TETRACHLOROETHYLENE

Two reviews on tetrachloroethylene are available (Berkowitz, 1979; National Institute for Occupational Safety & Health, 1976).

1. Chemical and Physical Data

1.1 Synonyms and trade names

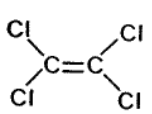
Chem. Abstr. Services Reg. No.: 127-18-4

Chem. Abstr. Name: Tetrachloroethane

Synonyms: Carbon bichloride; carbon dichloride; ethylene tetrachloride; per; perc; perchlor; perchlorethylene; perchloroethylene; perk; tetrachlorethylene; 1,1,2,2-tetrachloroethylene

Trade names: Ankilostin; Antisal 1; Dee-Solv; Didakene; Dow-Per; ENT 1860; Fedal-Un; Nema; Perclene; Percosolv; Perklone; PerSec; Tetlen; Tetracap; Tetraleno; Tetravec; Tetroguer; Tetropil

1.2 Structural and molecular formulae and molecular weight



C_2Cl_4 Mol. wt: 165.8

1.3 Chemical and physical properties of the pure substance

From Hawley (1977), unless otherwise specified

(a) Description: Colourless liquid

(b) Boiling-point: 121°C

(c) Freezing-point: -22.4°C

(d) Density: d_{20}^{20} 1.625

(e) Refractive index: n_D^{25} 1.5029

(f) Spectroscopy data: Infra-red, Raman and mass spectral data have been tabulated (Grasselli & Ritchey, 1975).

(g) Solubility: Practically insoluble in water (0.015 g/100 ml water at 25°C) (Hardie, 1964); miscible with ethanol, diethyl ether and oils in all proportions

(h) Volatility: Vapour pressure is 20 mm at 26.3°C (Perry & Chilton, 1973).

(i) Stability: Nonflammable; decomposes slowly in contact with water to yield trichloroacetic and hydrochloric acids. At 700°C in contact with active carbon, it decomposes to hexachloroethane and hexachlorobenzene (Hardie, 1964).

(j) Reactivity: Oxidized by strong oxidizing agents (sulphuric and nitric acids, sulphur trioxide); reaction with excess hydrogen in the presence of reduced nickel catalyst produces total decomposition to hydrogen chloride and carbon (Hardie, 1964).

(k) Conversion factor: 1 ppm in air is equivalent to 6.78 mg/m^3.

1.4 Technical products and impurities

Tetrachloroethylene is available in the US in the following grades: purified, technical, USP, spectrophotometric (Hawley, 1977) and dry-cleaning. The technical and dry-cleaning grades both meet specifications for technical grade and differ only in the amount of stabilizer added to prevent decomposition. Stabilizers are believed to include amines or mixtures of epoxides and esters. Typical analysis of the commercial grades is as follows: appearance, clear and free of suspended matter; specific gravity, 20°C/20°C, 1.624; nonvolatile residue, 0.0003%; free chlorine, none; moisture, no cloud at -5°C; 100% distillation range, 120.8-121.6°C.

USP grade contains not less than 99.0% and no more than 99.5% tetrachloroethylene, the remainder consisting of ethanol; it is available in the US in 0.2, 0.5, 1.0, 2.5 and 5 ml capsules intended for internal drug use (US Pharmacopeial Convention, Inc., 1975).

In Japan, tetrachloroethylene is available as a technical product with the following specifications: nonvolatile matter, 0.002% max; acidity (as HCl), 0.0001% max; and pH, 6.8.

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(a) Production

Tetrachloroethylene was first prepared in 1821 by Faraday by thermal decomposition of hexachloroethane (Hardie, 1964). The original commercial method of producing tetrachloroethylene involved a four-step process based on acetylene and chlorine as the raw materials. By July 1975, only one US plant with about 3% of total tetrachloroethylene capacity was using this process. Currently, the majority of tetrachloroethylene produced in the US is made by the oxyhydrochlorination, chlorination and/or dehydrochlorination of other hydrocarbons or chlorinated hydrocarbons. The raw materials include 1,2-dichloroethane (see monograph, p. 429), methane, ethane, propane, propylene, propylene dichloride and various other chlorinated materials such as 1,1,2-trichloroethane (see monograph, p. 533). An estimated 60% of the tetrachloroethylene produced in the US in 1974 was prepared from 1,2-dichloroethane, and about 40% from methane, ethane and propane.

In western Europe, tetrachloroethylene is produced by oxychlorination processes and by propylene chlorination.

In Japan, an estimated 60% of tetrachloroethylene is produced by chlorination of 1,2-dichloroethane and 40% by chlorination of methane and propane.

In 1972, worldwide demand for tetrachloroethylene was estimated to be 600 million kg.

It has been produced commercially in the US since 1925 (Hardie, 1964). In 1976, 9 US companies reported a total production of 304 million kg (US International Trade Commission, 1977). US imports in that year were 23.3 million kg, from the following countries (percent of total): France (34), Belgium (21), Italy (18), Japan (11), Canada (10), The Netherlands (4), and the Federal Republic of Germany (2) (US Department of Commerce, 1977a); exports were 22 million kg, and went to the following countries (percent of total): Mexico (38), the Federal Republic of Germany (18), The Netherlands (14), Belgium (9), Canada (5) and at least 5 other countries (16) (US Department of Commerce, 1977b).

Total annual production of tetrachloroethylene in western Europe is 250-500 million kg; the Federal Republic of Germany, France, Italy and the UK are the major producing countries, and Austria, Scandinavia, Spain, Switzerland and Benelux are minor producing regions. Annual production of tetrachloroethylene in eastern Europe is estimated to be 50-100 million kg.

Tetrachloroethylene has been produced commercially in Japan since 1952. In 1977, 8 companies produced an estimated 54.7 million kg; exports were 2.6 million kg in that year, none was imported.

(b) Use

In 1976, tetrachloroethylene was used in the US as follows: textile industry, 68%; industrial metal cleaning, 15%; chemical intermediate, 14%; and other applications, 3%.

Tetrachloroethylene is used in the textile industry for dry-cleaning and for processing and finishing. It is nonflammable, easily recoverable for reuse, does not hydrolyse appreciably, and can be used on all fabrics. In 1975, 70% of the dry-cleaners in the US used tetrachloroethylene, and it constituted over 65% of the total dry-cleaning solvent usage. In 1974, 18-27 million kg tetrachloroethylene were used for textile processing and finishing in the US.

It is used in both cold cleaning and vapour degreasing of metals; in 1974, about 80% of the total used in the US for metal cleaning was in vapour degreasing.

It is used as a chemical intermediate in the synthesis of Fluorocarbon 113 (1,1,2-trichloro-1,2,2-trifluoroethane), Fluorocarbon 114 (1,2-dichloro-1,1,2,2-tetrafluoroethane), Fluorocarbon 115 (chloropentafluoroethane), and Fluorocarbon 116 (hexafluoroethane).

Tetrachloroethylene is also used as a heat-exchange fluid, and as a drug against hookworms and some nematodes (National Institute for Occupational Safety & Health, 1978; US Pharmacopeial Convention, Inc., 1975).

In western Europe, use of tetrachloroethylene is as follows: dry-cleaning, 70-95%; metal cleaning and extraction, 5-15%; chemical intermediate, 0-10%; and other, 0-5%. Its use in Japan in 1977 was: dry-cleaning, 50%; metal cleaning, 21%; solvent and miscellaneous uses, 29%.

The US Occupational Safety and Health Administration's health standards for exposure to air contaminants require than an employee's exposure to tetrachloroethylene not exceed an 8-hr time-weighted average of 670 mg/m^3 (100 ppm) in the working atmosphere during an 8-hr work

shift of a 40-hr work week (US Occupational Safety & Health Administration, 1977). The corresponding standard in the Federal Republic of Germany is 670 mg/m^3; in the German Democratic Republic, 300 mg/m^3; in Sweden, 200 mg/m^3; and in Czechoslovakia, 250 mg/m^3; the acceptable ceiling concentration in the USSR is 10 mg/m^3 (Winell, 1975).

2.2 Occurrence

Tetrachloroethylene is not known to occur as a natural product.

(a) Air

About 85% of the tetrachloroethylene used annually in the US is lost to the atmosphere; in 1974, this amount was estimated to be 250 million kg (Fuller, 1976).

Numerous US studies have reported tetrachloroethylene in air [concentrations in parts per trillion (ppt[1]), unless otherwise specified]: (1) in rural air in central Michigan (30-50) (Russell & Shadoff, 1977); (2) in locations in California, including Los Angeles (673.3), Palm Springs (278.1), Badger Pass (30.7), Menlo Park (201.9) (Singh, 1976), Stanford Hills (38.3), Point Reyes (43.1) (Singh *et al.*, 1977), Pasadena (1.3-4.2 ppb[2]), West San Gabriel Valley to Manhatten Beach (< 0.01-3.8 ppb) and the Los Angeles Basin (0.37-3.84 ppb) (Simmonds *et al.*, 1974); (3) in New Brunswick, New Jersey (0.5 ppb) (Lillian *et al.*, 1976); (4) in rural south-eastern Washington state (20) (Grimsrud & Rasmussen, 1975); and (5) in various other locations (reported as mean concentrations), including Seagirt, New Jersey (0.32 ppb); New York City, New York (4.5 ppb), Sandy Hook, New Jersey (0.39 ppb), Delaware City, Delaware (0.24 ppb), Baltimore, Maryland (0.18 ppb), Wilmington, Ohio (0.15 ppb), White Face Mountains, New York (0.07 ppb) and Bayonne, New Jersey (1.63 ppb) (Lillian *et al.*, 1975).

In a UK study, tetrachloroethylene was detected in the air at the following locations (ppb): Runcorn Works perimeter (15-40), Runcorn Heath (0.2-5), Liverpool/Manchester suburban area (< 0.1-10), Moel Famau, Flintshire (< 0.1-2.5), Rannoch Moor, Argyllshire (0.3-1), and Forest of Dean, Monmouthshire (3) (Pearson & McConnell, 1975). In an air-sampling study conducted in central Exmoor and the moorlands of North Wales, tetrachloroethylene concentrations were found to range from 8-57 ng/m^3; in air over the north-east Atlantic Ocean between Cap Blanc and Lands End 1-9 ng/m^3 were detected (Murray & Riley, 1973). Tetrachloroethylene was also detected in the air over Adrigole, County Cork, Eire, at a level of 27.6 ppt (Cox *et al.*, 1976).

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[1] 1 ppt in air is equivalent to 6.78 ng/m^3.
[2] 1 ppb in air is equivalent to 6.78 µg/m^3.

(b) Water

Tetrachloroethylene may be formed in small quantities during chlorination of water: samples from 8 of 10 water utilities contained 0.07-0.46 µg/l (Safe Drinking Water Committee, 1977). It has also been detected in the municipal drinking-water at a number of localities [Bertsch *et al.*, 1975; (0.5 µg/l) Eurocop-Cost, 1976; (< 5 µg/l) Saunders *et al.*, 1975].

Rainwater has been found to contain up to 0.15 µg/l tetrachloroethylene. Average and maximum concentrations in sea-water were 0.12 µg/l and 2.6 µg/l and the maximum concentration in sediments 4.8 µg/l (Pearson & McConnell, 1975). Surface water from the Atlantic Ocean contained 0.2-0.8 ng/l tetrachloroethylene (Murray & Riley, 1973). It has also been detected in rivers and in subterranean water (Dowty *et al.*, 1975; Eurocop-Cost, 1976; Zürcher & Giger, 1976); and in commercial deionized charcoal-filtered water (Dowty *et al.*, 1975).

Tetrachloroethylene was detected in the influent to a sewage treatment plant at a level of 6.2 µg/l, in the effluent before chlorination, at 3.9 µg/l, and in the effluent after chlorination, at 4.2 µg/l (Bellar *et al.*, 1974). It has also been detected in the effluents from chemical production plants, an oil refinery and textile plants and in lake water (Shackelford & Keith, 1976).

(c) Food

Tetrachloroethylene has been detected in dairy produce (0.3-13 µg/kg), meat (0.9-5 µg/kg), oils and fats (0.01-7 µg/kg), beverages (2-3 µg/kg), fruit and vegetables (0.7-2 µg/kg), fresh bread (1 µg/kg) (McConnell *et al.*, 1975) and commercially available rendered fats and meat-and-bone meal (Ingr, 1976).

(d) Marine organisms

Tetrachloroethylene residues were detected in specific organs of the following fish (concentrations expressed as µg/kg on a dry-weight basis): 3 species of molluscs (0-176), eel (1-43), cod (0-8), coalfish (0-6), dogfish (0-13), and bib (0-27) (Dickson & Riley, 1976).

In another study, tetrachloroethylene residues were reported as follows (concentrations expressed as µg/kg of wet tissue): in 14 species of invertebrates (0.05-15), 3 species of marine algae (13-20), 15 species of fish (0-41), the organs and eggs of 8 species of sea and freshwater birds (0.7-39), and the organs of 2 species of mammals (0-19) (Pearson & McConnell, 1975).

(e) Humans

Tetrachloroethylene has been detected in post-mortem human tissue samples, at levels of less than 0.5-29.2 µg/kg (wet tissue) (McConnell *et al.*, 1975), and in expired air, at levels of 0.022-12 µg/hr/subject (Conkle *et al.*, 1975).

(f) Occupational exposure

Tetrachloroethylene was detected in the air of industrial installations at a concentration of 2 mg/m^3 (0.3 ppm) (Kiparisova & Stepanenko, 1976). Concentrations measured in dry-cleaning plants varied from 20-300 mg/m^3 (3-45 ppm) (Engels *et al.*, 1975).

2.3 Analysis

The determination of chlorinated hydrocarbons, including tetrachloroethylene, in ambient and alveolar air, workplace atmospheres, blood and urine has been reviewed (Walter *et al.*, 1976). Methods used for the analysis of tetrachloroethylene in environmental samples are listed in Table 1.

Grimsrud & Rasmussen (1975) report that difficulty in removing tetrachloroethylene from the carrier gas system limits the value of gas chromatography/mass spectrometry methods. This method was used by Coleman *et al.* (1976) to quantify halocarbons, including tetrachloroethylene, in drinking-water.

Carbon dioxide laser absorption spectrometry can be used to detect tetrachloroethylene in prepared samples of air pollutants, with a limit of detection of 9.5 µg/m^3 (1.4 ppb) (Schnell & Fischer, 1975).

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals[1]

(a) Oral administration

Mouse: Groups of 50 male and 50 female B6C3F1 mice, approximately 5 weeks old at the beginning of treatment, were administered tetrachloroethylene (USP grade) in corn oil by gavage on 5 consecutive days per week for 78 weeks. High-dose males received 900 mg/kg bw/day for 11 weeks,

[1]The Working Group was aware of studies in progress to assess the carcinogenicity of tetrachloroethylene in mice and rats by oral administration and in mice by skin application (IARC, 1978a).

TABLE 1. METHODS FOR THE ANALYSIS OF TETRACHLOROETHYLENE

ANALYTICAL METHOD				
SAMPLE TYPE	EXTRACTION/CLEAN-UP	DETECTION	LIMIT OF DETECTION	REFERENCE
Formulations				
Encapsulated liquids	Dilute (ethanol)	IR		Horwitz (1975)
Cough syrups	Dilute (ethanol) if necessary	IR		Horwitz (1975)
Air				
Workplace	Sample on charcoal, extract (carbon disulphide)	GC/FID	Useful range, 655-2749 mg/m^3	National Institute for Occupational Safety & Health (1977)
Ambient	Determine directly Enrich	GC	15 mg/m^3 2.5 mg/m^3	Krynska *et al.* (1976)
Ambient	Trap on Chromosorb 101, desorb by heating, retrap in line on GC column	GC	3.4 $\mu g/m^3$ (0.5 ppb)	Parkes *et al.* (1976)
Ambient	Sample in Drechsel flask fitted with rubber septum, sample with gas syringe	GC/ECD	1 $\mu g/m^3$	Bureau International Technique des Solvants Chlorés (1976)
Ambient	Sample on Porapak N, desorb by heating, retrap in line on GC column	GC/ECD, GC/MS	0.2 $\mu g/m^3$ (30 ppt)	Russell & Shadoff (1977)
Water				
Drinking- and sewage water	Bubble nitrogen through sample, concentrate	GC/FID; GC/MS	0.1 µg/l	Bellar *et al.* (1974)
Drinking-water	Extract (pentane), dry	GC/ECD	25 ng/l	Bureau International Technique des Solvants Chlorés (1976)
Drinking-water	Analyse directly	GC/ECD	0.5 µg/l	Nicholson *et al.* (1977)
Drinking-water	Analyse directly	GC/ECD	8 µg/l	Nicholson & Meresz (1975)

TABLE 1. METHODS FOR THE ANALYSIS OF TETRACHLOROETHYLENE (continued)

ANALYTICAL METHOD				
SAMPLE TYPE	EXTRACTION/CLEAN-UP	DETECTION	LIMIT OF DETECTION	REFERENCE
Miscellaneous				
Oil and liquid paraffin	Heat sample, use headspace	GC/FID		Drexler & Osterkamp (1977)
Tobacco smoke	Trap on Tenax GC and Carbopack BHT coated with 5 and 25% OV-101 silicon fluid	GC/FID; GC/MS		Holzer *et al.* (1976)

Abbreviations: IR - infra-red spectrometry; GC/FID - gas chromatography/flame-ionization detection; ECD - electron capture detection; MS - mass spectrometry

1100 mg/kg bw/day for 67 weeks followed by 12 weeks without treatment; high-dose females received 600 mg/kg bw/day for 11 weeks and 800 mg/kg bw/day for 67 weeks. Respective doses in low-dose animals were 450 and 550 mg/kg bw/day in males and 300 and 400 mg/kg bw/day in females. Time-weighted average doses were 536 and 1072 mg/kg bw/day in males and 386 and 772 mg/kg bw/day in females. Groups of 20 male and 20 female mice were either untreated or received corn oil alone. All surviving mice were killed 90 weeks after the start of the experiment. The times at which 50% of animals were still alive were 90 weeks for control animals of both sexes, 78 weeks for low-dose males, 43 weeks for high-dose males, 62 weeks for low-dose females and 50 weeks for high-dose females. The shorter lifespan in treated animals was due to early toxicity and high incidences of hepatocellular carcinomas in animals of both sexes: hepatocellular carcinomas occurred in 2/17 untreated control males, 2/20 vehicle control males, 32/49 low-dose males and 27/48 high-dose males; in females, the respective incidences were 2/20, 0/20, 19/48 and 19/48. Metastases were found in 1 untreated control male, in 3 low-dose males, in 1 low-dose female and in 1 high-dose female (National Cancer Institute, 1977).

Rat: Groups of 50 male and 50 female 7-week-old Osborne-Mendel rats were treated with tetrachloroethylene (USP grade) in corn oil by gavage on 5 days a week for 78 weeks. High-dose animals received 1000-1400 mg/kg bw/day, and low-dose animals 500-700 mg/kg bw/day. All surviving animals were then observed until 110 weeks after the start of treatment. The time-weighted average doses were 471 and 941 mg/kg bw/day in low- and high-dose males and 474 and 949 mg/kg bw/day in low- and high-dose females. Dose-related mortality was observed in animals of both sexes after 30 weeks. Groups of 20 male and 20 female untreated rats or vehicle-treated rats served as controls. The times at which 50% of animals were still alive were 44 weeks for high-dose males, 66 weeks for high-dose females, 66 weeks for control groups, over 88 weeks for low-dose males and 102 weeks for low-dose females. No increases in tumour incidences were observed. Toxic nephropathy was observed in treated rats that died as early as week 20 (National Cancer Institute, 1977) [The Working Group noted the poor survival of treated animals].

(b) Inhalation and/or intratracheal administration

Rat: In a study reported as an abstract, groups of 96 male and 96 female Sprague-Dawley rats were exposed by inhalation to 2 or 4 g/m^3 (300 or 600 ppm) tetrachloroethylene in air for 6 hrs per day on 5 days a week for 12 months, followed by observation up to 30 months. No statistically significant difference in tumour incidence between treated and control animals was found (Rampy *et al.*, 1977) [The Working Group noted the incomplete reporting of the experiment and the short duration of the exposure].

(c) Intraperitoneal administration

Mouse: Groups of 20 male A/St mice, 6-8 weeks old, were given thrice weekly i.p. injections of 80 mg/kg bw (14 injections), 200 mg/kg bw (24 injections) or 400 mg/kg bw (48 injections) tetrachloroethylene in tricaprylin. All survivors (15, 17, 18 mice in the three groups, respectively) were killed 24 weeks after the first injection. The average number of lung tumours per mouse was not increased compared with that in controls that received tricaprylin alone (Theiss *et al.*, 1977) [The Working Group noted the limitations of negative results obtained with this test system; see also General Remarks on Substances Considered, p. 34].

3.2 Other relevant biological data

(a) Experimental systems

Toxic effects

The toxic effects of tetrachloroethylene have been reviewed (Von Oettingen, 1964).

The oral LD_{50} of tetrachloroethylene in mice is 6.4-8 g/kg bw (Kohne, 1940), 8.85 and 10.8 g/kg bw; it was less toxic in oily solution than when undiluted (Dybing & Dybing, 1946). The inhalational LC_{50} in mice (4 hrs) is 35 g/m^3 (5200 ppm) (Friberg *et al.*, 1953), and the i.p. LD_{50} is 4.7 g/kg bw (Klaassen & Plaa, 1966). In rats, the oral LD_{50} is 13 g/kg bw (Smyth *et al.*, 1969). For rabbits, the minimum lethal dose (24 hrs) after s.c. injection is 2.2 g/kg bw; in dogs, the minimum lethal dose (30 min) after i.v. injection is 85 mg/kg bw (Barsoum & Saad, 1934). The i.p. LD_{50} in dogs is 3.5 g/kg bw (Klaassen & Plaa, 1967).

The minimal narcotic concentration of tetrachloroethylene for mice is 20 g/m^3 (2950 ppm) (Lazarew, 1929). Single exposure of rats to 13.6 g/m^3 (2000 ppm) for 5 hrs caused no loss of consciousness (Rowe *et al.*, 1952). Lamson *et al.* (1929) reported the narcotic concentration for dogs as 62 g/m^3 (9900 ppm).

Thirteen exposures to 17 g/m^3 (2500 ppm) tetrachloroethylene vapours for 7 hrs daily was fatal to the majority of rats (Rowe *et al.*, 1952). The average maximum tolerated oral dose of tetrachloroethylene over a period of 78 weeks was 941 mg/kg bw/day in male Osborne-Mendel rats, 949 mg/kg bw/day in females, 1072 mg/kg bw/day in male B6C3F1 mice, and 722 mg/kg bw/day in females (National Cancer Institute, 1977).

Repeated exposure to vapours has produced a variety of pathological changes in the liver, ranging from fatty degeneration to necrosis in rats, rabbits and guinea-pigs (Rowe *et al.*, 1952). Repeated exposure of male

Sprague-Dawley rats to 4 g/m^3 (600 ppm) vapour for 6 hrs/day on 5 days/week for 12 months resulted in reversible toxic effects in the liver (Pegg *et al.*, 1978). Oral doses of 0.3 g/kg bw produced degenerative changes and extensive atrophy of the liver in dogs (Hall & Shillinger, 1925).

Oral doses of tetrachloroethylene have lesser effects on the kidney: only a nearly lethal dose (4 g/kg bw) caused swelling of the convoluted tubules and hydropic degeneration in male mice (Klaassen & Plaa, 1966; Plaa & Larson, 1965). I.p. doses of 1.6-2.3 g/kg bw tetrachloroethylene caused slight calcification of the tubules of the kidneys in dogs (Klaassen & Plaa, 1967).

Embryotoxicity and teratogenicity

Groups of rats and mice were exposed by inhalation for 7 hrs daily on days 6-15 of gestation to 2 g/m^3 in air (300 ppm) tetrachloroethylene; no effects were observed on the average number of implantation sites per litter, litter size, incidence of foetal resorptions, foetal sex ratios or foetal body measurements. No treatment-related increase in the incidence of skeletal or visceral malformations was observed (Schwetz *et al.*, 1975).

Absorption, distribution, excretion and metabolism

Tetrachloroethylene is readily absorbed through the lungs and to some extent from the gastrointestinal tract (Von Oettingen, 1964). Fats and oils facilitate its absorption from the intestine after oral administration to dogs (Lamson *et al.*, 1929). Skin absorption of tetrachloroethylene in mice is low in relation to that of a series of chlorinated ethanes and ethylenes (Tsuruta, 1975).

The half-life of expiration of ^{36}Cl-labelled tetrachloroethylene in rats was about 7 hrs, regardless of dose or route of application (Pegg *et al.*, 1978).

Mice excreted about 90% of an inhaled dose of 1300 mg/kg bw ^{14}C-labelled tetrachloroethylene: 70% in the expired air, 20% in the urine and < 0.5 % in the faeces. The metabolites identified in the urine were trichloroacetic acid (52% of total urinary activity), oxalic acid (11%) and traces of dichloroacetic acid (Yllner, 1961). In contrast, Daniel (1963) found only 2% of an oral dose of about 1000 mg/kg bw ^{36}Cl-tetrachloroethylene in the urine of rats; trichloroacetic acid (0.6%) and inorganic chloride were the only metabolites detected.

When ^{14}C-labelled tetrachloroethylene was administered to adult male rats by gavage or by inhalation, approximately 70% of the body burden was expired as unchanged compound, 26% as CO_2 in expired air and as nonvolatile metabolites in urine and faeces and 3-4% remained in the carcass (Pegg *et al.*, 1978).

The hepatotoxicity of tetrachloroethylene was enhanced in rats treated with Aroclor 1254. Pretreatment of rats with phenobarbital or Aroclor 1254 orally considerably increased the urinary excretion of trichloro compounds after oral administration of tetrachloroethylene in oil (Moslen *et al.*, 1977).

In rat liver perfusion experiments, tetrachloroethylene was converted into trichloroacetic acid, the only metabolite detected (Bonse *et al.*, 1975).

The presence of an epoxide intermediate (oxirane) has been proposed in the metabolism of tetrachloroethylene on the basis of its oxidative metabolism (Henschler & Bonse, 1977).

Mutagenicity and other related short-term tests

Results reported in an abstract suggest that tetrachloroethylene is mutagenic in plate tests in *Salmonella typhimurium* TA100. In a host-mediated assay in mice, using *Salmonella typhimurium* TA1950, TA1951 and TA1952, there was a significant increase in the number of revertants with doses equivalent to the LD_{50} and to half the LD_{50}, but this was not dose-related (Černá & Kypěnová, 1977).

Tetrachloroethylene did not induce mutations to prototrophy at the *gal*, *arg* and *nad* loci in *Escherichia coli* K12 and had no effect on forward mutation frequency in the methyltryptophan resistance system at a nontoxic concentration of 0.9 mM (liquid tests) (Greim *et al.*, 1975).

There was no induction of chromosomal aberrations in bone-marrow cells of mice that had received either single (half LD_{50}) or 5 daily i.p. injections (one-sixth LD_{50}) of the chemical (Černá & Kypěnová, 1977).

(b) Humans

The effects of inhalation of various concentrations have been reviewed; these include irritation of the mucous membranes, skin irritation (Von Oettingen, 1964) and lung oedema (Patel *et al.*, 1977). The neurological effects of tetrachloroethylene on dry-cleaners have also been reviewed (Tuttle *et al.*, 1977).

Chronic exposure to tetrachloroethylene vapours caused irritation of the respiratory tract, nausea, headache, sleeplessness, abdominal pains and constipation (Chmielewski *et al.*, 1976; Coler & Rossmiller, 1953; Stewart *et al.*, 1970; Von Oettingen, 1964). Pathological findings (liver cirrhosis, hepatitis and nephritis) are rare (Stewart, 1969). Other reports of intoxications and fatalities due to tetrachloroethylene have been made (Eberhardt & Freundt, 1966; Larsen *et al.*,

1977; Stewart, 1969; Trense & Zimmermann, 1969). Therapeutic administration of tetrachloroethylene as an anthelminthic has occasionally produced side effects (Von Oettingen, 1964).

A case of 'obstructive jaundice' in a 6-week old infant has been attributed to tetrachloroethylene in breast milk. During her pregnancy, the mother had frequently visited her husband at his work place in a dry-cleaning plant. Liver function tests and serum transaminase levels in the parents were normal (Bagnell & Ellenberger, 1977).

Tetrachloroethylene vapours and liquid can be absorbed through the skin (Hake & Stewart, 1977; Stewart & Dodd, 1964) and through the lungs (Stewart *et al.*, 1961). Inhaled tetrachloroethylene is excreted very slowly: its biological half-life is 3-5 days, depending on the length of exposure (Stewart *et al.*, 1970). The half-life of tetrachloroethylene in alveolar air after dermal absorption of the liquid was approximately 8 hrs (Stewart & Dodd, 1964). After exposure to 0.7 g/m^3 (100 ppm) in air for 8 hrs, the concentrations in the alveolar air decreased exponentially, with an initial expiration half-life of 25-30 min (Fernandez *et al.*, 1976). The total body half-life was calculated to be 71.5 hrs (Guberan & Fernandez, 1974).

Inhalation of tetrachloroethylene is followed by a long-lasting excretion of metabolites in the urine (Ikeda & Imamura, 1973). Tetrachloroethylene is metabolized very slowly, and determination of its urinary metabolites can therefore not be taken as a satisfactory measure of exposure. Male volunteers exposed to 0.6 g/m^3 (87 ppm) tetrachloroethylene vapours in air for 3 hrs excreted about 1.8% of the dose in the urine as trichloroacetic acid in 67 hrs (Ogata *et al.*, 1971). At concentrations well below 678 mg/m^3 (100 ppm), both trichloroacetic acid and trichloroethanol concentrations in the urine reach a plateau (Ikeda, 1977).

Of 200 workers exposed to tetrachloroethylene vapours, 35% had more than 10 mg/l trichloroacetic acid in their urine. About half the subjects with these levels of urinary trichloroacetic acid had some symptoms of poisoning (Münzer & Heder, 1972).

3.3 Case reports and epidemiological studies[1]

No data were available to the Working Group.

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[1]The Working Group was aware of a mortality study in progress on dry-cleaning workers exposed to tetrachloroethylene (IARC, 1978b).

4. Summary of Data Reported and Evaluation

4.1 Experimental data

Tetrachloroethylene was tested in one experiment in mice and in one in rats by oral administration. In mice, it produced hepatocellular carcinomas in animals of both sexes. The experiment in rats was considered to be inadequate. Tetrachloroethylene was also inadequately tested by inhalation exposure in rats and by intraperitoneal injection in mice.

Tetrachloroethylene was not mutagenic in *Escherichia coli* and was negative in cytogenetic tests in mice.

4.2 Human data[1]

No case reports or epidemiological studies were available to the Working Group.

The extensive production and use of tetrachloroethylene over the past several decades, particularly for dry-cleaning purposes, indicate that widespread human exposure occurs. This is confirmed by many reports of its occurrence in air, water, fish and food samples.

4.3 Evaluation

There is *limited evidence* that tetrachloroethylene is carcinogenic in mice.

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[1]Subsequent to the meeting of the Working Group, the Secretariat became aware of a study of 330 deceased laundry and dry-cleaning workers who had been exposed to carbon tetrachloride, trichloroethylene and tetrachloroethylene. An excess of lung, cervical and skin cancers and a slight excess of leukaemias and liver cancers were observed (Blair *et al.*, 1979). In an abstract, Blair *et al.* (1978) described a clinical report of 5 cases of chronic lymphocytic leukaemia in a family that operated a dry-cleaning business.

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