JACC Report

No 12

1-Chloro-1,2,2,2-Tetrafluoroethane-(HFA-124)
CAS Reg. No. 2837-89-0

May 1990

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Joint Assessment of Commodity Chemicals

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1-CHLORO-1,2,2,2-TETRAFLUOROETHANE (HFA-124)

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Correction

Page 4 - Half life should read lifetime.

THE ECETOC SCHEME FOR THE

"JOINT ASSESSMENT OF COMMODITY CHEMICALS" (JACC)

This report has been produced as part of a programme for reviewing critically the toxicity and environmental hazards of selected industrial chemcials. A number of organisations world-wide produce such reviews so that, based on up-to-date knowledge, existing chemicals can continue to be produced and used safely. ECETOC is contributing to this with its JACC reviews.

In general, commodity chemicals, that is those produced in large tonnage by several companies and having widespread and multiple uses, are reviewed. Every effort is made to discover whether an adequate review exists already, but when this is not so a review is produced jointly by experts from a number of companies with interests in the chemical. Whenever good scientific reviews on certain toxicological or ecotoxicological aspects exist, their conclusions are summarised and only the subsequent literature is assessed. Only the uses of the chemical as such are considered; its occurrence as an impurity in other products is not normally taken into account.

In this document a critical assessment of the toxicology and ecotoxicology of chlorotetrafluoroethane is presented. Strictly this is not a commodity chemical, it is a product undergoing process development, but in view of the interest that exists in chlorinated fluorocarbons it is considered that an interim statement is needed on the state of knowledge that exists with respect to this group of chemicals.

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1. SUMMARY AND CONCLUSIONS

1-Chloro-1,2,2,2-tetrafluoroethane (chlorotetrafluoroethane) is a non-flammable, colourless gas under normal conditions. It is currently undergoing process development and is not available in commercial quantities. Since quantities produced are small, no information has been developed on biodegradation, bioconcentration or bioaccumulation.

Chlorotetrafluoroethane has a low calculated ozone depletion potential (ODP) of 0.016 - 0.024 compared to the fully halogenated chlorofluorocarbons; the reference compounds trichlorofluoromethane (CFC-11) and dichlorodifluoromethane (CFC-12) have an ODP of 1.0. Chlorotetrafluoroethane has a global warming potential (GWP) of 0.092 - 0.10, which is low compared to CFC-11 (GWP of 1.0).

There is no evidence that chlorotetrafluoroethane is genotoxic *in vitro*; negative results were obtained in microbial assays using *Saccharomyces cerevisiae* and *Salmonella typhimurium* with and without the addition of mammalian metabolic activation preparations.

Since chlorotetrafluorethane is a gas, studies of skin, eye irritation and dermal sensitisation have not been conducted.

Chlorotetrafluoroethane has a low order of acute toxicity. An approximate lethal concentration of 2,460,000 mg/m^3 was estimated for a 10-minute exposure in mice and the approximate anaestetic concentration was 837,000 mg/m^3. Anaesthesia in dogs was achieved at concentrations ranging from 2,230,000 - 3,910,000 mg/m^3.

Chlorotetrafluoroethane caused cardiac sensitisation at concentrations of 146,000 mg/m^3 or greater in dogs which received a challenge injection of adrenaline. The no-effect-level was 55,800 mg/m^3.

Chlorotetrafluoroethane has been evaluated in repeated exposures studies. Rats were exposed for 6h/d, 5d/w for 2 weeks at concentrations of 558,000 mg/m^3 and for 3 months at concentrations of 2,790, 5,580 or 27,900 mg/m^3 using a 6h/d, 5d/w regime. In the two week study no effects were observed. The only effects found in the 3-month inhalation toxicity study were increased liver weights in males at 5,580 and 27,900 mg/m^3 and decreased lung and adrenal weights at concentrations of 2,790 mg/m^3 and above. Clinical chemistry and histopathology did not show evidence of treatment related effects. Elevated urinary fluoride excretion was found in both sexes exposed to 27,900 mg/m^3 and in males exposed to all 3 levels both at 90 days and following a 30 day recovery period.

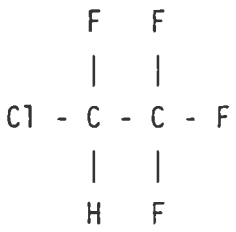
Specific kinetic and metabolism studies on chlorotetrafluoroethane are lacking but the increased urinary fluoride level in rats in a 90-day toxicity study suggests absorption and some metabolic transformation does take place.

Chlorotetrafluoroethane was not teratogenic to rats at a concentration of 27,900 mg/m^3.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 Identity

Chemical structure:



Chemical formulae:	$CHClF\text{-}CF_3$
Common name:	1-Chloro-1,2,2,2-tetrafluoroethane Chlorotetrafluoroethane
Common synonyms:	1,1,1,2-Tetrafluoro-2-chloroethane Fluorocarbon 124 HCFC-124; HFA 124*
CAS Registry Number:	2837-89-0
Conversion factors:	1 ppm = 5.58 mg/m^3 1 mg/l = 179 ppm

2.2 Physical and Chemical Properties

Chlorotetrafluoroethane is a nonflammable colourless gas. Some physical and chemical data for chlorotetrafluoroethane are given in Table 1.

* HFA-124 abbreviation means : Hydro Fluor Alkane C_2HF_4Cl

First figure = Number of C-Atoms minus 1	1
Second figure = Number of H-Atoms plus 1	2
Third figure = Number of F-Atoms	4
	HFA-124

The number of Cl-Atoms is not included in the abbreviation, but represents the rest to the total saturation of the formula.

2.3 Analytical Methods

A method of analysis has been described using gas chromatography with dual flame ionization detection (Brewer, 1977a).

3. PRODUCTION, STORAGE, TRANSPORT AND USE

There is no known natural source of chlorotetrafluoroethane. The manufacturing process is in the developmental stage; thus there is no information on producers and production levels and no known releases.

Chlorotetrafluoroethane is being developed as a substitute for some existing fully halogenated CFCs with comparable physical properties which may find applications as blowing agents and refrigerants.

4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

4.1 Introduction

Chlorotetrafluoroethane is undergoing development and is not available in commercial quantities. Information on biodegradation, bioconcentration and bioaccumulation is not yet available.

4.2 Environmental Factors

The physical and chemical properties of chlorotetrafluoroethane suggest that it would mix rapidly in the troposphere. Reaction with naturally occuring hydroxyl radicals (OH) in the troposphere is expected to be the primary degradation route. The estimated atmospheric half-life of this reaction is about 6.6 years (UNEP/WHO, 1989).

UNEP/WMO (1989) reported the ozone depletion potential (ODP) to be 0.016 -0.017 and 0.017-0.024 determined by one-dimensional and two-dimensional models, respectively. This is compared with an ODP-value of 1.0 for the fully halogenated trichlorofluoromethane (CFC-11). The estimates were made assuming that the reference compound, methyl chloroform, has a tropospheric lifetime of 6.3 years; chlorotetrafluoroethane has a shorter troposheric lifetime than that of trichlorofluoromethane and slightly longer than that of methyl chloroform. A marked latitudinal gradient is predicted for the ODP of chlorotetrafluoroethane, with the largest ODP's near summer poles and smaller values in the tropics.

The global warming potential (GWP) range for chlorotetrafluoroethane is reported by UNEP/WMO (1989) to be 0.092-0.10 as compared to CFC 11, which has a GWP of 1.0. The range was determined by one-dimensional models assuming a methyl chloroform-derived lifetime of 6.3 years.

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Environmental levels and human exposure are negligible, since chlorotetrafluoroethane is not in commercial production.

6. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

No data are available on the effects of chlorotetrafluoroethane on environmental organisms.

7. KINETICS AND METABOLISM

7.1 Animal Studies

Kinetic and metabolic studies are not available but increased urinary fluoride levels observed in a 90-day toxicity study in rats suggest absorption and metabolic transformation take place (see Section 8.2).

7.2 Human Studies

No data exist for human absorption, distribution, metabolic transformation or elimination of chlorotetrafluoroethane.

8. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO TEST SYSTEMS

8.1 Single Exposure

Coate (1976) reported that a single 6-hour exposure to chlorotetrafluoroethane at a concentration of 2,010,000 mg/m^3 was not lethal to rats but rapidly depressed motor activity and this was followed by anaesthesia after 1 hr. Rats exposed to 558,000 mg/m^3 were active for 30 minutes but then inactive until to termination of exposure. Body weight was not lost, but rats exposed to 2,010,000 mg/m^3 gained less weight than either the controls or the lower exposure group between days 1 and 8. This supports earlier work by Van Poznak and Artusio (1960) which demonstrated that chlorotetrafluoroethane caused anaesthesia in dogs exposed to concentrations between 2,230,000 and 3,910,000 mg/m^3. Wada (1977) reported an approximate lethal concentration in mice of 2,460,000 mg/m^3 for a 10-minute exposure to chlorotetrafluoroethane. No deaths were reported at a concentration of 2,230,000 mg/m^3. The

approximate anaesthetic concentration was given as 837,000 mg/m^3 with no observable effect at 558,000 mg/m^3. These data are consistent with those in rats reported by Coate (1976).

8.2 Repeated Exposure

Subacute and subchronic toxicity studies on chlorotetrafluoroethane are discussed here. Studies designed to examine effects on the cardiac system are described in Section 8.5.

Trochimowicz et al (1977) reported that no adverse effects were found on clinical examination and histopathological evaluation of rats exposed for 6 hrs/d, 5 d/wk for 2 weeks to chlorotetrafluoroethane at 558,000 mg/m^3.

Brewer (1977a) conducted a 3-month inhalation toxicity study of chlorotetrafluoroethane on four groups of 60 (35 M, 25 F) Sprague Dawley rats. Test groups were exposed to chlorotetrafluoroethane concentrations of 2,790, 5,580, or 27,900 mg/m^3 6 h/d, 5 d/wk for 3 months (a total of 64 exposures) and a control group was exposed to air only. Ten male rats and 10 female rats were examined and sacrificed after 45 days and a similar number after 92 days. Ten male and five female rats of each group were maintained without further exposure for an additional 30 day period after exposure. Clinical signs and body weight were determined and haematological clinical biochemical, organ weight and histopathological examinations carried out on all animals.

No statistically significant body weight changes were noted during the study. Haematology, clinical chemistry and routine urine analysis findings on treated rats were normal and comparable to findings in control animals. Urinary fluoride excretion was increased after 45 d exposure in both males and females (4.0 and 3.5 fold respectively) when exposed at 27,900 mg/m^2, determinations were not made at the two lower dose levels. After 95 days exposure at all 3 dose levels urinary fluoride was elevated in males only (1.5/1.7/1.8 fold), the effect persisted following the 30 day period free from exposure.

Gross and histopathological examination of all groups did not reveal any changes which could be attributable to the inhalation of chlorotetrafluoroethane. Statistically significant differences between treated and control rats were found with respect to organ weights at sacrifice of main study animals. Liver weights were increased significantly in males at both the 5,580 and 27,900 mg/m^3 exposure level, while the lung and adrenal weights were decreased significantly in males at all three exposure levels. In the absence of any histopathological changes, these organ weight changes are unlikely to have any biological significance. No statistically significant organ weight differences were found between treated and the group animals allowed a recovery period or in female animals of any group.

8.3 Long-Term Exposure

No data are available.

8.4 Skin and Eye Irritation. Allergic Sensitisation

As chlorotetrafluoroethane is a gas studies of skin and eye irritation and dermal sensitisation have not been conducted. No conclusions could be drawn from the 90-day inhalation study concerning these features.

8.5 Special Studies: Cardiovascular and Respiratory Effects

Mullin (1976) reported that the no-effect level for cardiovascular sensitisation in the dog was 55,800 mg chlorotetrafluoroethane/m^3 while exposure to concentrations of 146,000 mg/m^3 or greater were capable of inducing cardiac sensitisation after a challenge injection of adrenaline.

Van Poznak and Artusio (1960) found that chlorotetrafluoroethane caused anaesthesia in dogs at concentrations ranging from 2,230,000 to 3,910,000 mg/m^3; blood pressure was lowered proportionately to the concentration administered. Although ventilation was adequate at 3,910,000 mg/m^3 the femoral arterial systolic pressure fell as low as 40 mm Hg. Little or no

anaesthetic effect was seen at concentrations which did not depress blood pressure. Atropine had little effect on the degree of hypotension. Phenylephrine partially reversed the hypotension and caused several premature ventricular contractions but not ventricular fibrillation. Similar effects were produced by intravenous adrenaline.

8.6 Reproductive Performance, Embryotoxicity and Teratology

Chlorotetrafluoroethane did not induce teratogenic effects in albino rats (Brewer, 1977b). A group of 20 pregnant Ch.R-CD rats was exposed via inhalation 6 h/d at a concentration of 27,900 mg/m^3 during days 6 - 15 of gestation. Maternal body weights and clinical signs of exposed pregnant rats were similar to controls. No maternal deaths occurred. The incidence of resorption sites in the chlorotetrafluoroethane exposed group was slightly higher than in controls but within the range commonly experienced with the strain of rats employed. The numbers of corpora lutea, implantation sites and foetuses in the chlorotetrafluoroethane group were similar to those of the controls. Foetal body weights were not altered by chlorotetrafluoroethane exposure.

No data are available on the effects of chlorotetrafluoroethane on other aspects of reproductive performance.

8.7 Mutagenicity

8.7.1 In Vitro

Brusick (1976) evaluated chlorotetrafluoroethane for mutagenic activity in a series of plate and suspension assays using Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98 and TA100, and Saccharomyces cerevisiae strain D4. Results of both a 4 h and 24 h exposure in the plate test were negative, with and without metabolic activation. Suspension assay test results, with and without activation, were also negative.

Chlorotetrafluoroethane was again found to be nonmutagenic in plate assays using Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98 and TA100 incubated in atmospheres containing 1,116,000 or 2,233,000 mg/m^3 with a 6 h incubation period in the presence or absence of an S-9 metabolic activation system (Du Pont Co., 1976).

Longstaff et al (1984) also reported that chlorotetrafluoroethane was non-mutagenic in Salmonella typhimurium strains TA1535, TA1538, TA98 and TA100 both in the presence or absence of an S-9 metabolic activating system. The maximum concentration used with some strains was up to 2,790,000 mg/m^3.

8.7.2 In Vivo

No data are available

8.8 Carcinogenicity

No data are available

9. EFFECTS ON HUMANS

There are no reported adverse health effects which can be ascribed to chlorotetrafluoroethane.

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Table 1. Physical and Chemical Properties of Chlorotetrafluoroethane (1)

Molecular weight	:	136.5	
Physical form	:	gas	
Colour	:	colourless	
Boiling point, °C at 1030 HPa	:	-12	(2)
Liquid density at 11.3°C, g/ml	:	1.4	
Vapour density (air = 1)	:	3.5	
Vapour pressure, psia at 20.6°C at 1030 HPa	:	48	
Solubility in water at 20°C, g/l	:	17.1	(3)
Solubility in organic solvents	:	miscible with acetone, ethanol, petroleum solvents	(3)
Flammability	:	nonflammable	

1. From Allied-Signal Inc; Product Safety Data Sheet - HCFC-124, September 1989.

2. From Allied-Signal Inc., Unpublished Data, 1975.

3. From E.I. du Pont de nemours and Co., Inc., Haskell Laboratory, Unpublished Data; 1976.

APPENDIX 1

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