1-Chloro-1,2,2,2-tetrafluoroethane (HCFC 124) CAS No. 2837-89-0 (Second Edition)

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CONTENTS

EXECUTIVE SUMMARY

This report has been produced as part of the ECETOC Joint Assessment of Commodity Chemicals (JACC) programme. It updates an earlier ECETOC review [a] and presents a critical evaluation of the available toxicity and ecotoxicity data on 1-chloro-1,2,2,2-tetrafluoroethane (HCFC-124), including results of recent and unpublished toxicological studies conducted under the Programme for Alternative Fluorocarbon Toxicity Testing (PAFT) [b].

A non-flammable colourless gas, HCFC-124 is used as a replacement for some fully halogenated chlorofluorocarbons in refrigeration. In the atmosphere, HCFC-124 has a low ozone depletion potential of 0.022 relative to trichlorofluoromethane (CFC-11). Its overall lifetime is 5.8 years and its global warming potential 599, relative to carbon dioxide.

HCFC-124 has a low order of acute inhalation toxicity in experimental animals; the main effect is weak anaesthesia. HCFC-124 can induce cardiac sensitisation at high concentrations (26,000 ppm; 145,000 mg/m^3 and above).

In long-term studies at concentrations as high as 50,000 ppm (279,000 mg/m^3), rats and mice showed minimal toxic effects attributable to HCFC-124. There were no developmental effects at that exposure level, but there was minimal toxicity to the mother at 15,000 ppm (83,700 mg/m^3) and above.

HCFC-124 was not mutagenic in bacteria (Ames test), in yeast and cultured mammalian cells *in vitro* or in the mouse micronucleus (*in vivo*) assay. These data and the absence of long-term, compound-related tumorigenesis suggest that HCFC-124 is unlikely to present a carcinogenic hazard.

There are no reported effects of HCFC-124 in humans.

Although there are no experimental data, the predicted toxic concentration of HCFC-124 to either aquatic or terrestrial organisms is relatively high (more than 90 mg/l). In view of that, there should be no significant effects on organisms in the environment.

[a] ECETOC, 1994. Joint Assessment of Commodity Chemicals No. 25
[b] A co-operative programme (1987 - 2000) sponsored by 16 leading chlorofluorocarbon producers [http://www.afeas.org/paft/]

THE ECETOC SCHEME FOR THE JOINT ASSESSMENT OF COMMODITY CHEMICALS

This report has been produced as part of the ECETOC programme for preparing critical reviews of the toxicology and ecotoxicology of selected existing industrial chemicals.

In the programme, commodity chemicals, that are those produced in large tonnage by several companies and having widespread and multiple uses, are jointly reviewed by experts from a number of companies with knowledge of the chemical. It should be noted that in a JACC review only the chemical itself is considered; products in which it appears as an impurity are not normally taken into account.

This document presents a critical evaluation of the available data on the toxicology and ecotoxicology of 1-chloro-1,2,2,2-tetrafluoroethane (HCFC-124) (CAS No. 2837-89-0). It provides an update of an earlier ECETOC review (JACC No. 25, 1994).

Where relevant, the Task Force has graded the (eco)toxicological studies by means of a "code of reliability" (CoR) to reflect the degree of confidence that can be placed on the reported results. The codes and criteria used to assess reliability are included in Appendix A.

1. SUMMARY AND CONCLUSIONS

1-Chloro-1,2,2,2-tetrafluoroethane (HCFC-124[a]), a non-flammable colourless gas at room temperature, is used as a replacement for the fully halogenated chlorofluorocarbons dichlorodifluoromethane (CFC-12) and 1,2-dichlorotetrafluoroethane (CFC-114) in refrigeration systems.

Any HCFC-124 released into the environment is expected to enter the ambient air, where it will be degraded, mainly in the troposphere, by reaction with naturally occurring hydroxyl radicals. The overall atmospheric lifetime is approximately 5.8 years. HCFC-124 has a low ozone depletion potential (ODP) of 0.022 relative to CFC-11. Its global warming potential (GWP) relative to CO_2 is 599, integrated over a time horizon of 100 years.

Limited studies in rats to evaluate metabolic fate and pharmacokinetics suggest that HCFC-124 undergoes oxidative metabolism, resulting in the excretion of trifluoroacetic acid (TFA) and fluoride ion in the urine.

HCFC-124 has a low order of acute inhalation toxicity, with a 4-hour LC_{50} in rats between 230,000 and 300,000 ppm (1,280,000 - 1,670,000 mg/m^3). Weak anaesthesia is the main toxicological effect during exposure. As with many other halocarbons and hydrocarbons, inhalation of high concentrations of HCFC-124, followed by an intravenous epinephrine challenge to simulate stress, induces cardiac sensitisation in dogs. In these experimental screening studies, cardiac sensitisation (life-threatening arrhythmia) was seen at concentrations of 26,000 ppm (145,000 mg/m^3) and above. The no-observed effect level (NOEL) was 10,000 ppm (55,800 mg/m^3).

In a 2-week inhalation toxicity study, rats exposed to 100,000 ppm (558,000 mg/m^3) HCFC-124 showed no adverse effects. In 90-day studies at concentrations as high as 50,000 ppm (279,000 mg/m^3), rats and mice showed minimal toxic effects such as slight central nervous system depression and minor blood chemistry changes. The NOEL in these 90-day studies was 5,000 ppm (27,900 mg/m^3) for male rats. Due to effects of minor toxicological significance, a NOEL for male mice was not achieved. For female rats and mice, a NOEL of 15,000 ppm (83,700 mg/m^3) was established.

No evidence of embryotoxicity or teratogenicity of HCFC-124 was seen in developmental studies in rats and rabbits at inhalation exposure levels as high as 50,000 ppm (279,000 mg/m^3). In both studies, there was minimal evidence of maternal toxicity at and above 15,000 ppm (83,700 mg/m^3).

[a] The naming and numbering system for fluorocarbons is explained in Appendix B

In a combined chronic toxicity/carcinogenicity study, in which rats were exposed to 2000, 10,000 or 50,000 ppm HCFC-124 (11,200, 55,800 or 279,000 mg/m^3) no significant exposure-related effects on non-carcinogenic endpoints were observed. The NOEL was considered to be 50,000 ppm. The NOEL for the carcinogenic endpoint was also 50,000 ppm.

HCFC-124 was not mutagenic in *in vitro and in vivo* studies using bacteria, yeast or mammalian cell lines or in a mouse micronucleus assay. These data and the absence of long-term, compound-related tumorigenesis suggest that HCFC-124 is unlikely to present a carcinogenic hazard.

There are no reported effects of HCFC-124 in humans. The American Industrial Hygiene Association (AIHA) recommends an occupational exposure limit of 1,000 ppm (5,580 mg/m^3) as an 8-hour time-weighted average concentration.

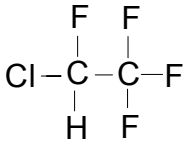
In the absence of experimental data, the predicted toxic concentration of HCFC-124 to aquatic or terrestrial organisms is relatively high (> 90 mg/l). Thus, there should be no significant effects on organisms in the environment.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 Identity

Name:	1-Chloro-1,2,2,2-tetrafluoroethane
IUPAC name:	Ethane, 2-chloro-1,1,1,2-tetrafluroro-
Synonyms:	Fluorocarbon 124 HCFC-124 HFA-124 1,1,1,2-Tetrafluoro-2-chloroethane
CAS name:	1-Chloro-1,2,2,2-tetrafluoroethane
CAS registry number:	2837-89-0
EC (EINECS) number:	220-629-6
Formula:	C_2HClF_4
Molecular mass:	136.5

Structural formula:



2.2 EC classification and labelling

1-Chloro-1,2,2,2-tetrafluoroethane (HCFC-124) is not classifiable according to the Dangerous Substances Directive 67/548/EEC and its subsequent amendments (EC, 2001).

2.3 Physical and chemical properties

HCFC-124 is a non-flammable, colourless and slightly ethereal (virtually odourless) gas at room temperature and normal pressure; it is moderately soluble in water. Physical and chemical properties are listed in Table 1.

Table 1: Physical and chemical properties

Parameter	Value, unit	Reference
Melting point	–199°C	DuPont, 2001a; Solvay, 2001; Ausimont, 2002
Boiling point at 1,013 hPa	–12.1°C	DuPont, 2002
	–12°C	Ausimont, 2002
	–11°C	DuPont, 2001; Solvay, 2001
Relative density of liquid, D_4^{25} (density of water at 4°C is 1,000 kg/m^3)	1.401	DuPont, 2002
	1.364	DuPont, 2001a
	1.360 [a]	DuPont, 1993; Ausimont, 2002
	1.355 [b]	McLinden, 1989
Viscosity of saturated liquid at 25°C	256.5 µPa·s	Ausimont, 2002
	310 µPa·s	Solvay, 2001
Viscosity of vapour at 25°C	11.85 µPa·s	Ausimont, 2002
Refractive index nD at 20°C	No data	
Vapour pressure at 25°C	3,860 hPa	DuPont, 2002
	3,850 hPa	DuPont, 1993
	3,820 hPa [c]	Ausimont, 2002
Vapour density at 25°C (air = 1)	4.7	DuPont, 1993
Threshold odour concentration	No data	
Surface tension at 20°C	9.7 mN/m	Ausimont, 2002
Solubility in water at 25°C	1.45 g/l [d]	DuPont, 1993; Solvay, 2001
	1.40 g/l [d]	Ausimont, 2002
Solubility of water in HCFC-124 at 25°C	0.8 g/l	Ausimont, 2002
Miscible with acetone, ethanol and petroleum solvents	Yes	DuPont, 1993; Solvay, 2001
Partition coefficient, log Kow	1.9 - 2.0 [e]	DuPont, 1993
(octanol/water) at 20°C	1.9	Solvay, 2001
	1.86 [f]	US-EPA, 2003
Partition coefficient, log Koc (organic carbon/water) at 20°C	1.7 - 1.9 [f]	DuPont, 1993; Solvay, 2001
Henry's Law constant at 25°C	9,536 Pa·m^3/mol [g]	This report
	9,414 Pa·m^3/mol [h]	ECETOC, 1994
Flash point (closed cup), flammability limits at 20 - 25°C	None	DuPont, 2001a; Ausimont, 2002
	Negligible	Solvay, 2001
Explosion limits in air at 1,013 hPa, at ambient temperature	No data	
Auto-flammability, ignition temperature	None	DuPont, 2001a, 2002

[a] Reported as 1.36 g/ml, refers to liquid HCFC-124 under pressure

[b] Reported as 1,355 kg/m^3 for the "saturated liquid density", i.e. the pressure is the saturated vapour pressure of HCFC-124 at 25°C

[c] Reported as 3.82 (1 bar = 1,000 hPa)

[d] In equilibrium with gaseous HCFC-124 at atmospheric pressure (1,013 hPa)

[e] Probably measured

[f] Calculated

[g] Calculated, vapour pressure x molecular weight / solubility, at 1 atm = 1,013 hPa

[h] Calculated, reported as 1.45 g/l·bar (ECETOC, 1994)

Typically, commercial HCFC-124 has a purity of > 99.0% (Solvay, 2001). Common impurities may include various other fluorocarbons, depending on the conditions of the production process (Section 3.1).

2.4 Conversion factors

Conversion factors for HCFC-124 concentrations in air at 25°C and 1,013 hPa are:

- 1 ppm = 5.579 mg/m^3 (1 ppt = 10^{-6} ppm)
- 1 mg/m^3 = 0.179 ppm

In this report, converted values are given in parentheses.

The generic formula, from which conversion factors for vapour concentrations in air are derived, is given in Appendix C. According to European standard conditions (20°C and 1,013 hPa) these would be: 1 ppm = 5.674 mg/m^3 and 1 mg/m^3 = 0.176 ppm.

2.5 Analytical methods

A method has been described for the analysis of HCFC-124 using gas chromatography (GC) with dual flame ionisation detection (FID). The method was used to monitor vapour concentrations in the range of 500 to 50,000 ppm (2,790 - 279,000 mg/m^3) (Malley, 1991a; Malley *et al*, 1998).

A halogen-selective detector, that combines specificity (without interference from other compounds) with a high sensitivity, can be used to monitor concentrations of HFC-124 in air at the workplace. Detection limits are below 5 ppm (< 27.9 mg/m^3) when used as an area monitor and less than 0.05 oz/y (< 1.4 g/y) when used as to pin-point leaks, e.g. when different refrigerants are used (Du Pont, 2002).

There are no standard methods for the specific analysis of low concentrations of HCFC-124 in water and air, but analysis can be conducted using a GC-FID combination. In this method, the gas sample (1 ml) is injected into the heated (200°C) injection port of a packed column and separated at 100°C isothermal (helium carrier gas); the limit of detection is 0.1 ppm (0.6 mg/m^3) (DuPont, 2001b).

3. PRODUCTION, STORAGE, TRANSPORT AND USE

3.1 Production

HCFC-124 is produced by the hydrofluorination of tetrachloroethylene or by the hydro-dechlorination of 1,1-dichloro-1,2,2,2-tetrafluoroethane (CFC-114a). The grade of purity obtained is greater than 99% (Solvay, 2001).

The world-wide production volume of HCFC-124 gradually increased from 0 kt in 1991 to 5.3 kt in 1998, but decreased thereafter to 2.3 kt/y in 2001 (AFEAS, 2003).

Under the Montreal Protocol, HCFC-124, in common with other hydrochlorofluorocarbons, will be virtually phased-out in the developed countries by the year 2020. In the European Union, the use of "virgin" hydrochlorofluorocarbons, including HCFC-124, will be banned from 1 January 2010, while in the USA, there will be specific regulation of HCFC-124 from 1 January 2015.

3.2 Storage and handling

HCFC-124 is stored and handled as a pressurised liquefied gas, in steel containers. The containers are stored in cool (< 52°C), dry and well-ventilated areas of low fire risk, avoiding sources of heat or ignition, and flammable substances, as mixtures with air at high pressure and/or air enriched with oxygen can become combustible. Hazardous decomposition products, including hydrogen fluoride (HF), hydrochloric acid (HCl), phosgene and fluorophosgene, can be formed from reaction at high temperature (open flame, hot metal surface) or with strong alkali metals, alkaline earth metals or powdered metals such as Al, Be and Zn. HCFC-124 vapour is heavier than air and can accumulate in depressed areas and near floor level (DuPont, 2001a, 2002; Solvay, 2001; Ausimont, 2002).

3.3 Transport

Pressurised HCFC-124 can be shipped as a "non-flammable (liquefied) gas, not otherwise specified (chlorotetrafluoroethane)" under US Department of Trade (DOT) (UN No. 1021, Class 2.2) regulations (DuPont, 2001a, 2002). In Europe, it is transported in 70 and 1,100 kg cylinders, and in bulk (Ausimont, 2002).

In Germany, HCFC-124 is classified as a low hazard to water (Wassergefährdungsklasse, WGK 1) (Umweltbundesamt, 2003).

3.4 Use

HCFC-124 has been developed as a substitute for fully halogenated chlorofluorocarbons. It is intended as a replacement for dichlorodifluoromethane (CFC-12) in refrigerant blends, or, in some applications, as an alternative to 1,2-dichlorotetrafluoroethane (CFC-114) as a "pure" refrigerant. HCFC-124 is generally stable in the presence of metals and lubricants commonly used in refrigeration systems (Ausimont, 2002; DuPont, 2002).

There is also a potential use for HCFC-124 as a fire extinguishant, as sterilising agent for surgical instruments and as a blowing agent for polystyrene and polyolefin foams (Ausimont, 2002; DuPont, 2002).

4. ENVIRONMENTAL DISTRIBUTION AND TRANSFORMATION

4.1 Emissions

There is no known natural source of HCFC-124.

For assessing certain aspects of the potential environmental impact of HCFC-124, ECETOC (1994) adopted a conservative upper limit of 25 kt/y for possible future annual emissions. More recent data collected during the alternative fluorocarbons environmental acceptability study (AFEAS) indicated a steady increase of annual releases from 0 to 3.2 kt from 1991 to 1997, followed by a decline to 2.4 kt/y from 1998 to 2001 (AFEAS, 2003).

4.2 Environmental distribution

The environmental partitioning of HCFC-124 has been assessed (Franklin, 2003) using the equilibrium criterion (EQC) Level I and Level III models (Mackay *et al*, 1996).

In the Level I model, a fixed quantity of a supposedly non-degradable chemical is introduced into a closed evaluative environment and equilibrium achieved between the various environmental compartments (air, water, soil, sediment). The Level III model simulates a situation in which a chemical is emitted at a constant rate into one or more of the compartments, in each of which it may degrade; the steady-state distribution between compartments is then calculated. Due to the resistance to mass transfer between compartments, the various phases are not in equilibrium and the steady-state partitioning depends on its "mode of entry", i.e. the compartment(s) into which the chemical is injected.

EQC modelling has been performed for HCFC-124 using the physical properties given in Table 1 and an atmospheric lifetime of 5.8 years, corresponding to a half-life of 4.0 years (Section 4.3.1). Degradation in other media was not taken into account. Table 2 below gives the percentage of HCFC-124 calculated to be present in each compartment.

Table 2: Partitioning (%) into the environment *(Franklin, 2003)*

Compartment	EQC level I	EQC level III	
		Emission to air alone	Emission to water alone
Air	99.94	99.95	19.9
Water	0.052	0.038	79.8
Soil	0.005	0.010	0.002
Sediment	0.0001	0.0002	0.33

The Level III simulation with emissions of HCFC-124 to air alone leads to a distribution close to the Level I equilibrium situation as far as the air and water compartments are concerned. However, a much greater steady-state proportion of HCFC-124 is found in the water compartment when the emissions are to water alone. This is due to the resistances to inter-media transfer (in particular from water to air) introduced in the Level III model.

The partition coefficient, log K_{ow}, is 1.9 to 2.0 (Table 1). From various correlations, log K_{oc} is estimated to lie in the range of 1.7 to 1.9, which suggests that HCFC-124 would be moderately mobile in soil. The atmospheric lifetime of HCFC-124 is much longer (about 5.8 years, Section 4.3.1) than either the intra-hemispheric or inter-hemispheric mixing times. Therefore this compound will become more or less uniformly distributed in the atmosphere on a global scale, at a concentration of approximately 1 ppt (v/v).

4.3 Environmental fate and biotransformation

4.3.1 Atmospheric fate and impact

Lifetime[a]

The atmospheric degradation of HCFC-124 occurs mainly in the troposphere, being initiated by reaction with naturally occurring hydroxyl radicals (•OH). Based on the most recent rate constant data and methodology, the lifetime with respect to this process has been estimated to be about 6.1 year, (WMO, 2002). Additionally, a minor amount of HCFC-124 will be transported to the stratosphere and degraded there by reaction with hydroxyl radicals and oxygen atoms, and by photolysis. The stratospheric lifetime has been estimated to be 111 years (Naik *et al*, 2000). The oceans would provide another sink to remove HCFC-124 from the atmosphere, with a lifetime of about 1,855 years (WMO, 2002). Thus, the overall atmospheric lifetime is estimated to be 5.8 years (WMO, 2002).

[a] Lifetime is the time necessary for 63% degradation: it is equal to the "half-life" divided by ln 2 (= 0.69)

Ozone depleting potential

The ODP expresses the stratospheric ozone loss due to emission of a unit mass of a given compound, divided by the ozone loss due to emission of the same mass of a reference compound.

The latest estimated semi-empirical ODP of HCFC-124 is 0.02, relative to a reference value of 1.0 for CFC-11 (WMO, 1999). A value of 0.022 was adopted for regulatory purposes in the 1992 amendment of the Montreal Protocol on ozone-depleting substances (WMO, 2002).

Global warming potential

The GWP of a greenhouse gas is the time-integrated radiative forcing resulting from emission to the atmosphere of a unit mass of a given substance, divided by the same quantity calculated for a reference substance. The radiative forcing is the additional earthward infrared radiation flux arising from the presence of the substance in the atmosphere. The GWP is calculated for a given "integration time horizon" (ITH). Depending on the reference substance, the ITH may be chosen to be finite (e.g. for CO_2) or infinite (e.g. for trichlorofluoromethane CFC-11). Almost invariably, GWP values are expressed relative to CO_2, for an ITH of 100 years.

The estimated 100-year GWP of HCFC-124 is 599, relative to a value of 1.0 for CO_2 (WMO, 2002).

Tropospheric ozone formation

HCFC-124 is too unreactive in the atmosphere to make any significant contribution to local urban tropospheric ozone formation and related photochemical smog, near the emission sources (WMO, 1989; Hayman and Derwent, 1997). A photochemical ozone creation potential of 0.1 has been given for HCFC-124, relative to a value of 100 for ethylene (Hayman and Derwent, 1997).

The US Environmental Protection Agency has excluded HFC-124 as a volatile organic compound from its ozone control programme (US-EPA, 1997).

Degradation mechanism and products

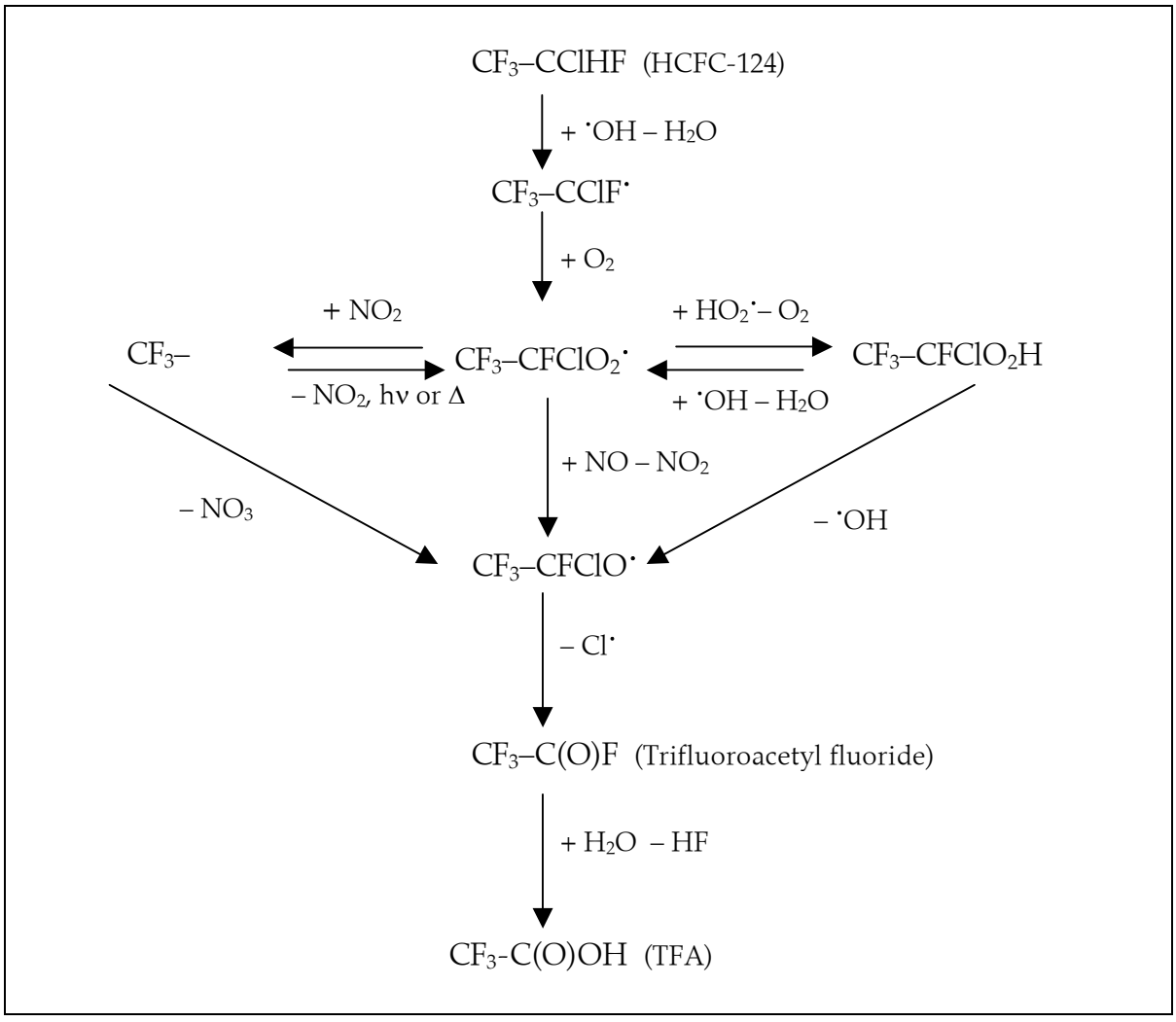
Support for the basic tropospheric degradation mechanism for HCFC-124 proposed in WMO (1989) has been provided by laboratory studies (WMO, 1991; Edney and Driscoll, 1992; Tuazon and Atkinson, 1993). Breakdown of HCFC-124 in the troposphere will be initiated by naturally occurring OH-radicals and will proceed via various free-radical intermediates to give HCl and trifluoroacetyl fluoride (CF_3COF). These breakdown products are expected to be removed from the atmosphere within a few days to a few months, by uptake into clouds, rain and the oceans;

CF_3COF will then rapidly hydrolyse into TFA and hydrofluoric acid (HF) (AFEAS, 1992; STEP/AFEAS, 1993; Franklin, 1993).

Although a peroxynitrate ($CF_3CFClO_2NO_2$) and a hydroperoxide (CF_3CFClO_2H) may be formed during the degradation of HCFC-124, neither is thought to play a significant role in the atmospheric degradation of HCFC-124. They are probably short-lived intermediates that undergo photolysis, thermal decomposition or reaction with OH radicals, leading to the regeneration of peroxy radicals (CF_3CFClO_2) or the formation of alkoxy radicals (CF_3CFClO) (Cox *et al*, 1995; Lelieveld *et al*, 1999).

The degradation mechanism of HCFC-124 is represented in Figure 1.

Figure 1: Tropospheric degradation mechanism[a]



[a] NO_2, NO and NO_3, free radicals

Contribution of degradation products to environmental chloride, fluoride and trifluoroacetate

Assuming an atmospheric release and degradation of 3 kt HCFC-124/y with complete conversion into HCl, HF and TFA (1 mol of each/mol HCFC-124) and uniform scavenging of the acids produced into the global average rainfall (5×10^{11} kt/y), the levels of chloride, fluoride and TFA produced would be low compared to those arising from other sources:

- Cl^- production from HCFC-124 would be 0.8 kt/y, i.e. only 0.004% of the combined natural and anthropogenic fluxes of HCl into the troposphere, and less than 1 ppm of the particulate chloride flux, mainly arising from sea-salt aerosols (Keene *et al*, 1999);
- F^- production would amount to 0.4 kt/y, i.e. an insignificant amount compared to the estimated atmospheric fluoride flux of 1,000 to 8,000 kt/y (WMO, 1989).

The contribution of HCFC-124 to TFA in rainwater would be about 5 ppt (w/w) (5 ng/l), which is low compared to currently observed values of around 100 ppt (w/w) (100 ng/l). The impact of TFA on the acidity of rainwater is discussed in ECETOC (2004). Boutonnet *et al* (1999) concluded that environmental levels of TFA, resulting from the breakdown of alternative fluorocarbons (including HCFC-123, HCFC-124 and HFC-134a), did not pose a threat to the environment. Furthermore, Frank *et al* (2002) demonstrated the existence of large natural sources of TFA.

4.3.2 Aquatic fate

No data are available.

4.3.3 Terrestrial fate

No data are available.

4.3.4 Biodegradation

In a closed-bottle assay for ready biodegradability (OECD Guideline 301D, without inhibition test) (OECD, 1981), HCFC-124 appeared to be stable in aqueous solution (1 - 2% loss) over a 4-week period (Tobeta, 1992; CoR 1b).

4.3.5 Bioaccumulation

No measured data are available.

Based on a log K_{ow} of 1.86 (Table 1), BcfWin software (US-EPA, 2003) predicts a bioconcentration factor of 5.4 for HFC-124. This indicates a low potential for passive bioaccumulation, as expected for a material with a high vapour pressure and low K_{ow}.

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1 Environmental levels

In the years 1998 and 2000, background atmospheric concentrations of HCFC-124 of 0.53 to 0.89 ppt (v/v) and 1.34 ppt (v/v) were reported (WMO, 2002).

5.2 Human exposure levels and hygiene standards

Data are available on human exposure, at the workplace or elsewhere.
The American Industrial Hygiene Association has recommended a workplace environmental exposure level (WEEL) of 1,000 ppm (5,580 mg/m^3) for HCFC-124 as an 8-hour time-weighted average concentration (AIHA, 1992).

6. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

No data are available on the effects of HCFC-124 on environmental organisms.

In the absence of experimental data, a modelling approach has been used to assess the effects of HCFC-124 on aquatic and terrestrial organisms.

6.1 Aquatic organisms

Using the estimated log K_{ow} of 1.86 (Table 1), the toxicity of HCFC-124 to fish, daphnia and algae was estimated using the US-EPA programme ECOSAR (Boethling *et al*, 1994; US-EPA, 2001) (Table 3).

***Table 3: Predicted acute toxicity to aquatic organisms** (US-EPA, 2001)*

Organism	Duration	Effect / Parameter	Concentration (mg/l)
		Lethality	
Fish	96 h	LC_{50}	137
		Immobility	
Daphnia	48 h	EC_{50}	145
		Growth inhibition	
Algae	96 h	EC_{50}	90

6.2 Terrestrial organisms

A 14-day LC_{50} of 927 mg HCFC-124/l was predicted for earthworms using the ECOSAR model (Boethling *et al*, 1994; US-EPA, 2001).

6.3 Evaluation

The predicted toxic concentration of HCFC-124 to aquatic or terrestrial organisms is relatively high (≥ 90 mg/l). There should be no significant effects on organisms in the environment.

7. KINETICS AND METABOLISM

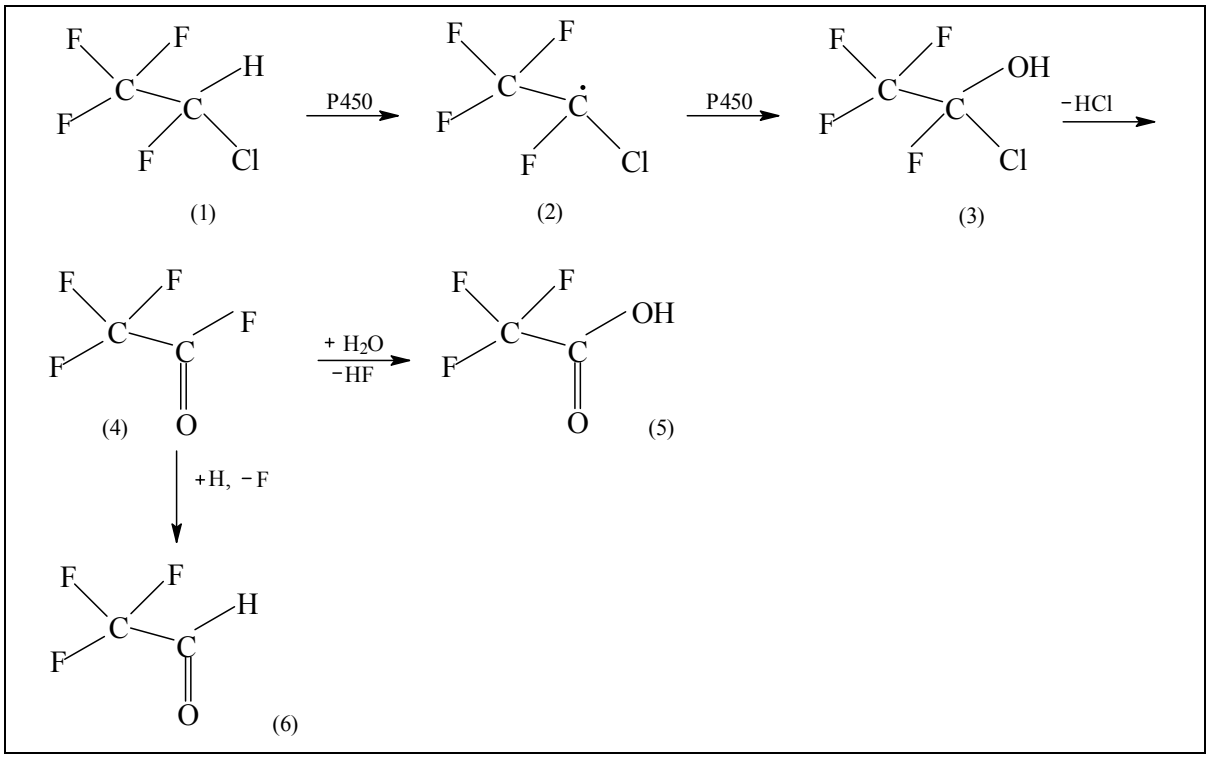
7.1 Animal studies

There are limited metabolic data on HCFC-124.

Olson *et al* (1991; CoR 1d) exposed rats by inhalation to 10,000 ppm HCFC-124 (558,000 mg/m^3) for 2 hours and found inorganic fluoride and TFA in the urine, both being products of an oxidative metabolism. Increases in urinary fluoride levels in rats exposed by subchronic inhalation to HCFC-124 had been reported previously by Brewer (1977a; CoR 3b) and by Malley (1991a; CoR 1a) (Section 8.3).

Additional evidence for an oxidative metabolism was provided by Harris *et al* (1992; CoR 1d) who exposed rats by inhalation to 1% HCFC-124 (10,000 ppm; 558,000 mg/m^3) for 6 hours and found trifluoroacetylated proteins in liver and TFA in urine; this similar to results reported previously by Harris *et al* (1991; CoR 1d). The oxidative metabolism was approximately 5-fold less for HCFC-124 than for 1-chloro-1-bromo-2,2,2-trifluoroethane and dichlorofluoroethane.
The proposed metabolic pathway for HCFC-124 is depicted in Figure 2.

Figure 2: Metabolic pathway for HCFC-124 *(adapted from Harris et al, 1992)*



(1) HCFC-124, (2) 1-chloro-1,2,2,2-tetrafluoroethyl radical, (3) 1-chloro-1,2,2,2-tetrafluoroethanol, (4) trifluoroacetyl fluoride, (5) TFA and (6) trifluroacetaldehyde (binding to protein)

HCFC-124 pharmacokinetics and metabolism were investigated in male rats, mice and hamsters. Rats were exposed by inhalation to 0, 500, 1,000, 2,000, 5,000 and 10,000 ppm for 6 hours, while mice and hamsters were exposed to 0, 1,000, 5,000 and 10,000 ppm for the same duration. At the end of exposure, the rodents were immediately placed in metabolism cages and urine collected for 24 hours. The partition coefficients at equilibrium, i.e. the ratio of chemical concentration in two different phases such as tissue:air, saline:air and tissue:blood, were determined by placing the tissue of interest in an air-tight vial containing the HCFC-124. The system was allowed to equilibrate and the headspace concentration measured in test and control vials. The difference between the amount of test substance in the headspace of the reference and control vials represented the amount of HCFC-124 present in the tissue. Tissue:air and blood:air partition coefficients were calculated from these data, and were then used to calculate the tissue:blood partition coefficients (Table 4) (Loizou and Anders, 1995). Results indicate that HCFC-124 partitioning into blood and fat, respectively, is poor to moderate.

Table 4: Partition coefficients in rat, mouse and hamster *(Loizou and Anders, 1995)*

Compartment	Rat	Mouse	Hamster
Blood:air	1.52	1.15	0.76
Fat:air	9.73	6.02	11.1
Liver:air	2.23	1.27	3.46
Muscle:air	1.43	0.67	1.99
0.9% saline:air	1.05	1.05	1.05
Olive oil:air	25.2	25.2	25.2

The uptake of HCFC-124 was quantified as the decrease in chamber concentration with time. Simulations of the observed uptake were used to provide kinetic constants for the rate and extent of HCFC-124 metabolism. In rats and mice, the uptake could be described by a model with both saturable and first-order components; in hamsters, only a first order uptake was observed. The simulated *in vivo* metabolic constants for rat, mouse and hamster, respectively, were: Michaelis-Menten constant, Km (mg/l, [mmol/l]) 1.2 [8.79], 1.2 [8.79] and not applicable; maximum velocity, Vmax (mg/kg/h [mmol/kg/h]) 0.35 [2.56], 1.78 [13.0] and not applicable; first-rate constant, k (/kg/h) 1.25, 4.08 and 1.47. (Comment by the Task Force: The Michaelis-Menten coefficient Km is a function of the affinity of HCFC-124 for the enzymes involved in its metabolism and Vmax represents the maximum rate of metabolism. When HCFC-124 concentration in the region of metabolising enzymes is near 1.2 mg/l, the rate of metabolism is approximately one half of the maximum rate possible.) The amount of TFA excreted increased as exposure to HCFC-124 increased. Simulated production and excretion of TFA, using metabolic constants, correlated well for rat and mouse data. Hamster data, however, could not be

satisfactorily simulated, perhaps due to the lack of data on physiological parameters, and the considerable variation in urine volume (Loizou and Anders, 1995).

7.2 Human studies

There are no data relating to the absorption, distribution, metabolic transformation or elimination of HCFC-124 in humans.

8. EFFECTS ON EXPERIMENTAL ANIMALS AND *IN VITRO* TEST SYSTEMS

8.1 Acute toxicity

8.1.1 Inhalation

Kelly (1990; CoR 1b) exposed (nose-only) Crl:CD BR rats (6 males/group) for a single 4-hour period to atmospheres containing 0, 48,000, 162,000, 230,000 or 300,000 ppm HCFC-124 vapour (0, 268,000, 904,000, 1,280,000 or 1,670,000 mg/m^3). Apart from a slight weight loss 1 day post exposure, rats exposed to the lowest exposure level showed no clinical signs of toxicity during or after exposure as compared with untreated controls. No deaths occurred at concentrations of 162,000 and 230,000 ppm, but rats did show a temporary weight loss, decreased acoustic-startle responses, prostration, lethargy and incoordination; these anaesthetic effects disappeared shortly after exposure. At 300,000 ppm, the same clinical signs occurred, but 6 out of 6 rats died during the 4-hour exposure. Under the conditions of this study, the 4-hour LC_{50} of HCFC-124 in rats was estimated to be between 230,000 and 300,000 ppm.

Wada (1977; CoR 3a) reported a 10-minute approximate lethal concentration of 440,000 ppm HCFC-124 (2,450,000 mg/m^3) for mice; exposure to 400,000 ppm (2,230,000 mg/m^3) for 10 minutes produced no mortality. Anaesthesia was observed at 150,000 ppm (837,000 mg/m^3), but no effects were seen at 100,000 ppm (558,000 mg/m^3).

A single 6-hour exposure to 360,000 ppm HCFC-124 (2,010,000 mg/m^3) was not lethal to rats but rapidly depressed motor activity; this was followed by anaesthesia after 1 hour. Rats exposed to 100,000 ppm (558,000 mg/m^3) were active for 30 minutes, but then inactive until termination of exposure. Rats exposed to 2,010,000 mg/m^3 gained less weight than either the controls or the lower exposure group in days 1 to 8 (Coate, 1976; CoR 2e).

When dogs were exposed to HCFC-124 for 10 minutes to concentrations ranging from 400,000 to 700,000 ppm (2,230,000 - 3,910,000 mg/m^3), alight surgical anaesthesia was rapidly induced. Complete recovery occurred within 7 to 10 minutes post exposure (Van Poznak and Artusio, 1960; CoR 3b).

Hartley guinea pigs were exposed (whole-body) by inhalation to 5,000 ppm HCFC-124 (27,900 mg/m^3) for 4 hours and killed at 24 and 48 hours after treatment. There was no significant change as compared with untreated controls in serum alanine aminotransferase and isocitrate dehydrogenase activities, or in hepatic GSH, cholesterol, glycerol and free fatty acid content at 24 or 48 hours after treatment; livers showed mild vacuolar (fatty) changes at 48 hours (Hoet *et al*, 2001; CoR 1d).

There was no evidence that HCFC-124 enhanced the hepatic toxicity of HCFC-123 following simultaneous exposure (whole-body, 1 x/4 h or 4 h/d) of Hartley guinea pigs (5 – 9 males/group)

by inhalation to 0 or 5,000 ppm HCFC-124 (0, 27,900 mg/m^3) blended with HCFC-123 (0, 31,200 mg/m^3) for 5 consecutive days. This observation was based on the evaluation of serum hepatic enzymes, on GSH, cholesterol, glycerol and free fatty acid content of the liver and on microscopic evaluation of liver tissue (Hoet *et al*, 2001; CoR 1d).

8.1.2 Other studies

In an experimental screening study, inhalation of high concentrations of HCFC-124 for 5 minutes, followed by an intravenous injection of adrenaline (approximately 8 µg/kgbw), induced cardiac sensitisation in dogs, at concentrations of 26,000 ppm (145,000 mg/m^3) and above. The NOEL for cardiac sensitisation was 10,000 ppm (55,800 mg/m^3) (Mullin, 1976; CoR 2c).

In repeated exposure studies by the inhalation route (Section 8.3), HCFC-124 concentrations as high as 50,000 to 100,000 ppm (279,000 - 558,000 mg/m^3) produced no clinical or histopathological evidence of respiratory irritation in mice or rats respectively.

Earlier studies to evaluate anaesthetic potency of HCFC-124 have been reported previously (ECETOC, 1990).

8.2 Skin and eye irritation/allergic sensitisation

No data are available.

As HCFC-124 is a gas at ambient temperature, studies to assess skin and eye irritation, as well as skin sensitisation, have not been carried out.

There was no evidence of skin or mucosal irritation in rats exposed to HCFC-124 by inhalation on an acute or repeated basis (Section 8.3).

8.3 Repeated exposure

Trochimowicz *et al* (1977; CoR 1a) reported no adverse effects in 10 rats exposed (6 h/d, 5 d/wk) by inhalation to 100,000 ppm HCFC-124 (558,000 mg/m^3) for 2 weeks.

Malley (1990; CoR 1a) exposed (6 h/d, 5 d/wk) CD-BR rats (10/sex/group) by inhalation to 0, 500, 2,000, 10,000 or 50,000 ppm HCFC-124 (0, 2,790, 11,200, 55,800, 279,000 mg/m^3) for 4 weeks. There were no compound related effects on body weight, food consumption, mortality, clinical laboratory parameters, organ weights or tissue morphology. During exposure, rats exposed to

50,000 ppm (279,000 mg/m^3) appeared to be lethargic and inco-ordinated. However, at the end of the daily exposure period, when the animals were removed from the chambers, no evidence of lethargy or inco-ordination was observed. The NOEL was considered to be 10,000 ppm (55,800 mg/m^3).

In a 90-day inhalation toxicity study, CD-BR rats (20/sex/group) were exposed (6 h/d, 5 d/wk) to HCFC-124 at concentrations of 0, 500, 15,000 or 50,000 ppm (0, 2,790, 83,700, 279,000 mg/m^3). A neurotoxicity evaluation using a functional observational battery with an additional 1-month recovery period was carried out on 10 rats/sex/group. There were no compound-related effects on body weight, food consumption, mortality, clinical signs, haematology, organ weights, and tissue morphology. During exposure, rats exposed to 50,000 ppm were less responsive to stimuli (as decreased reaction to a knock on the exposure chamber wall) than untreated controls. In addition, on the day following the last exposure, male rats exposed to 15,000 or 50,000 ppm had decreased arousal times (4/10 and 6/10 rats, respectively). At the 45-day clinical evaluation, males exposed to 15,000 or 50,000 ppm had lower serum triglyceride concentrations than controls and female rats at 50,000 ppm showed increased alkaline phosphatase activity. At all exposure levels, fluoride concentration in blood and urine was elevated at several sampling intervals during exposure and also at 1 month post exposure. Male rats exposed at the two highest exposure levels also showed a mild diuresis. This was probably a result of increased osmotic activity from the excreted fluoride ion, rather than a direct effect of HCFC-124. The NOEL for this 90-day study in rats was considered to be 500 ppm for males and 15,000 ppm for females (Malley, 1991a; CoR 1a).

Malley (1991b; CoR 1a) also conducted a 90-day inhalation toxicity study in CD-1(ICR)BR mice (20/sex/group) exposed (6 h/d, 5 d/wk) to the same concentration levels of HCFC-124 as used in the rat study (see above). Responses in mice and rats were similar, i.e. there were no compound-related effects on mortality, food consumption, clinical signs, haematology, organ weights and tissue morphology. In male mice killed at 90 days, body weights were 6 to 7% lower than controls (not dose-related) and hepatic □-oxidation activity was approximately 2-fold higher at all exposure levels, while serum triglyceride concentrations were decreased at the two highest exposure levels. During exposure, both male and female mice exposed at 279,000 mg/m^3 HCFC-124 were less responsive to stimuli (knocking on chamber window) than controls. All the effects seen in female and male mice during exposure disappeared within 30 days. The effects in male mice were slight and of negligible toxicological significance, but it was considered that no NOEL was achieved. For female mice, the NOEL was 15,000 ppm.

In a 90-day inhalation study reported earlier by ECETOC (1990), rats were exposed to HCFC-124 (unknown purity) at exposure levels of up to 5,000 ppm (27,900 mg/m^3) (Brewer (1977a; CoR 3b). The study is not discussed further since the more recent studies of Malley (1991a,b) in rodents at similar and higher exposure levels for longer duration failed to confirm these findings.

In conclusion, the minimal and reversible effects seen in the preceding studies are not considered to be adverse. Therefore the subchronic no-observed adverse effect level (NOAEL) of HCFC-124 for rats and mice is 50,000 ppm (279,000 mg/m^3).

8.4 Mutagenicity

8.4.1 *In vitro*

The mutagenic potential of HCFC-124 has been evaluated in several bacteria and cells. In a series of plate and suspension assays using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 exposed to various concentrations of HCFC-124 in the presence and absence of an S9 metabolic activation system. None of these studies showed any evidence of mutagenicity (Brusick, 1976; CoR 1d; Barsky, 1976; CoR 3a; Longstaff *et al,* 1984; CoR 3a; Reynolds, 1990; CoR 1a; May, 1991; CoR 1a). In addition, HCFC-124 was not mutagenic in other *in vitro* assays with *Escherichia coli* (May, 1991) and *Saccharomyces cerevisiae* (Brusick, 1976; CoR 1d).

Furthermore, HCFC-124 showed no evidence of clastogenic activity in cultured Chinese Hamster Ovary (CHO-K1) cells (Edwards, 1991; CoR 1a) or in human lymphocytes with or without S9 metabolic activation (Bentley, 1990; CoR 1a).

8.4.2 *In vivo*

HCFC-124 was tested for its ability to induce micronuclei in bone marrow polychromatic erythrocytes of male and female mice exposed (6 h/d, head-only) to 0 or 99,000 ppm (0, 552,000 mg/m^3) for 2 consecutive days. Bone marrow smears were prepared 24 and 48 hours after exposure. HCFC-124 did not induce micronuclei. Since central nervous system effects were observed in the acute inhalation toxicity studies at comparable exposure concentrations, it was assumed that the substance had reached the bone marrow. HCFC-124 was not mutagenic *in vivo* (Rickard, 1990; CoR 1a).

In conclusion, HCFC-124 is not mutagenic when tested *in vitro* and *in vivo.*

8.5 Chronic toxicity and carcinogenicity

In a combined chronic toxicity-carcinogenic study, male and female rats were exposed (6 h/d, 5 d/wk) to 0, 2,000, 10,000 or 50,000 ppm HCFC-124 (0, 2,790, 11,200, 55,800, 279,000 mg/m^3) for 2 years. Body weights were determined weekly for the first 3 months and then every alternate week. Food consumption was determined weekly. Clinical signs of toxicity were monitored throughout the study. An ophthalmological examination was performed on all animals prior to

the start of the study and all survivors were examined after approximately 3, 12 and 24 months. Clinical pathology was evaluated at 3, 6, 12, 18 and 24 months. There was an interim kill at 12 months; all surviving animals were necropsied at 24 months (Malley *et al*, 1998; CoR 1a).

There were no compound-related adverse effects on body weight, food consumption, survival, ocular lesions, and serum hormone concentrations. Compared to controls, urinary fluoride was increased in males and females at all exposure levels. This was not considered an adverse effect, since it indicated metabolism of the compound. There was no dental or osseous fluorosis. There was a slight, transient decrease in serum triglycerides in the 10,000 or 50,000 ppm males at 3 months, considered to be of questionable biological relevance. No lower responsiveness to auditory stimuli, as seen in the 90-day study, was observed in this study. This may be due to technical differences (e.g. noise perception) between the two studies. At the 12-month kill, there were incidences of minimal focal accumulations of yellow-brown pigment in the renal proximal tubules of all exposed male rats and in 50,000 ppm females. These changes were not observed at 24 months. This transient phenomenon was not considered to be toxicologically relevant when evaluated alongside other relevant renal and urinary changes observed at the same time. At terminal sacrifice, the incidence of focal hepatic necrosis and cholesterol clefts/granulomas in the lungs was significantly increased in the 50,000 ppm males. Although no comparison with historical controls was mentioned, the authors noted that such phenomena were common in aging rats. A statistically significant increase in mammary gland fibro-adenomas was observed in the 50,000 ppm exposed females when compared to controls. However, based on an identical incidence of mammary fibro-adenomas observed in untreated controls in another laboratory which used the same feeding regimen, the higher incidence observed in the 50,000 ppm females was not considered to be related to HCFC-124. No other exposure-related observations were made. Therefore, the NOAEL for male and female rats in this 2-year study was considered to be 50,000 ppm (279,000 mg/m^3) (Malley *et al*, 1998; CoR 1a).

8.6 Developmental and reproductive toxicity

In a developmental toxicity study, pregnant CD-BR rats (24/group) were exposed (6 h/d, (whole-body) by inhalation to 0, 5,000, 15,000 or 50,000 ppm HCFC-124 (0, 27,900, 83,700 or 279,000 mg/m^3) from day 6 to 15 of gestation. No evidence of embryotoxicity, foetotoxicity or teratogenicity was seen at any exposure level. Maternal toxicity was demonstrated at 50,000 ppm by a decreased rate of weight gain and food consumption during the first 4 days of exposure and by a reduced response to auditory stimuli during exposure, but not shortly thereafter. Under these study conditions, the NOAEL for HCFC-124 was 15,000 ppm for the dam and 50,000 ppm for the conceptus (Alvarez, 1990; CoR 1a).

Using the same exposure levels as in the preceding study, pregnant New-Zealand White rabbits (20/group) were exposed (6 h/d, whole-body) by inhalation to HCFC-124 from day 6 to 18 of

gestation. There was no evidence of embryotoxicity, foetotoxicity, or teratogenicity at any exposure level. As in rats, slight maternal effects were seen at 50,000 ppm (279,000 mg/m^3) as judged by decreased food consumption and decreased in-chamber activity. The NOEL for maternal effects was 15,000 ppm (83,700 mg/m^3) while the NOEL for developmental toxicity was 50,000 ppm (279,000 mg/m^3) (Schroeder, 1991; CoR 1a).

In a limited developmental toxicity study reported earlier by ECETOC (1990) 20 pregnant albino rats were exposed (6 h/d) to 50,000 ppm HCFC-124 (unknown purity) (27,900 mg/m^3) from day 6 to 15 of gestation. No evidence of maternal toxicity, foetotoxicity, embryotoxicity or teratogenicity was seen at this single exposure level (Brewer, 1977b; CoR 3b).

No data are available on which to evaluate the reproductive performance of male and female animals exposed to HCFC-124. However, in rats and mice exposed for 90 days by inhalation to HCFC-124 at concentrations as high as 50,000 ppm (279,000 mg/m^3), no histopathological effects were seen in the reproductive organs/tract of male or female animals (Malley, 1991a,b) (Section 8.3).

9. EFFECTS ON HUMANS

A case has been reported of repeated accidental exposure to a mixture of HCFC-123 and HCFC-124 (% not stated) used as a cooling fluid in a bridge crane of a Belgian metal smelter. The period of exposure and exposure levels were not specified, but several of the exposed workers showed different degrees of hepatitis. In some, focal hepatocellular necrosis was detected with trifluoracetyl adducted proteins in surviving hepatocytes (Hoet *et al*, 1997). In view of the toxicological profile of HCFC-124 described above in this report, it is highly improbable that HCFC-124 was involved in the hepatic effects seen in workers exposed to a mixture of HCFC-123 and HCFC-124. The observed effects can be explained by the toxicity of HCFC-123 (Hoet *et al*, 2001) (Section 8.1). The toxicology of HCFC-123 is reviewed elsewhere (ECETOC, 1996).

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APPENDIX A: CRITERIA FOR RELIABILITY CATEGORIES

Adapted from Klimisch *et al* (1997)

Code of Reliability (CoR)	Category of reliability
1	**Reliable without restriction**
1a	GLP guideline study (OECD, EC, EPA, FDA, *etc.*)
1b	Comparable to guideline study
1c	Test procedure in accordance with national standard methods (AFNOR, DIN, *etc.*)
1d	Test procedure in accordance with generally accepted scientific standards and described in sufficient detail
2	**Reliable with restrictions**
2a	Guideline study without detailed documentation
2b	Guideline study with acceptable restrictions
2c	Comparable to guideline study with acceptable restrictions
2d	Test procedure in accordance with national standard methods with acceptable restrictions
2e	Study well documented, meets generally accepted scientific principles, acceptable for assessment
2f	Accepted calculation method
2g	Data from handbook or collection of data
3	**Not reliable**
3a	Documentation insufficient for assessment
3b	Significant methodological deficiencies
3c	Unsuitable test system
4	**Not assignable**
4a	Abstract
4b	Secondary literature
4c	Original reference not yet available
4d	Original reference not translated
4e	Documentation insufficient for assessment

APPENDIX B: NAMING AND NUMBERING SYSTEM FOR FLUOROCARBON COMPOUNDS

The naming and numbering system currently used by industry was officially adopted as Standard 34 of the American Society of Heating, Refrigeration, and Air-conditioning Engineers (ASHRAE) on June 3, 1957 (Du Pont, 1999).

B.1 Prefixes

These prefixes are generally applicable:

- FC = Fluorocarbon
- CFC = Chlorofluorocarbon
- HFC = Hydrofluorocarbon
- PFC = Perfluorocarbon (also Perfluorocompound, Persistent Fluorinated Compound)
- HFOC = Hydrofluoroether
- HCFC = Hydrochlorofluorocarbon
- FOC = Fluoroether

B.2 Numbering code

The first digit from the right is the number of fluorine atoms in the molecule. The second digit from the right is one more than the number of hydrogen atoms in the molecule. The third digit from the right is one less than the number of carbon atoms in the molecule (omit if zero).

The number of chlorine atoms in the compound is calculated by subtracting the sum of fluorine and hydrogen atoms from the total atoms which can be connected to the carbon atoms. If some of the chlorine has been replaced by bromine, then the number is followed by a "B", then the number of chlorine atoms so replaced.

The fourth digit from the right indicates the number of double bonds in the molecule, for example:

- PFC-116 = 6 Fs, 0 Hs, 2 Cs and 0 Cls → C_2F_6
- HFC-23 = 3 Fs, 1 H, 1 C, and 0 Cls → CF_3H
- PFC-1216 = 6 Fs, 0 Hs, 3 Cs, 0 Cls with 1 double bond → C_3F_6 → CF_2=CF-CF_3

For cyclic molecules, the letter C is used before the identifying number, for example:

- PFC-C318 = 8 Fs, 0 Hs, 4 Cs and 0 Cls with cyclic structure → c-C_4F_8

For isomeric compounds, each has the same number designation, but the various isomers are indicated by a lowercase letter following the number; the letters are assigned based on the symmetry of the molecule. The most symmetrical structure has no letter, followed by the next most symmetrical isomer designated "a", and so on. The symmetry is determined by summing the atomic weights of all atoms attached to each carbon, and comparing the two numbers. The smaller their difference, the more symmetrical the molecule. For example $C_2H_2F_4$ can have two structural isomers:

- CF_2H-CF_2H, more symmetrical, HFC-134
- CF3-CFH_2, less symmetrical, HFC-134a

B.3 Extension to 3-carbon molecules

For C3s, the isomer designation is slightly different, and uses a two-letter code. The codes below are used to determine the substituents on the central carbon, which determines the first letter of the code. The second letter in the code designates the various isomers based on symmetry, with the most symmetrical structure designated "a", and so forth.

B.4 Letter central carbon

- a = CCl_2
- b = CClF
- c = CF_2
- d = CClH
- e = CHF
- f = CH_2

For example:

HFC-236fa = $C_3F_6H_2$ → Central carbon designated "f" → CH_2 → "a" designation → $CF_3CH_2CF_3$

B.5 C4 and larger molecules

For 4-carbon atom and larger molecules, string together the letter designations from the above and following lists to indicate the current isomer. Always start either at the molecule's more fluorinated end or at the end needing the least number of suffix letters to assign the structure. If a digit is larger than 9, it is offset by a dash.

- j = CCl_3
- k = CCl_2F

- l = $CClF_2$
- m = CF_3
- n = $CHCl_2$
- o = CH_2Cl
- p = CHF_2
- q = CH_2F
- r = CHClF
- s = CH_3
- t = C
- x = CCl
- y = CF
- z = CH

Example: HFC-43-10mee = 10 Fs, 2 Hs, 5 Cs, no Cls → $C_5H_2F_{10}$

m indicates CF_3 . . . CF_3

e indicates CHF, so CF_3CHF

e indicates CHF, so $CF_3CHFCHF$

HFC-43-10mee → $CF_3CHFCHFCF_2CF_3$

The assignment of a string of letters, to denote structural groups, is stopped when the structure is unambiguous (i.e. one does not need to call the compound HFC-43-10mee**cm**, since once one reaches "mee", one knows that 5 fluorine atoms still need to be attached to the remaining two carbons, so the rest of the molecule must be $–CF_2CF_3$).

APPENDIX C: CONVERSION FACTORS FOR VAPOUR CONCENTRATIONS IN AIR

Conversion factors for vapour concentrations in air can be calculated from the molar volume of an ideal gas at 0°C: 22.4136 litre.

$$1\ mg/m^3 = 22.4136/Mw \times 1{,}013.25/P \times (273+T)/273\ ppm \quad \text{.....(Eq. B.1)}$$

$$1\ ppm = Mw/22.4136 \times P/1{,}013.25 \times 273/(273+T)\ mg/m^3 \quad \text{.....(Eq. B.2)}$$

where Mw = molecular weight, T = temperature (°C) and P = pressure (hPa).

For European standard conditions, 20°C and 1,013.25 hPa (=1 atm = 760 mm Hg), the formulae become

$$1\ mg/m^3 = 24.0556/Mw\ ppm \quad \text{.....(Eq. B.3)}$$

$$1\ ppm = Mw/24.0556\ mg/m^3 \quad \text{.....(Eq. B.4)}$$

In the USA and other countries 25°C is used, and the formulae are:

$$1\ mg/m^3 = 24.4661/Mw\ ppm \quad \text{.....(Eq. B.5)}$$

$$1\ ppm = Mw/24.4661\ mg/m^3 \quad \text{.....(Eq. B.6)}$$

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No. 9	Chlorodifluoromethane
No. 10	Isophorone
No. 11	1,2-Dichloro-1,1-difluoroethane (HFA-132b)
No. 12	1-Chloro-1,2,2,2-tetrafluoroethane (HFA-124) (updated by JACC No. 25)
No. 13	1,1-Dichloro-2,2,2-trifluoroethane (HFA-123) (updated by JACC No. 33)
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No. 16	Dichlorofluoromethane (HCFC-21)
No. 17	1-Chloro-1,1-difluoroethane (HFA-142b)
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No. 19	Dicyclopentadiene (CAS: 77-73-6)
No. 20	Tris-/Bis-/Mono-(2 ethylhexyl) phosphate
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No. 22	Hydrogen Peroxide (CAS: 7722-84-1)
No. 23	Polycarboxylate Polymers as Used in Detergents
No. 24	Pentafluoroethane (HFC-125) (CAS: 354-33-6)
No. 25	1-Chloro-1,2,2,2-tetrafluoroethane (HCFC 124) (CAS No. 2837-89-0) (updated by JACC No. 46)
No. 26	Linear Polydimethylsiloxanes (CAS No. 63148-62-9)
No. 27	*n*-Butyl Acrylate (CAS No. 141-32-2)

No. 28 Ethyl Acrylate (CAS No. 140-88-5)
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No. 35 Methacrylic Acid (CAS No. 79-41-4)
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No. 37 Methyl Acrylate (CAS No. 96-33-3)
No. 38 Monochloroacetic Acid (CAS No. 79-11-8) and its Sodium Salt (CAS No. 3926-62-3)
No. 39 Tetrachloroethylene (CAS No. 127-18-4)
No. 40 Peracetic Acid (CAS No. 79-21-0) and its Equilibrium Solutions
No. 41 *n*-Butanol (CAS No. 71-36-3)
No. 42 Tetrafluoroethylene (CAS No. 116-14-3)
No. 43 *sec*-Butanol (CAS No. 78-92-2)
No. 44 1, 1, 1, 3, 3-Pentafluoropropane (HFC-245fa)
No. 45 1, 1-Difluoroethane (HFC-152a) (CAS No. 75-37-6)

Special Reports

No. Title

No. 8 HAZCHEM; A Mathematical Model for Use in Risk Assessment of Substances
No. 9 Styrene Criteria Document
No. 10 Hydrogen Peroxide OEL Criteria Document (CAS No. 7722-84-1)
No. 11 Ecotoxicology of some Inorganic Borates
No. 12 1,3-Butadiene OEL Criteria Document (Second Edition) (CAS No. 106-99-0)
No. 13 Occupational Exposure Limits for Hydrocarbon Solvents
No. 14 *n*-Butyl Methacrylate and Isobutyl Methacrylate OEL Criteria Document
No. 15 Examination of a Proposed Skin Notation Strategy
No. 16 GREAT-ER User Manual
No. 17 Risk Assessment Report for Existing Substances Methyl *tertiary*-Butyl Ether

Documents

No.	Title
No. 32	Environmental Oestrogens: Male Reproduction and Reproductive Development
No. 33	Environmental Oestrogens: A Compendium of Test Methods
No. 34	The Challenge Posed by Endocrine-disrupting Chemicals
No. 35	Exposure Assessment in the Context of the EU Technical Guidance Documents on Risk Assessment of Substances
No. 36	Comments on OECD Draft Detailed Review Paper: Appraisal of Test Methods for Sex-Hormone Disrupting Chemicals
No. 37	EC Classification of Eye Irritancy
No. 38	Wildlife and Endocrine Disrupters: Requirements for Hazard Identification
No. 39	Screening and Testing Methods for Ecotoxicological Effects of Potential Endocrine Disrupters: Response to the EDSTAC Recommendations and a Proposed Alternative Approach
No. 40	Comments on Recommendation from Scientific Committee on Occupational Exposure Limits for 1,3-Butadiene
No. 41	Persistent Organic Pollutants (POPs) Response to UNEP/INC/CEG-I Annex 1
No. 42	Genomics, Transcript Profiling, Proteomics and Metabonomics (GTPM). An Introduction
No. 43	Contact Sensitisation: Classification According to Potency, A Commentary

Workshop Reports

No.	Title
No. 1	Workshop on Availability, Interpretation and Use of Environmental Monitoring Data 20-21 March 2003, Brussels
No. 2	Strategy Report on Challenges, Opportunities and Research needs arising from the Definition, Assessment and Management of Ecological Quality Status as required by the EU Water Framework Directive based on the workshop EQS and WFD versus PNEC and REACH - are they doing the job ? 27-28 November 2003, Budapest