg/kg. The authors suggested that cleaning solvents in production areas and packaging materials were possible sources for the contamination.

Pellizari et al. (1982) analysed breast milk for 1,1,1-trichloroethane in four urban areas of Pennsylvania, New Jersey, and Los Angeles, USA. They sampled up to 12 women at each site, and eight samples out of 42 were analysed manually by experienced spectroscopists. 1,1,1-Trichloroethane was identified in all of the samples, but no actual levels were reported. Travis et al. (1988) also suggested contamination of human breast milk based on pharmacokinetic modelling.

Table 8 summarizes data on the concentrations of 1,1,1-trichloroethane reported in foods.

5.2.2 Drinking-water

An investigation of drinking-water from 100 cities in Germany showed a range of trichloroethane concentrations from < 0.1 to 1.7 µg/litre (Bauer, 1981).

A study of the daily average intake of trichloroethane in Germany revealed that 0.6%, i.e. 0.2 µg/day, of the intake came from drinking-water. These calculations were based on a daily intake of 1 litre of drinking-water containing 0.2 µg trichloroethane/litre of water (Düszeln et al., 1982).

In the USA, 23 wells out of 1611 tested contained 1,1,1-trichloroethane. Another investigation in the USA showed detectable concentrations in 835 of 1071 samples, with a maximum value of 607.8 µg/litre and a 90th percentile of 6.1 µg/litre (Fischer et al., 1982).

Pearson (1982) reported a value of 0.1 µg/litre as a typical level of 1,1,1-trichloroethane in drinking-water. Fielding et al. (1981) surveyed 14 drinking-water sources in the United Kingdom over a period of 9 months in 1976. 1,1,1-Trichloroethane was found at 3 out of 14 sites and, although no actual levels were reported, it was implied that concentrations were less than or equal to 1 µg/litre.

Table 8. Concentrations of 1,1,1-trichloroethane ($\mu\text{g}/\text{kg}$) in various foodstuffs^a

Foodstuff	Mean content	Range	Reference
Dairy products		0.1-10 0-0.6	Pearson (1982) Bauer (1981)
Meat		3-6	McConnell et al. (1975) Pearson (1982)
Vegetable oils		0.5-10 < 1 - > 100	Pearson (1982) Pfannhauser et al. (1988)
Margarine	45	n.d. - 500	Entz et al. (1982) Entz & Diachenko (1988)
Butter	16	10-7500	Entz et al. (1982) Miller & Uhler (1988)
Ice cream	2		Entz et al. (1982)
Cheese		7-9 < 1 - 100	Entz et al. (1982) Pfannhauser et al. (1988)
Bread	2		McConnell et al. (1975) Pearson (1982)
Potatoes		1-4	McConnell et al. (1975)
Fruit and vegetables		2-3	McConnell et al. (1975) Pearson (1982)
Fish flesh		0.7-5	McConnell et al. (1975) Pearson (1982)
Fish (cod) liver, muscle, stomach		5-7 ^b	Dickson & Riley (1976)
Tea (packet)	7		McConnell et al. (1975)
Rolled oats	770 ^c		Daft (1988)
Popcorn	5		Daft (1988)
Pinto beans	5		Daft (1988)
Chocolate products		< 1 - 100	Pfannhauser et al. (1988)
Fatty foods		< 1 - 10	Pfannhauser et al. (1988)

^a Fresh (wet) weight, unless specified otherwise; n.d. = not detected

^b Dry weight

^c Possibly from fumigant contamination

Dever (1986) reported levels of 1,1,1-trichloroethane in a contaminated water supply in Montgomery County, Maryland, USA. Both raw and treated potable water samples were analysed, and 1,1,1-trichloroethane levels of 180 $\mu\text{g}/\text{litre}$ and 30 $\mu\text{g}/\text{litre}$, respectively, were found.

Wallace et al. (1987) measured low levels of 1,1,1-trichloroethane in drinking-water collected in 3 states in the USA during 1981/1982. The average levels in New Jersey were 0.2–0.6 ng/litre (maximum levels were 1.6–5.3 ng/litre), and in North Carolina and North Dakota they were lower still, i.e. 0.03 ng/litre and 0.04 ng/litre , respectively.

An environmental monitoring study carried out near 1,1,1-trichloroethane production plants and user facilities in 1976/1977 yielded the following 1,1,1-trichloroethane levels in hotel tap water (US EPA, 1977):

Freeport, Texas (industrial area): 17 $\mu\text{g}/\text{litre}$;
Lake Charles, Louisiana (industrial area): 0.3 $\mu\text{g}/\text{litre}$;
Helena, Arkansas (rural area): 0.4 $\mu\text{g}/\text{litre}$.

Concentrations of 1,1,1-trichloroethane in Japanese tap water (Osaka City) were reported to range from 0.078 to 0.212 $\mu\text{g}/\text{litre}$ (Kajino & Yagi, 1980).

5.2.3 Air

In relatively non-polluted areas, the average concentration of 1,1,1-trichloroethane in air can be assumed to be around 540 ng/m^3 (100 ppt), increasing to 2700–5400 ng/m^3 (500–1000 ppt) in industrialized areas (Bouwer & McCarty, 1983a,b). In Germany, the average air concentration was found to be about 2 $\mu\text{g}/\text{m}^3$ (Düszeln & Thiemann, 1985).

In a monitoring study conducted in 1981 on 350 residents of New Jersey, USA, Wallace et al. (1986) found median indoor air concentrations of 17 $\mu\text{g}/\text{m}^3$ both at night and during the day. Concentration ranged from 0.16 to 333 000 $\mu\text{g}/\text{m}^3$. The median outdoor air level was 4.5 $\mu\text{g}/\text{m}^3$, the range being 0.05 to 470 $\mu\text{g}/\text{m}^3$. Analyses conducted on the breath of these individuals showed median levels of 6.6 $\mu\text{g}/\text{m}^3$ (ranging from 0.06 to 520 $\mu\text{g}/\text{m}^3$).

A study of the average daily intake of trichloroethane in Germany estimated that 89%, i.e. 32 μg of the daily intake of 35.8 μg , came from the air. This calculation was based on a daily inhalation of 20 m^3 air containing 1.6 μg trichloroethane/ m^3 (300 ppt) (Düszeln et al., 1982).

In Japan, 15 sites of Yokohama City and Kawasaki City were sampled from July 1985 to July 1986. Mean (of 5) concentrations of 14.6, 12.4, and 8.6 $\mu\text{g}/\text{m}^3$ were measured in industrial, commercial, and residential areas, respectively (Urano et al., 1988). The calculated average intake ($\mu\text{g}/\text{day}$) by inhalation in each area was 135, 114, and 81, respectively.

It can be concluded that, in general, inhalation is the most important source of human exposure to trichloroethane.

5.2.4 Consumer products and cosmetics

Trichloroethane is used as a solvent in aerosol and non-aerosol consumer products, and the concentration may be anywhere in the range 10-100% (IARC, 1979). In aerosol cans for cosmetics, a concentration of up to 35% is allowed in countries of the Economic European Community (EEC). Consumer use and abuse of such products may lead to considerable exposure to trichloroethane, which can be much higher than from other sources.

In a study by Otson et al. (1984), two fabric protectors (450 g of each) containing 75% and 97% 1,1,1-trichloroethane, respectively, were sprayed onto a sofa in a room with a volume of 28 m^3 . Initial concentrations were as high as 1800 mg/m^3 . Concentrations dropped rapidly to less than 150 mg/m^3 when the room was ventilated, but under unventilated conditions they remained above 1000 mg/m^3 for at least one hour and dropped below 500 mg/m^3 only after more than 2 h.

5.3 Occupational exposure

In general, exposure levels of trichloroethane at the workplace are much lower than established limit values for workplace air. The 8-h time-weighted average (TWA) concentrations measured in the United Kingdom in vapour-degreasing baths were typically 10.8-270 mg/m^3 (2-50 ppm) (HSE, 1990).

In addition to workers engaged in the manufacturing and production of trichloroethane and trichloroethane-containing

products, the workers most likely to be exposed to trichloroethane are those engaged in dry-cleaning or degreasing processes in the metallic and electronic industries. It was estimated that about 2.23 million workers were potentially exposed to trichloroethane in the USA (NIOSH Survey, 1983).

During the period 1983 to 1986, the Danish Labour Inspection Service made 476 measurements of trichloroethane at workplaces in Denmark (AMI, 1988). In 6% of the samples the levels were found to exceed the Occupational Limit Value of 540 mg/m³ (100 ppm).

6. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Appraisal

1,1,1-Trichloroethane is rapidly absorbed through the lungs. Absorption through the gastrointestinal tract and skin also occurs, but is of less importance than the inhalation route. In humans, the absorption from the lungs is about 25 to 40% of the inhaled dose over 6 to 8 h. 1,1,1-Trichloroethane is distributed widely to body tissues, especially to those with a high lipid content, e.g., brain and adipose tissue. It crosses the blood-brain and placental barriers. Less than 7% of an absorbed dose is metabolized. Metabolism appears to be saturable. Excretion by exhalation of unchanged compound accounts for > 90% of the absorbed dose. Less than 1% of 1,1,1-trichloroethane remains in the human body after 9 days.

6.1 Absorption

1,1,1-Trichloroethane is rapidly absorbed through the lungs and the gastrointestinal tract. Absorption through skin also occurs, but is of minor importance compared to uptake via inhalation.

6.1.1 *Animal studies*

6.1.1.1 *Inhalation*

The absorption in the lungs of rats exposed to 270 or 2700 mg 1,1,1-trichloroethane/m³ (50 or 500 ppm) has been shown to be time-dependent. The initial uptake was more than 80% of the dose. During the first hour the absorption decreased to around 50%, the decrease being greater in the high-dose group (Dallas et al., 1989). Because 1,1,1-trichloroethane is poorly metabolized (see section 6.3), absorption is expected to be low as steady state is approached.

In dogs exposed to 4.05, 8.1 or 10.8 g/m³ (750, 1500 or 2000 ppm) for one hour by inhalation, the cumulative uptake was 27, 45, and 71 mg/kg, respectively. This represented about 14% of inhaled amounts. Concentrations in arterial and venous blood did not attain a steady state during this period (Hobara et al., 1982).

6.1.1.2 Oral absorption

Oral toxicity data (see section 7.1, Table 10) suggest that 1,1,1-trichloroethane is readily taken up from the gastrointestinal tract (Reitz et al., 1988).

6.1.1.3 Skin absorption

The percutaneous penetration of 1,1,1-trichloroethane was studied in guinea-pigs by applying the solvent in a skin depot (a glass ring attached to the skin and covered with glass). Absorption was found to be rapid and to result in blood levels of 1.9 mg/litre during the first 30 min. These levels were higher than those found for carbon tetrachloride and perchloroethylene (1.1 mg/litre in both cases) in the same study (Jakobson et al., 1980, 1982). HSE (1984) calculated a rate of absorption through the skin of 6 $\mu\text{g}/\text{min}$ per cm^2 from this study.

Compared to methylene dichloride, chloroform, carbon tetrachloride, and 1,1,2-trichloroethane, the skin penetration of 1,1,1-trichloroethane in mice was found to be lower. The penetration rate of these solvents increased with the degree of water solubility (Tsuruta, 1975).

6.1.2 Human studies

The absorption of trichloroethane in humans has been studied following exposure by inhalation and by skin contact. No studies have so far been carried out using the oral route, but reports of intoxication following oral ingestion indicate that the chemical can be absorbed by this route (Stewart & Andrews, 1966, 1971).

6.1.2.1 Inhalation

The absorption of 1,1,1-trichloroethane in the lungs is lower than that of most other chlorinated solvents. This is due to the relatively low blood/air partition coefficient of 3.3 (US EPA, 1984).

Studies with human volunteers (males), exposed by inhalation to 1,1,1-trichloroethane at concentrations from around 200 mg/m^3 (35 ppm) to 2000 mg/m^3 (350 ppm) for 6-8 h, showed that about 25-40% of the trichloroethane inhaled was absorbed by the lungs, depending on its concentration in the inhaled air, duration of exposure, body weight and amount of adipose tissue, blood

circulation, and other factors (Astrand et al., 1973; Humbert & Fernandez 1977; Monster et al., 1979; Nolan et al., 1984). The amount absorbed increased with increasing work-load, due presumably to an increase in breathing rate (Monster et al., 1979).

6.1.2.2 Skin contact

Percutaneous absorption of 1,1,1-trichloroethane has been measured in human subjects. Following the immersion for a few minutes of a thumb or a hand in liquid 1,1,1-trichloroethane, it is possible to detect the solvent in the breath (Stewart & Dodd, 1964).

The absorption of trichloroethane through the skin is slower than for aromatic solvents and perchloroethylene, and is, in general, considered of minor importance compared to the more rapid uptake via the lungs (Humbert & Fernandez, 1977). Dermal application to human volunteers of 15 ml 1,1,1-trichloroethane under occlusion resulted in 16.2-27 mg/m³ (3-5 ppm) of the solvent in the exhaled air. This corresponded to a 2-h inhalation exposure of 54-108 mg/m³ (10-20 ppm) (Nakaaki et al., 1980).

Trichloroethane vapour can also be absorbed through the intact skin, but the amount absorbed in the body has been estimated to be a thousand times less than the amount absorbed by inhalation (Riihimaki & Pfaffli, 1978).

6.2 Distribution and retention

Compared with many other chlorinated hydrocarbon solvents, 1,1,1-trichloroethane has a high lipid/blood partition coefficient (108 at 37 °C). It would therefore be expected to distribute widely into body tissues, especially into those, such as brain and adipose tissue, with high lipid content (US EPA, 1984; CEC, 1986).

Blood and exhaled breath concentrations of 1,1,1-trichloroethane in rats increased rapidly after inhalation exposure, approaching, but not reaching, steady state after a 2-h exposure (Dallas et al., 1989).

6.2.1 Animal studies

When rats were exposed to 2700 mg/m³ (500 ppm) (6 h per day for 4 days), only trace amounts of 1,1,1-trichloroethane could be detected in the liver, brain, and blood 17 h after the end of the

exposure period. A higher concentration remained in adipose tissue, but this represented only about 5% of the concentration immediately after exposure (Savolainen et al., 1977). These data indicate that 1,1,1-trichloroethane does not accumulate in the tissues. This is supported by the observation that no significant tissue accumulation occurred in rats exposed to 8100 mg/m³ (1500 ppm), 6 h per day, 5 days per week, for 16 months (Schumann et al., 1982).

In a study by Danielsson et al. (1986), pregnant mice were exposed to ¹⁴C-labelled 1,1,1-trichloroethane by inhalation for 10 min on days 11, 14 or 17 of gestation. Radioactivity was detected in the brain, lungs, liver, and kidney of the maternal mouse immediately after exposure, the concentrations being approximately the same in all tissues. The fetal and placental uptake was measured at all stages of gestation studied. Although the fetal uptake was low compared with uptake to the maternal brain, the authors stated that 1,1,1-trichloroethane passes as easily through the placental barrier as through the blood-brain barrier. After exposure, 1,1,1-trichloroethane disappeared from both maternal and fetal bodies within 24 h. A small amount of non-volatile radioactivity was present in both the mother and fetus.

Concentrations of 1,1,1-trichloroethane in exhaled air from dogs exposed to 3780, 8100 or 10 800 mg/m³ (700, 1500 or 2000 ppm) increased rapidly for one hour, approaching steady-state levels at 80 to 90% of inhaled air concentrations. After one hour's recovery, 66 to 71% of the total uptake had been excreted through the lungs (Hobara et al., 1982).

6.2.2 Human studies

In a fatal case of 1,1,1-trichloroethane intoxication, residues of the solvent were determined in the bile, blood, brain, kidney, liver, and lung. The concentration was highest in the brain, followed by the kidney (Caplan et al., 1976). This indicates that 1,1,1-trichloroethane can also cross the blood-brain barrier in humans.

Samples of kidney, lung, and muscle tissues taken from hospital patients in Finland contained small amounts of 1,1,1-trichloroethane (0.1 to 0.4 µg/kg) (Kroneld, 1989). In human samples from the German Ruhr district, levels of 1.8 to 5.6 µg/kg (fresh weight) were found in the same tissues. In addition, 2.1 µg/kg was found in fat tissue and 1.9 µg/kg in liver tissue (Bauer, 1981).

6.3 Metabolic transformation

1,1,1-Trichloroethane is a fairly stable molecule, which is metabolized in mammals to a lesser degree than other trichlorinated solvents (Ikeda & Ohtsuji, 1972). As shown in Fig. 1, the principal metabolites are 2,2,2-trichloroethanol and trichloroacetic acid (Humbert & Fernandez, 1977). These metabolites are formed in the liver by microsomal oxidases (cytochrome P-450) (Ivanetich & Honert, 1981; US EPA, 1984). Trichloroethanol is conjugated with glucuronic acid before excretion in the urine.

6.3.1 Animal studies

In an early study in rats, less than 3% of a single intraperitoneal injected dose of about 700 mg 1,1,1-trichloroethane/kg body weight was metabolized within 25 h; the rest was expired unchanged. The metabolites identified, accounting for 1.6% of the dose, were the glucuronide of 2,2,2-trichloroethanol in the urine (53%) and $^{14}\text{CO}_2$ in the expired air (30%) (Hake et al., 1960).

When 1,1,1-trichloroethane (143 mg/kg) was administered in the drinking-water to rats over an 8-h period, the percentage of the dose recovered as metabolites within 56 h was 6%, of which 37% was excreted in the urine and 37% as $^{14}\text{CO}_2$ in the expired air (Reitz et al., 1988). Following repeated administration by gavage for 4 weeks, the percentage of the administered dose recovered as metabolites in male rats within 48 h was 4.2%. Under similar experimental conditions in mice, 6.1% of the administered dose was recovered as metabolites (Mitoma et al., 1985). A single inhalation exposure for 4 h at a concentration of 1188 or 2376 mg/m³ (220 or 440 ppm) resulted in, respectively, urine metabolite concentrations of 0.58 and 0.97 mg/kg body weight. Both trichloroethanol and trichloroacetic acid were identified as metabolites in the urine, trichloroethanol being excreted (as the glucuronide) much faster than trichloroacetic acid (Eben & Kimberle 1974).

Following a single inhalation exposure of rats to 810 and 8100 mg/m³ (150 and 1500 ppm), only a 2-4 times increase in excreted metabolites was found between the two doses, suggesting metabolic saturation. Repeated exposure to 8100 mg/m³ over 16 months did not change the amount of 1,1,1-trichloroethane metabolites. Similar results were obtained in mice. In both rats and mice, urine metabolites accounted for 40-70% of the total

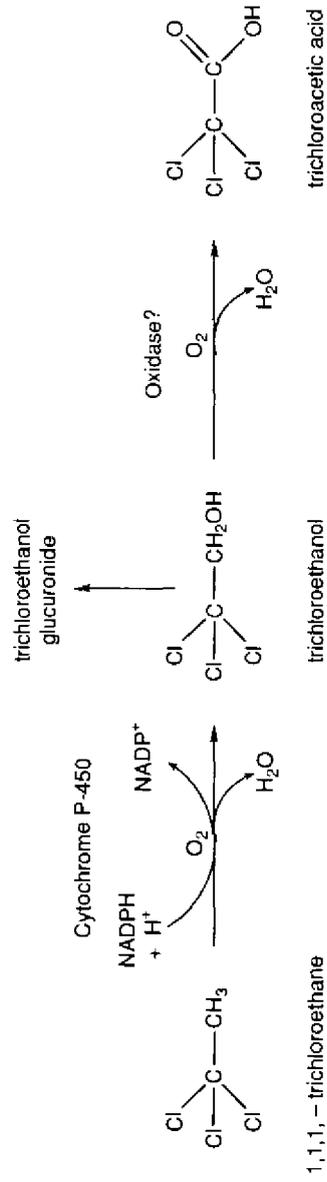


Fig. 1. Metabolic pathway of 1,1,1-trichloroethane.

amount metabolized. Overall, mice were found to biotransform approximately 5 times more 1,1,1-trichloroethane (per kg body weight) than rats. In rats and mice an age-related increase in the amount metabolized was observed in aged animals as opposed to young adults (Schumann et al., 1982).

6.3.2 Human studies

The average amount of metabolites excreted in the urine of humans (workers or volunteers) exposed to 1,1,1-trichloroethane in the air (22-1890 mg/m³, 4-350 ppm) was variable, but was typically between 3 and 7% of the absorbed dose. The ratio of the metabolites trichloroethanol glucuronide and trichloroacetic acid was about 2 to 1, but this increased with increasing exposure concentration (Seki et al., 1975; Humbert & Fernandez, 1977; Monster et al., 1979; Nolan et al., 1984).

6.3.3 Metabolic interactions

Simultaneous exposure to other solvents tends to increase the retention and decrease the metabolism of 1,1,1-trichloroethane (Savolainen et al., 1981). 1,1,1-Trichloroethane metabolism was accelerated in rats pre-treated with ethanol because of the induction of metabolic enzymes (Sato et al., 1980).

6.4 Elimination

Regardless of the route of administration, the main excretory route for 1,1,1-trichloroethane is exhalation via the lungs. This may be explained by the relatively low solubility in blood.

6.4.1 Animal studies

In rats and mice, 55% to 98% of the 1,1,1-trichloroethane was excreted unchanged in expired air after oral or intraperitoneal exposure (Hake et al., 1960; Reitz et al., 1988).

Following inhalation exposure, 94-98% of the absorbed 1,1,1-trichloroethane was excreted unchanged in the expired air of rats during 72 h. In mice, the corresponding figure was 87-97%. The rate of elimination was somewhat higher in mice; 85% was eliminated during the first 3 h compared to 65% in rats (Schumann et al., 1982).

A total of about 1-8% of an absorbed dose in rodents is excreted in the urine (Hake et al., 1960; Schumann et al., 1982).

After exposure to 1,1,1-trichloroethane vapour, the level in blood plasma decreases rapidly in a biphasic or triphasic manner, depending on the exposure level. Following exposure to 810 mg/m³ (150 ppm), the half-lives were 10 and 139 min, whereas with 8100 mg/m³ (1500 ppm), the half-lives were 36 and 238 min. In mice the half-lives were a little shorter (Schumann et al., 1982).

6.4.2 Human studies

Studies with human volunteers show that over 90% of the absorbed trichloroethane is excreted unchanged in the expired air. Only minor parts (5-7%) of the absorbed solvent are excreted in the urine (as trichloroethanol glucuronide and trichloroacetic acid) (Stewart et al., 1969; Humbert & Fernandez, 1977; Nolan et al., 1984). The main product was found to be 2,2,2-trichloroethanol glucuronide, the excretion of which was completed within 8 days. The secondary product was trichloroacetic acid; its excretion occurred somewhat later and was completed within 12 days (Humbert & Fernandez, 1977).

The elimination of 1,1,1-trichloroethane, measured as plasma concentration and concentration in expired air, in six human volunteers exposed to 191 or 1911 mg/m³ (35 or 350 ppm) for 6 h could be described by a three-compartment model with estimated half-lives of 44 min, 5.7 h, and 53 h, respectively. Less than 1% remained in the body after 9 days (Nolan et al., 1984).

In a study by Nolan et al. (1984), the trichloroethane concentrations in blood and expired air were proportional to the exposure concentration after 6 h of exposure and indicated that about 25% of the 1,1,1-trichloroethane inhaled during the exposure was absorbed.

6.5 Biological monitoring

Several options exist for the biological monitoring of exposure to 1,1,1-trichloroethane (Monster 1986). These include the determination of:

- the unchanged solvent in blood or alveolar air;
- the metabolite trichloroethanol in blood, alveolar air or urine;
- the metabolite trichloroacetic acid in blood and urine.

Table 9 indicates the mean concentrations of these parameters as a result of exposure of subjects for 8 h/day (5 days/week) to a time-weighted average (TWA) concentration of 270 mg/m³ (50 ppm) (Monster, 1986).

Table 9. Mean concentrations of 1,1,1-trichloroethane, trichloroethanol, and trichloroacetic acid in blood, alveolar air, and urine^a

Test	Time after exposure of sampling			
	End of exposure	5-15 min	16 h	64 h
Blood (mg/litre)				
1,1,1-trichloroethane		0.9		0.07
trichloroethanol		0.16		-
trichloroacetic acid		2.3		1.6
Alveolar air (mg/m³)				
1,1,1-trichloroethane ^b		210 (39)	13 (2.4)	8 (1.5)
trichloroethanol		0.014	0.007	-
Urine (mg/g creatinine)				
trichloroacetic acid	4.9		2.5	0.9
trichloroethanol	2.5		1.8	1.5

^a From: Monster (1986)

^b Values in parentheses are in ppm

Trichloroethane concentrations in blood measured after work on a Friday seem to be the best single parameter for estimation of the TWA-week exposure (Monster, 1986). For one-day exposure, the trichloroethane level in blood and urine is most useful (Monster, 1986).

Droz et al. (1989) suggested a physiological model for describing variability in the biological monitoring of solvent exposure. Standard statistical distributions are used to simulate variability in exposure concentration, physical workload, body fluid, liver function, and renal clearance. For groups of workers exposed daily, the model calculates air monitoring indicators and biological monitoring results, including levels in expired air,

blood, and urine. The calculated results obtained are discussed and compared with measured data for physiological and toxicokinetic parameters for six solvents including 1,1,1-trichloroethane and their metabolites. It is suggested that such mathematical models are applicable for prediction and management studies.

6.6 Bioaccumulation

Inhalation exposure of rats to 2700 mg/m³ (500 ppm) for 4 days, 6 h per day, led to an accumulation of 1,1,1-trichloroethane in the fat 17 h after the last exposure. Further exposure on the 5th day increased brain, liver, lung, and blood levels (Savolainen et al., 1981).

A study by Travis et al. (1988) indicated that bioaccumulation of organic chemicals, including 1,1,1-trichloroethane, perchloroethane, trichloroethylene, and dichloromethane, in human adipose tissues was positively correlated with their octanol-water partition coefficients. The information presented, however, was based on data from a human pharmacokinetic model.

7. EFFECTS ON LABORATORY MAMMALS AND IN VITRO TEST SYSTEMS

Appraisal

1,1,1-Trichloroethane administered by various routes has low acute toxicity for laboratory animals. The acute toxicity pattern is characterised by central nervous system depression and respiratory arrest at lethal levels. 1,1,1-Trichloroethane is a moderate skin and mild eye irritant.

Short-term inhalation exposure of rats to 4320-5400 mg/m³ (800-1000 ppm) or more produced an increase in liver weight. At similar concentrations in mice, the liver changes were more marked and included fatty infiltration and single cell necrosis. Minor cytoplasmic alterations were seen in mice exposed to 1350 mg/m³ (250 ppm). Studies on Mongolian gerbils using 1,1,1-trichloroethane concentrations down to 378 mg/m³ (70 ppm) revealed effects on DNA concentrations and other biochemical effects in several regions of the brain. The significance of these findings is uncertain. The no-observed-effect level (NOEL) for rats is about 2700 mg/m³ (500 ppm).

In long-term toxicity studies, 1,1,1-trichloroethane administration led to reduced weight gain in both rats and mice. Slight microscopic hepatic effects were seen, but only at the highest concentration of 8100 mg/m³ (1500 ppm). There was no evidence of carcinogenic potential in oral and inhalation studies on rats and mice. One study reported increased incidence of leukaemia but this study is considered inadequate.

1,1,1-Trichloroethane has been shown to have low genotoxic potential in a range of in vitro and in vivo studies.

In a multigeneration study on mice, there was no evidence of adverse reproductive effects (including effects on fertility) caused by 1,1,1-trichloroethane in drinking-water at concentrations up to 1000 mg/kg body weight. Inhalation studies on female rats and mice at 4590 mg/m³ (850 ppm) showed no evidence of teratogenic or fetotoxic effects. However, in rats exposed to 11 340 mg/m³ (2100 ppm), there was some evidence of fetotoxicity.

The data available are inadequate to assess the immunotoxic potential of 1,1,1-trichloroethane.

Enhanced toxicity of 1,1,1-trichloroethane was observed when exposure was combined with exposure to ethanol.

7.1 Acute toxicity

1,1,1-Trichloroethane has a very low acute toxicity in laboratory animals dosed by various routes of administration. Selected LD₅₀ and LC₅₀ values are given in Tables 10 and 11.

Table 10. Acute toxicity (LD₅₀) of 1,1,1-trichloroethane in experimental animals

Species	Sex	Route	LD ₅₀ (mg/kg body weight)	Reference
Rat	male	oral	14 300	Torkelson et al. (1958)
Rat	female	oral	11 000	Torkelson et al. (1958)
Mouse	female	oral	9700	Torkelson et al. (1958)
Guinea-pig	male & female	oral	8600	Torkelson et al. (1958)
Rabbit	male & female	oral	10 500	Torkelson et al. (1958)
Rabbit	male & female	skin	15 800	Torkelson et al. (1958)
Mouse	female	intraperitoneal	3700	Gradiski et al. (1974)
Mouse	male	intraperitoneal	5080	Klaassen & Plaa (1966)
Dog	male	intraperitoneal	4140	Klaassen & Plaa (1967)

The toxicological pattern of acute trichloroethane poisoning is central nervous system (CNS) depression, eventually culminating in respiratory arrest or cardiac failure at lethal exposure levels (Stewart, 1968).

The findings of rapid and shallow breathing in a dog following inhalation of 0.9% (by volume) 1,1,1-trichloroethane (corresponding to 48 600 mg/m³ or 9000 ppm) may be related to an increase in the activity of the lung stretch receptor in the vagus nerve (Kobayashi et al., 1986). A level of 1.3% increased the heart rate but 2.8% decreased it (Kobayashi et al., 1987).

Table 11. Acute toxicity by inhalation (LC₅₀) of 1,1,1-trichloroethane in experimental animals

Species	Sex	LC ₅₀ (g/m ³) (ppm)		Exposure duration	Reference
Rat	male & female	97.2	18 000	3 h	Adams et al. (1950)
Rat	male & female	76.9	14 250	7 h	Adams et al. (1950)
Rat	male	99.4	18 400	4 h	Siegel et al. (1971)
Rat	male	55.6	10 300	6 h	Bonnet et al. (1981)
Rat	male & female	205	38 000	15 min	Clark & Tinston (1982)
Mouse	male	120	22 240	30 min	Woolverton & Balster (1981)
Mouse	female	72.4	13 410	6 h	Gradiski et al. (1978)
Mouse	male	21.1	3910	2 h	Horiguchi & Horiguchi (1971)
Mouse	male	99.1	18 358	1 h	Moser & Balster (1985)
Mouse	male	111	20 616	30 min	Moser & Balster (1985)
Mouse	male	159	29 492	10 min	Moser & Baister (1985)

Non-lethal acute toxicity has also been investigated (see Table 12). In a study on rats, 50% of the experimental group showed loss of coordination (ataxia) after inhalation of 20 400 mg/m³ (3780 ppm) for 4 h, and loss of righting-reflex was observed at 45 800 mg/m³ (8480 ppm). Tremors and death were observed at 64 800 mg/m³ (12 000 ppm) within one hour of exposure (Mullin & Krivanek, 1982).

Cardiac sensitization to adrenaline was reported in dogs exposed to 37 800 mg/m³ (range: 21 600 to 59 400 mg/m³) for 5 min (Clark & Tinston, 1982). An increase in concentration (range: 37 300 to 373 000 mg/m³) and inhalation period (0.5 to 20 min) was accompanied by a decrease in the amount of adrenaline that induced arrhythmia (Kobayashi et al., 1982).

Reinhardt et al. (1973) reported that 1,1,1-trichloroethane caused cardiac sensitization to adrenaline in dogs at and above the

0.5% (v/v) level. The marked response was associated with ventricular fibrillation following the challenge dose of adrenaline. At this level, the solvent was also associated with excitement and struggling in the animals. Histopathological examination of samples from the dogs that developed fatal arrhythmias did not show any gross or microscopic abnormalities.

Table 12. Non-lethal acute toxicity in experimental animals exposed to 1,1,1-trichloroethane by inhalation

Species	Exposure level (mg/m ³)	Exposure duration	Effects	Reference
Rat	45 800	4 h	loss of righting reflex (EC ₅₀)	Mullin & Krivanek (1982)
Rat	20 400	4 h	loss of coordination (EC ₅₀)	Mullin & Krivanek (1982)
Mouse	31 000	1 h	inverted screen test performance (EC ₅₀)	Moser & Balster (1985)
Dog	37 800	5 min	cardiac sensitization to adrenaline	Clark & Tinston (1982)
Dog	21 600	a few min	decrease in blood pressure	Kobayashi et al. (1983)

The effect of 1,1,1-trichloroethane on liver enzyme activity in the serum of experimental animals has been investigated. An almost lethal intraperitoneal dose of 1,1,1-trichloroethane (0.87 ml/kg body weight) caused a significant elevation of ALAT (alanine aminotransferase) in dogs (Klaassen & Plaa, 1967), and one eighth of a lethal intraperitoneal dose caused a significant elevation in SDH (sorbitol dehydrogenase) (Lundberg et al., 1986). In both studies, the hepatotoxicity of 1,1,1-trichloroethane was relatively small compared to that of other organic solvents, e.g., chloroform, carbon tetrachloride, dimethylformamide (Lundberg et al., 1986), dichloromethane, 1,1,2-trichloroethane, and trichloroethylene (Klaassen & Plaa, 1967).

7.1.1 Irritation

Trichloroethane has been shown to produce "mild" skin irritation in rabbits when repeatedly applied topically under an occlusive dressing. Redness was noted and the skin became scaly, but the effect was transient, the skin rapidly returned to normal (Torkelson et al., 1958).

After guinea-pigs had been exposed to 1 ml of 1,1,1-trichloroethane via a skin depot (a glass ring attached to the skin and covered with glass), for 15 min, oedema was observed. Prolonged exposure for several hours led to more severe inflammatory reactions in the upper part of the dermis, and histological examination at 15 min and 1, 4, and 16 h showed a number of changes to the epidermis. The extent of these changes increased with duration of exposure (Kronevi et al., 1981).

Repeated topical application of trichloroethane to abraded and non-abraded rabbit skin for up to 90 days resulted in slight, reversible irritation (Torkelson et al., 1958). The same study showed that when trichloroethane was applied soaked in a cotton wool pad and bandaged to the shaven belly of a rabbit slight reddening and scaliness occurred, but this only increased slightly with repeated applications.

The application of 0.5 ml trichloroethane to the shaven skin of rabbits under an occlusive dressing for 24 h, resulted in moderate skin irritation (Duprat et al., 1976). In a recent study of OECD methods (4-h exposure under semi-occlusive dressing) trichloroethane was reported to be a skin irritant (van Beek, 1990).

Trichloroethane is a "mild" eye irritant. Slight to moderate pain and slight conjunctival irritation, but no corneal damage, was reported following a single application of 100 μ l trichloroethane to the eyes of rabbits (Torkelson et al., 1958). Duprat et al. (1976) also found that instillation of 0.1 ml trichloroethane to the eyes of rabbits produced slight irritation.

7.1.2 Short-term exposure

7.1.2.1 Inhalation

When groups of rats, guinea-pigs, rabbits, dogs, and squirrel monkeys were exposed to 1,1,1-trichloroethane (11 880 mg/m³,

2200 ppm) for 8 h/day, 5 days/week for 6 weeks, the only sign of toxicity was reduced body weight gain in rabbits and dogs. There were no effects on haematological parameters or serum urea nitrogen and no histopathological changes were observed (Prendergast et al., 1967).

In a study by Adams et al. (1950), rats were exposed to 0 or 27 000 mg/m³ (0 or 5000 ppm) for 7 h/day on 32 out of 45 days and guinea-pigs received 20 to 65 7-h exposures to 0, 3510, 8100, 16 200 or 27 000 mg/m³ (0, 650, 1500, 3000 or 5000 ppm) for a period of 1-3 months. Body weight gain was reduced in both species at all exposure levels used, but there were no other signs of toxicity and no effects were observed on blood urea nitrogen. The only 1,1,1-trichloroethane-related effect observed on histopathological examination was fatty degeneration, without necrosis, in the liver of guinea-pigs at 16 200 and 27 000 mg/m³.

Rats exposed to 2700 mg/m³ (500 ppm), 6 h/day for 5 days, showed no behavioural effects. However, there was a slight decrease in brain RNA content relative to controls (Savolainen et al., 1977). Inhalation of 1750 mg/m³ (320 ppm) for 30 days had no effects on the composition of brain lipids in rats (Kyrklund et al., 1988).

When rats were given 4320 mg/m³ (800 ppm) by inhalation 6 h/day, 5 days/week for 4 weeks, absolute and relative liver weights were increased but there was no induction of liver microsomal cytochrome P-450 (Toftgaard et al., 1981). A 1-h daily exposure to 54 000 mg/m³ (10 000 ppm) for 3 months resulted in a narcotic effect (sedation and transient sleep) and in an increase of relative liver weight in rats, but there was no evidence of organ damage (Torkelson et al., 1958).

When rats were exposed continuously for 100 days to 1350 or 5400 mg/m³ (250 or 1000 ppm), no effects were observed in the low-dose group but an increase in relative liver weight was seen in the high-dose group (McEwen & Vernot, 1974). No toxicity was observed in similar experiments with dogs and monkeys (McEwen & Vernot 1974).

Exposure of mice to 5400 mg/m³ (1000 ppm) continuously for 14 weeks resulted in marked liver changes (elevated relative liver weight, moderate liver triglyceride accumulation, and necrosis of individual hepatocytes). Electron microscopy showed extensive cytoplasmic modifications consisting of vesiculation of the rough

endoplasmic reticulum with loss of attached polyribosomes, increased smooth endoplasmic reticulum, microbodies (peroxisomes), and triglyceride droplets. The observed toxic effects were similar to, but much less severe than, those produced by carbon tetrachloride. Only minor cytoplasmic alterations were seen in mice exposed to 1350 mg/m³ (250 ppm) (McNutt et al., 1975).

No signs of toxicity were observed in rats, rabbits, guinea-pigs, dogs or monkeys exposed to 2730 mg/m³ (500 ppm) 7 h/day, 5 days/week for 6 months (Torkelson et al., 1958).

In a study by Prendergast et al. (1967), rats, rabbits, guinea-pigs, dogs, and monkeys were exposed continuously to 754 or 2059 mg/m³ for 90 days. At the higher dose level, there were no deaths in any species after 90 days, and the authors stated that no visible toxic signs were observed. However, at the lower dose level, some deaths occurred (2 out of 15 rats and 1 out of 3 rabbits). Varying degrees of lung congestion were noted in the surviving animals. In view of this and the deaths at the lowest dose tested, the authors stated that no positive conclusion could be drawn as to whether the effects were associated with the exposure.

No adverse effects were seen in male Wistar rats exposed to 1100 mg/m³ (204 ppm) 8 h/day, 5 days/week for 14 weeks (Eben & Kimmerle, 1974).

When young adult Mongolian gerbils (*Meriones unguiculatus*) were continuously exposed to 378, 1134 or 5400 mg/m³ (70, 210 or 1000 ppm) for 3 months, followed by a 4-month period without exposure, increased glial fibrillary acidic protein (GFA) was found in the cerebral cortex at the two highest exposure levels, indicating astrogliosis in this region of the brain (Rosengren et al., 1985). In a similar study by Karlsson et al. (1987), the DNA concentrations in several brain regions were decreased in animals exposed to 378 mg/m³ (70 ppm), the only exposure concentration used.

Table 13 summarizes data from short-term inhalation studies.

7.1.2.2 Oral administration

When rats were dosed orally with 1,1,1-trichloroethane in corn oil, 5 days/week for 6 weeks, a dosage of 3.2 g/kg body weight per day had no adverse effects. However, total doses of 5.6 g/kg body weight in females and 10 g/kg body weight in males induced

40% mortality and decreased the body weight of survivors (NCI, 1977). In mice no mortality was seen with a dose of 5.6 g/kg body weight. Thus, trichloroethane has low toxicity in rats and mice following repeated exposure by the oral route.

Table 13. Short-term toxicity (exposure-effect relationships) in experimental animals exposed to 1,1,1-trichloroethane by inhalation

Species	Exposure level (mg/m ³)	Exposure duration	Effects	Reference
Rat	5400	100 days	increased relative liver weight	McEwen & Vernot (1974)
Rat	1100	14 weeks, 8 h/day, 5 days/week	NOAEL	Eben & Kimberle (1974)
Gerbil	5400	3 months	reduced brain weight	Rosengren et al. (1985)
Gerbil	380	3 months	biochemical changes in the brain	Karlsson et al. (1987)
Mouse	5400	14 weeks	liver necrosis	McNutt et al. (1975)
Mouse	1350	14 weeks	minor liver effects	McNutt et al. (1975)
Rat, dog, rabbit, monkey, guinea-pig	2700	6 months, 7 h/day, 5 days/week	NOAEL	Torkelson et al. (1958)
Rat, dog, rabbit, monkey, guinea-pig	2000	90 days	NOAEL	Prendergast et al. (1967)

7.2 Long-term exposure

In the NCI (1977) carcinogenesis study (see section 7.5.1 for details of doses), reduced weight gain was noted in both rats and

mice during the exposure period at all dose levels. Furthermore, bloody discharge and crusting around the eyes of some rats was observed during the second year (NCI, 1977).

In an oncogenicity inhalation study, female rats exposed to the highest concentration (8100 mg/m³, 1500 ppm) of 1,1,1-trichloroethane exhibited a significant decrease in body weight, and both females and males showed very slight microscopic hepatic effects at 6, 12, and 18 months. At lower concentrations and in male rats and mice of both sex, no toxicity was observable (Quast et al., 1988).

7.3 Reproductive toxicity, embryotoxicity, and teratogenicity

Inhalation studies in female rats and mice gave no evidence of any teratogenic or fetotoxic effects followed exposure to 1,1,1-trichloroethane at a concentration of 4700 mg/m³ (875 ppm) for 7 h/day on days 6-15 of gestation (Leong et al., 1975). No signs of maternal toxicity were noted.

In a study of female rats exposed to a higher 1,1,1-trichloroethane concentration (11 340 mg/m³, 2100 ppm, 6 h/day, 5 days/week) for 2 weeks before mating and/or during 20 days of gestation (6 h/day, 7 days/week), there was some evidence of fetotoxicity. This consisted of reduced fetal weight in the group exposed during pregnancy only and minor visceral and skeletal abnormalities, such as delayed ossification, in the group exposed before and during pregnancy (York et al., 1982). No signs of maternal toxicity were observed.

In a two-generation fertility study incorporating teratogenicity and dominant lethal elements, mice received 0, 100, 300 or 1000 mg 1,1,1-trichloroethane/kg daily in the drinking-water (Lane et al., 1982). Two or three litters were produced from each of the two generations, and the parental animals and offspring were used variously to investigate fertility, developmental toxicity, and dominant lethal effects. No adverse effects on any aspect of reproduction were evident in this study. The level of 1,1,1-trichloroethane in the drinking-water in this study was reported to be up to 6000 mg/litre but was not actually measured. In a further study, rats exhibited slight aversion to 30 mg/litre in drinking-water (George et al. 1989).

Rats (Sprague-Dawley) and rabbits (New Zealand White) were exposed on days 6-15 and 6-18 of gestation, respectively, to 0,

5400, 16 200 or 32 400 mg/m³ (0, 1000, 3000 or 6000 ppm) for 6 h/day. 1,1,1-Trichloroethane was found to be developmentally toxic to both rats and rabbits at the highest dose level, producing an increase in unossified and poorly ossified cervical centra, decreased female fetal body weight, an increase in non-viable implantations in rats, and an increase in the frequency of bilateral extra 13th rib in rabbits. Both rats and rabbits showed a NOEL of 16 200 mg/m³ for developmental toxicity. For both species, the developmental toxicity was seen in the presence of maternal toxicity (Personal communication by E.Z. Francis to S. Ells, US EPA, Test Rules Development Branch, Existing Chemical Assessment Division. Review of Developmental Toxicity Studies on 1,1,1-Trichloroethane (TCE). OHEA, ORD. Sept. 28, 1988).

Dapson et al. (1984) reported that exposure to 10 mg 1,1,1-trichloroethane per litre drinking-water caused cardiac anomalies in developing Sprague-Dawley rats. The repeatability of this preliminary study was investigated by George et al. (1989), who exposed male and female CD rats to 3, 10 or 30 mg of 97% pure 1,1,1-trichloroethane per litre drinking-water using 0.05% Tween 80 as an emulsifying agent. The animals were exposed for a period of 14 days before and at least 13 days after co-habitation. Sperm-positive females continued to be exposed during pregnancy and lactation until postnatal day 21. No significant effects were noted concerning the reproductive competence of the parental animals or the postnatal growth and development of the offspring (fertility, length of gestation period, litter size, pup body weight, and pup survival were all investigated). In addition, there was no increase in the incidence of any cardiac malformations or other anomalies. Thus the finding of Dapson et al. (1984) was not confirmed using a different strain of rats and a 3-fold higher concentration of 1,1,1-trichloroethane.

7.4 Mutagenicity

Appraisal

1,1,1-Trichloroethane has been tested extensively for mutagenicity, both in vitro and in vivo, and the principal studies are summarized in Table 14. The results of most of the studies were clearly negative. The positive results seen in some in vitro tests give rise to some concern, but may well have been due to the presence of stabilizers and/or impurities. Some of the studies yielding negative results were of insufficient sensitivity. All of the in vivo tests gave negative results. Overall, it appears that 1,1,1-trichloroethane does not have significant mutagenic potential.

Table 14. Mutagenicity studies

Test method	Organism	Test conditions	Result	References
<i>In vitro</i> studies on microorganisms				
Bacterial mutagenicity	<i>Salmonella typhimurium</i> or <i>Escherichia coli</i>	many studies, using liquid or vapour, with and without S9 activation	mostly negative; some positive results attributed to stabilizers or impurities	Simmon et al. (1977), Snow et al. (1979), Nestmann et al. (1980), Gocke et al. (1981), Rowland & Sevm (1981), McDonald (1981), Nagao & Takahashi (1981), Richard & Jones (1981), Simmon & Shepherd (1981), Ichinotsubo et al. (1981), de Serres & Ashby (1981), HSE (1984), Shimada et al. (1985)
Bacterial DNA damage/repair tests	<i>E. coli</i> or <i>Bacillus subtilis</i>	several studies	mainly negative; occasionally equivocal results	Kada (1981), Ichinotsubo et al. (1981), Green (1981), Tweats (1981), Rosenkranz et al. (1981), de Serres & Ashby (1981)
Yeasts, gene mutation, gene conversion	<i>Saccharomyces cerevisiae</i> <i>Schizosaccharomyces pombe</i>	numerous studies	negative	HSE (1984), de Serres & Ashby (1981)
	<i>S. cerevisiae</i> and mice (host-mediated assay)	5000 mg/kg intraperitoneal	negative	Loprieno et al. (1979)

Table 14 (contd).

Test method	Organism	Test conditions	Result	References
<i>In vitro</i> mammalian cell studies				
Chromosome aberrations	CHO cells	± S9 activation	clear positive without S9; equivocal with S9	Galloway et al. (1987)
Gene mutation	L5178Y mouse lymphoma cells	± S9	equivocal with S9; negative without S9	Myhr & Caspary (1988)
Unscheduled DNA synthesis	rat, mouse hepatocytes; HeLa cells	± S9	negative	Althaus et al. (1982), Martin & McDermid (1981)
DNA repair	rat hepatocytes	± S9	mainly negative; some positive results attributed to presence of stabilizers or impurities	Williams (1983), Shimada et al. (1985)
Sister chromatid exchange	CHO cells	± S9	negative equivocal	Perry & Thomson (1981) Galloway et al. (1987)
Cell transformation	various cell types	± S9	both positive and negative results	Daniel & Dehnel (1981), Styles (1981), Price et al. (1978), Hatch et al. (1983) Tu et al. (1985), HSE (1984)
<i>Drosophila</i> studies				
Sex-linked recessive lethals		25 nM	negative	Gocke et al. (1981)

Table 14 (contd).

<i>In vivo</i> mammalian studies					
Chromosome aberrations (bone marrow)	rats	875 or 1750 ppm 6 h/day, 52 weeks	negative	Quast et al. (1978)	
Micronucleus	mice	34-67 mg/kg intrapitoneal	negative	Salamone et al. (1981)	
Micronucleus	mice	11-42 mg/kg intrapitoneal	negative	Tsuchimoto & Matter (1981)	
Micronucleus	mice	266-2000 mg/kg intrapitoneal	negative	Gooke et al. (1981)	
Dominant lethal	mice	100-1000 mg/kg per day oral	negative	Lane et al. (1982)	
Sperm morphology	mice	130-2680 mg/kg per day intraperitoneal	negative	Topham (1980)	
DNA binding (liver)	rats and mice		low binding	Prodi et al. (1988)	

7.5 Carcinogenicity

1,1,1-Trichloroethane has been investigated for carcinogenic effects in life-time bioassays on both rats and mice by oral administration or inhalation.

7.5.1 Oral administration

In a US National Cancer Institute (NCI) assay, 7 week-old Osborne-Mendel rats were fed by gavage a 75% solution of technical grade 1,1,1-trichloroethane in corn oil, 5 days/week for 78 weeks. The daily doses were calculated to be 750 or 1500 mg/kg body weight, and the study was terminated after 110 weeks. The number of animals in each treated group was 50 of each sex, and the control groups consisted of 20 animals of each sex, which were not vehicle dosed. No increased tumour incidence was found (NCI, 1977). However, because of an unusually high mortality both among treated and control animals (only 6 out of 240 animals survived the 110 weeks to the end of the experiment), this study was considered insufficient by US EPA (1984) and placed in class D (not applicable to assess human carcinogenicity).

In another NCI study with 5-week-old B6C3F₁ mice, technical grade trichloroethane containing 3% 1,4-dioxane was given by gavage as a 40-60% solution in corn oil at two dose levels (average daily doses: 2807 and 5615 mg/kg body weight) 5 days/week for 78 weeks. The same number of animals was used as in the NCI rat study reported above. All surviving animals were killed after 90 weeks of study. A variety of neoplasms was observed in the treated groups, but the incidence was not statistically significantly different from that of the control groups (NCI, 1977). Again the mortality rate was very high in both treated and control animals, although it was a little lower than in the rat study. Nevertheless this study was also considered insufficient (US EPA 1984).

In a study by Maltoni et al. (1986), groups of male and female rats were given 1,1,1-trichloroethane (500 mg/kg body weight) in olive oil by gavage (4 to 5 days/week for 104 weeks). The 1,1,1-trichloroethane contained about 4% 1,4-dioxane and 1% of other impurities. An increased incidence of "leukaemias" was detected in the exposed group. However, data were not evaluated statistically nor were any data for historical controls supplied.

7.5.2 Inhalation

In an inhalation study carried out by the Dow Chemical Co., 1-month-old Sprague-Dawley rats were exposed to technical 1,1,1-trichloroethane (6 h/day, 5 days/week for 12 months) and observed 18 months later, before the survivors were killed. Each dose group consisted of 96 rats of each sex. The unexposed control group consisted of the same number of rats as the two exposed groups together. The two exposure concentrations used were 4778 mg/m³ (875 ppm) and 9555 mg/m³ (1750 ppm). The treatment had no significant effect on mortality, and the tumour incidence in the treated animals was similar to that of the controls (Rampy et al., 1977). The purity of the 1,1,1-trichloroethane used was 96%, and the stabilizers were 3% 1,4-dioxane, 0.4% nitromethane, and 0.5% butylene oxide. In the validation of this study, it was pointed out that the exposure period was only 12 months and not lifelong, that no subchronic range-finding test had been done, and that the exposure concentration could have been too low (US EPA, 1984).

A more recent long-term inhalation study, this time on both rats and mice, has been carried out by the Dow Chemical Co. (Quast et al., 1988). Groups of male and female 4- to 6-week-old Fischer-344 rats and 5- to 6-week-old B6C3F₁ mice (80 of each sex per group) were exposed to 1,1,1-trichloroethane (technical formulation) vapour concentrations of 0 mg/m³, 820 mg/m³ (150 ppm), 2730 mg/m³ (500 ppm), 8190 mg/m³ (1500 ppm) 6 h/day, 5 days/week for 2 years. Ten animals of each sex from each group were predesignated for interim sacrifices after 6, 12, and 18 months of exposure. The purity of the formulation was 94% (by volume) 1,1,1-trichloroethane, 5% stabilizers (butylene oxide, *tert*-amyl alcohol, methyl butynol, nitroethane, and nitromethane) and < 1% minor impurities. In none of the treated animal groups, did the tumour incidence differ significantly from that of the controls.

The early studies with mice and rats were evaluated at IARC (International Agency for Research on Cancer) and considered inadequate (IARC, 1979; IARC, 1987).

7.6 Immunotoxicity and sensitization

Shmutter (1977) exposed rabbits to 1,1,1-trichloroethane concentrations of 2 mg/m³ (0.4 ppm), 10 mg/m³ (1.8 ppm), and 100 mg/m³ (18 ppm) by inhalation 3 h/day, 6 days/week for

8-10 months. At week 6, *Salmonella typhimurium* was injected subcutaneously to investigate the immune response over an 8-month period. The antibody response was depressed at both 10 mg/m³ and 100 mg/m³. This reduction in immune response was followed by an increased electrophoretic mobility of the antibodies toward α - and β -globulin fractions and also by a significant drop in the level of normal haemolysins to the Forsman's antigen of the sheep erythrocytes occurring during treatment.

7.7 Interactions

Interaction between 1,1,1-trichloroethane and ethanol was studied in mice given ethanol (0-2 g/kg body weight) by gavage 30 min before exposure to up to 120 000 mg trichloroethane/m³ (22 200 ppm) by inhalation. Different combinations of exposure to the solvents enhanced the toxicity of trichloroethane in the animals previous exposed to ethanol. The observed behavioural and lethal effects were dose related for each compound and additive (Woolverton & Balster, 1981).

When dogs anaesthetized with either pentobarbital sodium or chloralose plus pentobarbital sodium were acutely exposed to a commercial spot remover containing 1,1,1-trichloroethane, there was a dose-dependent biphasic decline in arterial pressure with an initial increase in the heart rate. A similar effect was obtained when 1,1,1-trichloroethane (99.5% by volume) was used instead of the commercial spot remover. It was found that the type of anaesthetic contributed in part to the effect. The authors reported that, in addition to the peripheral vascular effects, significant alterations in myocardial function occurred, and they concluded that the solvent acts by inhibiting myocardial contractility (Herd et al., 1974).

7.8 Mechanisms of action

1,1,1-Trichloroethane given to mice intraperitoneally or by short inhalation exposure has been shown to reduce the cyclic guanosine monophosphate (cGMP) content in the cerebellum, cerebral cortex, and brain stem. This was attributed to an increased rate of cGMP hydrolysis (Nilsson, 1986a). The cyclic adenosine monophosphate (cAMP) content in the brain stem of mice was increased in a dose-related and time-dependant manner. This might be mediated by adrenoceptor interaction stimulating the catalytic unit of adenylate cyclase (Nilsson, 1986b).

A study on isolated mouse brain synaptosomes exposed *in vivo* and *in vitro* showed that 1,1,1-trichloroethane increases calcium influx in the brain stem but not in the cerebellum and cerebral cortex. The data indicated that 1,1,1-trichloroethane may influence voltage-dependant calcium channels in brain stem nerve endings (Nilsson, 1987).

1,1,1-Trichloroethane suppressed the uptake of ovabain taurocholate and 2-aminoisobutyric acid, but not of cadmium chloride or 3-*O*-methyl-D-glucose, into isolated rat hepatocytes. Both the cellular ATP level and ATP-ase activities in isolated membrane fractions were also decreased. It was suggested that energy-dependant transport functions are disrupted, owing to decreased ATP levels and/or inhibition of membrane ATP-ases (Kukongviriyapan et al., 1990).

8. EFFECTS ON HUMANS

Appraisal

Both acute and long-term inhalation exposure to 1,1,1-trichloroethane can produce CNS effects ranging from slight behavioural changes to unconsciousness. Death may follow from respiratory failure or cardiac arrest. There is also the possibility of hepatic alterations and cardiac damage.

Ingestion and dermal exposure do not appear to be serious concerns, although skin irritation may occur.

1,1,1-Trichloroethane has properties (see chapter 2) that make it a dangerous compound in poorly ventilated areas and confined spaces such as tanks and vaults. The vapour is five times more dense than air, which may result in non-uniform distribution, and very high levels can occur in certain areas such as the bottom of empty tanks and container vessels. The combination of these properties has been the cause of some serious accidents, including fatalities. Solvent abuse has also produced a large number of fatalities.

There are insufficient studies to permit any conclusion concerning the reproductive and carcinogenic effects of this compound on humans.

Exposure to 1,1,1-trichloroethane may increase sensitivity to other compounds, e.g., anaesthetics.

The NOEL for humans appears to be in the region of 1350 mg/m³ (250 ppm).

Table 15 summarizes the toxic effects of 1,1,1-trichloroethane after inhalation exposure.

8.1 Controlled human studies

Several studies on volunteers under controlled conditions have investigated the effects of 1,1,1-trichloroethane on the CNS as measured by performance in certain behavioural tests. These studies have usually been conducted using the technical grade of 1,1,1-trichloroethane containing stabilizers, since this is the type of exposure that occurs most frequently.

Table 15. Toxic effects in humans related to inhalation exposure to 1,1,1-trichloroethane

Exposure concentration (mg/m ³)	Exposure concentration (ppm)	Duration of exposure	Effect	Reference
378 000	70 000	a few min	death	Northfield (1981)
54 000	10 000	2 min	general anaesthesia when given together with nitrous oxide (N ₂ O)	Dornette & Jones (1960)
> 27 000	> 5000	10 min	death	Kleinfeid & Feiner (1966)
27 000	5000	5 min	marked incoordination	Stewart (1968)
10 260	1900	5 min	disturbance of equilibrium	Torkelson et al. (1958)
5400	1000	short-term	mild eye and nasal discomfort, impairment of coordination	Stewart (1968)
5000	920	70-75 min	CNS disturbances (lightheadedness), slight eye irritation	Torkelson et al. (1958)
4860	900	73 min	impaired performance in Romberg's test, mild eye irritation	Stewart et al. (1961)
2700	500	6-7 h/day for 5 days	impaired performance in Romberg's test after 1 h of exposure, mild eye irritation, drowsiness, headaches	Stewart et al. (1969)

Table 15 (contd).

Exposure concentration (mg/m ³)	Exposure concentration (ppm)	Duration of exposure	Effect	Reference
2700	500	90-450 min	no CNS disturbances	Torkelson et al. (1958)
2430	450	30 min	dizziness, mild eye irritation	Salvini et al. (1971)
2430	450	30 min	reduced reaction time and perceptual speed	Gamberale & Hultengren (1973)
1890	350	30 min	reduced perceptual speed	Gamberale & Hultengren (1973)
1900	350	3.5 h	reduced psychomotor performance	Mackay et al. (1987)
< 1860	< 345	6.7 years	NOEL	Maroni et al. (1977)
< 1350	< 250	1-6 years	NOEL	Kramer et al. (1978)
1350	250	30 min	NOEL	Gamberale & Hultengren (1973)
950	175	3.5 h	reduced reaction time	Mackay et al. (1987)
540	100		odour threshold	Stewart (1968)

8.1.1 Single exposure period

In a study by Torkelson et al. (1958), four volunteers were exposed in an inhalation chamber to average trichloroethane levels of 4968 mg/m^3 (920 ppm) for 70-75 min. Symptoms of slight CNS disturbances (lightheadedness) were noted in three of the four subjects and slight eye irritation was noted in one individual. Two volunteers reported a strong odour during the experiment. Concentrations in the range of $2700\text{-}2970 \text{ mg/m}^3$ (500-550 ppm) for 90-450 min apparently produced no symptoms of CNS disturbance, but exposure to $10\ 260 \text{ mg/m}^3$ (1900 ppm) for 5 min produced a very noticeable odour and obvious disturbances in equilibrium. Unfortunately, full details of this study are not available.

Exposure to about 2700 mg/m^3 (500 ppm) trichloroethane for 78-186 min did not result in CNS toxicity or other effects (Stewart et al., 1961). However, exposure to about 4860 mg/m^3 (900 ppm) for up to 73 min resulted in CNS disturbances (light-headedness and impaired Romberg test performance) in approximately half of the subjects. Mild eye irritation was also observed. In another experiment in this series, the volunteers were exposed to increasing concentrations in the range of $0\text{-}14\ 310 \text{ mg/m}^3$ (0-2650 ppm) over a 15 min period. Signs of mild eye irritation were noted in six out of seven subjects when the concentration reached about 5400 mg/m^3 (1000 ppm), and there was a rapid increase in CNS symptoms, principally dizziness. Throat irritation was experienced by six out of seven subjects at about $10\ 800 \text{ mg/m}^3$ (2000 ppm). Severe CNS disturbances (imbalance, light-headedness) occurred at the end of the exposure period, when the concentration had reached $14\ 310 \text{ mg/m}^3$. In addition, minor effects on liver and kidney function were seen. The authors considered that all the effects were reversible.

The effect on young men of exposure to a mean trichloroethane level of 2430 mg/m^3 (450 ppm) for two periods of 4 h (separated by a lunch break of $1\frac{1}{2}$ h) was investigated by Salvini et al. (1971). The volunteers experienced dizziness and slight excitation, but only during the first 30 min of exposure, and mild eye irritation was noted. No significant change in performance in any of the behavioural tests was seen.

In a study by Gamberale & Hultengren (1973), 12 male volunteers were exposed to 1350 mg/m^3 (250 ppm) for 30 min, followed by 1890 mg/m^3 (350 ppm) for the next 30 min, and

2430 mg/m³ (450 ppm) and 2970 mg/m³ (550 ppm) for subsequent 30-min periods. At 2430 mg/m³, the reaction time, perceptual speed, and manual dexterity were reduced, and at 1890 mg/m³ the perceptual speed was reduced. The NOEL was 1350 mg/m³.

Mackay et al. (1987) reported the results of an exposure chamber study in which volunteers were exposed to 950 mg/m³ (175 ppm) and 1990 mg/m³ (350 ppm) for 3 to 5 h. Several human psychomotor behavioural tests were employed, including two new ones. One was concerned with distraction of attention and concentration (the Stroop test) and the other with analysing grammatical statements (the syntactic reasoning test). Performance deficits in the psychomotor behavioural tests were recorded in volunteers exposed to 1,1,1-trichloroethane; these depended on the time of exposure and the blood levels. The performance changes were rapid and occurred in some cases within 20 min. However, different effects were found. In the Stroop test, enhanced performance was observed following exposure, whereas the syntactic reasoning test was found not to respond to 1,1,1-trichloroethane exposure effects. Measures of short-term subjective well-being were not affected by exposure. Other parameters, such as simple reaction time and four-choice reaction time were increased.

The effect of exposure to trichloroethane on performance in a very extensive range of behavioural tests was investigated by Savolainen et al. (1981, 1982a, 1982b). Nine healthy male students (aged 20-25) were exposed in an inhalation chamber to 1080 and 2160 mg trichloroethane/m³ (200 and 400 ppm) for 4 h, with a 6-day interval between exposure at the two levels. There was no clear indication of any effects on the CNS, although some minor changes were noted in body-sway measurements when the subjects had their eyes closed.

8.1.2 Repeated exposure

The effect of repeated exposure of male volunteers to 2700 mg/m³ (500 ppm), 7 h/day for 5 days, was studied in an inhalation chamber (Stewart et al., 1969). Several subjective symptoms were noted, e.g., drowsiness, headaches, lightheadedness, and eye and nose irritation, but the absence of a control group made it difficult to assess the significance. No performance impairment in behavioural tests (modified Romberg test) was noted, apart from the inability of two subjects to perform the balance test on two occasions.

8.2 Accidental exposure

Respiratory system symptoms, such as cough, breathlessness, and chest tightness, are common in cases of acute poisoning (Boyer et al., 1987).

Since 1,1,1-trichloroethane is a very volatile solvent with a saturated vapour concentration of 864 g/m³ (160 000 ppm) at 25 °C, there is a potential for very high air concentrations in confined spaces, such as tanks and vaults. Furthermore, its vapour is five times more dense than air. This may result in non-uniform distribution in the workplace air and very high levels in certain areas such as just above degreasing vessels and at the bottom of empty tanks, even though levels elsewhere are low and safe. This property has been the cause of some serious accidents and fatalities.

A near-fatal childhood intoxication was described by Gerace (1981). A 4-year-old boy was playing under his bed covers with a flower-making kit which contained a 30-cm³ container of 1,1,1-trichloroethane. Because of some unusual noises heard by a sibling, the child was quickly discovered. However, he was not breathing at this point. He was resuscitated on the way to the hospital but remained comatose for about 12 min after arrival. The author suggested that the child was rendered unconscious by the 1,1,1-trichloroethane and that the noises heard were seizures caused by hypoxia. The child was released 48 h after admission. According to the author, clinical investigation during the child's hospital stay demonstrated some hepatic abnormalities with alteration in liver bilirubin.

Caplan et al. (1976) reported the death of a woman due to accidental exposure while cleaning a paint spill using a paint thinner in a poorly ventilated room. Autopsy results showed "mild fatty changes" in the liver and acute oedema and congestion of the lungs. The concentrations of 1,1,1-trichloroethane in the brain, kidney, liver, and blood were 36, 12, 5, and 2 mg/100 ml, respectively.

8.2.1 Confined spaces at workplaces

A man who had spent 10 min in a vault, where the concentration of 1,1,1-trichloroethane was estimated to be well in excess of 27 g/m³ (5000 ppm), collapsed and died shortly after leaving the vault (Kleinfeld & Feiner, 1966).

Seven fatalities from using trichloroethane to clean equipment on naval ships or aircraft tanks have been reported (Stahl et al., 1969; Hatfield & Maykoski, 1970). The exposure level in one of these cases was estimated to be in the order of 270 g/m^3 (50 000 ppm). In all cases the most significant pathological finding was pulmonary oedema. Liver damage was not seen.

Other case histories with accidental death due to 1,1,1-trichloroethane exposure in confined spaces have been reported (Stewart 1968; Bonventre et al., 1977).

During the period 1961-1980, the Factory Inspectorate in the United Kingdom revealed 52 incidents due to trichloroethane (McCarthy & Jones, 1983). Loss of consciousness was reported in 26 cases and death in three cases, all involving very young workers. In one case the worker died after leaning over an open tank of trichloroethane, apparently to wash his hands in the solvent. He was found unconscious slumped over the side of the tank, and the solvent concentration in his breathing zone was later estimated to be about 378 g/m^3 (70 000 ppm) (Northfield, 1981). In a second case, a worker was using trichloroethane for cleaning purposes in a closed room (Jones & Winter, 1983). He was found on the floor with chemical burns on the head and neck, which was consistent with prolonged skin absorption from spills of solvent on the floor. The third case was a teenage worker who cleaned the interior of a car with a cloth soaked in the solvent (Jones & Winter, 1983). Death was presumed to be from 1,1,1-trichloroethane intoxication and simultaneous inhalation of vomit.

8.2.2 Solvent abuse

During the 1960s, 110 cases of sudden death from solvent abuse were reported in the USA. Of these, spot remover containing 1,1,1-trichloroethane was identified as responsible for 29 cases (Bass, 1970). Death frequently occurred immediately following stressful activity. Where autopsies were performed, no abnormalities could be detected, and it was suggested that deaths was due to cardiac arrhythmia.

Over the period 1971-1981, 140 deaths from solvent abuse were reported in the United Kingdom; 20 of them were believed to be due to 1,1,1-trichloroethane, mainly in dry-cleaning fluid, domestic cleaners or plaster remover (Anderson et al., 1982).

In the case of a fatality due to the abuse of cleaning solvent containing 1,1,1-trichloroethane, very minor hepatic changes were seen (Hall & Hine, 1966). In four cases of deaths caused by inhalation of typewriter correction fluid containing 1,1,1-trichloroethane and trichloroethylene, the autopsies showed no evidence of kidney or liver damage (King et al., 1985).

According to Marjot & McLeod (1989), toluene and the chlorinated hydrocarbons 1,1,1-trichloroethane and trichloroethylene can cause permanent damage to the kidney, liver, heart, and lung in certain volatile substance abusers.

8.2.3 Medical use

Trichloroethane has been used as an anaesthetic on an experimental basis. General anaesthesia in humans has been rapidly induced by 2 min of exposure to 54 000 mg/m³ (10 000 ppm) given with a mixture of nitrous oxide (N₂O) and oxygen (80:20). Cardiovascular side effects (slight to severe hypotension, cardiac arrhythmias, and, in one case, cardiac arrest) were observed in several of the patients during anaesthesia. In view of these effects, the experimental use of 1,1,1-trichloroethane as an anaesthetic was discontinued (Dornette & Jones, 1960).

In the USA, after aerosol drug products containing 1,1,1-trichloroethane had been implicated in 21 deaths from their abuse or misuse, the Food and Drug Administration (FDA) removed the products from the market (US Food and Drug Administration, 1973). The medical products were mainly used as cough suppressants and contained 1,1,1-trichloroethane as a solvent for the active ingredients and to reduce the vapour pressure of the propellants. The FDA found lack of general recognition by qualified experts of the safety or effectiveness of 1,1,1-trichloroethane in aerosol drug products intended for inhalation.

Under 1977 rules from the FDA, it was stated that 1,1,1-trichloroethane is potentially toxic to the cardiovascular system by sensitizing the heart to adrenaline (Food and Drug Administration, 1977).

8.2.4 Ingestion

In a case of accidental ingestion of about 600 mg trichloroethane/kg, signs of severe gastrointestinal irritation (vomiting, diarrhoea) were evident shortly after the ingestion.

There was no evidence of any CNS disturbance or any liver or kidney dysfunction (Stewart & Andrews, 1966).

Ingestion of about 30 ml trichloroethane has been found to cause severe vomiting and diarrhoea (CEC, 1986).

8.2.5 Drinking-water contamination

In December 1981, a water well in Santa Clara County, California, USA, was removed from service after contamination with 1,1,1-trichloroethane and other solvents was detected. A 1,1,1-trichloroethane level of 1.7 mg/litre was detected at the well head, but the level of the other contaminants (dichloroethylene, isopropyl alcohol, and freon) was not reported. Subsequently suspicion of a cluster of spontaneous abortions and congenital heart anomalies from pregnancies conceived during 1980-1981 was reported by the local community. Epidemiological studies indicated that a cluster did exist, that the odds ratio for spontaneous abortion was 2.3 and the relative risk for congenital malformations was 3.1, but they were unable to draw a direct link between the ingestion of the contaminated water and these effects (Goldberg et al., 1990).

8.3 Effects on the skin and eyes

Prolonged or repeated skin contact with 1,1,1-trichloroethane may lead to dermatitis, due to its defatting action. However, despite its wide use only a few cases of skin irritancy have been reported (Torkelson et al., 1958).

Immersion of a hand in liquid 1,1,1-trichloroethane for 30 min resulted in mild erythema, which persisted for one hour (Stewart & Dodd, 1964).

Splashed in the eye, the compound may produce conjunctivitis (Stewart, 1968). However, accidental eye contact has been reported to produce only transient irritation (Savolainen et al., 1982a,b). Exposure to a vapour concentration of 2700 mg/m³ (500 ppm) may produce mild eye irritation (see section 8.1).

8.4 Long-term occupational exposure

A case study described a patient with liver cirrhosis after several years of heavy exposure to trichloroethylene followed by 3 months of work that frequently involved using aerosolized degreaser containing trichloroethane (Thiele et al., 1982).

An investigation of the neurotoxicity of trichloroethane was carried out on a group of 22 female workers exposed to the solvent for an average period of 6.7 years. The group was subdivided into three exposure groups (mean levels: 594 mg/m³ (110 ppm), 756-864 mg/m³ (140-160 ppm), and 1080-1863 mg/m³ (200-345 ppm)). Each woman had a general physical examination, and information about symptoms was obtained from a questionnaire. The measurement of nerve conduction velocity and psychometric functions indicated no differences between the exposed workers and an unexposed control group of 7 workers (Maroni et al., 1977).

Hodgson et al. (1989) reported that four out of ten clinical cases of fatty liver disease were associated with occupational exposure to 1,1,1-trichloroethane.

A matching-pair study of 151 pairs of workers at textile plants, with and without daily exposure to trichloroethane levels of up to 1365 mg/m³ (250 ppm), found no toxic effect among the exposed workers, the majority of whom were exposed to less than 810 mg/m³ (150 ppm) for a period of 1-6 years (Kramer et al., 1978).

In a case-control study of the effect of occupational exposure to various solvents on spontaneous abortion rates in Finland (1973-1983), a statistically significant elevation in relative risk was found for exposure to organic solvents in general. However, there were very few cases related specifically to 1,1,1-trichloroethane. The low statistical power, therefore, precludes any conclusion as to whether the data show an effect or not for 1,1,1-trichloroethane (Lindbohm et al., 1990)

There are no adequate epidemiological studies available concerning long-term exposure to 1,1,1-trichloroethane and carcinogenicity.

8.5 Interactions

Chronic cardiac arrhythmia developed in two cases, after routine halothane anaesthesia, in subjects with previous repeated long-term exposure to 1,1,1-trichloroethane (in one case, occupational and in the other, due to solvent abuse). The effects involved myocardial damage with either ventricular arrhythmia or deterioration of left ventricular function. In one of the cases, the pathologist suggested a subacute myocarditis superimposed on long-standing damage. The authors postulated that the interaction between the two chemicals may have caused the cardiac

deterioration and concluded that cardiac damage sustained after long-term exposure to 1,1,1-trichloroethane may be severe, life-threatening, and irreversible (McLeod et al., 1987)

Marjot & McLeod (1989) reported two cases, a 14-year-old boy exposed to 1,1,1-trichloroethane via solvent abuse and a 54-year-old man exposed occupationally, where the cardiac toxicity of 1,1,1-trichloroethane may have been increased by exposure to halothane (2-bromo-2-chloro-1,1,1-trifluoroethane) as an anaesthetic.

9. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD

Appraisal

1,1,1-Trichloroethane is not likely to be a significant hazard to non-target organisms in the environment. For example, 96-h LC₅₀ values for fish ranged from 33 mg/litre for dabs to 105 mg/litre for fathead minnows. The 48-h LC₅₀ for *Daphnia* was around 60 mg/litre. The EC₅₀ for carbon dioxide incorporation into algae was 5 mg/litre.

9.1 Microorganisms

A toxic threshold of 93 mg 1,1,1-trichloroethane/litre has been estimated for the inhibition of cell multiplication in the bacterium *Pseudomonas putida* (Bringmann & Kuhn, 1977). The 3-h EC₅₀ values, for inhibition of photosynthesis (measured by monitoring the uptake of ¹⁴CO₂), for the green algae *Chlamydomonas angulosa* (at a cell concentration of 5 x 10⁴ cells/ml) and *Chlorella vulgaris* (at a cell concentration of 20 x 10⁴ cells/ml) were 280 mg/litre and 153 mg/litre, respectively, under static conditions (Hutchinson et al., 1980). Bringmann & Kuhn (1978) calculated toxic thresholds of 350 mg/litre and 430 mg/litre, respectively, for inhibition of cell multiplication, over an 8-day period, of the cyano bacterium (blue-green alga) *Microcystis aeruginosa* and the green alga *Scenedesmus quadricauda*. The 96-h EC₅₀ for chlorophyll *a* and cell number in the green alga *Selenastrum capricornutum* was > 669 mg/litre (US EPA, 1980a,b). Pearson & McConnell (1975) assessed the toxicity of 1,1,1-trichloroethane to the unicellular alga *Phaeodactylum tricorutum* by measuring changes in the uptake of carbon, from ¹⁴CO₂, during photosynthesis, and obtained an EC₅₀ of 5 mg/litre.

9.2 Aquatic organisms

The acute toxicity of 1,1,1-trichloroethane to aquatic organisms is summarized in Table 16.

Flow-through tests gave much lower LC₅₀ values than static tests, suggesting that some loss via evaporation may be occurring. The 48-h LC₅₀ for aquatic invertebrates ranges from 7.5 mg/litre for barnacles in a flow-through test to > 530 mg/litre for daphnids in a static test. The 96-h LC₅₀ for fish ranges from 33 mg/litre for

Table 16. Acute toxicity of 1,1,1-trichloroethane to aquatic organisms

Organism	Age/ size	Stat/ flow ^a	Temperature (°C)	Hardness ^c	pH	Duration (h)	LC ₅₀ ^e (mg./litre)	Reference
Invertebrates								
Mysid shrimp (<i>Mysidopsis bahia</i>)		stat				96	31.2 n	US EPA (1980b)
Barnacle (<i>Eliminus modestus</i>)	nauplii	stat				48	7.5 n	Pearson & McConnell (1975)
Water flea (<i>Daphnia magna</i>)	< 24 h	stat	21-23	72	6.7-8.1	48	> 530 n	LeBlanc (1980)
	4-6 day	stat	21-25			48	59.6	Abernethy et al. (1986)
	4-6 day	stat				48	57.6	Bobra et al. (1984)
Fish								
Dab (<i>Limanda limanda</i>)	15-20 cm	flow				96	33 m	Pearson & McConnell (1975)
Sheepshead minnow (<i>Cyprinodon variegatus</i>)	8-15 mm	stat	25-31	10-31 ^d		96	71 (60-81) n	Heitmuller et al. (1981)

Table 16 (contd).

Organism	Age/ size	Stat/ flow ^a	Temperature (°C)	Hardness ^c	pH	Duration (h)	LC ₅₀ ^e (mg/litre)	Reference
Fish (contd)								
Bluegill (<i>Lepomis macrochirus</i>)	0.32-1.2 g	stat	21-23	32-48	6.7-7.8	24	110 n	Buccafusco et al. (1981)
	0.32-1.2 g	stat stat	21-23	32-48	6.7-7.8	96 96	72 (57-90) n 69.7 n	Buccafusco et al. (1981) US EPA (1980b)
Fathead minnow (<i>Pimephales promelas</i>)	1 g	stat	12		7.8-8.0	96	105 (91-126) n	Alexander et al. (1978)
	1 g	flow	12		7.8-8.0	96	52.8 (43.7-77.7) m	Alexander et al. (1978)
Guppy (<i>Poecilia reticulata</i>)	2-3 month	stat ^b				168	133	Konemann (1981)

^a stat = static conditions (water unchanged for the duration of the test) unless stated otherwise; flow = flow-through conditions (1,1,1-trichloroethane concentration continuously maintained)

^b static conditions but water renewed daily

^c hardness expressed as mg CaCO₃ per litre

^d value refers to salinity (‰), not hardness

^e n = nominal; m = measured

the dab (*Limanda limanda*) in flow-through tests to 105 mg/litre for the fathead minnow (*Pimephales promelas*) in static tests.

LeBlanc (1980) exposed the water flea *Daphnia magna* to 1,1,1-trichloroethane for 48 h under static conditions. At the highest concentration of 530 mg/litre, no discernible effect was observed. A no-observed-effect level (NOEL) of 43 mg/litre was estimated by Heitmuller et al. (1981) after exposing the sheepshead minnow (*Cyprinodon variegatus*) to 1,1,1-trichloroethane for 96 h.

When Thompson & Carmichael (1989) exposed the water flea *Daphnia magna* to 1,1,1-trichloroethane concentrations of between 1.3 and 23 mg/litre for 17 days under semistatic conditions (water renewed every 2 days), no effect on mortality or reproduction (as measured by number of offspring per parent) was observed at 1.3 mg/litre. However, the mortality increased with increasing concentration of 1,1,1-trichloroethane from 30% at 2.4 mg/litre to 100% at 23 mg/litre. The number of offspring per parent was significantly reduced at concentrations of 2.4 mg/litre or more.

Thompson & Carmichael (1989) also exposed the mirror carp *Cyprinus carpio* to 1,1,1-trichloroethane concentrations ranging from 1.4 to 30 mg/litre for 14 days under flow-through conditions. There was no mortality at any of the concentrations, but at the highest concentration the fish showed surfacing behaviour, loss of balance and coughing, and their mean weight decreased. The authors considered, therefore, that the NOEL was the next highest concentration, i.e. 7.7 mg/litre.

Alexander et al. (1978) observed fathead minnows (*Pimephales promelas*), during exposure to 1,1,1-trichloroethane for up to 96 h, for the following effects: loss of equilibrium, melanization, narcosis, and swollen, haemorrhaging gills. The concentration producing one or more of these observable effects in 50% of the fish (EC₅₀) was 11.1 mg/litre.

9.3 Terrestrial organisms

Thompson & Carmichael (1989) exposed emergent seedlings of crop sorghum (*Sorghum bicolor*) and oil seed rape (*Brassica napus*) to 1,1,1-trichloroethane in the gaseous phase at nominal concentrations of between 3.2 and 320 mg/litre (g/m³) for a period of 14 days (the test material was replenished after 7 days in a sealed vessel). Mean measured concentrations ranged from 58% to 75% of the nominal concentration, reflecting the decline of

1,1,1-trichloroethane in the gas phase concentration during the 7-day periods between toxicant renewal. In the case of *Sorghum bicolor*, the 14-day EC₅₀ (based on mean plant weight and a mean measured 1,1,1-trichloroethane concentration) was 48 mg/litre; the NOEL being 19 mg/litre. For *Brassica napus*, the 14-day EC₅₀ was 19 mg/litre and the NOEL 6.9 mg/litre, both values being based on mean measured concentrations.

Rajendran (1990) exposed 1- to 2-day-old pupae of the red flour beetle (*Tribolium castaneum*) to 1,1,1-trichloroethane in fumigation chambers. An LC₅₀ of 208.4 mg/litre was estimated after a 24-h exposure and a 20-day post-fumigation observation period. When pupae were exposed to a mixture of 1,1,1-trichloroethane and methyl bromide at a concentration of 2.5 mg/litre or 3.0 mg/litre, the toxicity was similar to that of the individual components.

In a contact toxicity test, red earthworms (*Eisenia foetida*) were exposed to 1,1,1-trichloroethane via filter paper in glass vials. An LC₅₀ of 83 µg/cm² was estimated (Neuhauser et al., 1986).

Elovaara et al. (1979) injected 1,1,1-trichloroethane, at concentrations ranging from 5 to 100 µmol/egg, into the air space of fertilized chicken eggs at 3 or 6 days of incubation, and the embryotoxicity was evaluated after 14 days of incubation. A clear dose-response relationship with respect to survival was found, irrespective of whether the eggs were injected after 3 or 6 days of incubation. The approximate LD₅₀ for 1,1,1-trichloroethane was between 50 and 100 µmol/egg.

10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT

10.1 Evaluation of human health risks

Humans are exposed to 1,1,1-trichloroethane principally by inhalation, where the substance is rapidly absorbed into the body. Exposure by skin absorption or ingestion may also occur but, compared to inhalation, is of lesser concern. 1,1,1-Trichloroethane is considered not to bioaccumulate. The acute and chronic toxicities are fairly low. Under conditions of high exposure there is a risk of toxic effects; such conditions may occur in occupational exposures, solvent abuse or accidents. Since 1,1,1-trichloroethane is volatile and the vapour is much more dense than air, toxic and explosive concentrations may occur unexpectedly in confined spaces. This has caused several fatal and near-fatal accidents at workplaces and elsewhere. The critical effect in humans relates to the central nervous system, leading to unconsciousness and respiratory arrest at high concentrations. 1,1,1-Trichloroethane is less toxic to the liver than most other organochlorine solvents. The no-observed-effect level for humans appears to be in the region of 1350 mg/m³ (250 ppm). Although one study suggested effects at a lower level, the interpretation of the results was unclear.

Studies on Mongolian gerbils involving 1,1,1-trichloroethane levels down to 378 mg/m³ (70 ppm) revealed effects on DNA concentrations and other biochemical effects in several brain regions. If these findings are validated and confirmed, this may be of significant concern.

No adequate study of carcinogenic effects on humans has been published. A long-term inhalation study on rats and mice exposed to 8100 mg/m³ (1500 ppm) gave no evidence of any carcinogenic effects. One study recorded increases numbers of "leukaemias", but it was performed under non-standard protocol. It gave no statistical evaluation and is, therefore, considered inadequate. It is unlikely that 1,1,1-trichloroethane itself presents a significant risk of genotoxic or carcinogenic effects in humans.

1,1,1-Trichloroethane is not teratogenic and elicits no developmental effects at doses that are not maternally toxic. The limited epidemiological evidence on reproductive effects is inconclusive due to the low statistical power of the study.

10.2 Evaluation of effects on the environment

1,1,1-Trichloroethane is released in large quantities to the environment. Due to its volatility and general stability it is a ubiquitous environmental contaminant.

Although the ozone-depleting and global-warming potentials of 1,1,1-trichloroethane are lower than those of many chlorofluorocarbons, the large-scale release of the compound into the atmosphere merits serious concern in these respects.

As a result of its widespread use and disposal and its mobility in soil, persistent 1,1,1-trichloroethane contamination of ground water, including deep aquifers, occurs.

Conditions under which 1,1,1-trichloroethane causes ecotoxicological effects are not found in the environment except after spills.

11. RECOMMENDATIONS FOR PROTECTION OF HUMAN HEALTH AND THE ENVIRONMENT

- a) Emissions of 1,1,1-trichloroethane should be reduced as far as is practicable in order to minimize exposure of workers and of the general population.
- b) The release of 1,1,1-trichloroethane into the environment must be reduced to the greatest extent possible in order to avoid damage to the ozone layer.
- c) Contamination of ground water by 1,1,1-trichloroethane from spills and waste disposal should be avoided.
- d) Safe substitutes for 1,1,1-trichloroethane should be identified.

12. FURTHER RESEARCH

- a) More study is needed to clarify the possible effects of 1,1,1-trichloroethane on the biochemistry of the central nervous system and their significance.
- b) More study is necessary to clarify the possible interaction between 1,1,1-trichloroethane and ethanol in humans.
- c) An adequate subchronic or long-term oral study is needed to assess the hepatotoxicity of 1,1,1-trichloroethane.
- d) Further epidemiological studies on reproductive effects are desirable.

13. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

IARC (International Agency for Research on Cancer) working groups have evaluated 1,1,1-trichloroethane and concluded that the evidence for genotoxicity is limited (IARC, 1979, 1987).

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RESUME

Le 1,1,1-trichloréthane est un hydrocarbure chloré produit par chloration du chlorure de vinyle ou du chlorure de vinylidène. En 1988, la production mondiale était d'environ 680 000 tonnes. C'est un liquide incolore et volatil à l'odeur caractéristique dont la vapeur est plus dense que l'air. On l'utilise essentiellement pour le dégraissage des surfaces métalliques et comme solvant dans un grand nombre de produits industriels et de produits de consommation, notamment des adhésifs, des détachants et des bombes aérosols. Il sert également d'intermédiaire en synthèse chimique. Le trichloréthane technique contient généralement 3 à 8% de stabilisants destinés à empêcher sa décomposition et la formation d'acide chlorhydrique; les parties métalliques sont ainsi protégées de la corrosion. Il est ininflammable dans les conditions normales mais la vapeur s'enflamme à haute température et, au cours du soudage, elle peut se décomposer en libérant du phosgène, un gaz toxique. Des réactions extrêmement violentes peuvent se produire en cas de contact avec de l'aluminium, du magnésium ou leurs alliages.

Le 1,1,1-trichloréthane pénètre facilement dans l'environnement. Comme il séjourne longtemps dans la troposphère (environ six ans) et qu'il n'est que lentement biodégradable, on le retrouve maintenant partout dans l'environnement, même à grande distance des zones industrielles. A proximité d'installations industrielles où ce composé est produit ou manipulé, on a trouvé du 1,1,1-trichloréthane à des concentrations atteignant $86 \mu\text{g}/\text{m}^3$ (16 000 ppm, p/p) dans des échantillons d'air.

Le trichloréthane se déplace dans le sol et parvient jusqu'aux eaux souterraines. On en a trouvé à des concentrations atteignant $1600 \mu\text{g}/\text{litre}$ dans les eaux souterraines ou les eaux de surface. Ce phénomène peut être à l'origine de la contamination des réserves d'eau potable.

On estime que 15% des émissions annuelles de 1,1,1-trichloréthane sont entraînées dans la stratosphère où elles peuvent endommager la couche d'ozone par libération d'atomes de chlore.

Des essais biologiques sur des crustacés et des poissons à des concentrations supérieures à $7 \text{ mg}/\text{litre}$ ont révélé des effets toxiques aigus. On possède quelques données selon lesquelles le composé ne s'accumulerait que faiblement chez les organismes

aquatiques. En raison du caractère limité des données disponibles, il est difficile d'évaluer les effets qu'il peut avoir sur les organismes terrestres.

L'exposition humaine au 1,1,1-trichloréthane est due principalement à l'inhalation de ce composé qui est ensuite rapidement résorbé par l'organisme. Il peut y avoir également exposition par contact cutané ou ingestion. Le trichloréthane se répartit largement dans les tissus de l'organisme et il traverse la barrière hématoencéphalique et placentaire. On le retrouve également dans le lait humain mais il ne semble pas qu'il s'accumule dans les tissus. Sa principale voie d'élimination est l'exhalation du composé non métabolisé.

La toxicité aiguë et chronique du 1,1,1-trichloréthane est relativement faible mais en cas de forte exposition, le risque d'intoxication est réel. Cela peut se produire en cas d'exposition professionnelle, d'accidents ou encore de toxicomanie aux solvants. Comme il s'agit d'un solvant volatil dont la vapeur est beaucoup plus dense que l'air, il peut se trouver à des concentrations inhabituellement fortes et dangereuses dans des espaces confinés comme les réservoirs "vides". Ce genre de situation a donné lieu à plusieurs intoxications mortelles ou qui auraient pu l'être sur les lieux de travail ou ailleurs.

Chez l'homme, l'effet critique s'exerce au niveau du système nerveux central. On observe des effets qui vont de légers troubles du comportement (accompagnés d'une légère irritation oculaire) à la dose de $1,9 \text{ g/m}^3$ (350 ppm), jusqu'à l'inconscience et à l'arrêt respiratoire lorsque la concentration est élevée. Dans certains cas, des anomalies cardiaques mortelles peuvent se produire. Le trichloréthane est moins toxique pour le foie que la plupart des autres solvants organiques chlorés. La dose sans effet observable pour l'homme se situe autour de $1,35 \text{ g/m}^3$ (250 ppm).

Aucune étude satisfaisante n'a été publiée sur les effets cancérogènes de ce solvant chez l'homme. Toutefois une étude par inhalation de longue durée sur des rats et des souris exposés à $8,1 \text{ g/m}^3$ (1500 ppm) n'a pas révélé le moindre effet cancérogène. Le 1,1,1-trichloréthane ne présente pas d'activité génotoxique significative.

Chez des rats et des lapins exposés au trichloréthane à des concentrations qui étaient toxiques pour les femelles gestantes, on n'a pas noté d'effets tératogènes, malgré la présence d'effets

toxiques sur le développement. Les données épidémiologiques relatives à ces effets sur la reproduction sont trop limitées pour permettre d'en tirer une conclusion.

RESUMEN

El 1,1,1-tricloroetano es un hidrocarburo clorado que se fabrica a partir del cloruro de vinilo o del cloruro de vinilideno por cloración. En 1988 la producción mundial fue de unas 680 000 toneladas. Es un líquido volátil e incoloro con un olor característico, y su vapor es más denso que el aire. Se utiliza principalmente en el desengrasado de metales y como disolvente en muchos productos industriales y de consumo, como adhesivos, quitamanchas y envases de aerosoles. Es también un producto químico intermediario. El tricloroetano de calidad técnica suele contener del 3% al 8% de estabilizadores que impiden la degradación y la formación de ácido clorhídrico a fin de proteger las partes metálicas de la corrosión. En condiciones normales no es inflamable, pero su vapor arde a altas temperaturas y, durante las operaciones de soldadura, su degradación produce fosgeno, un gas tóxico. Cuando entra en contacto con el aluminio, el magnesio y sus aleaciones puede provocar reacciones muy violentas.

El 1,1,1-tricloroetano llega fácilmente al medio ambiente. Su prolongada permanencia en la troposfera (unos seis años) y baja biodegradabilidad son razón de su actual omnipresencia en el medio ambiente, incluso lejos de las zonas industriales. En muestras de aire de zonas próximas a industrias que lo fabrican o lo manipulan se han detectado concentraciones de hasta 86 $\mu\text{g}/\text{m}^3$ (16 ppb, peso/peso).

El tricloroetano se desplaza en los suelos y alcanza las aguas subterráneas. Se han encontrado concentraciones de hasta 1600 $\mu\text{g}/\text{litro}$ en aguas subterráneas o superficiales. Esta puede ser una fuente de contaminación para suministros de agua potable.

Se estima que el 15% del volumen anual liberado llega a la estratosfera, donde libera átomos de cloro que contribuyen a la destrucción del ozono.

En bioensayos con crustáceos y peces se han observado efectos tóxicos agudos con concentraciones superiores a 7 mg/litro. Limitada información limitada disponible parece indicar que la bioacumulación en los organismos acuáticos es baja. La escasez de datos dificulta la evaluación de los posibles efectos en los organismos terrestres.

El ser humano está expuesto al 1,1,1-tricloroetano principalmente por inhalación, y luego el organismo absorbe

rápida mente la sustancia. También se puede dar la exposición por contacto cutáneo o ingestión. El tricloroetano se distribuye ampliamente por los tejidos y atraviesa las barreras hematoencefálica y placentaria. Aunque también se ha encontrado en la leche humana, no parece que se produzca bioacumulación. La principal vía de eliminación es la exhalación del compuesto inalterado.

Las toxicidades aguda y crónica del 1,1,1-tricloroetano son relativamente bajas, pero en condiciones de exposición intensa pueden producirse efectos tóxicos. Estas condiciones se pueden presentar en casos de exposición profesional, de abuso del disolvente o de accidentes. Dado que el disolvente es volátil y el vapor es mucho más denso que el aire, se pueden producir concentraciones inesperadamente elevadas y peligrosas en espacios reducidos, como depósitos de almacenamiento "vacíos". Así, se han producido algunas intoxicaciones mortales y casi mortales en lugares de trabajo y otros.

El efecto más importante en el ser humano se produce en el sistema nervioso central. Los efectos observables van desde ligeros cambios de comportamiento (acompañados de una leve irritación ocular) con $1,9 \text{ g/m}^3$ (350 ppm) hasta la pérdida del conocimiento y el paro respiratorio con concentraciones más elevadas. Sin embargo, también se pueden producir anomalías cardíacas fatales. La toxicidad hepática del tricloroetano es inferior a la de la mayoría de los disolventes organoclorados. El nivel sin efecto observado (NOEL) para la especie humana parece ser del orden de $1,35 \text{ g/m}^3$ (250 ppm).

No se han publicado estudios adecuados sobre los efectos carcinogénicos en la especie humana. Sin embargo, en los estudios de inhalación prolongada en ratas y ratones expuestos a $8,1 \text{ g/m}^3$ (1500 ppm) no se obtuvieron pruebas de ningún efecto carcinogénico. El 1,1,1-tricloroetano no tiene un potencial genotóxico importante.

En ratas y conejos se ha observado toxicidad en la fase de crecimiento, pero no teratogenicidad, con concentraciones que fueron tóxicas para las madres. Las escasas pruebas epidemiológicas en relación con sus efectos sobre la reproducción no son concluyentes.

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