FOREWORD **INTRODUCTION**

1-CHLORO-1,2,2,2-TETRAFLUOROETHANE

CAS N°: 2837-89-0

SIDS Initial Assessment Report

For

SIAM 16

Paris, France, 27-30 May 2003

1. Chemical Name: 1-chloro-1,2,2,2-tetrafluoroethane

2. CAS Number: 2837-89-0

3. Sponsor Country: United States

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4. Shared Partnership with: Honeywell

5. Roles/Responsibilities of the Partners:

- Name of industry sponsor /consortium: George Rusch
Honeywell
973-455-3672

- Process used: Honeywell produced the documents; EPA reviewed the documents and provided additional information where there were data gaps.

6. Sponsorship History Documents were prepared and reviewed by industry prior to submission to sponsor country. Sponsor country conducted reviews of submitted data and offered comments to industry. Industry prepared and resubmitted documents for consideration at SIAM 16. Further information is available in the IPCS EHC document 139 entitled "Partially Halogenated Chlorofluorocarbons (Ethane Derivatives)."

no testing (X)
testing ( )

- How was the chemical or category brought into the OECD HPV Chemicals Programme ?

7. Review Process Prior to the SIAM: The U.S. EPA reviewed this case

8. Quality check process:

9. Date of Submission: January 2003

10. Date of last Update: May 2005

11. Comments:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	2837-89-0
Chemical Name	1-chloro-1,2,2,2-tetrafluoroethane (HCFC-124)
Structural Formula	ClFHC-CF_3

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Rationale

The analogs HCFC-141b (1,1-dichloro-1-fluoroethane; CAS No. 1717-00-6) and HCFC-142b (1-chloro-1,1-difluoroethane; CAS No. 75-68-3) were used to supplement the SAR estimations for aquatic toxicity. These analogs were chosen based on similar functional groups (both analogs are two-carbon alkanes with chlorine and fluorine), similar molecular weights, and similar Log Kows.

Human Health

Metabolism/kinetic studies in animals indicate HCFC-124 is metabolised to a slight extent, primarily by cytochrome P450 IIE1 with consequent urinary excretion of trifluoroacetic acid and fluoride. It has been postulated that the intermediate metabolite (trifluoracetaldehyde) could result in covalently-bound protein adducts, but no toxic effects have been observed that support this hypothesis.

In rats, the 4-hr ALC was 230,000-300,000 ppm (1.3×10^6 - 1.7×10^6 mg/m^3). No rats died at the lower dose, and all rats died at 300,000 ppm (1,671,847 mg/m^3). The 6-hr LC50 was >360,000 ppm (2×10^6 mg/m^3). Exposure of dogs to concentrations of 2.5% (139,500 mg/m^3) or greater resulted in cardiac sensitisation to epinephrine. No studies specifically designed to identify eye or dermal irritation have been performed.

Repeated-dose studies via inhalation have been conducted in rodents for 4 weeks, 13 weeks, and 2 years (6 hrs/day, 5 days/wk). The highest tested concentration in all studies was 50,000 ppm (279,140 mg/m^3). Several clinical signs/symptoms were observed at this highest dose, including lethargy, uncoordinated movements and/or reduced noise stimuli responsiveness. A variety of clinical chemistry and some other parameters were affected at different time intervals and doses between 10,000 and 50,000 ppm. Specifically, effects observed in the 13-week study at higher doses included decreased arousal times in males at 15,000 and 50,000 ppm (55,838 and 279,140 mg/m^3) as well as decreased triglyceride levels at these doses. Increased alkaline phosphatase was observed in females at 50,000 ppm (279,140 mg/m^3). Based on effects observed at 50,000 ppm in the 4-week rat study, a NOAEL of 10,000 ppm (55,828 mg/m^3) was determined and the 13-week sub-chronic studies resulted in a NOAEL of 15,000 ppm (83,700 mg/m^3) in mice and female rats and 5,000 ppm (27,900 mg/m^3) in male rats. The toxicological significance of the effects observed in the chronic 2-year study were unclear.

In *in vitro* and *in vivo* genotoxicity studies, HCFC-124 has shown no mutagenic or clastogenic activity.

No effects were seen in reproductive organs in the repeated-exposure studies. HCFC-124 showed no developmental effects in pregnant rats and rabbits exposed to up to 50,000 ppm (279,000 mg/m^3) for 6 hours per day. In the dams, there was a transient decrease in food consumption (8% decrease in rats) and reduced noise stimuli responsiveness (rabbits) during exposure. The NOAELs for maternal effects were 5,000 ppm (28,000 mg/m^3) in rabbits and 15,000 ppm (83,700 mg/m^3) in rats. The NOAEL for developmental effects was 50,000 ppm (279,000 mg/m^3).

Environment

HCFC-124 (1-chloro-1,2,2,2-tetrafluoroethane, CAS no 2837-89-0) is a colorless gas with a faint ethereal odour at room temperature and atmospheric pressure. It has a melting point of -199ºC and a boiling point of -12ºC at 1013 hPa. It is soluble in water, has a log Kow of 1.94 and a vapour pressure of 3850 hPa.

Degradation of HCFC-124 will occur predominantly in the air by reaction with hydroxyl radicals. Breakdown is expected to proceed via intermediates resulting in formation of HCl and CF_3COF, which would be removed from the atmosphere within a few days to a few months by uptake into clouds, rain and the oceans. The CF_3COF will then rapidly hydrolyse to trifluoroacetic acid and hydrofluoric acid. The atmospheric half-life of HCFC-124 is estimated to be 6 years. Its ozone depleting potential (ODP), relative to CFC-11 (=1.0), has been estimated, giving results in the range 02-0.04. Global warming potential values range from 470 to 620. The value of 470 was adopted by the Kyoto Protocol.

According to the Model River and Lake Program (in EPIWIN), any HCFC-124 present in aqueous waste streams discharged directly into rivers ($t_{1/2}$ = 1.2 h) and lakes ($t_{1/2}$ = 4.6 d) is likely to evaporate rapidly. Results from Level I MacKay modelling also suggest that HCFC-124 would partition mostly to the atmosphere (99.986%), with approximately 0.013% in water and 0.001% in soil. The substance is not readily biodegradable. Its relatively low measured Log Kow (1.94) and estimated bioconcentration factor (6.22) indicate a low potential to bioaccumulate.

Due to the chemical's specific physicochemical properties and distribution in the environment, aquatic and terrestrial testing has not been performed. Using QSAR, a 96-hr LC50 for fish (137 mg/L), a 48-hr LC50 for daphnids (145 mg/L), a 96-hr LC50 for green algae (90 mg/L), and a 14-day LC50 for earthworm (927 mg/L) have been estimated. Measured data for analogs of HCFC-124 (HCFC 141b and HCFC 142b) show low to moderate aquatic toxicity and support the SAR data of HCFC-124.

Because of its ODP, the production and consumption of HCFC-124 will be phased out by the Montreal Protocol. In the case of developed countries, a phase-out of HCFC 124 and other hydrochlorofluorocarbons (HCFCs) is scheduled as follows: 35% in 2004, 65% in 2010, 90% in 2015, 99.5% in 2020. A total phase-out is scheduled in 2030. For developing countries, a freeze of the production is scheduled in 2016 and a total phase-out in 2040. In the European Union, the phase-out of ozone depleting substances is scheduled more rapidly than that required by the Montreal Protocol. The total ban of hydrochlorofluorocarbons is required on January 1, 2010.

Exposure

In the U.S., HCFC-124 is produced in closed systems. The world-wide production volume in 2001 was approximately 2,277 metric tonnes. Its use is limited to foam blowing agents and as a blend in refrigerants. The population exposed either directly or indirectly to HCFC-124 is expected to be limited. Occupational exposure is expected to be the primary exposure. Possible emissions during production are likely to be small. Because HCFC-124 is a gas and is used in anhydrous conditions, release of HCFC-124 to water systems is not expected. In cases of accidental emissions, it is expected to partition almost exclusively to the air.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

This chemical possesses properties indicating the potential for low to moderate hazard to aquatic organisms and low hazard for human health. Based on data presented by the Sponsor country, exposures are anticipated to be low. In addition, the chemical is being phased out under the Montreal Protocol due to its ozone depletion potential. Ozone depletion may have human health effect consequences. Therefore, this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

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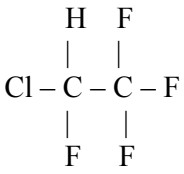
1 IDENTITY

1.1 Identification of the Substance

CAS Number: 2837-89-0
CAS Name: 1-chloro-1,2,2,2-tetrafluoroethane
EINECS No: 220-629-6
Empirical Formula: C_2HClF_4
Structural Formula:



Molecular Weight: 136.5
Common Name: HCFC-124

1.2 Purity/Impurities/Additives

The purity of the substance is about 99.7%. Impurities include a variety of saturates and unsaturates.

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value
Physical state	Gas at room temperature and pressure. Clear, colourless liquid under pressurized conditions
Melting point	- 199°C
Boiling point	-12°C at 1013 hPa
Liquid density	1.36 g/cm^3 at 25°C (pressure not given)
Vapour pressure	3850 hPa at 25°C
Water solubility	1450 mg/L at 25°C and 1013 hPa
Log K_{ow}	1.94 at 25°C
Odour	Ethereal
Flammability	No flash point

The physicochemical values presented here are mainly as reported in the Joint Assessment of Commodity Chemicals (JACC) report for HCFC-124 (JACC, 2003). Water solubility values available for HCFC-124 include values that range from 1,400 to 14,000 mg/L. Based on a several data for analogs (see below), as well as estimated values (see IUCLID), and the fact that 1400 – 1450 mg/L are quoted most often, 1450 mg/L was chosen as the most credible value.

1.4 Analog Justification

The analogs HCFC-141b (1,1-dichloro-1-fluoroethane; CAS No. 1717-00-6) and HCFC-142b (1-chloro-1,1-difluoroethane; CAS No. 75-68-3) are used to supplement the data for HCFC-124. These analogs were chosen based on similar functional groups (both analogs are two-carbon alkanes with chlorine and fluorine), similar molecular weights, and similar Log K_{ow}s. The physicochemical properties of HCFC-124 and the analogs are tabulated below

	HCFC-124	**HCFC-141b***	**HCFC-142b***
	$CFClCF_3$	$CFCl_2CH_3$	CF_2ClCH_3
Molecular Weight	136.48	116.95	100.50
Boiling Point (°C)	-12	32	-9.2
Melting Point (°C)	-199	-103.5	-130.8
Vapour Pressure (hPa)	3850	763	339
Water Solubility (g/L)	1.45	4.0	1.4
Log K_{ow}	1.94	2.3	1.64

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes, Manufacturing Processes, and Use Patterns

Production Volume

According to AFEAS (2002), the production volume in the year 2001 was 2,277 +/- 200 metric tonnes. This figure is based on a survey of companies in Argentina, Australia, Brazil, Canada, the European Union, Japan, Mexico, the United States, and Venezuela. The HCFC-124 data gathered in the survey account for 90 % of all non-feedstock HCFC-124 production. The major global producers of HCFC-124 are Du Pont and Ausimont.

Manufacturing Information

Common methods of production of HCFC-124 are hydrofluorination of tetrachloroethylene or hydrodechlorination of 1,1-dichloro-1,2,2,2-tetrafluoroethane (CFC-114a). The grade of HCFC-124 purity obtained from either process is greater than 99% (as indicated in Section 1.2). In at least one manufacturing plant (in Italy), the production unit is equipped with an incineration unit to burn any exhaust and off gas quantities. HCFC-124 is stored in closed steel cylinders at ambient conditions either outside in open air or inside in half-open sheds with a roof to protect the cylinders from direct sunlight, and it is transported in the same steel cylinders. At the production plant in Italy, pressure tanks are used to store HCFC-124 as a liquid. All tank-venting systems are also connected to the central incineration unit in order to prevent any releases to the environment.

Uses

HCFC-124 is classified as a partially halogenated chorofluorocarbon and was developed as a substitute for fully halogenated chlorofluorocarbons. HCFC-124's main use is in commercial applications as a blowing agent for polystyrene and polyolefin foams in addition to being a component in refrigerant blends. HCFC-124 is used either in closed systems (for refrigeration uses) or in well-ventilated areas with exhaust systems (in the case of appliance manufacturing).

2.2 Environmental Exposure and Fate

Based on manufacturing and commercial use of HCFC-124, any release is likely to be to the atmosphere (estimated Henry's Law constant 37517 $Pa.m^3/mol$) rather than to soil or water. Also, due to its high vapour pressure (3850 hPa at 25°C), HCFC-124 will partition almost exclusively into the air when released to air.

2.2.1 Sources of Environmental Exposure

HCFC-124 is produced in a closed reactor and my potentially be released to the environment during final distillation of the product or during equipment maintanence. There may be accidental release during loading/unloading of storage tanks or refrigeration units. It's use as a foam-blowing agent could lead to environmental release.

2.2.2 Photodegradation/Indirect Photolysis

Degradation of HCFC-124 will occur predominantly in the air. Most of the atmospheric breakdown (95%) will occur in the troposphere, by reaction with naturally-occurring hydroxyl radicals. Breakdown will proceed via various free radical and molecular intermediates to produce HCl and CF_3COF. The latter two species are expected to be removed from the atmosphere within a few days to a few months by uptake into clouds, rain and the oceans. The CF_3COF will then rapidly hydrolyse to trifluoroacetic acid and hydrofluoric acid. Support for this degradation mechanism has been provided by laboratory studies (Edney and Driscoll, 1992 and Tuazon and Atkinson, 1993). Using the AOP model in EPIWIN, the half-life of HCFC-124 is estimated to be 2174 days (6 years), based on a hydroxyl reaction rate of $0.005*10^{-12}$ cm^3/molecule*sec.

Because processes in addition to reaction with OH radicals also operate to remove HCFC-124 from air (e.g., oceanic uptake and stratospheric degradation), an overall atmospheric lifetime can be calculated. A value of 5.8 years has been estimated with a corresponding half-life of 4 years (WMO, 2002).

2.2.3 Stability in Water

There are no data on the hydrolysis of HCFC-124 in water.

HCFC-124 that might be present in aqueous waste streams discharged directly into rivers and lakes would be expected to have a volatilization half-life of a few days, based upon predictions using EPIWIN ($t_{1/2}$ = 1.2 hours in river water and 4.6 days in lake water).

2.2.4 Transport between Environmental Compartments

Results from the Level I MacKay modeling suggest that HCFC-124 would partition nearly exclusively into the atmosphere (100%), with less than 0.01% in water and soil. The Level I model assumes a one-time release and equilibrium conditions. The Level III model, which assumes continuous release, shows that using a scenario in which all HCFC-124 was released into the air, the chemical also would remain nearly exclusively in the atmosphere (100%).

2.2.5 Biodegradation

There are little experimental data on biodegradation of HCFC-124. Biotic degradation in a closed bottle test with activated sludge showed only 2 % degradation after 28 days (Krume Research Laboratories, 1992). It can therefore be concluded that HCFC-124 is not readily biodegradable.

However, under environmental conditions in soil and water, HCFC-124 would be expected to volatilize to the atmosphere more rapidly than it would biodegrade, as suggested by the closed bottle test results and its physicochemical properties (e.g. Henry's Law Constant).

2.2.6 Bioaccumulation

A measured log K_{ow} of 1.94 (Krume Research Laboratories, 1991) and an estimated bioconcentration factor of 6.22 suggests that HCFC-124 has a low potential to bioaccumulate.

2.2.7 Other Information on Environmental Fate

Stability in Soil

The calculated soil K_{oc} is 29.7, indicating limited potential for the chemical to adsorb to soil. HCFC-124 present in surface or groundwater would have little tendency to partition into biota or onto soil based on its relatively low log K_{ow} (1.94), bioconcentration factor (6.22), and soil K_{oc} (29.7).

Ozone Depletion Potential

HCFC-124's ozone depleting potential relative to CFC-11 (=1.0) has been estimated to range from 0.02-0.04 for different isomers as presented in the Montreal Protocol (UNEP, 2000). The specific isomers associated with each value, however, are not stated. The ODP value used for regulatory purposes (and stated as representing a commercially viable HCFC-124 product) is 0.022 (UNEP, 2000).

Global Warming Potential

Global warming potential values relative to carbon dioxide over a time horizon of 100 years ranges from 470 to 620. The value of 470 was adopted by the Kyoto Protocol (IPCC, 1995). Relative to CFC-11, the global warming potential of HCFC-124 has been estimated to be 0.1 (AER, 1992).

2.3 Human Exposure

HCFC-124 is a gas at room temperature. It is used in systems or applications that are contained within the atmosphere (rather than water or soil) and therefore the main route of human exposure is via inhalation. The main exposure groups are likely to be occupational groups and the population residing in the vicinity of production/processing facilities

2.3.1 Occupational Exposure

Potential exposures to HCFC-124 can occur during production, as a result of loading or unloading, or its use as a blowing agent or refrigerant. HCFC-124 is produced on a small scale in closed vessel reactors. It is stored in open air away from direct sunlight in closed steel cylinders at ambient conditions, and it is transported in the same steel cylinders. During use, HCFC-124 is kept in closed systems or in well-ventilated areas. The potential for occupational exposure is limited if proper controls are used. No monitoring data are available. The American Industrial Hygiene Association (AIHA) occupational exposure limit (8 hr time-weighed average) is 1,000 ppm (5583 mg/m^3) (AIHA, 1992).

2.3.2 Consumer Exposure

HCFC-124 is not used in consumer products. Therefore, overall consumer exposure is expected to be limited. However, no data were located for direct or indirect consumer exposure to HCFC124 blown products.

2.3.3 Indirect Exposure via the Environment

HCFC-124 is not known to occur naturally. After release, however, the chemical will partition into the air based on its high vapour pressure of 3850 hPa. It also has a low affinity for soil, and is not expected to accumulate in water based on its high vapour pressure and Henry's Law constant. With a log K_{ow} of 1.94 and estimated bioconcentration factor of 5.4, it is not expected to show significant bioconcentration in aquatic organisms.

2.3.4 Regulatory Controls

An international agreement, known as the **Montreal Protocol**, controls the production and consumption of ozone-depleting substances. In developed countries, the 1996 production of HCFCs is 'frozen' to the baseline level calculated for each country using the following formula: 2.8 percent of Ozone Depletion Potential (ODP)-weighted production in 1989 of chlorofluorocarbons (CFCs) augmented by 100 percent of ODP weighted production in 1989 of HCFCs. Furthermore, time limits for consumption were also given by authorizing 100 percent of maximum value of consumption (calculated as above) until January 1, 2004 and then applying every five years a decreasing threshold to this authorized maximum:

65% as from January 1, 2004

35% as from January 1, 2010

10% as from January 1, 2015

0.5% as from January 1, 2020

A total ban on HCFCs (including HCFC-124) is planned for 2030 for developed countries.

For developing countries, a freeze of the production and consumption of HCFCs is planned on January 1, 2016 to the baseline level of 2015 and a total ban of consumption on January 1, 2040.

In the European Union (EU), the phase out of ozone depleting substances is scheduled more rapidly than that required by the Montreal protocol. The total ban of hydrochlorofluorocorbons (HCFCs) is required on January 1, 2010.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Metabolism/kinetic studies in animals indicate HCFC-124 is metabolised to a slight extent, primarily by cytochrome P450 IIE1 with consequent urinary excretion of trifluoroacetic acid and

fluoride (Olson *et. al.* 1991). It has been postulated that the intermediate metabolite (trifluoracetaldehyde) could result in covalently-bound protein adducts, but no toxic effects have been observed that support this hypothesis.

3.1.2 Acute Toxicity

Studies in Animals

In rats , the approximate lethal concentration following 4-hr inhalation exposure in rats was in the range of 230,000-300,000 ppm (1,274,049 – 1,671,847 mg/m^3) (Haskell Laboratory, 1990a). There were no clinical signs observed during exposure to 48,000 ppm (267,974 mg/m^3) HCFC-124. The main clinical effects during exposure to 160,000 and 230,000 ppm (893,248 - 1,274,049 mg/m^3) were reduced activity, anaesthesia, reduced acoustic startle and tail pinch responses. At 300,000 ppm (1,671,847 mg/m^3) exposure, all rats died. In a separate study, the 6-hr LC_{50} following inhalation exposure was determined to be >360,000 ppm (>2,007,816 mg/m^3) (Hazleton Laboratory, 1976). In this study rats showed reduced activity during exposure to 100,000 ppm (558,280 mg/m^3) HCFC-124 and were anaesthetised for the major part of exposure to 360,000 ppm (2,007,816 mg/m^3) HCFC-124. There were no mortalities at any concentrations.

Conclusion

Because these two inhalation studies in rats show somewhat different results, the LC_{50} value is somewhat uncertain. However, in both cases the value is greater than 230,000 ppm (1,274,049 mg/m^3).

3.1.3 Irritation

There are no skin or eye irritation studies available

3.1.4 Sensitisation

Exposure of dogs to concentrations of 2.5% (139,500 mg/m^3) or greater combined with concurrent injection of epinephrine (adrenalin) at 0.008 mg/kg resulted in cardiac sensitisation to the epinephrine (Haskell Laboratory, 1976a).

3.1.5 Repeated Dose Toxicity

Studies in Animals

In a 4-week repeated-dose inhalation study with exposures of 6 hours per day for 5 days a week in rats, the no-observable-adverse-effect level (NOAEL) was judged to be 10,000 ppm (55,828 mg/m^3) (Haskell Laboratory, 1990b). In 13-week studies, the NOAEL was 15,000 ppm (83,742 mg/m^3) in mice (Haskell Laboratory, 1991a) and female rats and 5,000 ppm (27,914 mg/m^3) in male rats (Haskell Laboratory, 1991b). The highest exposure level in these studies, 50,000 ppm (279,140 mg/m^3), induced lethargy, uncoordinated movements and/or reduced noise stimuli responsiveness during exposure. These observations were made while the animals were being exposed in the inhalation chamber; therefore, they were general in nature. There were no clinical signs of toxicity seen in either the rats or mice. In the FOB, 4/10 male rats at 15,000 ppm (83,742 mg/m^3) and 6/10 male rats at 50,000 ppm (279,140 mg/m^3) showed decreased arousal times at week 13 but not at week 4, 8 or 16. The FOB analysis was not conducted in the mouse study. In male rats, serum triglyceride levels were reduced significantly (41% at both exposure levels) at day 45 in the15,000 and 50,000 ppm (83,742 and 279,140 mg/m^3) exposure levels. The serum triglyceride levels remained low at day 90, but were not statistically significant. In female rats, alkaline

phosphatase activity was increased at day 90, but not days 45 or the end of recovery in the 50,000 ppm (279,140 mg/m^3) exposure group. No treatment–related haematological or histopathological changes were noted in any exposure level group. There was no treatment-related mortality or difference in organ weights in any of the three studies. Urinary and plasma fluoride levels increased in a dose-related pattern at all exposure levels, but this is a result of metabolism and not a toxic effect (Malley *et. al*., 1996; Haskell Laboratory, 1990b; Haskell Laboratory, 1991a and Haskell Laboratory, 1991b).

In a whole-body inhalation lifetime study, rats were exposed to HCFC-124 concentrations of 0, 2,000, 10,000 or 50,000 ppm (11,166, 55,828 or 279,140 mg/m^3) for 6 hours per day for 5 days per week. Clinical signs observed during exposure in the subchronic studies were not duplicated. In males, 3-month serum triglyceride levels were lower, but not significantly, at 10,000 and 50,000 ppm (55,828 and 279,140 mg/m^3) with a dose-related trend. The 24-month male serum triglyceride levels were higher at 10,000 ppm (55,828 mg/m^3) and lower at 50,000 ppm (279,140 mg/m^3). The effect on serum triglyceride at 3 months was not substantiated at 24 months and therefore, the toxicological significance of changes in triglyceride levels is unclear. There were changes in organ weights, although these were not accompanied by gross or microscopic changes**.** At 24 months, male rats in the 50,000 ppm (279,140 mg/m^3) group had increased incidence of focal hepatic necrosis and cholesterol clefts in the lungs; although these are common in aging rats, it is important to note the differences in these effects compared with control animals. There were some statistically-significant differences in hematological and hormonal parameters. However, the changes were not dose-related, were not sustained throughout the study, and in the case of the hematological measures, were not substantiated by closely-related parameters. Urinary fluoride levels were higher in all animals at each exposure level, as were 12-month female plasma fluoride levels. These were expected results of metabolism, and were not considered a toxic effect. Consistent with an increase in grossly identified mammary gland masses in the 50,000 ppm females relative to control, there was a statistically significant higher incidence of mammary gland fibroadenoma in the 50,000 ppm females (36%) compared to controls (23%). The effects seen in the above study were either not related to treatment or the toxicological significance was unclear and the no-observable-adverse-effect level (NOAEL) for systemic toxicity was judged to be 50,000 ppm (279,140 mg/m^3) (Haskell Laboratory, 1995 and Malley *et al*., 1998).

Studies in Humans

There are no experimental studies on effects in humans resulting from exposure to HCFC-124. Accidental worker exposure to a mixture of HCFC-123 (1,1-dichloro-2,2,2-tetrafluoroethane) and HCFC-124 has been reported. The investigators concluded that repeated human exposure to HCFC-123 and HCFC-124 can result in serious liver injury in a large proportion of the exposed population. Although it is not clear which HCFC compound is responsible, the discussion focuses on HCFC-123's known hepatotoxicity and greater extent of metabolism (Hoet *et. al.,* 1997). A guinea-pig study (4-hr exposure to 5,000 ppm HCFC-123 for 1 or 5 days) showed toxicity of HCFC-123 was not increased by concurrent exposure to 5,000 ppm (27,914 mg/m^3) HCFC-124 (Hoet *et. al.,* 2001).

Conclusion

In subchronic repeated-dose studies using rats and mice, HCFC-124 induced lethargy, uncoordinated movements and/or reduced noise stimuli in males and females of both species at 50,000 ppm (279,140 mg/m^3). In male rats, serum triglyceride levels were reduced at 15,000 and 50,000 ppm (55,828 and 279,140 mg/m^3). In females at 50,000 ppm (279,140 mg/m^3), there was an increase in alkaline phosphate activity. In the 13-week rat study FOB, 4/10 male rats at 15,000 ppm (83,742 mg/m^3) and 6/10 male rats at 50,000 ppm (279,140 mg/m^3) showed decreased arousal times at week 13 but not at week 4, 8 or 16.

Of the subchronic animal studies, the 4-week repeated-dose inhalation study was judged to have a NOAEL of 10,000 ppm (55,828 mg/m^3). In 13-week studies, the NOAEL was 15,000 ppm (83,742 mg/m^3) in mice and female rats and 5,000 ppm (27,914 mg/m^3) in male rats.

In lifetime animal studies, the effects were either not related to treatment or the toxicological significance was unclear. Therefore, the NOAEL for systemic toxicity was judged to be 50,000 ppm (279,140 mg/m^3).

The lack of HCFC-124 toxicity in the animal studies and the results of report of human exposure support the theory that worker toxicity may be due to HCFC-123 and not HCFC-124.

3.1.6 Genotoxicity

Studies in Animals

In vitro Studies

HCFC-124 was negative in all *in vitro* genotoxicity studies. HCFC-124 was non-mutagenic in bacterial tests with *Salmonella typhimurium* (up to 60% exposure level), *Escherichia coli* (up to 50% exposure level) and the non-bacterial test (yeast) *Saccaromyces cerevisiae* (Haskell Laboratory , 1976b; Litton Bionetics , 1976; Haskell Laboratory , 1990c, and Life Science , 1991a). In tests with hamster CHO-K1 cells (up to 60% exposure level) (Life Science, 1991b) and human lymphocytes (up to 100% exposure level) (Haskell Laboratory , 1990d), it was shown to be non-clastogenic.

In vivo Studies

A micronucleus test was performed in male and female mice after 6-hr whole-body inhalation exposure to 100,000 ppm (558,280 mg/m^3) HCFC-124 on two consecutive days. There was no significant difference in the percent micronucleated PCEs between the controls and HCFC-124-treated mice. Therefore, HCFC-124 was determined to be negative in the mouse micronucleus assay (Haskell Laboratory, 1990e and Malley *et al*., 1998).

Conclusion

All available studies show that HCFC-124 is negative for genetic toxicity.

3.1.7 Carcinogenicity

Studies in Animals

In a whole-body inhalation lifetime study in which rats were exposed to HCFC-124 concentrations of 0, 2,000, 10,000 or 50,000 ppm (11,166, 55,828 or 279,140 mg/m^3) for 6 hours per day for 5 days per week, compound-related carcinogenicity was not observed (Haskell Laboratory, 1995 and Malley *et al*., 1998). HCFC-124 did not produce neoplastic changes in male or female rats at any exposure level. At 24 months, male rats in the 50,000 ppm (279,140 mg/m^3) group had increased incidence of granulomas in the lungs compared with the controls. There was a statistically-significant increase in incidence of mammary gland fibroadenomas (36 %) in the 50,000 ppm (279,140 mg/m^3) females compared with controls (23 %). Incidence in the 2,000 and 10,000 ppm (11,166 and 55,828 mg/m^3) groups appeared lower (at 16 and 22 %) compared with the controls. A high incidence (36 %) was observed in controls in a study that was likely to have been conducted in another laboratory (Keenan *et al.*, 1995).

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility

In two repeated-dose 90-day inhalation studies, rats (Haskell Laboratory, 1991b and Malley *et al*., 1996) and mice (Haskell Laboratory, 1991a and Malley *et al*., 1996) were exposed to 0, 5,000, 15,000 or 50,000 ppm (0, 27,914, 55,828, or 279,140 mg/m^3). In both studies, several reproductive organs of males (testes, epididymis and prostate) and females (uterus, ovaries and vagina) were evaluated both macro- and microscopically (control and 50,000 ppm (279,140 mg/m^3) groups only). No treatment-related findings were observed at any of the administered doses.

Developmental Toxicity

Pregnant rats (gestation days 7-16) and rabbits (gestation days 6-18) were exposed to levels of 0, 5,000, 15,000 or 50,000 ppm (0, 27,914, 55,828, or 279,140 mg/m^3) for 6 hrs/day. Maternal rats on gestation days 7-9 had lower body weight (93%) and post-treatment weight of maternal rabbits exposed to 50,000 ppm (279,140 mg/m^3) was higher (118%). There were no differences at any other times in body weight gains. In the pregnant rats, there was a trend in decreased food consumption during exposure (days 7-13), but only significantly for days 9-11 (8%) of gestation for the 50,000 ppm (279,140 mg/m^3) group. After exposure there was a significant trend for increased food consumption, but only significantly (10%) in the 15,000 ppm (55,828 mg/m^3) group. In the pregnant rabbits, food consumption was significantly lower during exposure and significantly higher after exposure in the 50,000 ppm (279,140 mg/m^3) group. During exposure, the pregnant rats and rabbits exposed to 50,000 ppm (279,140 mg/m^3) were less responsive to noise stimuli (tap on the exposure chamber wall) (Haskell Laboratory, 1991c; Biodynamics, 1991a; Malley *et al.,* 1996).

In rats, increased mean nidations per litter (5,000 ppm or 27,914 mg/m^3) and increased mean corpora lutea counts (15,000 ppm or 55,828 mg/m^3) were observed. For rabbits, the mean pre-implantation loss ratio was higher for the 50,000 ppm (279,140 mg/m^3) group but not significantly, and for the other exposure groups, the rate was comparable to controls.

In rats, there were significant reductions in mean fetal weights (combined 5%, and by sex 4-7%) in the 5,000 and 15,00 ppm (27,914 and 55,828 mg/m^3) groups but there was no significant trend. There were no other fetal effects (Haskell Laboratory, 1991c and Malley *et. al*., 1996). In rabbits, no fetal effects were seen (Biodynamics, 1991a).

The NOAEL for maternal effects was 15,000 ppm (279,140 mg/m^3) for both rats and rabbits.[1] The NOAEL for developmental toxicity for both rats and rabbits was 50,000 ppm (279,140 mg/m^3) (the highest dose tested).

Conclusion

No effects on reproductive organs were observed at doses of 50,000 ppm (279,140 mg/m^3) in rats and mice in subchronic studies. In addition, HCFC-124 did not cause developmental effects in rats or rabbits at exposures up to 50,000 ppm (279,140 mg/m^3) in full developmental studies. However, dose levels were high enough that some maternal toxicity (decreased response to noise stimulus, reduced mean food consumption) was seen at 50,000 ppm (279,140 mg/m^3) in these studies.

[1] The maternal NOAELs from range-finding studies used to determine doses for these full studies were 5,000 ppm for rabbits (based on decreased activity) and 10,000 ppm for rats (based on lethargy and uncoordinated movement) (Biodynamics, 1991b; Haskell Laboratory, 1990f).

3.2 Initial Assessment for Human Health

HCFC-124 has a 4-hr rat inhalation ALC between 230,000 and 300,000 ppm (1,274,049 and 1,671,847 mg/m^3). In dogs at exposure levels of 2.5% (139,500 mg/m^3)or greater it was a cardiac sensitizer to the effects of exogenous adrenaline. In repeated-dose studies (male/female, rats/mice) at 50,000 ppm (279,140 mg/m^3), HCFC-124 induced lethargy, uncoordinated movements and/or reduced noise stimuli in all groups. In male rats, serum triglyceride levels were reduced at 15,000 and 50,000 ppm (55,828 and 279,140 mg/m^3). In females at 50,000 ppm (279,140 mg/m^3), there was an increase in alkaline phosphate activity. HCFC-124 did not show any activity in *in vitro* or *in vivo* genotoxicity studies. In a lifetime study in rats, study authors concluded that HCFC-124 did not produce tumours at exposure levels up to 50,000 ppm (279,140 mg/m^3). The toxicological relevance or relationship to treatment of other observed effects was unclear. HCFC-124 did not cause teratogenic effects in rats or rabbits with exposures up to 50,000 ppm (279,140 mg/m^3). However, dose levels were high enough that some maternal toxicity was seen at 5,000-15,000 ppm (27,914 - 55,828 mg/m^3) (decreased activity during exposure, reduced mean food consumption).

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

There are no experimental data available on HCFC-124 for the aquatic compartment. HCFC-124's high vapour pressure and Henry's Law constant suggest that it will partition to the air. Since SAR estimations in ECOSAR for this class of chemicals (neutral organics) rely on a large amount of data, it is believed that these estimations plus data and estimations from analogs are sufficient to meet the SIDS required endpoints for acute aquatic toxicity to fish, daphnids and algae. The available information is summarised in the following text and tabulated at the end of this section.

4.1.1 Acute Toxicity Test Results

Acute Toxicity to Fish

Using ECOSAR modeling, the HCFC-124 96-hr LC_{50} for fish is estimated to be 137 mg/L.

For HCFC-141b the 96-hr LC_{50} for Zebra fish was 126 mg/L in a static, sealed vessel test (Bazzon and Hervouet, 1989), compared with an estimated value of 45.3 mg/L. For HCFC-142b the 96-hr EC_{50} for Guppies (Poecilia reticulta) was 220 mg/L in a semi-static, sealed vessel test (Groeneveld and Kuijpers, 1990a), with an estimated value of 162 mg/L.

Acute Toxicity to Aquatic Invertebrates

ECOSAR modeling predicts an HCFC-124 48-hr LC_{50} of 145 mg/L for daphnids.

For HCFC-141b the 48-hr LC_{50} for daphnids was 31.2 mg/L, in a sealed vessel test (Brian and Hervouet, 1989); the estimated value is 45.9 mg/L. For HCFC-142b the 48-hr LC_{50} for daphnids was 160 mg/L, in a sealed vessel test (Groeneveld and Kuijpers, 1990b), while the value estimated by ECOSAR is 170 mg/L.

Acute Toxicity to Algae

Using ECOSAR modeling, the HCFC-124 96-hr LC_{50} for green algae is estimated to be 90 mg/L. For HCFC-141b the algae 72-hr biomass and growth rate EC_{50} was >44 mg/L (highest dose tested)

in a sealed vessel test (Groeneveld and Kuijpers, 1991). ECOSAR estimations for HCFC-141b and HCFC-142b are 31.5 and 104 mg/L, respectively.

		HCFC-124	HCFC-141b	HCFC-142b
Fish (mg/L)	Experimental	No Data	126 (96-hr LC_{50})	220 (96-hr EC_{50})
	Estimated 96-hr LC_{50}	137	45.3	162
Daphnid (mg/L)	Experimental	No Data	31.2 (48-hr LC_{50})	160 (48-hr LC_{50})
	Estimated 48-hr LC_{50}	145	45.9	170
Algae (mg/L)	Experimental	No Data	>44 (72-hr EC_{50})	No Data
	Estimated 96-hr EC_{50}	90	31.5	104

4.2 Terrestrial Effects

There were no experimental data concerning terrestrial effects. However, using the ECOSAR model, the 14-day LC50 for the earthworm is estimated to be 927 mg/L.

4.3 Other Environmental Effects

4.4 Initial Assessment for the Environment

HCFC-124 is expected to be released almost exclusively to the air compartment. Its physicochemical properties dictate that it will remain in the air compartment after release. The majority of HCFC-124 would be broken down in the lower atmosphere by hydroxyl radicals to ultimately yield trifluoroacetic acid and hydrofluoric acid. HCFC-124 has an atmospheric half-life of 6 years, a halocarbon global warming potential of 0.10 and a stratospheric ozone depletion potential in the range of 0.02-0.04. Global warming potential values relative to carbon dioxide for an integration time horizon of 100 years, was 470, as adopted by the Kyoto Protocol. Bioaccumulation in aquatic organisms is of low concern because of its low log K_{ow} of 1.94 and estimated bioconcentration factor of 6.22. The substance is not readily biodegradable.

Based on the MacKay Level I modelling data and the physicochemical properties of HCFC-124, the concentration in the aquatic compartment is likely to be low.

Based on the physicochemical properties of HCFC-124, the SAR for aquatic toxicity was deemed to be appropriate, using the chemical class of neutral organics.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work. This chemical possesses properties indicating the potential for low to moderate hazard to aquatic organisms and low hazard for human health. Based on data presented by the Sponsor country, exposures are anticipated to be low. In addition, the chemical is being phased out under the Montreal Protocol due to its ozone depletion

potential. Ozone depletion may have human health effect consequences. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

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I U C L I D

D a t a S e t

Existing Chemical	ID: 2837-89-0
CAS No.	2837-89-0
EINECS Name	1-Chloro-1,2,2,2-tetrafluoroethane
Tag name	HCFC 124
Producer Related Part	
Company:	Solvay S.A.
Creation date:	08-SEP-2002
Substance Related Part	
Company:	Solvay S.A.
Creation date:	08-SEP-2002
Memo:	OECD HPV Chemicals programme, SIDS Dossier, approved at SIAM 16 (27-30 May 2003)
Printing date:	15-NOV-2005
Revision date:	
Date of last Update:	14-NOV-2005
Number of Pages:	89
Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 Applicant and Company Information

1.0.2 Location of Production Site, Importer or Formulator

1.0.3 Identity of Recipients

1.0.4 Details on Category/Template

1.1.0 Substance Identification

IUPAC Name: Ethane, 2-chloro-1,1,1,2-tetrafluorethane
Mol. Formula: C2HClF4
Mol. Weight: 136.5

Source: Daxa Borkhataria Northaw
30-MAY-2002

1.1.1 General Substance Information

Substance type: organic
Physical status: gaseous
Purity: 99.7 - % v/v
Colour: colourless
Odour: Faint etheral odour

Remark: The 99.7% purity value is the current commercial specification for HCFC-124.
Source: Daxa Borkhataria Northaw
21-MAY-2003

1.1.2 Spectra

Type of spectra: IR

Remark: Wavenumber for stretch (/cm) C-H 3000, C-F 1100-1300 and C-Cl 700
Source: Daxa Borkhataria Northaw
19-JUN-2002 (47)

1.2 Synonyms and Tradenames

HCFC-124, Hydrofluorocarbon 124, Fluorocarbon 124, HFA-124, Chlorotetrafluoroethane, Flon 124, F 124, FC 124, Genetron 124 and G 124

Source: Daxa Borkhataria Northaw
03-MAY-2003

1.3 Impurities

Remark: Impurities - typical for commercial specification
< 300 ppm saturates

< 300 ppm unsaturates
Source: Daxa Borkhataria Northaw
21-MAY-2003

1.4 Additives

1.5 Total Quantity

Quantity: 2277 tonnes produced in 2001

Source: Daxa Borkhataria Northaw
21-MAY-2003 (2)

1.6.1 Labelling

1.6.2 Classification

1.6.3 Packaging

1.7 Use Pattern

Type: type
Category: Use in closed system

Source: Daxa Borkhataria Northaw
01-JUL-2002

Type: industrial
Category: Chemical industry: used in synthesis

Source: Daxa Borkhataria Northaw
23-AUG-2002

Type: industrial
Category: other: refrigerant (sealed system) foam blowing (well ventilated area with exhaust systems)

Source: Daxa Borkhataria Northaw
23-AUG-2002

1.7.1 Detailed Use Pattern

1.7.2 Methods of Manufacture

Source: Daxa Borkhataria Northaw
01-JUL-2002

1.8 Regulatory Measures

1.8.1 Occupational Exposure Limit Values

Type of limit: OES (UK)
Limit value: 1000 other: ppm

Remark: Occupational exposure limit from the American Industrial Hygiene Association's workplace environmental exposure level (WEEL) guide, 1992
Source: Daxa Borkhataria Northaw
06-MAY-2003 (3)

1.8.2 Acceptable Residues Levels

1.8.3 Water Pollution

1.8.4 Major Accident Hazards

1.8.5 Air Pollution

1.8.6 Listings e.g. Chemical Inventories

1.9.1 Degradation/Transformation Products

1.9.2 Components

1.10 Source of Exposure

1.11 Additional Remarks

1.12 Last Literature Search

1.13 Reviews

2.1 Melting Point

Value: = -199 degree C

Remark: Listed in test substance data in report on Measurement of Dissociation constant, Krume Research Laboratories, Japan, Test No 80647, December 1991

Reliability criteria: 2g (reliable with restriction, data from handbook or collection of data).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003

2.2 Boiling Point

Value: = -12 degree C at 1013 hPa

GLP: no data

Remark: Value listed in JACC Report, 2003.

Reliability criteria 2g (reliable with restriction, data from handbook or collection of data).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (15)

Value: = -11 degree C

Remark: Value listed in various study reports.

Reliability criteria 2g (reliable with restriction, data from handbook or collection of data).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003

2.3 Density

Type: density
Value: = 1.36 g/cm³ at 25 degree C

Remark: Liquid density value from JACC report, 2003.
Pressure is not given.

Reliability criteria 2g (reliable with restriction, data from handbook or collection of data).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (15)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: ca. 3850 hPa at 25 degree C

GLP: no data

Remark: Vapour pressure values in JACC report, 2003, range from 3820 to 3860 hPa. Value of 3850 hPa is a Dupont, 1993 referenced value.

Reliability criteria 2g (reliable with restriction, data from handbook or collection of data).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (15)

Remark: Vapour pressure estimated using EPIWIN with a boiling point input value of -12 degrees C

2870 mm Hg (3825 hPa) Antoine method
2690 mm Hg (3585 hPa) Modified Grain method
2450 mm Hg (3266 hPa) Mackay method

Conversion factor (at 20 degrees C):-
1,103 hPa = 1 atm = 760 mm Hg

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

2.5 Partition Coefficient

Partition Coeff.: octanol-water
log Pow: = 1.94 at 25 degree C

Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year: 1991
GLP: yes

Remark: 6.1 mg of HCFC-124 was added to a vessel containing water:octanol in the following ratios: 5:97, 10:92 and 82:20. Distribution between the two phases was determined in duplicate for each ratio.

Mean value of six determinations reported.

Reliability criteria 1a (GLP guideline study).
Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99.99%.
Reliability: (1) valid without restriction
30-SEP-2003 (47)

2.6.1 Solubility in different media

Solubility in: Water
Value: at 25 degree C

Test substance: other TS

Remark: These values are listed in the JACC report, 2003.

1.45 g/l at 25 degrees C (Material safety data sheet HCFC-124, Dupont 1993 and Solkane 124 safety data sheet, Solvay 2001).

1.40 g/L at 25 degrees C (Meforex 124 safety data sheet, Ausimont, 2002) and

Reliability criteria 4c (not assignable, original reference not yet available).
Source: Daxa Borkhataria Northaw
Reliability: (4) not assignable
13-JAN-2004 (15)

Solubility in: Water
Value: = 14 g/l

Remark: This value is reported in "Test on 1-octanol/water partition coefficient of Flon 124", Krume Research Laboratories, Japan, Test No. 80646, December 1991. The method used to determine solubility is not given.

Reliability Criteria 4e (not assignable, documentation insufficient for assessment).
Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99.99%.
Reliability: (4) not assignable
13-JAN-2004 (48)

Solubility in: Water

Remark: The water solubility of HCFC-124 at 25 degrees C and 1 atmosphere is reported to be between 1.40-1.45 g/L. There is also a value of 14 g/L reported in a Japanese study report.

Below are two additional sources of information which support the lower value of the solubility at 1 atmosphere partial pressure.

1) Maassen (1996)

In a doctoral dissertation, Maassen determined the Henry's Law constant (HLC) for partitioning of gaseous HCFC-124 to water. Maassen defines (in his Fig. 3.2) the HLC as being the ratio of the gas-phase partial pressure of a substance to its aqueous-phase mole fraction. Maassen's value for the "infinite dilution" HLC of HCFC-124 at 298.13 K (25°C) is given in his Table A.1.1.a as 533.7 MPa (per unit mole fraction). This value can be converted into a solubility at

1 atmosphere partial pressure as follows:

· Consider a very dilute aqueous solution with, say, a mole fraction of 0.001 of HCFC-124. This corresponds to 1 mole (136.5 g) of HCFC-124 per 999 moles (17997 g) of water.

· The concentration of HCFC-124 is therefore 136.5 g/17.997 kg water. The density of water at 25°C being 0.997 kg/L, this is equivalent to a concentration of 136.5/18.051 = 7.56 g HCFC-124 per L water. The value expressed in g HCFC-124 per L solution will be approximately the same, given the high dilution.

· Since we have considered a solution with a mole fraction of 0.001, the gas-phase partial pressure in equilibrium with it will be 0.001 * 533.7 MPa = 5.337 bar.

· Recapitulating, at a gas-phase partial pressure of 5.337 bar, the aqueous-phase concentration of HCFC-124 will be 7.56 g/L.

· Therefore, at a gas-phase partial pressure of 1 atmosphere (1.013 bar), the aqueous-phase concentration of HCFC-124 will be 7.56 * 1.013/5.337 = 1.43 g/L.

In conclusion, Maassen's Henry's Law constant corresponds to an HCFC-124 solubility of 1.43 g/L at 25°C and 1 atmosphere partial pressure.

2) Irmann (1965)

Irmann does not report any experimental results for the solubility of HCFC-124, but gives a correlation enabling it to be calculated.

The equation used by Irmann is :

- log10s = a + Sum of bini + sum of cjnj

where :

· "s" is the solubility at 25°C, expressed in g solute/g water (for gases, this refers to equilibrium at the saturated vapour pressure of the substance : see note g of Irmann's Table 3)

· "a" is a constant for a given family of compounds (0.50 for HCFC-124)

· "bi" is a contribution for each type of atom present (0.25 for C, 0.125 for H, 0.28 for F attached to a saturated aliphatic C and 0.375 for Cl attached to a saturated aliphatic C)

· "ni" is the number of atoms of each type present

· "cj" is a contribution for various types of structural elements present (the only relevant one for HCFC-124 has a value of -0.30)

· "nj" is the number of such structural elements (i.e. 1 for HCFC-124)

In the case of HCFC-124, we therefore have, at 25°C and the saturated vapour pressure :

- log10s = 0.50+(0.25*2+0.125*1+0.28*4+0.375*1)-0.30*1 = 2.32

Therefore, s = 4.79*10-3 g HCFC-124 per g water, or 4.79 g HCFC-124/kg water. The vapour pressure of HCFC-124 at 25°C

being approximately 3.8 atmospheres, the solubility of HCFC-124 at 25°C and 1 atmosphere partial pressure is estimated to be 4.79/3.8 g/kg water, i.e. approximately 1.3 g/L.

Reliability Criteria 4 (not assignable).
Source: Daxa Borkhataria Northaw
Reliability: (4) not assignable
13-JAN-2004 (31)

Solubility in: Water

Remark: Data from EPIWIN model.

Equation used to estimate water solubility:
Log S (mol/L) = 0.693 - 0.96logKow - 0.0092(Tm-25) - 0.00314MW + correction

Where Log Kow = 1.86 (estimated value)
Tm (melting point) = -199 deg C
Correction (for plyfluoroalkane) = -0.945

Log S (mol/L) = -2.467
Water solubility (mg/L) at 25 deg C = 466.1

Reliability criteria 4 (not assignable).
Source: Daxa Borkhataria Northaw
Reliability: (4) not assignable
13-JAN-2004 (17)

Solubility in: Organic Solvents

Remark: Miscible with acetone, ethanol and petroleum solvents

Reliability criteria 2g (reliable with restriction, data from handbook or collection of data).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
13-JAN-2004 (15)

2.6.2 Surface Tension

Test type: other

Remark: The chemical is a gas at ambient temperature and atmospheric pressure, hence surface tension is not relevant.
Source: Daxa Borkhataria Northaw
30-MAY-2002

2.7 Flash Point

Method: other:

Remark: The compound is non-flammable.
Source: Daxa Borkhataria Northaw
11-JUN-2002 (15)

2.8 Auto Flammability

2.9 Flammability

Result: non flammable

Remark: Reported in JACC Report, 2003.
Source: Daxa Borkhataria Northaw
30-MAY-2002 (15)

2.10 Explosive Properties

2.11 Oxidizing Properties

2.12 Dissociation Constant

Acid-base Const.: The substance does not dissociate

Method: OECD Guide-line 112
Year: 1991
GLP: no data

Remark: Reliability criteria - 1b (comparable to guideline study).
Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99.99% (abbreviated to Flon 124).
Reliability: (1) valid without restriction
30-SEP-2003 (36)

2.13 Viscosity

2.14 Additional Remarks

Memo: OTHER

Remark: Henry's Law Constant (VP/Wsol):-

Henry's Law Constant 0.0941 atm.m3/mol (estimated using vapour pressure of 1370 mm Hg or 182607 Pa and water solubility of 1450 mg/L).

Henry's Law Constant 37517 Pa.m3/mol (estimated using vapour pressure of 2888 mm Hg or 385035 Pa and water solubility of 1450 mg/L).

Based on EPIWIN SRC model.

Reliability criteria - 2f (accepted method of calculation).

Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

3.1.1 Photodegradation

Type: other

Remark: The official value adopted by the Kyoto protocol (1995) for HCFC-124 global warming potential (GWP) relative to carbon dioxide is 470 for an integration time horizon (ITH) of 100 years.

The most recently (2001) calculated GWP, relative to carbon dioxide, is 620.
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (30)

Type: other

Remark: The Global Warming Potential of HCFC-124 is 0.1 (where CFC-11 = 1.0)
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (1)

Type: other

Remark: HCFC-124 Global warming potential estimated by the method of de Leeuw, 1993 gives a value of 0.19 where CFC-11 is 1.0.
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (13)

Type: other

Remark: Estimates of ozone depletion potential (ODP) of HCFC-124 using 3 different atmospheric models give results of 0.016, 0.020 and 0.034.

The "semi-empirical" ODP of HCFC-124 is 0.022 (where CFC-11 = 1.0) and is the value adopted by the Montreal Protocol for regulatory purposes.
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (53)

Type: air
Light source: Xenon lamp
Conc. of subst.: at 25 degree C
INDIRECT PHOTOLYSIS
Sensitizer: other: Chlorine
Degradation: = 33 % after 28 minute(s)

GLP: no data

Remark: Mixture of CHClCF3 (1.23 E+14 molecules/cm3) and Cl2 (2.0 E+14 molecules/cm3) irradiated.

Experiments conducted at 298 +/- 2K and 740 Torr of synthetic air (80% nitrogen and 20% oxygen).
Irradiation time 15-130 minutes (variable for different HFCs or HCFCs.)

33 and 62% reaction after 28 and 36 minutes, respectively.
Single breakdown product, CF3C(O)F, accounted for total breakdown.

The production of a single breakdown product is consistent with an earlier publication showing the same.

Reliability criteria - 1d (test procedure in accordance with generally accepted scientific standards and described in sufficient detail).

Source: Daxa Borkhataria Northaw
Test condition: Radiation provided by 24 kW xenon-arc, wavelengths <= 300 nm removed.
Reliability: (1) valid without restriction
30-SEP-2003 (51)

Type: air
Light source: Xenon lamp
Conc. of subst.: at 25 degree C
INDIRECT PHOTOLYSIS
Rate constant: ca. .0000000000000027 cm^3/(molecule * sec)

GLP: no data

Remark: Photolysis of Cl-HCFC-124-methane (reference compound) in air was conducted at 740 Torr and 298 +/- 2K.
A relative rate technique was used to determine rate constants for the Cl atom reaction.
HCFC-124 was investigated with a series of other HCFC/HFCs.

Concentration range used (exact values not given)
HCFC-124: 1.2-7.2 E+14 molecules/cm3
Cl2: 4.1-16 E+14 molecules/cm3
Methane: >= 2.4 E+14 molecules/cm3
Irradiation period 15-100 min.

The relative rate reaction constant (HCFC-124/methane) was determined to be 0.0271 +/- 0.0010.
Using the known rate constant for the Cl atom and methane reaction (1.0 +/- 0.2 E-13 cm3/molecule.s) at 298 K, rate constant for the HCFC-124-Cl reaction was calculated as 2.7 +/- 0.6 E-15 cm3/molecule.s.

Reliability criteria - 1d (Test procedure in accordance with generally accepted scientific standards and described in sufficient detail.)

Source: Daxa Borkhataria Northaw
Test condition: Radiation provided by 24 kW xenon-arc, filtered to provide wavelengths > 300 nm.
Reliability: (1) valid without restriction
30-SEP-2003 (52)

Type: air
Light source: other: 96 fluorescent lamps (72 black-light and 24 sun lamps)
Conc. of subst.: at 25 degree C

GLP: no data

Remark: The method does not specify concentration of HCFC-124 and Cl2 that were used. Typical conditions consisted of irradiating cell contents for 20 min., collecting IR spectra every 5 min., at a cell temperature of 25 +/- 3 degrees C. From the IR spectrum obtained, one major carbon containing product was detected and quantified.

CF3CF(O) was the only product and accounted for yield of 1.00 +/- 0.04. Absence of other bands in the IR spectrum, other than CF3CF(O) and HCl, suggested scission of the C-C bond was insignificant.

Reliability criteria - 2e (study well documented, meets generally accepted scientific principles, acceptable for assessment).

Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (16)

3.1.2 Stability in Water

Method: other:

Remark: No experimental data are available.
Volatisation half-lives in surface waters of rivers and lakes were calculated using the EPIWIN model with input values for water solubility (1450 mg/L), vapour pressure (2888 mm Hg):

	River	Lake
Water Depth (m)	1	1
Wind velocity (m/sec)	5	0.5
Current velocity (m/sec)	1	0.05
Half-life (hours)	1.2	111

Reliability criteria - 2f (accepted calculation method).

Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

3.1.3 Stability in Soil

Type: other:

Remark: No experimental data are available.

Given its low boiling point and its low log Pow value, HCFC-124 will evaporate into the atmosphere. See also transport between environmental compartments (3.3.1)

Source: Daxa Borkhataria Northaw
03-DEC-2002

3.2.1 Monitoring Data (Environment)

3.2.2 Field Studies

3.3.1 Transport between Environmental Compartments

Type: volatility
Media: other
Air: 99.9856 % (Fugacity Model Level I)
Water: .0132 % (Fugacity Model Level I)
Soil: .0012 % (Fugacity Model Level I)

Remark: As HCFC-124 is a gas, it is expected to move to air from soil.

The level III Fugacity Model has been run with the following input parameters:-

Vapour pressure	3.85 e+05 Pa
Temperature	25 degrees C
Henry's Law constant	9413 Pa.m3/mol
Water solubility	5583 g/m3 (40.9 mol/m3)
Air reaction half-life	37039 h
Reaction half-life	1.00 e+11 (all other environment)
Log Kow	1.94
Emission	3000 kg/h to air alone

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (%)	Advection (%)
Air	1.83e-7	0.112	3000	3.74e-3	100
Water	1.36e-7	3.47e-12	5.01e-4	1.16e-13	1.67e-15
Soil	1.85e-7	1.02e-12	0	3.39e-14	0
Sediment	1.46e-7	2.77e-15	8.01e-9	9.25e-17	2.67e-10

Residence time
Total = 2.00 h
Reaction = 53453 h
Advection = 2.00 h

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

3.3.2 Distribution

Media: other: soil adsorption
Method: other (calculation)

Remark: Soil Koc = 29.7
Calculated using EPIWIN.

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, domestic
Contact time: 28 day(s)
Degradation: ca. 2 % after 28 day(s)
Control Subst.: other: sodium n-dodecylsulfate
Kinetic: 28 day(s) 93 %

Method: Directive 84/449/EEC, C.6 "Biotic degradation - closed bottle test"
Year: 1992
GLP: no data

Remark: The activated sludge contained 46000000 bacteria/mL. One drop was added to 1 litre of final volume.
100 mL test solution, cultivated in the dark at 20 degrees C for 28 days.

2% biodegradation assessed by two methods (direct GC measurement of HCFC-124 and biochemical oxygen demand).

Reliability criteria - 1b (comparable to guideline study).
Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99.99%.
Reliability: (1) valid without restriction
30-SEP-2003 (49)

Remark: Calculated fate in wastewater treatment facility using STP Fugacity model in EPIWIN with following input values:-

Water solubility (mg/L)		1450
Vapour pressure (Pa)		385035
	(atm)	3.8
	(mm Hg)	2888
Henry's Law Constant (atm.m3/mol)		0.358
Air-water partition coefficient		14.6
Octanol-water partition coefficient (Kow)		72.4
Log Kow		1.86
Biomass to water partition		15.3
Temperature (deg C)		25

Total biodegradation = 0.02%.

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

Remark: No experimental data are available.

Biodegradability was calculated with the BIOWIN model.
Linear biodegradation probability is 0.051.
Non-linear biodegradation probability is 0.0016.
Both values indicate HCFC-124 does not biodegrade fast.

Primary and ultimate biodegradation is 3.3 and 2.2, respectively and indicates biodegradation is in a period of

weeks (primary) and months (secondary).

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

3.6 BOD5, COD or BOD5/COD Ratio

Method: other
Year:
Method:
Remark: No experimental data are available.
Source: Daxa Borkhataria Northaw
19-JUN-2002

3.7 Bioaccumulation

BCF: = 5.4

Remark: BCF calculated using EPIWIN model and estimated Log Kow of 1.86.

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (18)

BCF: = 6.22

Remark: BCF calculated using EPIWIN model and measured Log Kow of 1.94.

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
04-JUL-2003 (17)

3.8 Additional Remarks

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: other: calculated
Species: other: fish
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: ca. - 137 calculated

Remark: Calculated using the ECOSAR program in EPIWIN model.
Input values - water solubility (1450 mg/L), vapour pressure (2888 mm Hg), boiling point (-12 deg C), melting point (-199 deg C) and log Kow (1.86, estimated).

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

Type: static
Species: other: Brachydanio rerio (Zebra fish)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 126 - measured/nominal

Method: other: ISO Standard 7346/1 (1984); OECD Method 203 4 April 1984 and EEC Directive 84/449, Method C1
Year: 1989
GLP: yes
Test substance: other TS

Remark: Groups of 20 fish and nominal test concentrations of 60, 120 and 264 mg/mL were used.
Survival was noted at 24, 48, 72, and 96 hours from initiation of the study. There was no renewal of test substance.
LC50 values are estimated using the nominal test concentration although actual concentration at 96 hr was estimated using gas chromatography.
Result: Highest non-lethal level at 24 hours - 96 mg/ and at 48-96hours <60 mg/L.
Estimated LC 50 for 24 hr - 276 mg/L, 48 hr - 192 mg/L, 72 hrs -174 mg/L and 96 hrs - 126 mg/L.

The actual test concentrations measured at 96 hours were 66.8 mg/mL (nominal 60 mg/mL), 100.8 mg/mL(nominal 120 mg/mL) and 200.4 mg/mL (nominal 264 mg/mL).

Reliability criteria: 1
Source: Daxa Borkhataria Northaw
Test substance: 1,1-dichloro-1-fluoroethane (CAS no 1717-00-6; HCFC-141b), purity >99.5%
Reliability: (1) valid without restriction
30-SEP-2003 (7)

Type: other: semistatic (renewal each 24 hours)
Species: other: Poecilia reticulata (guppies)
Exposure period: 96 hour(s)

Unit: Analytical monitoring: yes

Method: other: OECD guideline 203 (1984) and EPA guidelines 72-1 (1982)
Year: 1990
GLP: yes
Test substance: other TS

Remark: 3200 mL test flasks completely filled with ISO water and tightly closed with aluminium stoppers with rubber septum.
Renewal of the test solutions each 24 hours.
Number of replicates, fish per replicate: 8 fish per concentration using 2 replicates of 4.
Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed
pH variations: around 7 over 28 days in the control and test samples
Dissolved oxygen: below 5 mg/l at high concentrations (170 and 300mg/L).
Test temperature range: 22 ± 1°C

Result: Nominal concentrations (as mg/L): 0, 30, 53, 94, 170, 300
Measured concentrations (as mg/L): 0, 33, 56, 106, 189, 321 (mean measured concentrations)
Unit: results expressed in mg/L
EC50 = 220 mg/L at 96 hours based on the mean measured concentrations
NOEC = 110 mg/L based on the mean measured concentrations
STATISTICAL RESULTS: 95% confidence interval 190-310 mg/L

Mortality of guppies
Control: 1/8 fish died at 96 hours
33 mg/L: 0/4
56 mg/L: 0/8
106 mg/L: 0/8
189 mg/L: 1/8 died at 24 hours
321 mg/L: 8/8 died at 24 hours (4/8 were dead within 5 hours).

CONCLUSIONS
Based on this key study, 1-chloro-1,1-difluoroethane (HCFC 142b) is of low toxicity to fish.

Reliability Criteria: 2e (4 fish used instead of 5 and oxygen content low at high test concentration).

Source: Daxa Borkhataria Northaw
Test substance: 1-chloro-1,1-difluoroethane (CAS no 75-68-3; HCFC-142b), purity >99.99 %
Reliability: (2) valid with restrictions
30-SEP-2003 (22)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: other: calculated
Species: other: Daphnid
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC50: ca. - 145 calculated

Remark: Calculated using the ECOSAR program in EPIWIN model.

Input values - water solubility (1450 mg/L), vapour pressure (2888 mm Hg), boiling point (-12 deg C), melting point (-199 deg C) and log Kow (1.86, estimated).

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

Type: other: calculated
Species: other: Mysid shrimp
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC50: ca. - 44 calculated

Remark: Calculated using the ECOSAR program in EPIWIN model.
Input values - water solubility (1450 mg/L), vapour pressure (2888 mm Hg), boiling point (-12 deg C), melting point (-199 deg C) and log Kow (1.86, estimated).

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC50: = 31.2 - measured/nominal

Method: other: French standard T 90 301 Jan 1983; OECD Method 202, 4 April 1984 and EEC Directive 84/449, Method C
Year: 1989
GLP: yes
Test substance: other TS

Remark: Four replicates containing five daphnia each were exposed to the nominal concentrations of 25.4, 38.1, 63.5 and 114.3 mg/L. As the test substance was volatile, the jars were sealed. At the end of the 48 hour exposure period, the level of HCFC 141b was determined by gas chromatographic analysis.
Recovery ranged from 83.9 to 95.7% of nominal concentration.

Reliability criteria: 1
Source: Daxa Borkhataria Northaw
Test substance: 1,1-dichloro-1-fluoroethane (HCFC-141b; CAS no 1717-00-6), purity >99.5%
Reliability: (1) valid without restriction
30-SEP-2003 (8)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: yes
EC50: = 160 - measured/nominal

Method: other: OECD guideline 202 (1984) and EPA Guideline 72-2 (EPA,

1982)
Year: 1990
GLP: yes
Test substance: other TS

Remark: Test design: 30 daphnids per concentration using 3 replicates of 10. Immobilisation was checked after 15 minutes, 24 hours and 48 hours
Method of calculating mean measured concentrations: arithmetic mean measured concentrations in 1hour sample
Exposure period: 48 h
Analytical monitoring: Gas Chromatography with flame ionisation detector
The mean response factor of all calibration was 1.85 with a coefficient of variation of 7 %(n=40; 3 point calibration).
Result: Nominal concentrations : 30, 53, 94 , 170, 300 mg/l
Measured concentrations : 33, 58, 106,197, 348 mg/l (in 1h samples)
Unit : mg/l
EC50 : 160 at 48 hours
NOEC : 106

Statistical results : 95 % Confidence Interval : 70 - 200

Biological observations
Number immobilized (%) at 48 h:

Control	22
33 mg/L	37
58 mg/L	25
106 mg/L	41
197 mg/L	75
348 mg/L	100

The control mortality was higher than expected. A few daphnids were stuck between the water level and the rubber septum at test termination, caused by the method used to minimise the evaporation of the test material. No other abnormalities were observed after 48 hours.

CONCLUSION

On the basis of this key study, 1-chloro-1,1-difluoroethane (HCFC 142b) is of low toxicity to daphnia

Reliability criteria: 2e (because of the control mortality).
Source: Daxa Borkhataria Northaw
Test substance: 1-chloro-1,1-difluoroethane (HCFC-142b; CAS No 75-68-3), purity >99.9%
Reliability: (2) valid with restrictions
30-SEP-2003 (21)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: yes

Method: other: OECD guideline 202 (1984) and EPA Guideline 72-2 (EPA, 1982)
Year: 1989

GLP: yes
Test substance: other TS

Remark: Test design: 20 daphnids per concentration using 2 replicates of 10. Immobilisation was checked after 24 hours and 48 hours
Method of calculating mean measured concentrations: no immobilisation observed during the test
Exposure period: 48 h
Analytical monitoring: Gas Chromatography using head space analysis
Result: Nominal concentrations: no indication
Measured concentrations (at the beginning and at the end of the test) : 8, 14, 20,40, 69, 110, 190 mg/l
EC50 : at 48 hours no immobilisation up to 190 mg/l.
Statistical results : -

Reliability criteria: 2e (not enough documented).
Source: Daxa Borkhataria Northaw
Test substance: 1-chloro-1,1-difluoroethane (HCFC-142b; CAS No 75-68-3), purity >99.9%
Reliability: (2) valid with restrictions
30-SEP-2003 (14)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: other algae
Endpoint: other: calculated
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC10: - calculated
EC50: ca. - 90

Remark: Calculated using the ECOSAR program in EPIWIN model.
Input values - water solubility (1450 mg/L), vapour pressure (2888 mm Hg), boiling point (-12 deg C), melting point (-199 deg C) and log Kow (1.86, estimated).

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

Species: Selenastrum capricornutum (Algae)
Exposure period: 72 hour(s)

Method: other: OECD Guideline 201 (1984); EPA guideline 40 CFR Part 797 & 1060 (1989)
Year: 1991
GLP: yes
Test substance: other TS

Remark: The test was conducted under static conditions in a sealed apparatus. Difficulty was experienced in dissolving the HCFC 141b in the test medium resulting in large differences between nominal and analytical concentrations. As a result, 44 mg/L was the highest achievable level. Results were based on analytical determinations.

Concentrations tested 16, 20, 35 uL/L (35uL/L equivalent to 44 mg/L).
Result: The 72 hour no-observed effect concentration for both growth rate and biomass for algae was >44 mg/L (>35 uL/L).

Reliability criteria: 1
Source: Daxa Borkhataria Northaw
Test substance: 1,1-dichloro-1-fluoroethane (HCFC-141b; CAS no 1717-00-6), purity >99.5%
Reliability: (1) valid without restriction
30-SEP-2003 (20)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: other:

Remark: No data available.
Source: Daxa Borkhataria Northaw
19-JUN-2002

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Method: other:

Remark: No data available.
Source: Daxa Borkhataria Northaw
05-JUN-2002

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Method: other:

Remark: No data available.
Source: Daxa Borkhataria Northaw
05-JUN-2002

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

Method: other:

Remark: No data available.
Source: Daxa Borkhataria Northaw
05-JUN-2002

4.6.2 Toxicity to Terrestrial Plants

Method: other:

Remark: No data available.
Source: Daxa Borkhataria Northaw
05-JUN-2002

4.6.3 Toxicity to Soil Dwelling Organisms

Type: other: calculated
Species: other soil dwelling worm
Exposure period: 14 day(s)
Unit: mg/kg soil dw
LC50: ca. - 927 calculated

Method: other:

Remark: Calculated using the ECOSAR program in EPIWIN model.
Input values - water solubility (1450 mg/L), vapour pressure (2888 mm Hg), boiling point (-12 deg C), melting point (-199 deg C) and log Kow (1.86, estimated).

Reliability criteria - 2f (accepted calculation method).
Source: Daxa Borkhataria Northaw
Reliability: (2) valid with restrictions
30-SEP-2003 (17)

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

Method: other:

Remark: No data available.
Source: Daxa Borkhataria Northaw
05-JUN-2002

4.7 Biological Effects Monitoring

Memo: No data available

Source: Daxa Borkhataria Northaw
05-JUN-2002

4.8 Biotransformation and Kinetics

Type: other:

Remark: No data available.
Source: Daxa Borkhataria Northaw
05-JUN-2002

4.9 Additional Remarks

Memo: See remarks.

Remark: Due to the specific physical chemical properties of HCFC-124, aquatic and terrestrial toxicity tests have not been performed. In order to achieve and maintain adequate

test concentrations, specific containment techniques would need to be used (semi static, flow through, closed vessel without head space etc.). Use of such systems would likely lead to changes (lack of carbon dioxide in algal media, oxygen depletion in closed vessels etc.) and hence give artefact results. In addition, such conditions would not represent natural environmental conditions.

Source: Daxa Borkhataria Northaw
06-MAY-2003

Source: Daxa Borkhataria Northaw
05-JUN-2002

5.0 Toxicokinetics, Metabolism and Distribution

In Vitro/in vivo:	In vivo
Type:	Metabolism
Species:	other: rats, mice and hamsters
Doses, males:	Rats - 500, 1,000, 2,000, 5,000 or 10,000 ppm Mice and hamsters 1,000, 5,000 or 10,000 ppm
Vehicle:	other: air
Exposure time:	6 hour(s)

Remark: HCFC-124 uptake pharmacokinetics and metabolism were investigated in male animals.
Rats and hamsters were exposed individually and mice in groups of 6 in a 1.67 L closed-chamber re-circulating system. Immediately after the end of exposure the rodents were placed in metabolism cages and urine collected for 24 hours. Urinary trifluoroacetic acid concentrations were determined. Various tissue:air partition coefficients were determined.

Data were analysed with Student's t test (unpaired), with $p<0.05$ used for acceptance or rejection of the null hypothesis.

Partition coefficients (rat, mouse, hamster, respectively)
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
Additionally,
0.9% saline:air was 1.05 and olive oil:air was 25.2

Animal HCFC-124 uptake was quantified as the decrease in chamber concentration with time. Simulation of the observed uptake were used to provide kinetic constants. 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 were (rat, mouse, hamster, respectively):

Michaelis-Menten constant, Km (mg/L, [mmol/L])
1.2 [8.79], 1.2 [8.79], not applicable
maximum velocity, Vmax (mg/kg.hr [mmol/kg.hr])
0.35 [2.56], 1.78 [13.0], not applicable
first rate constant, k (/kg.hr)
1.25, 4.08, 1.47

The excretion of trifluoroacetic acid (TFA) increased with increasing HCFC-124 exposure concentrations. Simulated production and excretion of TFA, using metabolic constants, provided a good fit for rat and mouse data. Hamster data

could not be satisfactorily simulated - possible reasons for this could be the lack of data on physiological parameters, and the considerable variation in urine volumes.

The observed species differences provide useful information in assessing the risks to humans and in designing future

experiments. Tissue dosimetry is dependent on body uptake and the data are important in risk assessment. The blood:air partition is therefore an important parameter in determining the amount of chemical that can be taken up by the body during inhalation exposure.

Reliability criteria - 1d (Test procedure in accordance with generally accepted scientific standards and described in sufficient detail).

Source: Daxa Borkhataria Northaw
Test substance: HCFC-124, purity not given.
Reliability: (1) valid without restriction
30-SEP-2003 (34)

In Vitro/in vivo:	In vivo
Type:	Metabolism
Species:	rat
No. of animals, males:	6
Doses, males:	1.0 % (10,000 ppm)
Vehicle:	other: air
Exposure time:	6 hour(s)

GLP: no data

Remark: Male Fischer 344 rats were used: in the same study rats were similarly exposed to halothane (1.1%, n=6), HCFC-123 (1.1%, n=6), HCFC-125 (0.97%, n=6) and HCF-134a (1%, =3). Chamber oxygen depleted during exposure was supplemented. After the end of exposure, animals were placed in metabolism cages, 12 hour urine collected and stored frozen until analysis by 19F-NMR. At the end of 12 hours, animals were sacrificed and liver microsomes prepared. Proteins were separated by SDS-PAGE and immunoblotted with anti-TFA-protein serum.

HCFC-124 has been studied with the other halocarbons due to structural similarities (all contain a geminal dihalomethyl group [-CHX2]) with halothane, a known hepatotoxin. Only the results for HCFC-124 and it's comparison to the other compounds is discussed here.

Trifluoroacetic acid (TFA) was excreted in urine following 6 hour exposure to 1% HCFC-124 - 15.6 umol/12hour/kg. TFA excretion rank order HCFC-123=halothane>HCFC-124>HCFC-125.

HCFC-124 showed a pattern of TFA-proteins (microsomal and cytosolic) similar to that seen following halothane exposure, although the immunoreactivity of individual bands was lower. TFA-protein formation rank order halothane=HCFC-123>>HCFC-124>HCFC-125.

A predictive model for hydrogen atom abstraction was used to calculate enthalpies of activation for the compounds. The calculated enthalpy values correlated well with the observed TFA excretion.

The proposed bioactivation scheme for halothane and HCFC-124 is: cytochrome P-450 catalyzed hydrogen abstraction to yield the intermediate 1,1-dihalo-2,2,2,-trifluoroethyl radical: oxygen rebound would give the geminal halohydrin: loss of HX

would give trifluoroacetylchloride or fluoride which may undergo oxidation to give TFA or may react with nucleophilic sites in proteins to give TFA-protein.

The data support the theory that cytochrome P-450-catalyzed formation of halohydrins is the rate-limiting step in the production of TFA and TFA-protein adducts. The data demonstrates increasing fluorination on the dihalomethyl group (CHX2) decreases in vivo metabolism.

Reliability criteria - 1d (Test procedure in accordance with generally accepted scientific standards and described in sufficient detail).

Source: Daxa Borkhataria Northaw
Test substance: HCFC-124, purity not given.
Reliability: (1) valid without restriction
30-SEP-2003 (23)

In Vitro/in vivo:	In vivo
Type:	Excretion
Species:	rat
No. of animals, males:	2
Doses, males:	1% (10,000 ppm)
Vehicle:	other: air
Exposure time:	2 hour(s)

GLP: no data

Remark: Fischer rats, 200g, were individually exposed in a small exposure chamber, which was periodically "topped up" with oxygen. Following the end of exposure, animals were immediately transferred into a metabolism cage, 20 hour urine collected and stored frozen until analysis by 19F-NMR.

During the exposure, chamber concentrations of HCFC-124 decreased with time, with similar rates of decrease between 30-90 minutes of the 2 hour exposure. The reduction demonstrates uptake by the rat.

The 19F-NMR analysis showed the urine sample contained trifluoroacetic acid (TFA, 156 umol) and fluoride (not quantified). No other metabolites were detected. Average excretion rate of 1.3 umol of TFA/24 hours was estimated.

Reliability criteria - 1d (Test procedure in accordance with generally accepted scientific standards and described in sufficient detail).

Source: Daxa Borkhataria Northaw
Test substance: HCFC-124, 1,1,1,2-tetrafluoro-2-chloroethane. Gas phase purity >99.7%.
Reliability: (1) valid without restriction
30-SEP-2003 (40)

In Vitro/in vivo:	In vitro
Type:	Metabolism
Species:	rat

GLP: no data

Remark: Hepatic microsomes from Fischer 344 male rats, untreated, pretreated with pyridine (100mg/kg daily for 5 days) or

phenobarbital (0.1% in drinking water for 7 days), were prepared.

Microsomal incubations with HCFC-124 were performed to assess the effect of heat, CO, NADPH, HCFC-124 concentration in the headspace above the microsomes, addition of anti-P450IIE1 and reduced oxygen tension. The supernatant was analysed by potentiometry (fluoride) and/or 19F-NMR (organic).

Defluorination: heat and CO-sensitive and NADPH dependant.
Three metabolites identified following aerobic microsomal metabolism (pyridine pretreated rats) - fluoride, trifluoroacetic acid (TFA) and unknown.
The in vitro data demonstrate HCFC-124 is biotransformed at low rates via oxidative (24.2% exposure concentration, 0.8 nmol fluoride/mg protein/15min) and reductive P-450 mediated pathways.
Urinary excretion of TFA in vivo, verifies the in vitro oxidative metabolism.
Induction of P450 IIE (by pyridine) greatly increased rates of defluorination (24.2% exposure concentration, 4.9 nmol fluoride/mg protein/15 min), whilst induction of P450 IIB1 and P450 IIB2 (by phenobarbital) marginally suppressed defluorination.
Metabolism in vitro decreased in microsomes containing antibodies to P450 IIE1.
The data suggest that P450 IIE1 is efficient at the oxidative metabolism of HCFC-124.

Reliability criteria - 1d (Test procedure in accordance with generally accepted scientific standards and described in sufficient detail).

Source: Daxa Borkhataria Northaw
Test substance: HCFC-124, purity >99.7%.
Reliability: (1) valid without restriction
30-SEP-2003 (40)

Type: Metabolism

Remark: Predictions of possible metabolism of HCFCs are made in this publication. It contains no data on HCFC-124, but postulates possible metabolism based on structure.

HCFC-124 is structurally similar to HCFC-123 (1,1-dicholor-2,2,2-trifluorethane) and halothane (2-bromo-2-chlro-1,1,1-trifluoroethane) and both these have been shown to have:
i) same urinary metabolite (trifluoroacetic acid),
ii) same trifluoroacetylated microsomal and cytosolic proteins (N-trifluoroacetyllysine)
iii) same immunoreactions with polyclonal, hapten-specific antitrifluoroacetyl protein antibodies.

The publication postulates the metabolic fate of HCFC-124, will be analogous to that described for HCFC-123 and halothane. There is insufficient data to predict rates of metabolism, although generally metabolism decreases with increasing fluorination.

Reliability criteria - 4b (Secondary literature).
Source: Daxa Borkhataria Northaw
Reliability: (4) not assignable
30-SEP-2003 (6)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

5.1.2 Acute Inhalation Toxicity

Type: other: approximate lethal concentration (ALC)
Species: rat
Strain: other: Crl: CD BR
Sex: male
No. of Animals: 24
Vehicle: other: air
Doses: 48,000; 160,000; 230,000 and 300,000 ppm
Exposure time: 4 hour(s)
Value: ca. 230000 - 300000 ppm

Method: other
Year: 1990
GLP: yes

Remark: Four groups of 6 rats/group were exposed, nose-only for a single 4 hour period to HCFC-124.

Rats were weighed prior to exposure and were observed for clinical signs of toxicity during and immediately after exposure. Rats were weighed and observed daily for 14 days post-exposure (except weekends).

Chamber HCFC-124 concentrations (measured every 30 min.) were found to be close to target (overall range 88-106%), with a maximum coefficient of variability of 6%.

300,000 ppm - all six rats died during exposure.
48,000; 160,000 and 230,000 ppm - no deaths.
160,000 and 230,000 ppm - rats showed depressed acoustic-startle and tail-pinch response. Immediately following exposure, rats showed clinical signs of toxicity including incoordination, lethargy and prostration.
48,000 ppm - no clinical signs of toxicity during or immediately following exposure.

All exposure groups showed slight (<10g) to moderate (10-20 g) weight loss on the day following exposure. One rat exposed to 48,000 ppm HFCF-124 that appeared to have been injured by its cage mate, exhibited severe (>20g) weight loss on the day following exposure. Thereafter all rats had a normal weight gain rate (approximately 5-10 g per day).

Based on 4-hour exposure, the ALC was between 230,000 and 300,000 ppm.

Reliability criteria - 1b (Comparable to guideline study, GLP).

Critical study for SIDS endpoint.
Source: Daxa Borkhataria Northaw
Test substance: HCFC-124, purity >99.9%.
Reliability: (1) valid without restriction
07-OCT-2003 (19)

Type: LC50
Species: rat
Strain: no data
Sex: male
No. of Animals: 30
Vehicle: other: air
Doses: 0 (air control), 100,000 and 360,000 ppm
Exposure time: 6 hour(s)
Value: > 360000 ppm

Method: other: not stated
Year: 1976
GLP: no data

Remark: Two groups of 10 rats/group were exposed to HCFC-124. A third group was treated similarly with air (control).

Rats were observed during exposure and for a 14-day post exposure period. Rat weights were recorded immediately prior to exposure, and post exposure on days 8 and 15 (fasted weight on day 15). At day 15 all animals were sacrificed and necropsied.

No deaths occurred at 100,000 or 360,000 ppm, however, no more material was available to test higher concentrations.

Air control. All rats were normal during exposure and the 14 day post-exposure period.

HCFC-124 exposure. Rats in 100,000 ppm group active for first 30 minutes of exposure then inactive for remainder of time. Rats in 360,000 ppm group, inactive for first 60 minutes, then anaesthetised. During 14 day post-exposure period, all rats appeared normal.
Gross pathology revealed no exposure related changes.
There was no sign of HCFC-124 having an affect on weight gain.

None of the effects noted were considered to be toxic.
Since no animals died a LC50 could not be assigned.

Reliability criteria - 2e (well documented, meets generally accepted scientific principles, acceptable for assessment).
Source: Daxa Borkhataria Northaw
Test substance: G124, purity not given.
Reliability: (2) valid with restrictions
30-SEP-2003 (33)

Type: other: Anaesthetic activity and fatality
Species: mouse
Strain: no data
Sex: male
No. of Animals: 36
Vehicle: other: air

Doses: 10.65, 13.36, 15.26, 17.40, 19.95% and 39.9, 42.5, 45.9 and 48.3%
Exposure time: 10 minute(s)

Method: other
Year: 1977
GLP: no

Remark: Groups of 4 mice were exposed at various concentrations for 10 minutes to determine the approximate anaesthetic concentration (AAC) (10.65-19.95%) and approximate lethal concentration (ALC) (39.9% and 48.3%) .

AAC is given as 15%, with no effect at 10.65%.
ALC is given as 44%, with no effect at 39.9%

Reliability criteria - 3a (documentation insufficient for assessment).
Source: Daxa Borkhataria Northaw
Test substance: F-124, purity not given.
Reliability: (3) invalid
30-SEP-2003 (12)

Type: other: determination of anaesthetic concentration
Species: dog
Strain: other: strain not specified
Sex: no data
No. of Animals: 6
Vehicle: other: oxygen

Method: other
GLP: no data
Test substance: no data

Remark: HCFC-124 was investigated along with a series of other fluorinated compounds, in this 1960 published study.

Six dogs unselected for age, sex or weight were used. They were exposed through a cuffed endotracheal tube with a non-rebreathing valve. Electroencephalogram and electrocardiogram were recorded continuously. Duration of anaesthesia varied from 10-90 minutes.

HCFC-124 caused anaesthesia at 40-70%, with a dose dependent depression of blood pressure. Atropine had little effect on the hypotension. Phenylephrine (0.1 mg) partially reversed the hypotension, caused several premature contractions but did not cause ventricular fibrillation. Epinephrine (iv, 2-8 ug/kg) produced similar effects.

Reliability criteria - 3b (significant methodological deficiencies).
Source: Daxa Borkhataria Northaw
Test substance: 1,1,1,2-tetrafluoro-2-cholorethane, purity not given.
Reliability: (3) invalid
30-SEP-2003 (42)

5.1.3 Acute Dermal Toxicity

5.1.4 Acute Toxicity, other Routes

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

5.2.2 Eye Irritation

5.3 Sensitization

5.4 Repeated Dose Toxicity

Type:	Chronic	
Species:	rat	Sex: male/female
Strain:	other: Crl: CD BR	
Route of administration:	inhalation	
Exposure period:	5/days a week for 24 months	
Frequency of treatment:	6 hours/day	
Post exposure period:	None	
Doses:	0, 2000, 10000, 50000 ppm	
Control Group:	yes	
NOAEL:	= 50000 ppm	

Method: other: EPA OTS 798.3320 and OECD test guidelines 453
Year: 1995
GLP: yes

Remark: Four groups of 87 rats per sex, per group were exposed. Four 4000 L chambers made of stainless steel and glass were used. Chambers were operated in a one-pass flow-through mode with the air flow rates adequate to maintain sufficient oxygen (approx. 19%). Animal cages placed within the chamber for exposure were rotated daily.

Body weights were recorded weekly for first three months and then every other week till study end. Food consumption was monitored weekly. Clinical signs of toxicity were monitored through out the study. An ophthalmological examination was performed on all animals prior to study start and at 3, 12 and 24 months. At 3, 6, 12, 18 and 24 months hematology, clinical chemistry and urinanalysis was performed on 10 rats/sex/group. The rats used for the 12 month clinical pathology also underwent an study interim sacrifice. All surviving rats were necropsied at 24 months. Selected tissues were weighed and tissues collected for microscopic evaluation.

STATISTICAL METHODS - Body and organ weights, body weight gains and clinical laboratory measurements were analysed by one-way analysis of variance. If group mean differences were significant (F-test), Dunnett's test was used to make pairwise comparisons between test and control.
Incidence of clinical observations was evaluated by the Cochran-Armitage test for trend. If the trend was positive for the intermediate and high groups ($p<0.05$), incidence observed in the lowest concentration group was compared to

control using the Fisher's Exact test. Survival among groups was compared with the Cochran-Armitage test and the Fisher's Exact test.
Bartlett's test for homogeneity of variance was performed on clinical laboratory data and organ weights and when results were significant, the Kruskal-Wallis test (clinical laboratory) and the Mann-Whitney U test (organ weight) was used to compare group means to control.
The Cochran-Armitage trend test was applied to all microscopic observations in those cases where all tissues were evaluated in a group. If the trend was positive for the intermediate and high groups ($p<0.05$), the lowest group were compared to control using Fisher's Exact test. For tissues not examined microscopically in all groups, Fisher's Exact test was used to compare lesion incidences in the control and the high group. If $p<0.05$, for a lesion in a given tissue, then it was microscopically evaluated in all animals and exposure groups, unless scientifically deemed unwarranted. When all tissues had been evaluated, the incidence of lesions in question were evaluated using the Cochran-Armitage trend test. When there was significant lack of fit (LOF<0.05) for the Cochran-Armitage trend test, Fisher's exact test with Bonferroni correction was used to compare test groups to control. Data were maintained separately by sex. Tests were judged significant at $p = 0.05$ (except Bartlett's test, alpha = 0.005).

CHAMBER CONCENTRATIONS - Overall mean chamber concentrations were close to nominal: 0, 2,020, 10,000 an 50,095 ppm. Mean daily temperature (21-22 degrees C) and mean daily relative humidity (54-55%) were similar for the four chambers.

BODY WEIGHT, FOOD CONSUMPTION AND EFFICIENCY - Mean cumulative body weight gains were significantly higher in

males at 10,000 (11%) and 50,000 ppm (9%) and females at 2,000 (17%), 10,000 (24%) and 50,000 ppm (14%). A dose-related trend was not apparent in either gender for cumulative weight gain or absolute weight and therefore the differences are considered not to be compound related. There were no compound related effects on food consumption or food efficiency in either gender.

CLINICAL OBSERVATIONS AND LABORATORY EVALUATIONS - Animal responsiveness to an alerting sound during exposure was similar in all exposure groups, including control. There were no adverse, compound related effects on the incidence of clinical observations or survival at any exposure concentration. There were no compound related effects on the eye at any exposure level (ophthalmoscopically visible or morphological changes).

There were no adverse, compound related effects on serum hormone (estradiol, follicle stimulating hormone (FSH), luteninizing hormone (LH) and testosterone (males only)) concentrations at any exposure concentration in the 1 week, 3, 6 and 12 month evaluations. Serum testosterone was significantly higher in the 50,000 ppm males at the 1 week evaluation and in the 10,000 ppm males at the 6 month evaluation. Serum FSH was significantly higher at 3 month

evaluation for 50,000 ppm males. In females, significantly higher estradiol values were noted for the 50,000 ppm group at the 3 month evaluation. Serum LH was significantly higher in the 2,000 ppm females at the 1 week evaluation. Serum FSH was significantly lower in the 2,000; 10,000 and 50,000 ppm females at the 3 month evaluation. Statistically significant differences when observed, were not dose-related, nor sustained throughout the study and therefore considered not to be compound related.
There were no compound related changes in hematology parameters at any exposure concentration. Statistically significant differences were not substantiated by changes in related parameters, were not dose-related or sustained through to study end.

Compound related adverse effects on clinical chemistry parameters did not occur at any exposure concentration. Group mean serum triglyceride levels at 3 months were slightly lower (not significant) than control in 10,000 and 50,000 ppm exposed males and there was a dose-related trend, suggesting a possible compound related effect. At 24 months, serum triglycerides were significantly higher and lower in males exposed to 10,000 and 50,000 ppm HCFC-124, respectively. Since a dose relation was not evident at 24 month, the effect small and not sustained through the study, the effect was considered biologically unimportant. Quantitative data were not available.

Urinary fluoride concentrations were significantly higher than controls in at all exposure concentrations and at each sampling time. At the 12 month evaluation, plasma fluoride was increased in females at all exposure concentrations. These results are indicative of metabolism of HCFC-124 and not an adverse effect. Quantitative data were not available.

PATHOLOGY - At the 12 and 24 month sacrifices, there were no compound related effects on mean absolute or mean relative (to body or brain weight) organ weights in males or females at any exposure concentration.
At the 12 month sacrifice, female absolute heart weights at 50,000 ppm and heart weights relative to brain weight at 2,000; 10,000 and 50,000 ppm were significantly higher compared to control. Absolute brain weights were significantly lower in the 2,000 and 50,000 ppm females and relative brain weight was significantly lower in the 50,000 ppm females.
At the 24 month sacrifice, in males mean brain weight relative to body weight was significantly lower in the 10,000 and 50,000 ppm groups; mean absolute spleen weights were significantly higher in the 2,000 and 50,000 ppm groups; mean absolute heart weight was significantly higher in the 50,000 ppm group; spleen and heart weights relative to brain weight were significantly higher in the 50,000 ppm group and mean absolute liver weight was higher in the 2,000 ppm group. In females, mean brain and heart weights relative to body weight were significantly lower in all treated groups; absolute liver and liver weight relative to brain weight were significantly higher in the 10,000 and 50,000 ppm group.
All the significant differences in weight (at 12 and 24

months) were not correlated by gross or microscopic change and the differences were considered not an adverse effect. In most instances the differences are most likely attributable to higher mean final rat body weights. Gross-observations at 12 and 24 months revealed no compound related effects in either males or females at any exposure concentration.

In the 12 month sacrificed animals, there were no compound related microscopic findings at any exposure concentration. Increased incidence of minimal, focal accumulation of yellow-brown pigment in renal proximal tubules present in males at all exposure levels and 50,000 ppm females was the only statistically significant effect. The increase was slight compared to controls, was not present in the 24 month sacrificed animals and was not associated with cytotoxic changes. It was thus considered toxicologically insignificant.

In the 24 month sacrificed males, there were no compound related microscopic finding at any exposure concentration. In 50,000 ppm males there were significantly increased incidences of focal hepatic necrosis (15/77 compared to 6/77 in the control group) and cholesterol clefts/granulomas in the lung (10/77 compared to 2/77 in the control group; but no corresponding increase in alveolar histiocytosis). All of these are common in the aging rat and the severity and distribution of this change was not consistent with a compound related effect. In the 24 month sacrificed females, there were no compound related non-neoplastic lesions at any exposure concentration.

HCFC-124 was not toxic in rats exposed for 24 months to up to 50,000 ppm HCFC-124. Based on the results of this study the no-observed-adverse-effect level was considered to be 50,000 ppm.

Reliability criteria - 1a (GLP guideline study).

Critical study for SIDS endpoint.

Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity minimum 99%.

14-NOV-2005 (10)

Type:	Sub-chronic	
Species:	rat	Sex: male/female
Strain:	other:Crl: CD BR	
Route of administration:	inhalation	
Exposure period:	5 days/week for 90 days	
Frequency of treatment:	6 hours/day	
Post exposure period:	1 month	
Doses:	0, 5,000, 15,000 or 50,000 ppm	
Control Group:	yes, concurrent no treatment	

Method:	other: comparable to OECD 413
Year:	1991
GLP:	yes

Remark: Four groups of 20 male and 20 female rats per group were exposed to HCFC-124. Subgroups of rats were held for a 1 month recovery period and the same subgroup had a functional observational battery (FOB) conducted at 0, 4, 8, 13 and 16

weeks. Clinical pathology evaluations, were conducted at days 45, 90 and after 1 month recovery. At end of final exposure or end of 1 month recovery, rats underwent gross and microscopic evaluations and liver samples were taken, from 5 rats/group at the day 90 sacrifice, for determination of peroxisome proliferation activity.

Four 1400 L chambers made of stainless steel and glass were used. Chambers were operated in a one-pass flow-through mode with the air flow rates adequate to maintain sufficient oxygen. Animal cages placed within the chamber for exposure were rotated daily. Male and female rats received 65 and 66 exposures, respectively.

STATISTICAL METHODS - Body and organ weights, body weight gains and clinical laboratory measurements were analysed by one-way analysis of variance. If group mean differences were significant (F-test), Dunnett's test was used to make pairwise comparisons between test and control.
Incidence of clinical observations was evaluated by Fischer's Exact test with a Bonferroni correction and the Cochran-Armitage test for trend. Bartlett's test for homogeneity of variance was performed on organ weights and clinical laboratory data and when significant, the Kruskal-Wallis test was employed and the Mann-Whitney U test was used to compare group means to control. Beta-oxidation activity data were evaluated by one-way analysis of variance. Pairwise comparisons were made with the least significant difference test.
Test were judged significant at alpha = 0.05 (except Bartlett's test, alpha = 0.005).

CHAMBER CONCENTRATION - The mean daily concentrations (measured every 30 min.) were within 90 -110% of nominal. The overall mean concentrations were very close to nominal, with a coefficient of variation of less than 3%.
The 13-week mean temperature (24-25 degrees C) and relative humidity (55-58%) were similar for all chambers.

BODY WEIGHTS - Rats were weighed weekly. There were no statistically significant differences between any of the exposure groups in mean body weights. The mean body weight gains in males exposed to 15,000 and 50,000 ppm (days 14-21, 13-15%) were statistically lower and higher (days 49-56, 41%) compared to control. There were no other statistically significant differences in mean body weight gains between any exposure groups.

FOOD CONSUMPTION AND EFFICIENCY - There were no differences between any of the exposure groups in the mean weekly or the overall mean food consumption. Similarly, there were no differences at any time period, between any of the exposure groups in the mean food efficiency.

CLINICAL OBSERVATIONS AND MORTALITY - Rats in the 50,000 ppm exposure group were generally less responsive to auditory stimuli during exposure, compared to the other exposure groups. The incidence of clinical observations was similar in all the groups.
There was no compound related effect on ocular tissues.
There were no compound-related mortalities.

CLINICAL LABORATORY EVALUATIONS - Biologically significant compound-related hematology effects were not observed in any parameters. Any observed differences were within biological variation.

Serum triglyceride concentrations were significantly lower in males exposed to 15,000 and 50,000 ppm at day 45 (41%, both exposure levels) sampling compared to control. The values remained low (16-23%, not significant) at day 90 and were low in 4/10 animals in the recovery group. The data are equivocal because of the variability in control values but are still considered to be compound related.
Alkaline phosphotase activity at day 90 was doubled in females exposed to 50,000 ppm compared to control. It was similar to control at day 45 and at end of recovery. The effect is considered to be compound related.
Plasma fluoride was significantly increased in all exposure groups at day 90 (males 31-44%; females 25-32%) compared to control and the levels remained elevated at the end of recovery (males 9-21%; females 14-17%).
Urinary fluoride concentration was higher (2-5 fold in males, and 4-10 fold in females) for all exposure concentrations at days 45 and 90. At the end of the recovery period the levels were ca. two fold higher than control.
The fractional clearance rate of fluoride (FCR) was significantly higher than control at day 90 in all exposure groups. The FCR remained elevated at the end of recovery, but was significant only in male rats.
Compared to males, females had higher FCR and amount excreted.
Males exposed to 15,000 and 50,000 ppm exhibited mild diuresis, which is considered to be the result of increased osmotic activity.
These data are expected physiological consequences as a result of HCFC-124 metabolism and are considered not to be an adverse event.

PATHALOGICAL EVALUATION - Absolute and relative organ weight (% of body weight) were similar to control values for all exposure groups at day 90. In male rats sacrificed at the end of recovery, relative lung weights were significantly lower in the 15,000 ppm group (10%) but the effect was considered to be biologically insignificant. All other absolute and relative organ weights were similar to control. There were no compound-related gross or microscopic morphological changes at any exposure concentration.

HEPATIC MICROSOMAL PROLIFERATION - There was no significant increase in hepatic beta-oxidation activity between control and any male or female exposure groups.

FOB - 4/10 males in the 15,000 ppm group and 6/10 males in the 50,000 ppm group had significantly decreased arousal in a free roaming space during the week 13 assessment. This effect was not observed in females. There were no differences at the baseline, week 4, week 8 and week 16 (recovery period) observations.

No-observable-adverse-effect level considered to be 5,000

ppm for males and 15,000 ppm for females.

Reliability criteria - 1b (GLP, comparable to a guideline study).

Critical study for SIDS endpoint.

Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99.9%.
Reliability: (1) valid without restriction
10-OCT-2003 (44)

Type: Sub-chronic
Species: rat Sex: male/female
Strain: other:Crl: CD BR
Route of administration: inhalation
Exposure period: 5 days/week for 4 weeks
Frequency of treatment: 6 hours/day
Post exposure period: None
Doses: 0, 500, 2,000, 10,000 or 50,000 ppm
Control Group: yes, concurrent no treatment
NOAEL: = 10000 ppm

Method: other: comparable to OECD 412
Year: 1990
GLP: yes

Remark: Five groups of 10 male and 10 female rats per group were exposed to HCFC-124 during the same eight-hour period of the day. Males and females received a total of 21 and 22 days exposure, respectively.

An additional 6 female rats were exposed concurrently for a probe teratology study. This is reported separately (Haskell Laboratory Report No 108-90).

Five 150 L chambers made of stainless steel and glass were used. Chambers were operated in a one-pass flow-through mode with the air flow rates adequate to maintain sufficient oxygen. Animal cages placed within the chamber for exposure were rotated daily.

Food consumption and body weight were monitored. A day prior to end of study, blood samples were collected followed by 15-hour urine sample collection.
Following the final exposure, all animals were sacrificed and necropsied. Liver samples from rats in control and 50,000 ppm exposure groups were taken for determination of peroxisome proliferation activity.

STATISTICAL METHODS - Body and organ weight, body weight gain and clinical laboratory measurements were analysed by one-way analysis of variance. If group mean differences were significant (F-test), Dunnett's test was used to make pairwise comparisons between test and control.
Incidence of clinical observations was evaluated by Fischer's Exact test with a Bonferroni correction and the Cochran-Armitage test for trend. Bartlett's test for homogeneity of variance was performed on clinical laboratory data and when significant, the Kruskal-Wallis test was employed and the Mann-Whitney U test used to compare group means to control.

Beta-oxidation activity data were evaluated by one-way analysis of variance. Pairwise comparisons were made with the least significant difference test.
Test were judged significant at alpha = 0.05 (except Bartlett's test, alpha = 0.005).

CHAMBER CONCENTRATION - The mean 4-week chamber concentrations (measured daily at 60 min. intervals) were very close to nominal (99-101%), with a coefficient of variation of less than 5%. The daily concentrations were also close to nominal, within 92 -114%.
The 4-week mean temperature (24-25 degrees C) and relative humidity (49-51%) were similar for all chambers.

BODY WEIGHTS - Rats were weighed on study days 1, 8, 15, 22 and 29. There were no statistically significant differences between any of the exposure groups in mean body weights or mean body weight gains.

FOOD CONSUMPTION AND EFFICIENCY - There were no differences between any of the exposure groups in the mean weekly or the overall mean food consumption. Similarly, there were no differences at any time period, between any of the exposure groups in the mean food efficiency.

CLINICAL OBSERVATIONS AND MORTALITY - During exposure, rats in the 50,000 ppm exposure group, were lethargic and had uncoordinated movement. During the first exposure only, rats in the 10,000 ppm exposure group also appeared lethargic with uncoordinated movement; this was considered to be biologically not significant. During all other exposures and in all other exposure groups there were no observable clinical effects. Following the end of exposure there were no observable clinical effects. There were no compound-related mortalities.

CLINICAL LABORATORY EVALUATIONS - Biologically significant compound-related hematology effects were not observed in any parameters. Male rats in the 500, 10,000 and 50,000 ppm exposure groups had significantly lower neutrophil count (37-51%), but the control group values were elevated and the values per se were within biological variation.
There were no compound related effects on clinical chemistry parameters.
Plasma fluoride was significantly lower in 2,000 ppm males (11%) and 500 ppm females (11%), but significantly higher for 2,000 ppm females (11%). However these differences were all within normal variation and biologically insignificant.
Urinary fluoride concentration was significantly higher than control values in females (36-320%) at all exposure levels and in males (147-329%) at all but the lowest (500 ppm) exposure levels; at 500 ppm, urinary fluoride was higher than control (28%), but not significantly so. This effect is not an adverse effect since fluoride is an expected metabolite and hence it is a marker of exposure.

PATHALOGICAL EVALUATION - There were no compound-related effects on absolute and relative organ weight (% of body weight), which were similar to control values for all exposure groups. There were no gross or microscopic

morphological changes at any exposure concentration.

HEPATIC MICROSOMAL PROLIFERATION - There was no difference in the in vitro hepatic beta-oxidation activity in liver samples from control and 50,000 ppm exposed rats.

No-observable-adverse-effect level is considered to be 10,000 ppm based on results described above.

Reliability criteria - 1b (GLP, comparable to a guideline study).

Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99.9%.
Reliability: (1) valid without restriction
22-MAY-2005 (45)

Type: Sub-chronic
Species: mouse Sex: male/female
Strain: other: Crl: CDE-1 (ICR) BR
Route of administration: inhalation
Exposure period: 5 days/week for 90 days
Frequency of treatment: 6 hours/day
Post exposure period: 1 month
Doses: 0, 5,000, 15,000 or 50,000 ppm
Control Group: yes, concurrent no treatment
NOAEL: = 15000 ppm

Method: other: comparable to OECD 413
Year: 1992
GLP: yes

Remark: Four groups of 20 male and 20 female mice per group were exposed to HCFC-124. Subgroups of mice were held for a 1 month recovery period. Clinical pathology evaluations were conducted at days 45, 90 and after 1 month recovery. At end of final exposure or end of 1 month recovery, mice underwent gross and microscopic evaluations and liver samples were taken, for determination of peroxisome proliferation activity.

Four 150 L chambers made of stainless steel and glass were used. Chambers were operated in a one-pass flow-through mode with the air flow rates adequate to maintain sufficient oxygen. Animal "modules" housing individual mice placed within the chamber for exposure were rotated daily. Male and female mice received 65 and 66 exposures, respectively.

STATISTICAL METHODS - Body and organ weights, body weight gains and hematology measurements were analysed by one-way analysis of variance. If group mean differences were significant (F-test), Dunnett's test was used to make pairwise comparisons between test and control. Incidence of clinical observations was evaluated by Fischer's Exact test with a Bonferroni correction and if significant, then the Cochran-Armitage test for trend. Bartlett's test for homogeneity of variance was performed on organ weight and clinical laboratory data and when results were significant, the Kruskal-Wallis test was employed and the Mann-Whitney U test was used to compare group means to control.
Beta-oxidation activity data were evaluated by one-way analysis of variance. Pairwise comparisons were made with

the least significant difference test.
Test were judged significant at alpha = 0.05 (except Bartlett's test, alpha = 0.005).

CHAMBER CONCENTRATION - The mean daily concentrations (measured every 60 min.) were within 90 -110% of nominal. The overall 13-week mean concentrations were very close to nominal, with a coefficient of variation of less than 5%. The mean temperature (24.5-25.6 degrees C) and relative humidity (52.1-52.6%) were similar for all chambers.

BODY WEIGHT - Mice were weighed weekly. In male mice exposed to 5,000 or 15,000 ppm, body weight was significantly lower than control at weeks 12, 13 and 15 (4-7%, recovery mice). These differences are considered to be compound related, but not important toxicologically. Female body weights were similar to control at all exposure concentrations. Body weight gains in both male and female mice were generally similar to control. A few statistically significant observed differences were sporadic, not dose related or persistent and hence were considered to be biologically not significant.

FOOD CONSUMPTION AND EFFICIENCY - There were no differences between any of the exposure groups in the mean weekly or the overall mean food consumption. Similarly, there were no differences at any time period, between any of the exposure groups in the mean food efficiency.

CLINICAL OBSERVATIONS AND MORTALITY - Mice in the 50,000 ppm exposure group, were generally less responsive to auditory stimuli during exposure, compared to the other exposure groups. They recovered quickly after the end of exposure and responsiveness was similar to controls. The incidence of clinical observations was similar in the groups and there were no biologically significant differences between groups. There were no compound-related mortalities, although several unscheduled deaths occurred.

CLINICAL LABORATORY EVALUATIONS - Biologically significant compound-related hematology effects were not observed in any parameters at either day 90 or the end recovery. Any observed differences were within biological variation or within normal reference values.

At day 90, serum triglyceride levels were significantly lower than control in males exposed to 15,000 (29%) and 50,000 ppm (34%); they were lower in males exposed to 5,000 ppm (17%), but not significantly. The effect is considered to be compound related. At day 45 and at the end recovery, there were no compound related effects in both males and females. Differences observed were with normal reference ranges and were considered biologically insignificant.

PATHALOGICAL EVALUATION - Mean body weight for day 90 sacrifice were significantly lower than control, but the differences were small (6-7%), not dose related and were considered insignificant. At the end of the 1 month recovery, there were no differences in the mean body weights.
There were no toxicologically significant differences in

mean organ or relative weights in the day 90 or recovery animals.
There were no compound-related gross or microscopic morphological changes at any exposure concentrations.

HEPATIC MICROSOMAL PROLIFERATION - In male mice at day 90, beta-oxidation was two fold higher than control at all exposure concentrations and at the end of recovery it was higher in males exposed to 5,000 ppm. This effect is toxicologically insignificant, since the effect is small compared to classic beta-oxidation inducers and there was no effect on liver weight. For female mice there was no significant difference in activity between control and exposure groups at day 90 or end of recovery.

No-observable-adverse-effect level is considered to be 15,000 ppm for females. In males a NOAEL was not achieved because of lower body weight, lower serum triglycerides and increased hepatic activity. However, since all of these are considered to be toxicologically insignificant, a NOAEL of 15,000 ppm is assigned to males as well.

Reliability criteria - 1b (GLP, comparable to a guideline study).

Critical study for SIDS endpoint.

Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity minimum 99.9%.
Reliability: (1) valid without restriction
22-MAY-2005 (43)

Type: Sub-chronic
Species: guinea pig Sex: male
Strain: Hartley
Route of administration: inhalation
Exposure period: 4 hours
Frequency of treatment: Once or for 5 days
Post exposure period: 24 or 48 hours
Doses: 5,000 ppm (blended with HCFC-123 5,000 ppm)
Control Group: yes, concurrent vehicle

Remark: Male guinea-pigs were used to assess the hepatotoxicity of HCFC-123 and possible potentiation by HCFC-124. Animals were exposed whole-body in a 300 L chamber, at 22-25 degrees C and 50-60% relative humidity (60 air changes per hour).

A preliminary study determined the exposure concentration of HCFC-123 required to produce no liver effect and moderate hepatotoxicity but without massive hepatic necrosis. Animals were exposed to HCFC-123 for 4 hours to 500, 1,000, 2,000 or 5,000 ppm and killed 48 hours post exposure.
In the main study the possible interaction of HFCF-123 and HCFC-124 was investigated. Animals (n=5-9) were exposed for 4 hours to 5,000 ppm HCFC-123 or a combination of 5,000 ppm HCFC-123 plus 5,000 ppm HCFC-124 (blend of HCFC-123/124). Animals were exposed once or for 5 consecutive days. An additional group was exposed to 5,000 ppm HCFC-124 alone (single exposures only) and concurrent controls were exposed to air. At the end of exposure urine was collected until animals were killed at either 24 or 48 hours post exposure.

Blood was collected for analysis, liver slices taken for histological processing, liver homogenates analysed. Urine samples were analysed for metabolites.

Main study. Single exposure.
1) Great variability in the response to HCFC-123 or blend of HCFC-123/124
2) Increased mean serum levels of alanine aminotransferase (ALT, 24 hours) and isocitrate dehydrogenase (ICDH, 24 and 48 hours) indicates a transient cytolytic action of HCFC-123; the liver injury being confirmed by liver pathology that showed minor to moderate lesions
3) Absence of liver toxicity with HCFC-124
4) Very limited evidence of a potentiation of HCFC-123 liver toxicity by HCFC-124
5) Absence of any metabolic interaction. Urinary excretion. Animals exposed to HCFC-124 alone excreted very low levels of trifluoroacetic acid (TFA - 0.61 mg/24 h). Animals exposed to the blend of HCFC123/124 and HCFC-123 excreted similar amounts of TFA (approx 6.4 mg/24 h), chlorodifluoroacetic acid (CDFA) and fluoride.

Main study. Repeated exposure.
1) Great variability in the response to HCFC-123 or blend of HCFC-123/124

2) Increased mean serum levels of ALT (24 hours) and ICDH (24 and 48 hours) indicates a transient cytolytic action of HCFC-123; the liver injury being confirmed by liver pathology that showed minor to moderate lesions
3) Biochemistry and liver pathology evidence of steatosis.
4) Metabolite accumulation during the week.
5) Very limited evidence of a potentiation of HCFC-123 liver toxicity by HCFC-124
6) Absence of any evidence of metabolic interaction.

The study confirmed HCFC-123 hepatotoxicity but found very limited indication of potentiation by HCFC-124.

Reliability criteria - 1d (Test procedure in accordance with generally accepted scientific standards and described in sufficient detail).

Source: Daxa Borkhataria Northaw
Test substance: HCFC-124, purity >99.9%.
Reliability: (1) valid without restriction
09-OCT-2003 (25)

Type: Sub-chronic
Species: rat Sex: male
Strain: other: Chr-CD
Route of administration: inhalation
Exposure period: 5 days/week for 2 weeks
Frequency of treatment: 6 hours/day
Post exposure period: 14 days
Doses: 10% (v/v) (100,000 ppm)
Control Group: other: air

Year: 1977
GLP: no data

Remark: Inhalation toxicity of HCFC-124 was evaluated along with seven other fluorocarbons. 10 rats/group were exposed. Clinical laboratory examination was performed (hematology, blood chemistry, urine analysis) on five rats from each group after the last exposure and after 14 days. The rats were sacrificed and tissue samples taken for histopathalogical evaluation.

The data showed HCFC-124 produced no adverse changes.

These data are in an abstract without details of any effect.

Reliability criteria - 3a (documentation insufficient for assessment).
Source: Daxa Borkhataria Northaw
Test substance: FC-124, purity not given.
Reliability: (3) invalid
09-OCT-2003 (50)

5.5 Genetic Toxicity 'in Vitro'

Type: Chromosomal aberration test
System of testing: Cultured Chinese hamster ovary (CHO-K1) cells
Concentration: 15, 30 and 60%
Metabolic activation: with and without
Result: negative

Method: other: OECD Guideline 473O, US EPS TSCA guidelines (1985, amended 1987) and Japanese MITI (1987 and MHW (1990) guidelines
Year: 1991
GLP: yes

Remark: Cultured Chinese hamster ovary cells (CHO-K1) cells were treated with HCFC-124.
Positive control: Mitomycin-C (absence of S-9 mix) and cyclophosphamide (presence of S-9 mix).
Negative control: Air

Exposure times, in the absence of S-9 mix, were 4, 24 and 48 hours and in the presence of S-9 mix, 4 hours.
Culture vessels were incubated at 37 degrees C on a rotating shaker. Following the end of the 4 hour incubation, culture medium was renewed and incubation continued for a further 20 hours in an atmosphere of 5% carbon dioxide. Two hours prior to the end of incubation, Colcemid was added to arrest cell division, prior to harvesting.

The test atmosphere concentration was determined by GC and found to be both close to nominal and stable for the duration of exposure.

Test concentrations were chosen based on preliminary toxicity studies with 10-60% HCFC-124. In the absence of S-9 mix, a mean mitotic index reduction of 30-39% was observed at each concentration of HCFC-124. In the presence of S-9 mix, there was no reduction in mean mitotic index.

Mitotic indices (number of metaphases observed per 1000 cells) were calculated after scoring at least 1000 cells.

100 metaphases were scored for each culture and frequencies of aberrant metaphases calculated, both including and excluding gap-type aberrations.

Statistical Method: Fishers Exact Probability test was used to evaluate the incidence of aberrant metaphases.

Mitotic Indices (% reduction in mean mitotic index at 15, 30 and 60% HCFC-124, respectively):
4 hour exposure (- S-9 mix); 0, 18 and 22%
4 hour exposure (+ S-9 mix); 0, 28 and 42%
24 hour exposure (- S-9 mix); 29%, 0 and 18%
48 hour exposure (- S-9 mix); No reduction at all HCFC-124 exposure concentration.

Chromosomal aberrations
4, 24 and 48 hour exposure (absence of S-9 mix)
No statistically nor biologically significant increases in the frequency of metaphases with chromosomal aberrations observed.
4 hour exposure (presence of S-9 mix)
There was a small, statistically significant (p=0.03) increase in the frequency of aberrant metaphases, gaps excluded, in cultures exposed to 15% HCFC-124 in the presence of S-9 mix. This effect is considered to be biologically insignificant because it was not dose related and the frequencies of aberrant metaphases (4 and 5%) were within the normal range of the laboratory. There were no statistically significant increases in the absence of S-9 mix.

The positive controls both induced significant ($p<0.001$) increases in the frequency of aberrant metaphases.

HCFC-124 is not clastogenic, under the conditions of the test, either in the presence or absence of S-9 mix.

Reliability criteria - 1a (GLP guideline study).

Critical study for SIDS endpoint.
Source: Daxa Borkhataria Northaw
Test substance: HCFC-124, purity >99%.
Reliability: (1) valid without restriction
30-SEP-2003 (27)

Type: Chromosomal aberration test
System of testing: Human peripheral blood lymphocytes
Concentration: 10, 50, 75 and 100%
Metabolic activation: with and without
Result: negative

Method: other: EPA OTS 798.5375 and OECD Guide-line 473
Year: 1990
GLP: yes

Remark: Cytotoxicity and chromosome aberration tests with HCFC-124 were performed with human lymphocytes obtained from two different pairs of male and female donors.

CYTOTOXICITY ASSESSMENT
Tissue culture flasks were placed in specially designed

glass chambers (1.65 L volume) and exposed HCFC-124. Negative controls were air or nitrogen. At each test concentration duplicate cultures were exposed. Cells were incubated for 3 hours at 37 degrees C. Following exposure, the cultures were rinsed, fresh medium containing 5-bromodeoxyuridine (BrdU) was added and incubation continued for 23 hours. Two hours prior to end of incubation time, Colcemid was added to arrest cell division. Cultures were handled under yellow-filtered light.

For each culture, 50 metaphase cells were scanned and scored as having gone through one (M1), one-to-two (M1+), two (M2), two-to-three (M2+) or three (M3) DNA replication cycles. The mean number of cell cycles (MCC) and the average generation time (AGG) were obtained using the following formulae:

MCC = [1(M1) + 1.5(M1+) + 2(M2) + 2.5(M2+) + 3(M3)] divided by total number of metaphases scored

AGT = [time in BrdU(hrs)]/MCC

HCFC-124 concentrations within the chamber were not always close to nominal but were stable and showed no substantial decrease for the duration of exposure.
HCFC-124 at atmospheric concentrations of 0-100% showed no clear increase in AGT of human lymphocytes in the absence or presence of S-9 mix.

For the subsequent chromosome aberration tests, a harvest time of 18 hours post-treatment (to allow an estimated 1 to 1.5 cell cycles to elapse) and HCFC-124 concentrations of 10, 50, 75 and 100% were selected.

CHROMOSOME ABERRATION ASSESSMENT
Culture treatment as described for CYTOTOXICITY ASSESSMENT, except (i) 10, 50, 75 and 100 % HCFC-124, (ii) no BrdU (iii) 3 hour incubation and 18 hour harvest times were used, (iv) positive controls included and (v) two independent trials were performed.
Positive Controls: Mitomycin C (absence S-9 mix) and cyclophosphamide (presence S-9 mix).
Negative Controls: Air and nitrogen (for 100% HCFC-124)

Where possible, a minimum of 100 cells, 50 per replicate, were evaluated for chromosome aberration in well-spread metaphase cells.

Statistical Method. For each trial, the proportion of abnormal cells and the proportion of cells with more than one aberration at each treatment level were compared to those of nitrogen control using Fisher's Exact Test and judged significant at the 5% level. A Cochran-Armitage test for linear trend (concentration-response) was performed where appropriate and judged significant at the 1% level. Chromatid and isochromatid gaps were excluded from the statistical evaluation.

No statistically significant increases in chromosome aberrations were observed for culture in the presence or absence of S-9 mix in either of the duplicate trials, nor

were there any concentration related trends. Mitotic indices were not appreciably depressed at any HCFC-124 concentration.

The positive controls both induced significant ($p<0.01$) increases in the frequency of aberrant metaphases, demonstrating the suitability of the test system and the metabolic activity of the S-9 mix.

HCFC-124 did not exhibit clastogenic activity in human lymphocytes either in the presence or absence of S-9 mix. Under the conditions of the assay, HCFC-124 is non-mutagenic.

Reliability criteria - 1a (GLP guideline study).
Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroeethane, purity 99.99%.
Reliability: (1) valid without restriction
30-SEP-2003 (28)

Type: other: Salmonella typhimurium and Escherichia coli reverse mutation assays
System of testing: Salmonella typhimurium, strains TA 98, TA 1538, TA 100, TA 1535 and TA 1537 and Escherichia coli, strain WP2 uvrA
Concentration: 3.125, 6.25, 12.5, 25 and 50%
Metabolic activation: with and without
Result: negative

Method: other: OECD Guide-line 471 and 472, and EPA OTS 798.5265.
Year: 1991
GLP: yes

Remark: Five histadine-dependant auxotrophs of Salmonella typhimurium, and one tryptophan-dependant auxotroph of E. coli, were used.
TA 1537, TA 1538 and TA 98 allow detection of frame shift.
TA 1535, TA 100 and WP2 uvrA allow detection of base substitution.
Positive control: Dichloromethane, benzo[a]pyrene, 2-nitrofluorene, 2-aminoanthracene, 9-aminoacridine, N-ethyl-N'-nitro-N-nitrosoguanadine and sodium azide.
Negative control: Air.

Plated bacteria, placed in racks inside a stainless steel vessel, were exposed to HCFC-124 and incubated at 37 degrees C for 48 hours. The plates were then removed from the vessels and incubated a further 24 hours. Each test in each strain was performed on two separate occasions.

Test concentrations were selected based on preliminary toxicity studies in strains TA 98 and WP2 uvrA using exposure concentrations of 10, 20, 30, 40, 50, 60 and 70% v/v HCFC-124.

Test atmosphere concentration was determined and results indicated that achieved concentrations were close to nominal and maintained through out the study.

The revertant colonies were counted in all concentration groups and compared to the number of revertant colonies in

the control group. No statistical methods are given.

No increases in reversion to prototrophy were obtained with any of the strains following exposure to HCFC-124 in the presence or absence of S-9 mix.
Inhibition of growth (reduction in revertant colony numbers), occurred in all strains following exposure to 50% HCFC-124 in the presence or absence of S-9 mix.
Marked increases in the number of revertant colonies were induced by the positive controls.

HCFC-124 tested on Salmonella typhimurium strains TA 98, TA 1538, TA 100 and TA 1535 and TA 1537 and Escherichia coli, strain WP2 uvrA was not mutagenic in the absence or presence of S-9 mix. Under the conditions of the assay, HCFC-124 is not mutagenic.

Reliability criteria - 1a (GLP guideline study).
Source: Daxa Borkhataria Northaw
Test substance: HCFC-124, purity >99%.
Reliability: (1) valid without restriction
30-SEP-2003 (24)

Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium strains TA 1535, TA 97, TA 98, TA 100
Concentration: 0, 40% (without activation) and 60% (with activation)
Metabolic activation: with and without
Result: negative

Method: other: EPA OTS 798.5265 and OECD guideline 471
Year: 1990
GLP: yes

Remark: Four Salmonella typhimurium strains were used.
Positive control: 2-aminoanthracene, 2-nitrofluorene, sodium azide and ICR-191 Acridine.
Negative control: Air.

The plated cultures were incubated and exposed to HCFC-124 for 48 hour at 37 degrees.

Test concentrations were based on preliminary studies on toxicity of 0, 10, 25, 50, 75 and 100% HCFC-124 to strain TA 98. Excessive toxicity was observed at concentrations of 50% without activation and 75% with activation.

The revertant colonies were counted in all concentration groups and compared to the number of revertant colonies in the control group.

Statistical methods. Mutant frequency (MF) data were first transformed using the formula Y=(MF to the power of 0.2).

The average transformed MF was compared to the solvent control using Dunnett's t-test. Dose-response relationship was examined by a two-way (concentration and experiment) analysis of variance. Linear, quadratic and higher order effects were tested for significance using the F-test.

HCFC-124 tested on Salmonella typhimurium strains TA 1535,

TA 97, TA 98 and TA 100 was not mutagenic in the presence or absence of rat liver homogenate preparation. Under the conditions of the assay, HCFC-124 is not mutagenic.

Reliability criteria - 1a (GLP guideline study).
Source: Daxa Borkhataria Northaw
Test substance: HCFC-124, purity 99.988%.
Reliability: (1) valid without restriction
30-SEP-2003 (39)

Type: Salmonella typhimurium reverse mutation assay
System of testing: Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98, TA 100
Concentration: 0, 20 and 40%
Metabolic activation: with and without
Result: negative

Method: other
Year: 1976
GLP: no data

Remark: Five Salmonella typhimurium histadine auxotrophs were used (TA 1535 and TA 100 used to detect base-pair substitution mutation and remainder to detect frameshift mutation). Positive control: Ethylene (20%).

The cultures were exposed to HCFC-124 in glass chambers for 6 hours at 37 degrees C after which the chamber was flushed with air for several minutes and incubation continued at 37 degrees C for a further 42 hours.

HCFC-124 concentration within the exposure chamber was determined by GC and found to agree well with nominal values.

Test concentrations were chosen based on lack of toxic effect and lack of inhibition of bacterial growth.

The revertant colonies were counted in all concentration groups and compared to the number of revertant colonies in the control group. Statistical method used not mentioned.

HCFC-124 tested on Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100 was not mutagenic in the absence or presence of rat liver homogenate preparation - it did not significantly increase frequency of spontaneous mutation.

Reliability criteria - 2e (Study well documented, meets generally accepted scientific principles, acceptable for assessment).
Source: Daxa Borkhataria Northaw
Test substance: 1-chloro-1,2,2,2-tetrafluoroethane, purity not given.
Reliability: (2) valid with restrictions
30-SEP-2003 (29)

Type: other: bacterial reverse mutation and yeast gene mutation assay
System of testing: Bacteria strain: Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98, TA 100.
Yeast strains: Saccharomyces cerevisiae, strain D4

Concentration: Report not explicit, but could be 5%.
Metabolic activation: with and without
Result: negative

Method: other
Year: 1976
GLP: no data

Remark: Salmonella typhimurium (bacteria) and Saccaromyces cerevisiae (yeast) were used.
Positive controls: Non-activation - Ethylmethanesulfonate, methylnitrosoguanidine, 2-nitrofluorene and Quinacrine mustard. Activation - 2-Anthramine, 2-Acetylaminofluorene, 8-Aminoquinolone and Dimethylnitrosamine.
Negative control: air.

The report uses time (5 or 24 h) as an indicator of exposure level, and does not clearly state concentration used. A maximum of 5% exposure is mentioned.

Plate test: incubated at 37 degrees C with HCFC-124 for 5 or 24 hours and then incubation completed to 48 hours. Untreated controls were run with each indicator strain.

Suspension tests: incubated at 37 degrees C for 15 minutes to 4 hours in a rotating shaker. Negative controls received no gas. Following treatment, aliquots of flask contents were removed, diluted and plated on the appropriate complete media. Bacterial plates were scored after incubation for 48 hours at 37 degrees C. Yeast plates were incubated for 3 to 5 days at 30 degrees C before scoring.

The revertant colonies were counted compared to the number of revertant colonies in the control group. Statistical method used not mentioned.

Plate test: Plate test exposures of the compound with or without activation were negative. The positive control had at least 5 fold greater reverse mutations.

Suspension tests: Results of the nonactivation and activation suspension tests were negative. Nonactivation tests with strains TA 100 and TA 1538 and activation tests with TA 1537 and TA 1538 were repeated because the first tests showed slightly increased mutant frequencies. All repeat tests were negative.

HCFC-124 tested on Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100 and Saccharomyces cerevisiae, strain D4, was not mutagenic with or without activation.

Reliability criteria - 2e (Study well documented, meets generally accepted scientific principles, acceptable for assessment).
Source: Daxa Borkhataria Northaw
Test substance: Genetron 124, purity not given.
Reliability: (2) valid with restrictions
30-SEP-2003 (38)

Type: Salmonella typhimurium reverse mutation assay

System of testing: Salmonella typhimurium strains TA 1535, TA 1538, TA 98 or TA 100.
Concentration: not specified
Metabolic activation: with and without
Result: negative

Method: other
GLP: no data

Remark: HCFC-124 was tested using the basic methodology of the Ames test. Method details are not explicit in the publication. A group of methane and ethane analogues have been studied. Various test gas concentrations, not specified, and exposures up to 72 hours have been used. Tests were performed in the presence and/or absence of S-9 mix.

Data are presented only for incubations with S-9 mix, since essentially identical data were obtained for incubations without S-9 mix.

HCFC-124 was found to be non-mutagenic with respect to each tester strain.

Reliability criteria - 3a (documentation insufficient for assessment).
Source: Daxa Borkhataria Northaw
Test substance: FC-124, purity 99.5%.
Reliability: (3) invalid
30-SEP-2003 (35)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay
Species: mouse Sex: male/female
Strain: other: Crl:CD-1 (ICR)BR
Route of admin.: inhalation
Exposure period: 6 hours/day, 2 consecutive days.
Doses: 0 and 100,000 ppm
Result: negative

Method: other: EPA OTS 798.5395 and OECD draft guideline 474
Year: 1990
GLP: yes

Remark: Male and female mice were exposed to HCFC-124 and sacrificed at 24 or 48 hours (remaining animals) after the second exposure and bone marrow smears prepared.
Control (air): 5 mice/sex/time point
HCFC-124: 6 mice/sex/time point.

Positive control: 5 mice/sex were dosed ip with 20 mg/kg cyclophosphamide (CP) and sacrificed 24 hours later.

The HCFC-124 exposure concentration selected was based on preliminary range finding study to estimate maximum tolerated concentration.

Parameters evaluated. 1000 polychromatic erythrocytes (PCEs) per animal were scored for the presence of micronuclei within the same field, the number of normochromatic

erythrocytes (NCEs) seen were also recorded. The PCE:NCE ratio was determined.

Statistical method. Data for percent micronucleated PCEs and proportion of PCEs among 1000 erythrocytes were transformed (arcsine square-root function) prior to analysis. Data were analysed by a one-way analysis of variance. Weight data were not transformed and positive indicator data were not included in the analysis. All analyses one-tailed and significant at the 5% level.

The overall HCFC-124 concentration was 99,000 ppm, relative humidity and temperature ranged between 26-32% and 22-26 degrees C, respectively.

There were no statistically significant differences in percent micronucleated PCEs between mice treated with HCFC-124 compared to control, at either sampling time. The positive control mice showed significant increases in micronucleated PCEs ($p<0.05$) compared to the control group. No significant decrease in the PCE:NCE ratio was observed.

Under the test conditions, HCFC-124 did not induce micronuclei in mice bone marrow cells - the compound is non-mutagenic.

Reliability criteria - 1a (GLP guideline study).

Critical study for SIDS endpoint.
Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99%.
Reliability: (1) valid without restriction
07-OCT-2003 (37)

5.7 Carcinogenicity

Species: rat Sex: male/female
Strain: other: Crl: CD BR
Route of administration: inhalation
Exposure period: 5/days a week for 24 months
Frequency of treatment: 6 hours/day
Post exposure period: None
Doses: 0, 2000, 10000 and 50000 ppm
Result: negative
Control Group: yes

Method: other: EPA OTS 798.3320 and OECD test guidelines 453
Year: 1995
GLP: yes

Remark: Four groups of 87 rats per sex, per group were exposed. Four 4000 L chambers made of stainless steel and glass were used. Chambers were operated in a one-pass flow-through mode with the air flow rates adequate to maintain sufficient oxygen (approx. 19%). Animal cages placed within the chamber for exposure were rotated daily.

Body weights were recorded weekly for first three months and then every other week till study end. Food consumption was monitored weekly. Clinical signs of toxicity were monitored

through out the study. An ophthalmological examination was performed on all animals prior to study start and at 3, 12 and 24 months. At 3, 6, 12, 18 and 24 months hematology, clinical chemistry and urinanalysis was performed on 10 rats/sex/group. The rats used for the 12 month clinical pathology also underwent an study interim sacrifice. All surviving rats were necropsied at 24 months. Selected tissues were weighed and tissues collected for microscopic evaluation.

STATISTICAL METHODS - Body and organ weights, body weight gains and clinical laboratory measurements were analysed by one-way analysis of variance. If group mean differences were significant (F-test), Dunnett's test was used to make pairwise comparisons between test and control.
Incidence of clinical observations was evaluated by the Cochran-Armitage test for trend. If the trend was positive for the intermediate and high groups ($p<0.05$), incidence observed in the lowest concentration group was compared to control using the Fisher's Exact test. Survival among groups was compared with the Cochran-Armitage test and the Fisher's Exact test.
Bartlett's test for homogeneity of variance was performed on clinical laboratory data and organ weights and when results were significant, the Kruskal-Wallis test (clinical laboratory) and the Mann-Whitney U test (organ weight) was used to compare group means to control.
The Cochran-Armitage trend test was applied to all microscopic observations in those cases where all tissues were evaluated in a group. If the trend was positive for the intermediate and high groups ($p<0.05$), the lowest group were compared to control using Fisher's Exact test. For tissues not examined microscopically in all groups, Fisher's Exact test was used to compare lesion incidences in the control and the high group. If $p<0.05$, for a lesion in a given tissue, then it was microscopically evaluated in all animals and exposure groups, unless scientifically deemed unwarranted. When all tissues had been evaluated, the incidence of lesions in question were evaluated using the Cochran-Armitage trend test. When there was significant lack of fit (LOF<0.05) for the Cochran-Armitage trend test, Fisher's exact test with Bonferroni correction was used to compare test groups to control. Data were maintained separately by sex. Tests were judged significant at $p = 0.05$ (except Bartlett's test, alpha = 0.005).

CHAMBER CONCENTRATIONS - Overall mean chamber concentrations were close to nominal: 0, 2,020, 10,000 an 50,095 ppm. Mean daily temperature (21-22 degrees C) and mean daily relative humidity (54-55%) were similar for the four chambers.

BODY WEIGHT, FOOD CONSUMPTION AND EFFICIENCY - Mean cumulative body weight gains were significantly higher in males at 10,000 (11%) and 50,000 ppm (9%) and females at 2,000 (17%), 10,000 (24%) and 50,000 ppm (14%). A dose-related trend was not apparent in either gender for cumulative weight gain or absolute weight and therefore the differences are considered not to be compound related. There were no compound related effects on food consumption or food efficiency in either gender.

CLINICAL OBSERVATIONS AND LABORATORY EVALUATIONS - Animal responsiveness to an alerting sound during exposure was similar in all exposure groups, including control. There were no adverse, compound related effects on the incidence of clinical observations or survival at any exposure concentration.

PATHOLOGY - At the 12 and 24 month sacrifices, there were no compound related effects on mean absolute or mean relative (to body or brain weight) organ weights in males or females at any exposure concentration.

At the 12 month sacrifice, female absolute heart weights at 50,000 ppm and heart weights relative to brain weight at 2,000; 10,000 and 50,000 ppm were significantly higher compared to control. Absolute brain weights were significantly lower in the 2,000 and 50,000 ppm females and relative brain weight was significantly lower in the 50,000 ppm females.

At the 24 month sacrifice, in males mean brain weight relative to body weight was significantly lower in the 10,000 and 50,000 ppm groups; mean absolute spleen weights were significantly higher in the 2,000 and 50,000 ppm groups; mean absolute heart weight was significantly higher in the 50,000 ppm group; spleen and heart weights relative to brain weight were significantly higher in the 50,000 ppm group and mean absolute liver weight was higher in the 2,000 ppm group. In females, mean brain and heart weights relative to body weight were significantly lower in all treated groups; absolute liver and liver weight relative to brain weight were significantly higher in the 10,000 and 50,000 ppm group. All the significant differences in weight (at 12 and 24 months) were not correlated by gross or microscopic change and the differences were considered not an adverse effect. In most instances the differences are most likely attributable to higher mean final rat body weights. Gross-observations at 12 and 24 months revealed no compound related effects in either males or females at any exposure concentration.

The incidences of C-cell adenoma were increased in treated groups of male rats, but were considered not compound related for the following reasons:- i) the incidences were not increased in a dose-response manner and thus were not statistically significant by the Cochran-Armitage trend test, ii) incidences of C-cell hyperplasia (a precursor to C-cell adenoma) or C-cell carcinoma were not increased in treated groups of male rats and iii) there were no significant increases in any proliferative C-cell lesion in female rats.

Consistent with an increase in grossly identified mammary gland masses in the 50,000 ppm females relative to control, there was a statistically significant higher incidence of mammary gland fibroadenoma in the 50,000 ppm females (36%) compared to controls (23%). Although the increase was significant by the Cochran-Armitage trend test, it was not significant by the Fisher's exact test and there was not a clear dose response - in the 2,000 (16%) and 10,000 ppm groups (22%), incidence was lower than control. There was

also no increase in multiplicity of fibroadenoma or incidence of primary mammary neoplasm. The author of the report states in a publication (Malley et al, 1998) that an incidence of 36% for mammary fibroadenoma has been observed in untreated rats feed according to the same regimen as used in this chronic study (see section 5.9, Specific Investigations). The rats in this study were housed 3 per cage, gender separated and were supplied with a feeder filled daily with approximately 50 (females) or 70 (males) g of Purina Rodent Chow #5056 (chunk). For all the reasons, the effect was considered not to be compound related.

At the 24-month sacrifice, the incidence of focal necrosis in the liver of male rats was significantly higher in the 50,000 ppm group (15/77 vs 6/77 in the control group). The minimal severity and generally focal distribution were inconsistent with a compound related effect. There was also no associated detectable change in liver function and focal hepatic necrosis is common in aging rats. The effect was not considered compound related.

The incidence of cholestrol clefts/granulomas in the lungs was significantly higher in the 50,000 ppm males (10/77 vs 2/77 in the control group) at 24 months. The change was generally minimal in severity, focally distributed, and is common in aging rats. Cholestrol granuloma are a result of alveolar histiocytosis which was not significantly increased in treated groups compared to controls. The effect was not considered compound related.

HCFC-124 was not carcinogenic in rats exposed for 24 months to up to 50,000 ppm HCFC-124.

Reliability criteria - 1a (GLP guideline study).

Critical study for SIDS endpoint.
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity minimum 99%.
Reliability: (1) valid without restriction
14-NOV-2005 (11)

5.8.1 Toxicity to Fertility

5.8.2 Developmental Toxicity/Teratogenicity

Species:	rat	Sex: female
Strain:	other: Crl:CD BR	
Route of administration:	inhalation	
Exposure period:	days 7-16 of gestation	
Frequency of treatment:	6 hours/day	
Doses:	0, 5,000, 15,000 and 50,000 ppm	
Control Group:	yes	
NOAEL Maternal Toxity:	= 15000 ppm	
NOAEL Teratogenicity:	= 50000 ppm	

Method: other: EPA OTS 798.4900 and OECD Guide-line 414
Year: 1991
GLP: yes

Remark: Groups of 24 female rats were exposed. Day 1 of gestation

(Day 1G) was day copulation was confirmed.
Exposures were concurrent with a subcronic study which is reported separately (HLR 79-91).

Four 1400 L stainless steel and glass chambers were used. Chambers were operated in a one-pass flow-through mode with the air flow rates adequate to maintain sufficient oxygen. Animal cages (2 animals/cage) placed within the chamber for exposure were rotated daily.

Body weight - day after arrival, before mating and Days 1, 7-17 and 22G.
Feed weight - Every other day for Days 1-19 and 22G.
Clinical signs on Days 1-22G.
Sacrificed on Day 22G and gross pathology performed. Types of nidations and relative positions recorded. The uterus of each "non=pregnant" rat was examined for possible early resorptions.
Live fetuses were weighed, sexed, and examined. For each litter, the maximum stunted weight (MSW) was calculated and any stunted fetuses (weight <= MSW) were omitted from the mean litter weight. First live fetus in a litter, every other thereafter, all stunted and malformed fetuses were decapitated (fixed and examined) and examined for visceral alterations. All remaining fetuses examined for skeletal alterations.

STATISTICAL METHODS - The level of significance was alpha = 0.05 (except Bartlett's test, alpha = 0.005).
Incidence of pregnancy, clinical observations, maternal mortality and females with total resorptions -
Cochran-Armitage test for trend and Fisher's exact test for pairwise comparisons.
Maternal weight, weight change and feed consumption -
linear combination of dose ranks from ANOVA and if this was significant, pairwise comparisons using Dunnett's test.
Live fetuses, dead fetuses, resorptions, nidations, corpora lutea, pre- and post-implantation losses, fetal weight and incidence of fetal alterations - Jonckheere's test for trend and pairwise comparisons performed using the Mann-Whitney U test. If 75% ties occurred in reproductive and fetal parameters, the Cochran-Armitage test and the Fishers exact test replaced Jonckheere's and Mann-Whitney U tests, respectively.

CHAMBER CONCENTRATION - The mean daily chamber concentrations (measured hourly) were close to target, overall range 90.9-105.1% of nominal for all chambers. The temperature (overall range, 21-27 degrees C) and relative humidity (overall range, 48-61%) were similar for all chambers. Oxygen concentrations were 20-21% for all chambers, based two daily measurements.

BODY WEIGHT GAINS - No significant differences in body weight changes for the pre and post exposure periods. During the exposure phase, a single significant decrease in body weight gain was observed in the 50,000 ppm group (93%) for Days 7-9G and the finding was accompanied by a significant trend.

FOOD CONSUMPTION - During exposure (Days 7-9, 9-11 and

11-13G), there was a significant trend in decreased food consumption; the reduction was significant only on Days 9-11G in the 50,000 ppm group (8%). Post exposure there was a significant trend in increased food consumption; the increase was significant only in the 15,000 ppm group (10%). No other effects were seen.

CLINICAL OBSERVATIONS AND MORTALITY - During exposure, rats in the 50,000 ppm exposure group, were less responsive to a noise stimulus. No significant differences in the incidence of clinical findings were observed.
There were no mortalities.

PATHALOGICAL EVALUATION - There were no gross changes at any exposure concentration.

REPRODUCTIVE EFFECTS - No significant effects on reproductive parameters, except for significant increases in mean nidations per litter (5,000 ppm group) and mean corpora lutea counts (15,000 ppm group). Overall pregnancy rate was 79.2, 83.3, 70.8 and 83.3 % for 0, 5,000, 15,000 and 50,000 ppm groups.

FETAL FINDINGS - There were significant reductions in mean fetal weights (combined 5%, and by sex 4-7%) in 5,000 and 15,000 ppm exposure groups, but there was no significant trend. There was no effect on the incidence of stunted fetuses.
No significant trends or differences from control values were found in the incidence of fetuses per litter with external, visceral, head or skeletal malformations or overall litter incidence.

No significant differences in the overall incidence of variations or in any categories were seen and no trends were detected.

Maternal and fetal no-observable-adverse-effect level was considered to be 15,000 ppm and 50,000 ppm, respectively.

Reliability criteria - 1a (GLP guideline study).

Critical study for SIDS endpoint.

Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity >99%.
Reliability: (1) valid without restriction
30-SEP-2003 (46)

Species: rabbit Sex: female
Strain: New Zealand white
Route of administration: inhalation
Exposure period: Days 6-18 of gestation
Frequency of treatment: 6 hours/day
Doses: 0, 5,000, 15,000 and 50,000 ppm
Control Group: yes
NOAEL Maternal Toxity: = 15000 ppm
NOAEL Teratogenicity: = 50000 ppm

Method: EPA OTS 798.4900
Year: 1991
GLP: yes

Remark: Twenty rabbits per group were exposed. Gestation Day O (Day 0G) was defined the day coitus was observed with two separate males.

6000 L stainless steel and glass chambers were used. Animals cages placed within the chamber were rotated daily.

Physical observations - twice daily. Detailed physical exam on Days 0, 6-18 (after removal from chamber), 24 and 30G. Beginning on day 11 of exposure, animals were observed through the glass walls of the chamber mid-way through exposure and specifically, response to a tap on the side of the chamber wall noted.
Body weight - Days 0, 6, 9, 12, 15, 19, 24 and 30G
Feed weight - Recorded for intervals of 0-1, 3-4, 5-6, 6-7, 7-8, 8-9, 9-10, 10-11, 11-12, 12-13, 13-14, 14-15, 15-16, 16-17, 17-18, 18-19, 19-20, 24-25 and 29-30G.
Sacrificed on Day 30G and gross pathology performed. Liver weights recorded. The uterus was removed, weighed, opened and numbers and locations of following recorded; live and dead fetuses, late and early resorptions, and implantation sites. Ovaries were evaluated for presence and number of corpora lutea. The uterus of each "non=pregnant" rabbit was examined. Females showing signs of premature delivery were killed. Reproductive systems were examined, fetuses/delivered pups recovered were evaluated for external malformations, eviscerated and processed for staining of skeletal structures.
All fetuses were examined grossly, weighed and sacrificed. Killed fetuses were evaluated for visceral malformations/variations and sexed. Eviscerated fetuses were skinned and eyes and brain ventricles examined grossly. The specimens were stained for fetal skeletal evaluations. Late resorptions were weighed, examined grossly and discarded.

STATISTICAL METHODS - Mean body weight and body weight changes, gravid uterine weight, Day 30G corrected weights and net maternal weight (Days 6-30G), mean food consumption, mean organ weight (absolute and relative to corrected Day 30G body weight) and reproductive data: Bartlett's test performed to determine if groups had equal variance. If equal variance (parametric), one way ANOVA using the F distribution used to assess significance. If significant, Dunnett's test used for pairwise comparison. Standard regression used to test for trends and lack of fit. If unequal variance (non-parametric), Kruskal-Wallis test used and if differences indicated, a summed rank test (Dunn) was used for pairwise comparison. Jonckheere's test for monotonic trend used. The Bartlett's test conducted at 1%, two-sided risk level. All others at 5% and 1%, two-sided risk level. All ratios arc sine transformed prior to analysis.
Incidence of litter resorption sites, mortality rates, pregnancy rates, incidences of fetus malformations/ variations and incidences of litters containing fetuses with malformations/variations: Contingency tables used. A standard chi-square test was first performed to determine if incidence proportions differed between groups. Next each treatment group compared to control using a 2x2 Fishers

Exact test with a Bonferroni correction. Third, Armitage's test for linear trend was performed. All tests reported at the 5% and 1% level of significance.

CHAMBER CONCENTRATION - The mean daily chamber concentrations were close to target (100-101%), the coefficient of variation was <3.0%. Overall mean temperature (range 20-22 degrees C) and relative humidity (range 46-53%) of each chamber were very similar.

MATERNAL DATA
No mortalities.
Pregnancy rates were 95, 100, 95 and 100% in 0, 5,000, 15,000 and 50,000 ppm groups, respectively.
Mean body weights were comparable between control and treated groups.
Pre-treatment and during treatment mean body weight changes were comparable between control and treated groups.
Post-treatment body weight gains were higher (significantly in the 50,000 ppm, 118%) in the treated groups.
Corrected Day 30G weights were comparable between groups.

Mean food consumption was significantly lower during treatment and significantly higher post-treatment in 50,000 ppm group compared to control; there were no other significant differences.
No adverse treatment effect was evident from physical evaluations.
During exposure (days 11 to 21), animals in the 50,000 ppm group showed decreased activity which was noted by a tap on the chamber wall. In all other groups a normal and similar response to the tap on the wall.
Incidence of premature deliveries were comparable between control and treated groups.
No aborted pregnancies were seen.
The mean number of corpora lutea and uterine implantations per pregnant females were similar between control and treated groups. The mean pre-implantation loss ratios were comparable between control and 5,000 and 15,000 ppm groups. The 50,000 ppm group ratio (0.16) was higher than control (0.08) but not significantly.
The mean numbers of viable fetuses per pregnant female were comparable between control and treated groups and no dead fetuses were recovered in utero, in any group. The mean number of resorptions, ratio of resorption/implants and incidence of resorptions in utero were comparable between control and treated groups.
Mean liver weight, absolute and relative to corrected Day 30G weights, were comparable between control and treated groups.
Gross morphological findings occurred at a similar level between control and treated groups and were considered not to be treatment related.

FETAL DATA
Mean fetal weights (combined or by sex) were similar between control and treated groups.
The number of males and female fetuses per pregnant female and the ratio of viable male/female fetuses per group was comparable between control and treated groups.
The incidence of external variations and visceral

malformations were not significantly different between control and treated groups.
There were no malformations in the fetuses/pups recovered from females that delivered prematurely.
The incidences of visceral variations, on a per fetus and per litter basis, were comparable between control and treated groups.
The incidences of fetuses with skeletal malformations did not differ significantly between control and treated groups.
The incidence of litters containing at least one fetus with ossification variation was 100% for all groups. The incidences did not differ significantly between control and treated groups.

Maternal and fetal no-observable-adverse-effect level was considered to be 15,000 ppm (based on decreased activity during exposure and reduced mean food consumption during treatment periods) and 50,000 ppm (no signs of either embryo- or fetotoxicity), respectively.

Reliability criteria - 1a (GLP guideline study).

Critical study for SIDS endpoint.

Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, considered to be a 100% pure.
Reliability: (1) valid without restriction
30-SEP-2003 (4)

Species: rat Sex: female
Strain: other: Crl:CD BR
Route of administration: inhalation
Exposure period: days 7-16 of gestation
Frequency of treatment: 6 hours/day
Doses: 0, 500, 2000, 10,000 and 50,000 ppm
Control Group: yes
NOAEL Maternal Toxity: = 10000 ppm

Year: 1990
GLP: yes

Remark: Groups of seven female rats were exposed. Day 1 of gestation (Day 1G) was defined as the day copulation was confirmed.

The study was conducted in conjunction with a four-week toxicity study in the rat (HLR No. 257-90) which has been reported separately.

Five 150 L chambers made of stainless steel and glass were used. Chambers were operated in a one-pass flow-through mode with the air flow rates adequate to maintain sufficient oxygen. Animal cages placed within the chamber for exposure were rotated daily.

Animals weighed - day after arrival, before mating and Days 1, 7-17 and 22G.
Feed weighed - Every other day for Days 1-19 and 22G.
Clinical signs on Days 1-22G.
Sacrificed on Day 22G and gross pathology performed. The uterus was removed and types of nidations and relative

positions recorded. The uterus of each "non=pregnant" rat was examined for possible early resorptions. Live fetuses were weighed, sexed, and examined. For each litter, the maximum stunted weight (MSW) was calculated and any stunted fetuses (weight <= MSW) were omitted from the mean litter weight.

STATISTICAL METHODS - The litter was considered the experimental unit. The level of significance was alpha = 0.05 (except Bartlett's test, alpha = 0.005).

Incidence of pregnancy, clinical observations, maternal mortality and females with total resorptions - Cochran-Armitage test for trend and Fisher's exact test for pairwise comparisons.
Maternal weight, weight change and feed consumption - linear combination of dose ranks from ANOVA and if this was significant, pairwise comparisons using Dunnett's test.
Live fetuses, dead fetuses, resorptions, nidations, fetal weight and incidence of fetal alterations - Jonckheere's test for trend and pairwise comparisons performed using the Mann-Whitney U test. If 75% ties occurred in reproductive and fetal parameters, the Cochran-Armitage test and the Fishers exact test replaced Jonckheere's and Mann-Whitney U tests, respectively.

CHAMBER CONCENTRATION - The mean daily chamber concentrations (measured hourly) were within +/-12% of target. The temperature (overall range, 17-27 degrees C) and relative humidity (overall range, 34-58%) were similar for all chambers. Oxygen concentrations were 20 +/- 1% for all chambers, based on a single daily measurement.

BODY WEIGHT GAINS - No significant differences in body weight changes for any time during the study.

FOOD CONSUMPTION - There were no significant differences at any time period, between any of the exposure groups.

CLINICAL OBSERVATIONS AND MORTALITY - During exposure, rats in the 50,000 ppm exposure group were lethargic, had uncoordinated movement and were less responsive to a noise stimulus for the first 15 minutes of exposure. They displayed normal activity thereafter. There were no mortalities.

PATHALOGICAL EVALUATION - There were no gross changes at any exposure concentration.

REPRODUCTIVE EFFECTS - No significant differences or trends observed for any reproductive parameter (pregnancy rate, incidence of totally resorbed litters, mean number of resorptions, number of live fetuses per litter or sex ratio).

FETAL FINDINGS - No differences detected in mean females, mean males and combined mean fetal weights. There were no exposure-related increases in the number of stunted fetuses. There were no developmental alterations detected, except for a single exencephalic fetus in the control litter.

Maternal no-observable-adverse-effect level was considered to be 10,000 ppm based on results described above. Although this pilot study did not fully evaluate developmental toxicity, no indication of such toxicity was evident at any exposure level.

Reliability criteria - 1b (comparable to guideline study).

Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity >99%.
Reliability: (1) valid without restriction
30-SEP-2003 (41)

Species:	rabbit	Sex: female
Strain:	New Zealand white	
Route of administration:	inhalation	
Exposure period:	Days 6-18 of gestation	
Frequency of treatment:	6 hours/day	
Doses:	0, 5,000, 15,000 and 50,000 ppm	
Control Group:	yes	
NOAEL Maternal Toxity:	= 5000 ppm	
NOAEL Teratogenicity:	= 50000 ppm	

Method: other
Year: 1991
GLP: yes

Remark: Groups of seven rabbits were exposed. Gestation Day O (Day 0G) was defined the day coitus was observed with two separate males.

Wahmann 1000 L stainless steel and glass chambers were used. Animals were housed in partitioned areas within the chamber; animal placement rotated daily.

Physical observations - twice daily and once during each exposure. Detailed physical exam on Days 0, 6-18 (after end of exposure), 24 and 30G.
Body weight - Days 0, 6, 9, 12, 15, 18, 24 and 30G
Feed weight - Recorded for intervals of 0-1, 5-6, 6-7, 7-8, 8-9, 9-10, 10-11, 13-14, 16-17, 18-19, 19-20, 24-25 and 29-30G.
Sacrificed on Day 30G and gross pathology performed. Liver weights recorded. The uterus was removed, weighed, opened and numbers and locations of following recorded; live and dead fetuses, late and early resorptions, and implantation sites. Ovaries evaluated for presence and number of corpora lutea. The uterus of each "non=pregnant" rabbit was examined. All fetuses were examined grossly, weighed and sacrificed. Late resorptions were weighed, examined grossly and discarded.

STATISTICAL METHODS - None, due to small sample size.

CHAMBER CONCENTRATION - The mean daily chamber concentrations were close to target (100-101%), the coefficient of variation was <3.5%. Overall mean temperature (range 24-25 degrees C) and relative humidity (range 40-44%) were similar for each chamber.

MATERNAL DATA - No mortalities.
Pregnancy rates were 100, 87.5, 87.5 and 100% in 0, 5,000,

15,000 and 50,000 ppm groups, respectively.
Mean body weight change and mean food consumption were similar between treated and control groups at all times (pre, during and post-treatment). Mean corrected Day 30G weights were similar between treated and control groups. During exposure, animals in the 15,000 and 50,000 ppm groups showed decreased activity. No adverse effects were noted for any exposure level during detailed physical examination. There were no abortions or premature deliveries. The mean number of corpora lutea and uterine implantations per pregnant females were similar between control and treated groups. The mean pre-implantation loss ratios were lower in each treatment group (0.0-0.12) compared to control (0.21). This is not an adverse effect. The mean numbers of viable fetuses and resorptions per pregnant female were similar between control and treated groups and no dead fetuses were recovered in any group.
Mean liver weight, absolute (5-22%) and relative to corrected Day 30G weights (3-17%), were lower than controls in each treated group. However they were within the range of control values and there was no dose relationship, hence effect not considered adverse. Gross morphological findings occurred at a similar level between control and treated groups and were considered not to be treatment related.

FETAL DATA
Mean fetal weights were similar between control and treated groups.
No external malformations or variations seen in any control or treated groups.

Maternal and fetal no-observable-adverse-effect level considered to be 5,000 ppm (based on decreased activity during exposure) and 50,000 ppm (no signs of either embryo- or fetotoxicity), respectively.

Reliability criteria - 1b (comparable to guideline study).
Source: Daxa Borkhataria Northaw
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity >99.0%.
Reliability: (1) valid without restriction
30-SEP-2003 (5)

5.8.3 Toxicity to Reproduction, Other Studies

Type: other: Sub-chronic
In Vitro/in vivo: In vivo
Species: rat
Strain: other: Crl: CD BR Sex: male/female
Route of administration: inhalation
Exposure period: 5 days/week for 90 days
Frequency of treatment: 6 hours/day
Doses: 0, 5,000, 15,000 or 50,000 ppm
Control Group: yes, concurrent no treatment

Method: other: comparable to OECD 413
Year: 1991
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: This study is reported in full in section 5.4. Data

relevant to reproductive organs is summarized separately here in section 5.8.3.

Four groups of 20 male and 20 female rats per group were exposed to HCFC-124. Subgroups of rats were held for a 1 month recovery period. Pathology evaluations were conducted after approximately 90 days on test (test days 95 and 96) and after approximately 1 month recovery (test days 128 and 129). At end of final exposure or end of 1 month recovery, rats were sacrificed and necropsied. The following reproductive system organs were collected (testes and ovaries were weighed):
Females:- Mammary gland, Ovaries, Uterus and Vagina
Males:- Prostrate, Testes, Epididymides and Seminal Vesicles.
Tissues underwent gross and microscopic evaluations.

STATISTICAL METHODS - Organ weights were analysed by one-way analysis of variance. If group mean differences were significant (F-test), Dunnett's test was used to make pairwise comparisons between test and control.

RESULTS - Absolute and relative organ weights were similar to control values for all exposure concentrations in males and females at 90-day and 1-month recovery sacrifices. There were no compound-related gross or microscopic morphological changes detected at any exposure concentration.

Reliability criteria - 1b (GLP, comparable to a guideline study).

Critical study for SIDS endpoint.
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99.9%.
22-MAY-2005 (44)

Type: other: Sub-chronic
In Vitro/in vivo: In vivo
Species: rat
Strain: other: Crl: CD BR Sex: male/female
Route of administration: inhalation
Exposure period: 5 days/week for 4 weeks
Frequency of treatment: 6 hours/day
Doses: 0, 500, 2,000, 10,000 or 50,000 ppm
Control Group: yes, concurrent no treatment

Method: other: comparable to OECD 412
Year: 1990
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: This study is reported in full in section 5.4. Data relevant to reproductive organs is summarized separately here in section 5.8.3.

Five groups of 10 male and 10 female rats per group were exposed to HCFC-124 during the same eight-hour period of the day. Males and females received a total of 21 and 22 days exposure, respectively.

An additional 6 female rats were exposed concurrently for a probe teratology study. This is reported separately (Haskell Laboratory Report No 108-90).

Following the final exposure, all animals were sacrificed and necropsied. The following reproductive system organs were collected (testes and ovaries were weighed):
Females:- Mammary gland, Ovaries, Uterus and Vagina
Males:- Prostrate, Testes, Epididymides and Seminal Vesicles.
Tissues underwent gross and microscopic evaluations.

STATISTICAL METHODS - Organ weight were analysed by one-way analysis of variance. If group mean differences were significant (F-test), Dunnett's test was used to make pairwise comparisons between test and control.

RESULTS - There were no compound-related effects on absolute and relative organ weight (% of body weight), which were similar to control values for all exposure groups. There were no gross or microscopic morphological changes at any exposure concentration.

Reliability criteria - 1b (GLP, comparable to a guideline study).
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99.9%.
22-MAY-2005 (45)

Type: other: sub-chronic
In Vitro/in vivo: In vivo
Species: mouse
Strain: other: Crl: CDE-1 (ICR) BR Sex: male/female
Route of administration: inhalation
Exposure period: 5 days/week for 90 days
Frequency of treatment: 6 hours/day
Doses: 0, 5,000, 15,000 or 50,000 ppm
Control Group: yes, concurrent no treatment

Method: other: comparable to OECD 413
Year: 1992
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: This study is reported in full in section 5.4. Data relevant to reproductive organs is summarized separately here in section 5.8.3.

Four groups of 20 male and 20 female mice per group were exposed to HCFC-124. Subgroups of mice were held for a 1 month recovery period. At end of final exposure (test days 96-97) or end of 1 month recovery (test days 123-124), mice were sacrificed and necropsied. The following reproductive system organs were collected for gross and microscopic evaluations:
Females:- Mammary gland, Ovaries, Uterus and Vagina
Males:- Prostrate, Testes, Epididymides and Seminal Vesicles.

RESULTS - There were no compound-related morphological changes at any exposure concentrations inn either males or

females at the 90-day or 1-month recovery sacrifices.

Reliability criteria - 1b (GLP, comparable to a guideline study).

Critical study for SIDS endpoint.
Test substance: 2-chloro-1,1,1,2-tetrafluoroethane, purity 99.9%.
22-MAY-2005 (43)

5.9 Specific Investigations

Endpoint:	other: cardiac sensitisation study
Species:	dog
Strain:	Beagle Sex: male
Route of administration:	Inhalation
Vehicle:	other: air
Doses:	1.0, 2.5 or 5.0%
Control Group:	no
Result:	HCFC-124 concentration of 2.5% or greater were capable of sensitising the beagle heart to the action of exogenous epinephrine.

Method: other
Year: 1976
GLP: no data

Remark: Healthy male beagle dogs were exposed to HCFC-124 via a face mask and had an electrocardiogram recorded throughout the experiment. Five minutes prior to exposure, they had a control iv injection of epinephrine, 0.008 mg/kg, and a challenge injection of same, five minutes after exposure.

Exposure concentrations were close to nominal (overall range 100-101%) with a maximum coefficient of variation of 5%.

The development, after challenge epinephrine, of an arrhythmia not present prior to exposure was considered a serious threat to life (multiple ventricular beats (MVBs) or ventricular fibrillation) and constituted a "marked response".

1%. 0/10 "marked response". No serious arrthymias were observed when 10 dogs were exposed.

2.5%. 4/10 "marked response". Four out of ten dogs exposed had the following responses:-
dog #1523 - (MVBs) of 4 second duration
dog #1515 - 2 episodes of MVBs of 10 second duration
dog #1489 - MVBs borderline fibrillation, recovered.
dog #1511 - 3 MVBs, fibrillation and cardiac arrest.

5%. 2/2. Both dogs exposed had "marked response" consisting of MVBs, one for 20 seconds, the other for 31 seconds.

HCFC-124 concentration of 2.5% or greater was capable of sensitizing beagle heart to the action of exogenous epinephrine.

Reliability criteria - 2e (study well documented, meets

generally accepted scientific principles, acceptable for assessment).
Source: Daxa Borkhataria Northaw
Test substance: 1-chloro-1,2,2,2-tetrafluoroethane, purity not given.

30-SEP-2003 (9)

Endpoint: other
Type: other: Diet and neoplasms in rats
Species: rat
Strain: Sprague-Dawley Sex: male/female
Route of administration: oral, diet
No. of animals: 700
Doses: See remarks

Remark: This study is mentioned in the summary in section 5.7.

5 experimental groups contained 70 rats/sex/group, in a study designed to compare the effects of ad libitum (AL) overfeeding and moderate dietary restriction of two different diets on rat 2-yr survival and the development of spontaneous neoplasms.

Groups were fed as follows:-

a) Purina Certified Rodent Chow 5002 pellets fed AL, approximately 24 (females) or 33 (males) g/day.

b) Purina Certified Rodent Chow 5002 pellets fed AL for approximately 6.5 hr/day during light cycle.

c) Purina Certified Rodent Chow 5002 pellets fed in measured daily amounts at approximately 65% of daily AL food consumption. This was approximately 16 (females) or 21.5 (males) g/day.

d) Purina Certified Rodent Chow 5002-9 extruded pellets AL.

e) Purina Certified Rodent Chow 5002-9 extruded pellets AL, fed in measured amounts to provide same calorific intake as animals in Group C. This was approximately 20.8 (females) and 28.8 (males) g/day.

Results.
Only the incidence of (and in brackets the number of deaths due to) mammary gland fibroadenoma are summarised here:

Group
a) 32/70, 46% (8)
b) 20/70, 29%
c) 25/70, 36% (2)
d) 18/70, 26% (3)
e) 12/70, 17%

This study concluded that moderate dietary restriction delayed death due to fatal cardiovascular or renal degenerative disease and spontaneous tumours, particularly those of the pituitary or mammary gland. The moderate

dietary restriction appeared only to delay onset, but not the progression of the spontaneous tumors.
Source: Daxa Borkhataria Northaw
09-OCT-2003 (32)

5.10 Exposure Experience

Type of experience: Human

Remark: HCFCs are used increasingly in industry. An epidemic of liver disease in nine industrial workers who had had repeated accidental exposure to a mixture of HCFC-124 and HCFC-123 has been investigated. The investigators aimed to test whether HCFC-123 and 124 could result in serious liver damage.

One worker liver biopsy was obtained and immunohistochemical
staining confirmed the presence of trifluoroacetyl protein adducts in surviving hepatocytes. The liver biopsy revealed
hepatocellular necrosis which was prominent in perivenular zone 3 and extended focally from portal tracts to portal tracts and centrilobular area. Serum of six affected workers and five control workers were tested for autoantibodies that react with human liver cytochrome P450 IIE1 and P58 protein disulphide isomerase isoform. These autoantibodies (previously associated with halothane hepatitis) were detected in the serum of five affected workers.

The investigators conclude repeated human exposure to HCFC-123 and 124 can result in serious liver injury in a large proportion of the exposed population. Although it is not clear which HCFC is responsible, the discussion focuses on HCFC-123 and its known hepatotoxicity and greater extent of metabolism.

Reliability criteria - 1d (Test procedure in accordance with
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Source: Daxa Borkhataria Northaw
Reliability: (1) valid without restriction
30-SEP-2003 (26)

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