FOREWORD **INTRODUCTION**

1,1,1,2,2-PENTAFLUOROETHANE

CAS N°: 354-33-6

SIDS Initial Assessment Report

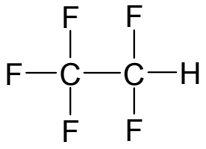
For

SIAM 20

Paris, France, 19-21 April 2005

1.	**Chemical Name:**	1,1,1,2,2-pentafluoroethane
2.	**CAS Number:**	354-33-6
3.	**Sponsor Country:**	United States
4.	**Shared Partnership with:**	Solvay Fluor; Dupont De Nemours S.A.; Honeywell Fluorine Products
5.	**Roles and Responsibilities of the Partners:**	Industry sponsors – initial preparer of documents U.S. Environmental Protection Agency – reviewer of the documents.
	• Name of industry sponsor /consortium	Marco Binaglia SOLVAY S.A. tel: +39 02 29092440
	• Process used	The industry sponsor prepared the documents, which relied on data obtained from a search of the databases described in Annex 1. The U.S. Environmental Protection Agency reviewed the documents and provided edits and changes where necessary in an iterative process with the industry sponsor.
6.	**Sponsorship History**	
	• How was the chemical or category brought into the OECD HPV Chemicals Programme?	Proposal of European Fluorocarbon Technical Committee (EFCTC)
7.	**Review Process Prior to the SIAM:**	Please see 5 above
8.	**Quality check process:**	Solvay (lead Company) drafted the documents in cooperation with co-sponsor Companies. At U.S. EPA, the documents underwent internal peer review.
9.	**Date of Submission:**	21 January 2005
10.	**Date of last Update:**	September 2005
11.	**Comments:**	

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	354-33-6
Chemical Name	1,1,1,2,2-pentafluoroethane (HFC-125)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Analog Rationale

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 pentafluoroethane for the aquatic toxicity endpoints. These substances are justified as analogs because they have molecular weights, functional groups, and Log Kow values that are similar to pentafluoroethane (HFC-125).

Human Health

In an inhalation toxicokinetics study, exposure by rats to concentrations of 1,000, 5,000, and 50,000 ppm (4,909, 24,544, and 245,440 mg/m^3) for 6 hours did not result in significant absorption or distribution in the body. In an acute inhalation toxicity test, HFC-125 administered to rats at a concentration of 800,000 ppm (3,927,000 mg/m^3) did not result in death. However, ataxic gait and abnormal respiration were observed during exposure and ceased one hour after exposure ended. No signs of dermal or ocular irritation were observed during acute exposure (up to 800,000 ppm) or repeated whole-body exposure (up to 50,000 ppm, 245,440 mg/m^3). Skin sensitization was not observed during repeated-dose studies.

In a 28-day inhalation study, rats were administered doses up to 50,000 ppm (245,440 mg/m^3) 6 hours per day, 5 days per week. Ten rats per sex per dose were used in the study. No clear treatment-related effects were observed and the highest tested concentration was considered to be the NOAEC. In a 90-day inhalation study, groups of ten males and ten females were also administered HFC-125 at doses of 5,000, 15,000, and 50,000 ppm (24,544, 73,630, and 245,440 mg/m^3) by inhalation for 6 hours/day for 5 days/week. Gross pathological effects observed at the highest dose included a cyst in the kidney of one animal, a cyst in the ovary of another, enlarged lymph nodes of a third animal, and white patches in the liver of a fourth animal. Due to the limited number of animals and different organs affected as well as the lack of statistical significance, these effects were considered incidental. Therefore, the highest dose (50,000 ppm) was considered the NOAEC for the 90-day study.

In vitro genotoxicity studies (a bacterial reverse mutation test and two mammalian chromosomal aberration tests) and an *in vivo* study (a mammalian erythrocyte micronucleus test) showed negative results at non-cytotoxic concentrations.

Fertility studies are not available. Results of organ weight and tissue analyses of male and female reproductive organs in both the 28-day and 90-day studies did not reveal any treatment-related effects.

In a developmental study in rats, groups of 40 females were exposed to concentrations up to 50,000 ppm (245,440 mg/m^3) HFC-125 during days 6 to 15 of pregnancy for 6 hrs/day. Twenty-four rabbits per exposure group were also dosed with concentrations up to 50,000 ppm during days 6 to 18 of pregnancy for 6 hours/day. No changes in embryo-foetal viability, incidence of malformations, anomalies or variants were observed. Therefore 50,000 ppm (245,440 mg/m^3) can be considered as both the maternal and the foetal NOAEC in the developmental studies.

A study on cardiac sensitisation was carried out in dogs exposed to HFC-125 and concurrently injected with

adrenaline. Cardiac sensitisation was observed in animals exposed to an atmosphere containing 100,000 ppm (490,880 mg/m^3) HFC-125 and above. The NOAEC for this study was 75,000 ppm (368,160 mg/m^3).

Environment

HFC-125 is a gas with a melting point of -103 °C, a boiling point of -48 °C, a vapor pressure of 1.4 x 10^4 hPa at 25°C an estimated water solubility range of 432-1071 mg/l at atmospheric pressure and a Log K_{ow} of 1.48.

According to the Level III Fugacity-based Multimedia Environmental Model, HFC-125 will partition almost exclusively into the atmosphere in an exposure scenario using 100 percent release into the air. No experimental data on abiotic degradation are available. However, calculated half-lives for hydrolysis are 1166 days at pH7 and 117 days at pH 8. Due to its vapor pressure and Henry's Law constant (28.2 KPa m^3/mol), the estimated volatilization half life 1 hour for a river and 105 hours for a lake. HFC-125 was not readily biodegradable in a closed-bottle test. Hydroxyl radical-mediated photodegradation in the troposphere results in a calculated global atmospheric lifetime of 29 years. Because of the low atmospheric degradation rate, HFC-125's potential to form ozone in the troposphere is considered negligible. Based on the ozone depletion potential value of 3 x 10^{-5} compared to CFC-11 (ODP = 1), HFC-125 does not contribute to atmospheric ozone depletion. Its global warming potential relative to CO_2 is 3,400 for a time horizon of 100 years and thus it has the potential to contribute to global warming upon release. Using the Log K_{ow} value, the estimated BCF is 2.75. Therefore, HFC-125 is not expected to bioaccumulate in aquatic organisms to any appreciable extent.

No ecotoxicity experimental data are available for HFC-125. ECOSAR calculations predicted the hazard potentials shown in the following table. This estimation is supported by the low aquatic toxicity of HFC-125 structural analogs. The analogs are likely to be more biologically reactive because of the presence of chlorine atoms in the chemical structures as well as the higher water solubilities.

	HFC-125	HCFC-141b	HCFC-142b
Fish (mg/L)	96-hr LC_{50} 274 (QSAR calculation)	96-hr LC_{50} 126 (experimental)	96-hr EC_{50} 220 (experimental)
Daphnia (mg/L)	48-hr LC_{50} 283 (QSAR calculation)	48-hr LC_{50} 31.2 (experimental)	48-hr LC_{50} 160 (experimental)
Algae (mg/L)	96-hr LC_{50} 172 (QSAR calculation)	72-hr EC_{50} >44 (experimental)	No data

Exposure

Greater than 99 percent of HFC-125 is used as a blend component for commercial refrigeration and air conditioning systems, while the rest is used as a fire extinguishing agent, as minor applications in plastic foam blowing, and as a solvent in special applications. The production of HFC-125 from three producers was approximately 16,000 tonnes in 2002. Occupational exposure to HFC-125 may occur during production and mainly during repair/maintenance operation in refrigeration systems. Since refrigeration units and fire extinguishing systems are hermetically sealed, consumer exposure would occur most likely from slow leaks. However, when used to extinguish fires, there may be some short term exposure to HFC-125 as well as thermal degradation products such as hydrogen fluoride. Environmental monitoring data performed between 1998 and 2000 detected a maximum mixing ratio of 1.4 ppt HFC-125 in the atmosphere. The use and disposal of equipment containing HFC-125 is regulated in the USA under the Clean Air Act (FR V68, 162, 2003).

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

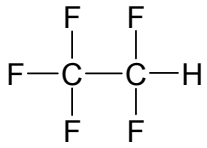
The chemical is currently of low priority for further work due to its low hazard profile for human health and the environment (fish, invertebrates, and algae). Its global warming potential is acknowledged and being addressed by other programs.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 354-33-6
IUPAC Name: 1,1,1,2,2-pentafluoroethane
Molecular Formula: $C_2H_1F_5$



Structural Formula: $F_3C\text{-}CHF_2$
Molecular Weight: 120.02 g/mol
Synonyms: HFC-125

1.2 Purity/Impurities/Additives

The purity of the marketed substance is >99.5 % v/v.

1.3 Physico-Chemical Properties

Table 1. Summary of Physico-Chemical Properties

Property	Value	Reference
Physical state	Gas	
Melting point	-103 °C	Kirk-Othmer Encyclopedia of Chemical Technology
Boiling point	-48.5 °C	Kirk-Othmer Encyclopedia of Chemical Technology.
Liquid density	1.53 g/cm^3 at -48.5 °C	Kirk-Othmer Encyclopedia of Chemical Technology
Vapour pressure (25 °C)	13,999 hPa	Daubert and Danner, 1989
Water solubility (25 °C)*	432 mg/l (estimated) 1071 mg/l (estimated) 905.5 mg/l (estimated,) 5,970 mg/l (estimated, at saturated vapour pressure)	Abraham et al., 2001 EPIWIN v3.12 EPIWIN v3.12 TGD, 2003
Partition coefficient n-octanol/water (log value)	1.48	Kawara and Tsutsumi, 1992
Dissociation constant	Dissociation not observed. HFC-125 is not dissociated in water solutions.	Tsutsumi, 1992
Henry's Law Constant (25 °C)	28.2 kPa m^3/mol (estimated)	TGD, 2003
The substance may undergo thermal decomposition resulting in the formation of hydrogen fluoride		

* Note on water solubility: a wide range may be identified for water solubility of HFC-125 (400-1000 mg/l at atmospheric pressure). However, due to the relatively low reliability of the QSAR programs for the estimation of water solubility of fluorinated compounds, the water solubility value estimated by the Ostwald solubility coefficient (Abraham et al., 2001) has been used in the dossier.

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 HFC-125 for the aquatic toxicity endpoints. These analogs were chosen based on similar functional groups, similar molecular weights, and similar Log K_{ow} values. The physico-chemical properties of HFC-125 and the analogs are reported in Table 2.

Table 2: physico chemical properties of HFC-125 and two structural analogs

	HFC-125	**HCFC-141b***	**HCFC-142b***
	CF_3CHF_2	$CFCl_2CH_3$	CF_2ClCH_3
Molecular Weight	120.02	116.95	100.50
Boiling Point (°C)	-48	32	-9.2
Melting Point (°C)	-103	-103.5	-130.8
Vapour Pressure (hPa)[a]	13,999	763	3390
Water Solubility (mg/L)	432[b]	4,000 (measured)	1,400[b] (measured or derived from measured HLC of 7400 Pa m^3/mol)
Log K_{ow}	1.48	2.3	1.64

*as presented at SIAM 12

[a] data at 25 °C

[b] data at 25 °C and at 1 atm of partial pressure of the solute

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Production Volumes

The 2002 Alternative Fluorocarbons Environmental Acceptability Study (AFEAS) estimated that 16400 tonnes were globally produced by ten companies (AFEAS, 2004). The 2002 Inventory Update Rule database reports that between 10 and 50 million pounds (4,540 to 22,700 tonnes) of HFC-125 were produced or imported annually in the United States by one company, Honeywell International, Inc. (U.S. EPA, 2004a)

Manufacturing Method

Pentafluoroethane is synthesized in a closed reactor by hydrofluorination of chlorotetrafluoroethane (HFC-124) and subsequent purification by distillation. The production facilities identified for each company within the consortium that is sponsoring HFC-125 in the OECD SIDS program are as follows:

DuPont	Deepwater, NJ (USA)
Honeywell	Geismer, La (USA)
Solvay	Porto Marghera (Italy)

It is possible that other companies not represented by the consortium may produce HFC-125.

Uses

According to the AFEAS database (AFEAS, 2004), more than 99% of HFC-125 produced worldwide by the reporting companies is used as a blend component for commercial refrigeration and air conditioning systems. The use as a fire-extinguishing agent in total flooding systems is another application of HFC-125 (EFCTC, 2004). Minor applications include the use of HFC-125 in plastic foam blowing and as a solvent in special applications (AFEAS, 2004).

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

There is no natural source of pentafluoroethane. The HFC-125 production and the applications of refrigeration and air conditioning are carried out in closed systems. Release of HFC-125 into the atmosphere may occur during manufacturing and during repair/maintenance work on refrigeration systems. Slow leaks from refrigeration and air-conditioning systems and emissions occurring during the short-term applications, such as plastic foam blowing may be also identified as relevant sources of environmental release. Leakage rates from refrigeration systems are estimated to range between ≤1% – 22%/year, depending on the application field (domestic or commercial refrigeration systems) and on the technological design of the refrigerating units (IPCC/TEAP, 2004). According to these figures, an eventual complete release of the refrigerating agents can be considered to occur during the life-cycle of less technologically-improved refrigerating systems. AFEAS (2004) estimated a global release of about 3,500 tonnes HFC-125 in 2002, principally due to HFC-125 already present in the market. Of the 2002 production volume (16,400 tonnes), fugitive emissions (which occur during transport and transfer operations) have been estimated to be less than 10 tonnes (AFEAS 2004). These estimations have been carried out by using the HFC-134a emission function and are considered provisional values. A possible release of HFC-125 is predictable also during the dismantling operations of refrigeration systems, although the recovery of the refrigerating agents can considerably limit the environmental emission in this process.

HFC-125 is stored in hermetically sealed units when used for fire extinguishing applications. In this case only infrequent environmental release is predictable, which can result in release of hydrogen fluoride (and which has its own toxic properties).

Environmental release can be considered to occur exclusively in the air compartment during production, processing and use of HFC-125.

2.2.2 Photodegradation

The atmospheric degradation pathway for HFC-125 involves the initial reaction with hydroxyl radicals in the troposphere. The molecular breakdown proceeds via various free-radical intermediates to give the stable molecule $C(O)F_2$ and CF_3O radical. $C(O)F_2$ is expected to be removed from the atmosphere by uptake into clouds, rain and the oceans and to be hydrolysed to HF and CO_2 within a few days to a few months. The environmental fate of CF_3O radical involves the probable formation of CF_3OH and the further degradation to CO_2 and HF, which are thus considered the main degradation end products of HFC-125. The proposed degradation pathway is supported by several studies (Tuazon and Atkinson, 1993; Edney and Driscoll, 1992; STEP/AFEAS, 1993; Franklin, 1993; and Hasson et al., 1997).

Lifetimes for CF_3O radicals with various species are reported in Franklin (1993). If considering the contribution of all the possible reactions (CH_4, NO, formaldehyde, et cetera), a lifetime < 1 s (thus also a half-life < 1 s) can be assumed for CF_3O.

Table 3 Partial lifetimes of CF_3O radicals in the atmosphere (adapted from Franklin, 1993)

Species (X)	Rate constant (cm^3 $molecule^{-1}$ s^{-1})	Concentration, [X] (molecule cm^{-3})	Lifetime s
NO	$(2.5 \pm 0.4) \times 10^{-11}$	$1.0 \times 10^8 – 2.5 \times 10^{10}$	1.6 – 400
NO_2	$(9.0 \pm 1.5) \times 10^{-12}$	$7.5 \times 10^7 – 5.0 \times 10^{10}$	2.2 – 1500
CO	$(4.4 \pm 0.6) \times 10^{-14}$	$5.0 \times 10^{12} – 2.5 \times 10^{13}$	0.9 – 4.5
CH_4	$(2.1 \pm 0.2) \times 10^{-14}$	3.3×10^{13}	1.4
C_2H_6	$(1.2 \pm 0.2) \times 10^{-12}$	$\sim 1 \times 10^{10}$	~ 80
C_2H_4	$(2.8 \pm 1.2) \times 10^{-11}$	$\sim 5 \times 10^9$	~ 7
H_2CO	$(7.3 \pm 1.0) \times 10^{-12}$	7.8×10^{10}	1.8

Talukdar et al. (1991) measured a rate constant of $1.9 \pm 0.27 \times 10^{-15}$ cm^3 /molecule/sec for reaction of HFC-125 with hydroxyl radicals at 298 K. A similar value of 2×10^{-15} cm^3 /molecule/sec is listed in Evaluation Number 14 of JPL NASA (2003), as a result of a combined fit of different experimental data.

The global atmospheric lifetime of HFC-125 is listed in WMO Report 47 (2002) and in IPCC third assessment (2001). An official value of 29 years was estimated considering the tropospheric lifetime, relative to CH_3CCl_3, calculated by means of an OH-mediated photodegradation rate proposed by JPL NASA (2003) at 272 K, a default stratospheric loss of 8% of the tropospheric loss and a negligible oceanic lifetime of 10650 years (Yvon-lewis and Butler, 2002).

Due to the low atmospheric degradation rate, HFC-125 potential to form ozone in the troposphere is considered negligible (Hayman and Derwent, 1997).

2.2.3 Stability in Water

There are no data on the hydrolysis of HFC-125 in water.

EPIWIN v3.1 (2001) calculated a rate constant of 6.877 × 10-2 l/mol/sec for alkaline hydrolysis of HFC-125 at 25 °C, corresponding to a half-life of 117 and 1166 days at pH = 8 and pH = 7, respectively.

However, due to the high values of vapour pressure (13999 hPa) and Henry's Law Constant (28.2 kPa m3/mol), volatilisation from the water compartment can be considered the most important process of HFC-125 removal. Volatility from rivers or lakes was calculated by EPIWIN v3.10 (2001). The estimated volatilisation half-lives are 1 hour from a river (1 m of water depth, 5m/sec of wind velocity and 1 m/sec of current velocity) and 105 hours from a lake (1 meter of water depth, 0.5 m/sec of wind velocity and 0.05 m/sec of current velocity).

2.2.4 Partitioning between Environmental Compartments

Fugacity-based Multimedia Environmental Model Level III (2002) was used to estimate the partitioning of HFC-125 into the environment, under the assumption that 100% is released to air. The Level III model's results indicated that HFC-125 would partition mainly into the air compartment (~100%) and less than 0.02% and 0.005% in water and soil compartment, respectively.

2.2.5 Biodegradation

A closed bottle test with activated domestic sewage sludge was carried out to establish the biodegradability of HFC-125 (Tobeta, 1992). A biodegradation of 5% was observed after 28 days. HFC-125 was judged to be not readily biodegradable under the test conditions. BIOWIN v4.00 (EPIWIN, 2001) estimated a low biodegradation probability for HFC-125 with all the available models.

2.2.6 Bioaccumulation

BFCWIN v2.14 (EPIWIN, 2001) estimated a bioconcentration factor of 2.75 for HFC-125.

2.2.7 Other Information on Environmental Fate

A soil adsorption coefficient K_{oc} was estimated with PKOC v1.66 (EPIWIN, 2001) to be 154 l/kg.

Ozone Depletion Potential

The ozone depleting potential (ODP) of HFC-125 relative to CFC-11 (ODP=1.0) was calculated with a model developed by World Meteorological Organization (WMO, 2002) to be below 3×10^{-5}. Due to the absence of chlorine and bromine atoms in the molecule, the contribution of HFC-125 to atmospheric ozone depletion can be considered negligible.

Global Warming Potential

Global Warming Potential (GWP) values of 5,970, 3,450 and 1,110 relative to carbon dioxide (GWP = 1) were calculated for integration time horizons of 20, 100 and 500 years, respectively (WMO, 2002). An official value of 2,800 was adopted by the Kyoto protocol (IPCC, 1996) for a time horizon of 100 years, indicating a potential contribution to global warming.

Under the Significant New Alternatives Policy (SNAP) Program for protection of stratospheric ozone administered by U.S. Environmental Protection Agency, the GWP of HFC-125 was considered in evaluating blends using this compound as alternatives for refrigeration, air conditioning products, and fire extinguishing uses. In particular, SNAP lists R-407C (which contains 25% HFC-125) as an acceptable alternative for HCFC-22, CFCs, HCFC blends, and R-502 in various refrigeration and air conditioning end uses (U.S. EPA, 2003; 2004b). The GWP of R-407C is lower than HCFC-22 and alternatives to HCFC-22 used in bus air conditioners and lower than other substitutes for R-502 (U.S. EPA, 2003; 2004b). EPA also finds ISCEON 89 (86% HFC-125) as an acceptable substitute for R-13B1 in very low temperature refrigeration. ISCEON 89 has a lower GWP than most other alternatives to R-13B1 for this use. However, EPA does recommend that leaks must be promptly identified and repaired (U.S. EPA, 2003). ISCEON 79 (containing 85.1% HFC-125) is also acceptable in new or retrofit equipment for other refrigerants for several types of uses; this mixture has a comparable or lower GWP than most other common refrigeration substitutes (U.S. EPA, 2004b). For fire extinguishing uses, HFC-125 and NAF S-125 have GWPs comparable or lower than Halon 1301 and substitutes for Halon 1301 (U.S. EPA, 2004b).

Monitoring Data

The tropospheric concentration of HFC-125 was measured from 1998 to 2000. A maximal mixing ratio of 1.4 ppt was detected (WMO, 2002).

2.3 Human Exposure

2.3.1 Occupational Exposure

Regular monitoring data for occupational exposure to HFC-125 during production and formulation are not carried out, since this chemical has a low toxicity and is produced and formulated in closed systems. However, exposure due to fugitive emissions might occur during production and processing of HFC-125.

HFC-125 is mainly used as a blend component for commercial refrigeration. Occupational exposure may occur during determinate routine operations on refrigeration systems. Gjølstad et al. (2003) measured the occupational exposure to halogenated refrigerants during 30 maintenance/repair operations in refrigeration systems. Among others, measures of the workroom air concentration and 10 personal samplings of exposed workers to a mixture containing 44% of HFC-125 were performed. Using personal sampling methods, measures of HFC-125 in the mixture showed a concentration range of 4.9-182 mg/m^3 (1-37 ppm), with a sampling time of 20-210 minutes. Workroom air concentration measures showed peak values within the time of exposure. The peaks for HFC-125 ranged from 64 to 5891 mg/m^3 (13-1,200 ppm) with a duration of 3-18 minutes. Considering an exposure for 390 minutes to 600 ppm HFC-125 as a worst-case scenario for occupational exposure during maintenance/repair work on refrigeration systems, the 8-hour weighted exposure is 488 ppm.

Process exhausts generally are delivered to a thermal oxidation installation and destroyed during the manufacturing process. The overall process is carried out in a closed system.

Some occupational exposure might occur from the minor applications, which include the use of HFC-125 in plastic foam blowing and as a solvent in special applications (AFEAS, 2004).

2.3.2 Consumer Exposure

HFC-125 is mainly used in commercial refrigeration, air conditioning equipment and as a fire-extinguishing agent. Information on potential exposure of the general public to HFC-125 was not identified. Eventual slow leaks from the refrigeration and air conditioning systems may occur. However, refrigeration units and fire extinguishing systems are hermetically sealed and maintenance is carried out only by professionals.

Direct consumer exposure to HFC-125 has to be considered when it is used as a fire-extinguishing agent. In this application HFC-125 may undergo a thermal decomposition, resulting in the release of hydrofluoric acid (which has its own toxic characteristics) and other degradation products.

Minor applications include the use of HFC-125 in plastic foam blowing and as a solvent in special applications (AFEAS, 2004). It is not clear whether consumer exposure might occur from these applications.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Studies in Animals

In vivo Studies

Although the mechanism of halothane hepatotoxicity has never been clarified, it has been hypothesized that trifluoroacetic acid, as a major hepatic metabolite of halothane, may be the active species implicated in halothane hepatitis (Gut et al., 1993; Kitterigham et al., 1995; DECOS 2002). Therefore, HFC-125 was assessed for the potential to be metabolised to trifluoroacetic acid in liver, in comparison with other halogenated-ethanes. Male Fisher rats were exposed to halothane, HCFC-124, HFC-125, HCFC-123 and HFC-134a. At the end of the exposure, animals were placed in metabolism cages and urinary trifluoroacetic acid excretion was measured. The presence of trifluoroacetylated-hepatic protein was assessed by means of SDS-PAGE and immunoblotted with anti-TFA-protein serum. The potential to form trifluoroacetylated-hepatic protein has the following decreasing order: Halothane ≥ HCFC-123 >> HCFC-124 > HFC-125. TFA-proteins were not detected in samples from rats exposed to HFC-134a. 19F-NMR analysis of urinary TFA excretion confirmed the previous order of reactivity. The increased fluorination on the dihalomethyl group (-CX_2H) decreases the metabolism of these compounds in vivo. HFC-125 showed a lower potential to form TFA in liver when compared to other halogenated ethanes.

Sprague Dawley rats were exposed to 1,000, 5,000 and 50,000 ppm (4,900, 24,500 and 245,000 mg/m^3) HFC-125 for 6 hours in individual inhalation chambers (Anders, 1993). Absorption was calculated by measuring the decrease of HFC-125 concentration in atmosphere within the period of exposure. Results indicated a slight uptake at the end of the exposure period. Due to the low absorption of HFC-125, kinetic constants of uptake and metabolism were not calculated.

Conclusion

HFC-125 is very poorly absorbed via inhalation. Compared with other halogenated ethanes, HFC-125 is less likely to be metabolised to TFA in the liver or will be metabolized at a slower rate.

3.1.2 Acute Toxicity

Studies in Animals

Inhalation

In an OECD guideline study (Nakayama et al., 1992a), 10 Sprague Dawley rats (5 males and 5 females) were exposed to 800,000 ppm (3,927,000 mg/m^3) HFC-125 in atmosphere for 4 hours. Another 10 animals were exposed to normal air for control. No mortality was observed within 14 days after the exposure. During the exposure, clinical signs typical of an anaesthetic effect, such as abnormal respiration and ataxic gait, were observed. These effects disappeared within 1 hour after the end of the exposure period. A slight decrease in mean body weight was registered in the exposed males, in comparison with the control males. No remarkable findings were observed during the autopsy. The lowest lethal dose (LDLo) was > 800,000 ppm (highest dose tested) for this study.

Cardiac sensitisation potential of HFC-125 following adrenaline injection was studied in beagle dogs (Hardy et al., 1992). The animals were initially tested for cardiac sensitivity to adrenaline alone, in order to establish the response dose (varying from 1 to 12 μg/kg for different animals). HFC-125 effects were compared to Halon 13B1 and to the reference (positive control) CFC-11. CFC-11 at a concentration of 25,000 ppm (122,720 mg/m^3) in air gave fatal ventricular fibrillation and multiple ectopic beats in 2/2 tested dogs. Six dogs were first exposed to 50,000 Halon 13B1, and then the same dogs were exposed to 100,000 HFC 125; these dogs were alternately exposed to increasing concentrations of Halon 13B1 and HFC 125. The same dogs were used for each successive exposure until a clear positive response was observed (5 or more apparently multifocal ventricular ectopic beats or ventricular fibrillation). Any dog with a positive response was removed from the experiment; it was assumed that the dogs exhibiting a positive response would also exhibit positive responses at all higher concentrations of the subject compound. Halon 13B1 and HFC-125 gave positive responses at 200,000 ppm (981,759 mg/m^3) (2/6 animals) and 100,000 ppm (490,879 mg/m^3) (1/6 animals), respectively. In this study the EC50 of HFC-125 for cardiac sensitisation potential was between 100,000 and 150,000 ppm (490,879 and 736,319 mg/m^3) in air, and the NOEC was 75,000 ppm (368.160 mg/m^3). Two dogs exposed respectively to 200,000 and 300,000 ppm HFC-125 showed fatal ventricular fibrillation. Because normal human plasma concentration of adrenaline is less than 140 pg/ml, the relevance of these studies using exogenous adrenaline concentrations well above physiologic range is not clear, and the significance of such finding is difficult to evaluate (U.S. EPA, 1993).

A similar study was performed with a mixture of 36.5/63.5% v/v HFC-23/HFC-125 (Hardy and Kieran, 1993). Exposure to 100,000 ppm (490,879 mg/m3) of this mixture in air gave a positive response (fatal ventricular fibrillation) in one of six dogs.

Conclusion

HFC-125 has a very low acute toxic potential by inhalation when mortality is considered. During exposure abnormal respiration and ataxic gait were observed. These effects disappeared within an hour after exposure ceased. Concentrations of 100,000 ppm (490,879 mg/m^3) or greater of HFC-125 in air induced cardiac sensitisation in dogs concurrently injected with adrenaline.

3.1.3 Irritation

There are no skin or eye irritation studies available. No signs of irritation were observed during whole-body exposure in acute or repeated-dose inhalation studies.

3.1.4 Sensitisation

There are no dermal sensitisation studies available. No sensitisation responses were observed during whole-body exposure in repeated-dose inhalation studies.

3.1.5 Repeated-Dose Toxicity

Studies in Animals

Inhalation

Two OECD guideline studies are available for inhalation exposure to HFC-125 for 28 and 90 days, respectively.

Groups of 10 male and 10 female Sprague Dawley rats were exposed to 0, 5000, 15,000 and 50,000 ppm (0, 24.544, 73,632 and 245,440 mg/m^3) HFC-125 for 28 days (6 hours/day, 5 days/week).

Two additional groups were exposed to 0 and 50,000 ppm HFC-125 and were allowed to recover for two weeks after the exposure period (Nakayama et al., 1992b).

No mortality was observed in this study. There were no treatment-related clinical signs of toxicity and differences in body weight and food consumption among the treated and the control groups, neither after the exposure nor after the recovery period. Some effects were observed in the haematology and blood chemistry analysis. In particular, a very slight, not dose-related increase in mean corpuscular haemoglobin concentration was measured in the males of all the treatment groups at the end of the exposure period; only the increase at the highest dose was statistically significant in comparison with the controls. Males exposed to 5,000 and 15,000, but not to 50,000 ppm, showed a slightly lower serum albumin content. A slight increase in serum phospholipids concentration was measured in the males of high-dosed group, at the end of exposure period. No haematological findings were observed in the recovery groups.

Neither macroscopic nor microscopic changes were observed during gross pathology and histological examinations, respectively. Study of peroxisomal proliferation gave equivocal results, since a slightly higher activity of peroxisomal beta-oxidation was measured in the males of the high-dosed group in comparison to control; while a lower activity was measured in the females of the same group.

The toxicological significance of the above effects is not clear. This fact and because of the equivocal nature of most of the effects, the 50,000 ppm concentration was considered the NOAEC of this study.

In 13-week study, groups of 10 male and 10 female Sprague-Dawley rats were exposed to 0, 5,000, 15,000 and 50,000 ppm (0, 24.544, 73,632 and 245,440 mg/m^3) HFC-125 (6 hrs/day, 5 days/week). Additional groups of 10 male and 10 female rats were designated for a 4-week recovery period (Nakayama et al., 1993). No mortality was found at any dose. There were no treatment-related clinical signs of toxicity or significant differences in body weight gains and food consumption among the control and the treated groups. No statistical differences were observed in haematology, blood biochemistry and urinalysis, in organ weights and in peroxisomal β-oxidation activities. Gross pathology examinations revealed a white patch in the liver of one male and a cyst in the kidney of another male dosed at 50,000 ppm and thick ear of one female of 5,000 ppm group, one of 50,000 ppm group and one in the control group. Enlargement of the lymph node in one female and a cyst in the ovary of another female were observed in the 50,000 ppm group at the end of the recovery period. These findings were considered incidental. No treatment-related histopathological changes were observed and 50,000 ppm, was considered the NOAEC for this study.

Conclusion

In the 4-week repeated-dose study in rats, HFC-125 exposure up to 50,000 ppm by inhalation did not induced mortality and no clinical signs were observed. The NOAEC of the 13-week study was also determined to be 50,000 ppm.

Some findings were observed in the haematology and blood chemistry examinations of males in the 4-week study (increase in mean corpuscular haemoglobin concentration at all the tested concentrations, increase in serum phospholipids concentration of males dosed at 50,000 ppm and a decrease in serum albumin content in the groups exposed at 5,000 and 15,000 ppm). However, some of these findings were not dose-related or showed equivocal results. These findings were not reproducible in the 13-week study.

3.1.6 Mutagenicity

In Vitro Studies

Four *in vitro* tests of genetic toxicity were carried out for HFC-125.

A reverse mutation assay study was performed with five histidine-dependent strains of *Salmonella typhimurium* and one tryptophan-dependent strain of *Escherichia coli* with and without metabolic activation. No increased incidence of mutation was observed in cells exposed for 48 hours to concentrations up to 100% (4,908,000 mg/m^3) HFC-125 in atmosphere, although cytotoxicity was observed at the highest tested concentration, both in the presence and in the absence of metabolic activation (May and Watson, 1992).

A limited Ames test was used by Longstaff et al. (1984) as a screening test to select the molecules to be tested in a chronic exposure study in rats. HFC-125 up to 200,000 ppm (982,000 mg/m^3) was tested in 2 strains of *Salmonella typhimurium,* with and without metabolic activation. Negative results were obtained with both strains and no chronic toxicity study was carried out for HFC-125.

A cytogenetic assay for the study of chromosomal aberrations was carried out in Chinese hamster ovary cells exposed to concentrations up to 700,000 ppm (3,436,000 mg/m^3) for 4 hours and up to 600,000 ppm (2,945,000 mg/m^3) for 24 and 48 hours, with and without metabolic activation. Positive results were observed only after 48 hours of exposure to 600,000 ppm HFC-125 in the absence of metabolic activation. However, the increased incidence of chromosomal aberration, observed under this experimental condition was concurrent with clear evidence of cytotoxicity (Dance, 1992a).

A further chromosomal aberration test was carried out in human lymphocytes exposed up to 700,000 ppm (3,436,000 mg/m^3) HFC-125 for 3, 24 and 48 hours, with and without metabolic activation. This study gave clearly negative results (Dance, 1992b).

In vivo Studies

An erythrocyte micronucleus test was performed by exposing groups of 5 male and 5 female mice up to 600,000 ppm (2,945,000 mg/m^3) HFC-125 in atmosphere for 6 hours. Mice were killed 24, 48 and 72 hours after exposure. The highest tested concentration produced clinical signs of toxicity (hunched posture, tremors, slow respiration), but no statistically-significant increased frequency of micronucleated erythrocytes was observed at any tested concentration, in comparison with control. No significant changes were observed in the ratio of polychromated to mature cells among the control group and the groups treated with HFC-125 (Edwards, 1992).

Conclusion

HFC-125 was not shown to be genotoxic in vitro and in vivo studies.

3.1.7 Carcinogenicity

There are no carcinogenicity studies available for HFC-125.

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility and Reproductive Organs

No specific fertility studies were conducted for HFC-125. In two repeated-dose inhalation studies (discussed in Section 3.1.5), rats were exposed to 0, 5,000, 15,000 or 50,000 ppm (0, 24.544, 73,632 and 245,440 mg/m^3) HFC-125 for 28 (Nakayama, 1992b) and 90 (Nakayama, 1993) days. In both studies, several reproductive organs of males (testes, epididymis and prostate) and females (uterus, ovaries and vagina) were evaluated both macro- and microscopically. No treatment-related findings were observed at any of the administered doses.

Developmental Toxicity

Groups of 40 pregnant female rats were exposed to levels of 0, 5,000, 15,000 or 50,000 ppm (0, 24.544, 73,632 and 245,440 mg/m^3) for 6 hrs/day during the gestation days 6-15 and sacrificed on day 20 of gestation (Masters et al., 1992). Adult female rats exhibited an unsteady gait during the exposure period, but no other treatment-related signs were observed. No significant differences were observed in body weight gain and food consumption among the control and the treated groups. Autopsies of adult females did not reveal any treatment-related finding.

No treatment-related findings were observed in litter size, embryofetal loss and litter and fetal weight in the rat study. The incidence of fetal malformation was 1/317, 2/341, 11/342, 5/366 for 0, 5,000, 15,000 and 50,000 ppm, respectively. However, 10 fetuses in the 15,000 ppm group and 3 fetuses in the 50,000 ppm group were affected by bilateral forelimb flexure, associated with distorted ribcage and thickened ribs. This syndrome is considered spontaneous and thus not treatment-related. No statistically-significant differences in the incidence of anomalies and variants were observed during visceral and skeletal examination of fetuses among the control and the treated groups. The fetal and maternal NOAECs are both considered to be 50,000 ppm for this study.

Groups of 24 pregnant female rabbits were exposed to levels of 0, 5,000, 15,000 or 50,000 ppm (0, 24.544, 73,632 and 245,440 mg/m^3) for 6 hrs/day during the gestation days 6-18 and sacrificed on day 29 of gestation (Brooker et al., 1992). Two animals in the control group and one in the 5,000 ppm group were sacrificed due to the poor condition. Another animal treated at 5,000 ppm showed weight loss during the early days of exposure and aborted on days 20/21. There were no other instances of abortion during the study. Treated animals showed an increased incidence of cold ears during the exposure period, in comparison with control animals. This finding was considered a response to stress. Adults treated at 50,000 ppm, but not at 5,000 and 15,000 ppm, showed reduced food consumption in comparison with the control. No significant differences were observed in body weight gain. No treatment-related findings were apparent at terminal autopsy.

A slightly increased incidence of early and late in utero deaths was observed at 50,000 ppm in comparison with the control. However, statistical significance was not achieved. The results were also within background incidence when compared with 9 studies carried out by the same laboratory in 1991, except for total embryonic deaths at 50,000 ppm (in which results were slightly higher than historical controls (1.5 /litter versus 0.7-1.4/litter in historical control). The incidence of foetal malformation was 2/165, 1/193, 7/215 and 2/169 for 0, 5,000, 15,000 and 50,000 ppm, respectively. There was no evidence of any treatment-related morphological change or of increased incidence of visceral and skeletal anomalies or variants. The maternal and fetal developmental NOAECs for this study were 50,000 ppm.

Conclusion

No effects were observed in reproductive organs of male and female rats exposed up to 50,000 ppm (245,440 mg/m^3) HFC-125 by inhalation for 90 days.

Full developmental studies carried out in rats and rabbits did not show any developmental toxicity for HFC-125 at concentrations up to 50,000 ppm (245,440 mg/m^3) in atmosphere. The rabbit study showed a slightly increased incidence of early and late in utero deaths at 50,000 ppm (245,440 mg/m^3).

3.2 Initial Assessment for Human Health

HFC-125 has a lowest lethal dose LDLo> 800,000 ppm (3,927,000 mg/m^3) for inhalation acute exposure in rats. In dogs previously injected with adrenaline, cardiac sensitisation was observed at concentration > 75,000 ppm (368,200 mg/m^3). Although no studies specifically evaluating irritation to skin and eyes are available, no skin or eye irritation were observed either in acute or in repeated inhalation studies. Also, no studies that specifically measured dermal sensitization were available. However, no signs of dermal sensitisation were observed in repeated inhalation studies. No treatment-related findings were observed in repeated-dose studies in male and female rats exposed by inhalation to HFC-125 up to 50,000 ppm (245,440 mg/m^3) for 4 weeks or for 13 weeks. HFC-125 gave negative responses in both *in vitro* and *in vivo* genotoxicity tests. The developmental study in rats did not show any developmental effects for exposure to HFC-125 up to 50,000 ppm (245,440 mg/m^3). Although a slight increased incidence in *in utero* deaths occurred in rabbits, it was not statistically significant.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

There are no experimental data available on HFC-125 for the aquatic compartment. Due to its high values of vapour pressure and Henry's Law constant, HFC-125 will partition mainly to the air compartment. The estimation of HFC-125 ecotoxicity has been carried out by using the QSAR model ECOSAR v0.99g (EPIWIN, 2001). Moreover, ecotoxicological data from structural analogs are also presented to meet the SIDS-required endpoints for acute aquatic toxicity to fish, daphnids and algae.

Acute Toxicity to Fish

ECOSAR v0.99g calculated a 96-hr LC_{50} of 274 mg/l for HFC-125. ECOSAR v0.99g calculated a 96-hr LC_{50} of 45 mg/l and 162 mg/l for HCFC-141b and HCFC-142b, respectively.

A semistatic, sealed vessel 96-hr toxicity test in Guppies (*Poecilia reticulata*) was carried out for HCFC 142b (Groenveld and Kuijpers, 1990a). The 96-hr LC_{50} based on measured concentrations was 220 mg/l in this study. However, the low oxygen levels measured in the samples exposed to high concentration groups likely affected the mortality rate in these groups and thus the overall determination of the LC50.

For HCFC 141b, the 96-hr LC_{50} for Zebra fish (*Brachydanio rerio*) was 126 mg/L in a static, sealed vessel test (Bazzon and Hervouet, 1989).

Acute Toxicity to Aquatic Invertebrates

ECOSAR v0.99g calculated a 48-hr EC_{50} of 283 mg/l for HFC-125 in daphnia. ECOSAR v0.99g calculated a 48-hr EC_{50} of 49 mg/l and 170 mg/l for HCFC-141b and HCFC-142b, respectively.

A static acute immobilisation test on daphnia was carried out in sealed vessels using HCFC 141b (Brian and Hervouet, 1989). The 48-hr EC_{50} was 31.2 mg/l in this study.

A similar study carried out for HCFC 142b gave a 48-hr EC_{50} of 160 mg/l (Groenveld and Kuijpers, 1990b).

Acute Toxicity to Algae

ECOSAR v0.99g calculated a 96-hr EC_{50} of 172 mg/l for HFC-125 in green algae. ECOSAR v0.99g calculated a 96-hr EC_{50} of 31 mg/l and 104 mg/l for HCFC-141b and HCFC-142b, respectively.

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).

4.2 Terrestrial Effects

Acute Toxicity Test Results

ECOSAR v0.99g calculated a 14-day LC_{50} of 1,068 mg/kg dry soil for earthworms.

4.3 Other Environmental Effects

No data are available.

4.4 Initial Assessment for the Environment

Due to its physico-chemical properties and existing information on its current release pattern (please see Section 2.2.1), HFC-125 is expected to be released only in the atmosphere. Fugacity-based Multimedia Environmental Model Level III (2002) simulation suggested an almost total partitioning of HFC-125 into the air compartment. HFC-125 environmental fate is likely determined by hydroxyl radical-mediated degradation in the troposphere. The products of hydroxyl radical-mediated HFC-125 photochemical breakdown are expected to be $C(O)F_2$ and CF_3OH, which can be further degraded to CO_2 and HF. HFC-125 has an atmospherical lifetime of 29 years and a global warming potential relative to carbon dioxide of 3450 for a time horizon of 100 years. Its ozone depleting potential relative to CFC-11 is below 3×10^{-5}. AGAGE measured tropospheric concentration of HFC-125 from 1998 to 2000. A maximal mixing ratio of 1.4 ppt was detected (WMO, 2002).

Experimental ecotoxicity data for HFC-125 in the aquatic compartment are not available. ECOSAR v0.99g results for HFC-125 are summarised in Table 4 together with experimental and calculated ecotoxicity data for the structural analogs:

Table 4: Aquatic ecotoxicity of HFC-125 and of two analogs

	HFC-125	**HCFC-141b**		**HCFC-142b**	
Fish (mg/L)	96-hr LC50 274 (QSAR calculation)	96-hr LC50 126 (experimental)	96-hr LC50 45 (QSAR calculation)	96-hr LC50 220 (experimental)	96-hr LC50 162 (QSAR calculation)
Daphnia (mg/L)	48-hr LC50 283 (QSAR calculation)	48-hr LC50 31.2 (experimental)	48-hr LC50 49 (QSAR calculation)	48-hr LC50 160 (experimental)	48-hr LC50 170 (QSAR calculation)
Algae (mg/L)	96-hr EC50 172 (QSAR calculation)	72-hr EC50 >44 (experimental)	96-hr EC50 31 (QSAR calculation)	No data	96-hr EC50 104 (QSAR calculation)

Bioaccumulation of HFC-125 in aquatic organisms is expected to be low because of its log Kow of 1.48 and estimated bioconcentration factor of 2.75. HFC-125 was not readily biodegradable in a closed-bottle test.

HFC-125 is not expected to distribute into the aquatic compartment. Mackay Level III calculated a partitioning lower than 0.002% in water, following emission of HFC-125 in the atmosphere. Furthermore EPIWIN predicted a short half-life in the water compartment because of volatilisation.

5 RECOMMENDATIONS

HFC-125 is currently of low priority for further work due to its low hazard profile for human health and the environment (fish, invertebrates and algae). Its global warming potential is acknowledged and being addressed by other programmes.

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ANNEX 1: DATABASES CONSULTED

AQUIRE [TOXICITY TO FISH AND OTHER MARINE ORGANISMS]
BIODEG [BIODEGRADATION DATA]
BIOLOG [BIODEGRADATION BIBLIOGRAPHIC REFERENCES]
CCRIS (CHEMICAL CARCINOGENESIS RESEARCH INFORMATION SYSTEM)
CHRIS (HAZMAT DATA)
DART/ETIC (DEVELOPMENTAL AND REPRODUCTIVE TOXICOLOGY)
DATALOG [ENVIRONMENTAL FATE BIBLIOGRAPHIC REFERENCES]
EMIC (ENVIRONMENTAL MUTAGEN INFORMATION CENTER)
ENVIROFATE [ENVIRONMENTAL FATE DATA]
GENETOX (GENETIC TOXICOLOGY)
GIABS [INDEX TO GASTROINTESTINAL ABSORPTION STUDIES, 1957-1987]
HSDB SUBSET [HAZARDOUS SUBSTANCES DATA BANK]
IRIS (INTEGRATED RISK INFORMATION SYSTEM)
MEDLINE (TOXICITY & CARCINOGENICITY BIBLIOGRAPHIC REFERENCES)
NIOSHTIC (HAZMAT BIBLIOGRAPHIC REFERENCES)
OHMTADS [HAZMAT DATA FROM THE US EPA]
PHYTOTOX [TOXICITY TO PLANTS]
PUBMED
RISKLINE (SWEDISH NATIONAL CHEMICALS INSPECTORATE)
RTECS [TOXICITY, CARCINOGENICITY, TUMORIGENICITY, MUTAGENICITY, TERATOGENICITY]
TERRETOX [TOXICITY TO TERRESTRIAL ANIMALS]
TOXCENTER (TOXICOLOGY LITERATURE ONLINE)
TOXLINE (TOXICOLOGY LITERATURE ONLINE)
TSCATS (UNPUBLISHED HEALTH AND SAFETY STUDIES SUBMITTED TO EPA)

S I D S

Dossier

Existing Chemical : ID: 354-33-6
CAS No. : 354-33-6
Structural Formula : CF3-CF2H
Product name : HFC-125

Producer related part
Company : Solvay S.A.
Creation date : 05.09.2003

Substance related part
Company : Solvay S.A.
Creation date : 05.09.2003

Status :
Memo :

Printing date : 23.06.2005
Revision date :
Date of last update : 23.06.2005

Number of pages :

Chapter (profile) :
Reliability (profile) :
Flags (profile) :

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	Manufacturer
Name	:	Solvay Fluor; Dupont De Nemours S.A.; Honeywell Fluorine Products
Contact person	:	
Date	:	
Street	:	
Town	:	
Country	:	
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

22.06.2005

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	:	1,1,1,2,2-pentafluoroethane
Smiles Code	:	C(F)(F)(F)C(F)(F)
Molecular formula	:	CF3-CHF2
Molecular weight	:	120.02
Petrol class	:	

10.10.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	Organic
Physical status	:	Gaseous
Purity	:	>= 99.5 % v/v
Colour	:	Colourless
Odour	:	faint etheral odour

10.12.2003

1.1.2 SPECTRA

Type of spectra	:	mass spectrum

Remark : Spectrum description (principal fragmentations and relative abundance)

m/z	fragment characterisation
51.00	(CHF2)+
69.00	(CF3)+
101.00	(CF3CHF)+
119.00	(CF3CF2)+

Source : Dupont-Mitui fluorochemicals
Reliability : (1) valid without restriction
29.10.2003 (39)

Type of spectra : IR

Remark : Spectrum description:

wavelenght (cm-1)	
3000	C-H stretching
1305	
1210	
1140	C-F stretching
870	
730	

29.10.2003 (35)

1.2 SYNONYMS AND TRADENAMES

HFC-125, HFA-125, pentafluoroethane, Solkane 125, Suva-125, R-125, FE-125

20.01.2004

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No : 354-33-6
EC-No : 206-557-8
EINECS-Name : Pentafluoroethane
Molecular formula : CF3-CHF2
Value : > 99.5 % v/v

Remark : Impurities:
CFC-115 < 0.4% wt
Source : Dupont-Mitui fluorochemicals
10.11.2003 (34)

1.4 ADDITIVES

10.12.2003

1.5 TOTAL QUANTITY

Quantity : ca. 16000 - tonnes produced in 2002

Remark : The 2002 Alternative Fluorocarbons Environmental Acceptability Study (AFEAS) estimated that 16400 tonnes were globally produced by ten companies

23.01.2004 (2)

1.6.1 LABELLING

Labelling : no labelling required (no dangerous properties)
Specific limits :

06.10.2003

1.6.2 CLASSIFICATION

Classified : no classification required (no dangerous properties)
Class of danger :
R-Phrases :
Specific limits :

10.12.2003

1.6.3 PACKAGING

Memo : Ordinary Steel

21.01.2004

1.7 USE PATTERN

Type of use : Industrial
Category : other: Refrigerant (sealed system); fire extinguishing agent; air conditioner; solvent; plastic foam blowing

Remark : 99.8% (16,406/16,431) tonnes of produced HFC-125 has been used in refrigeration (which includes air conditioning). 7 tonnes have been sold for solvent applications. The 8 tonnes reported as HFC-125 sold for closed cell foam applications have to be likely interpreted as the volume used for fire extinguishing systems. The 10 tonnes listed under the category "other short-term uses" may be considered as fugitive emissions occurring during production and down-stream uses of HFC-125.

13.06.2005 (2)

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

Origin of substance : Synthesis
Type : Production

Remark : Pentafluoroethane is synthetised in closed reactor by hydrofluorination of chlorotetrafluoroethane (HFC-124) and subsequent purification by distillation.

20.01.2004

1.8 REGULATORY MEASURES

Type of measure : OEL
Legal basis :

20.01.2004

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : Other
Limit value : 1000 other:ppm

Remark : An exposure limit for HFC-125 of 1,000 ppm (8-hour time-weighted average) has been recommended by the American Industrial Hygiene Association, Workplace Environmental Exposure Limit (WEEL) Committee.

30.10.2003

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

Classified by : other: none
Labelled by :
Class of danger :

12.12.2003

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

Type : EINECS
Additional information : 206-557-8

06.10.2003

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Source of exposure : Human: exposure by production
Exposure to the : Substance

10.12.2003

Source of exposure : Human: exposure of the operator by intended use
Exposure to the : Substance

10.12.2003

Source of exposure : Environment: exposure from production
Exposure to the : Substance

10.12.2003

Source of exposure : Environment: exposure from intended use
Exposure to the : Substance

10.12.2003

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

Type of search : Internal and External
Chapters covered : 3, 4, 5
Date of search : 12.12.2003

23.01.2004

1.13 REVIEWS

2.1 MELTING POINT

Value : = -103 °C
Sublimation :
Method :
Year : 1992
GLP : no data
Test substance :

Remark : Data from handbook
Source : .
Reliability : (2) valid with restrictions
2g Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
09.12.2003 (30)

Value : = -162.1 °C
Sublimation :
Method : other
Year :
GLP :
Test substance :

Remark : Estimated value - EPIWIN calculation (MPBWIN v1.40):
Input: MW 120.02 g/mol

Output:

Melting point (°C)	Method
-170.49	Adapted Joback
-153.65	Gold and Ogle
-162.07	mean value

Result : 2f Accepted calculation method
Reliability : (2) valid with restrictions
09.12.2003 (16)

2.2 BOILING POINT

Value : = -48.5 °C at 1013.25 hPa
Decomposition :
Method :
Year : 1992
GLP : no data
Test substance :

Remark : Data from handbook
Source : .
Reliability : (2) valid with restrictions
2g Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
09.12.2003 (30)

Value : = -68.5 °C at
Decomposition :
Method : other
Year :
GLP :
Test substance :

Remark : Estimated value - EPIWIN calculation (MPBWIN v1.40):
Input: MW 120.02 g/mol

Output:
Boiling point (°C) Method
-68.48 Adapted Stein and Brown
Reliability : (2) valid with restrictions
2f Accepted calculation method
09.12.2003 (16)

2.3 DENSITY

Type : Density
Value : = 1.53 g/cm³ at °C

Remark : .
Liquid density at -48.5 °C
Source : .
Reliability : (2) valid with restrictions
2g Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
09.12.2003 (30)

2.3.1 GRANULOMETRY

Type of distribution : other: not applicable
Precentile :

06.10.2003

2.4 VAPOUR PRESSURE

Value : = 13998.6 hPa at 25 °C

Remark : calculated from experimentally-derived coefficients
Source : .
Reliability : (2) valid with restrictions
2g Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
10.12.2003 (10)

Value : = 13810 hPa at 25 °C
Decomposition :
Method :
Year : 1992
GLP : no data
Test substance :

Remark : Value from ECETOC JACC Report no.24, 1994
Source : Dupont-Mitui fluorochemicals
Reliability : (2) valid with restrictions
2g Data from handbook or collection of data
10.12.2003 (13)

Value : = 9492 hPa at °C

Remark : Vapour pressure estimations at 25 °C (MBPWIN v1.40):

Used data:
Boiling point = -48.5 °C

8770 mm Hg (11692 hPa) - Antoine method
5470 mm Hg (7292 hPa) - Modified Grain method
6400 mm Hg (8532 hPa) - MacKay method

selected vapour pressure:
7120 mm Hg (mean of Antoine and Grain methods)

Reliability : (2) valid with restrictions
2f Accepted calculation method

10.12.2003 (16)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = 1.48 at 25 °C
pH value : ca. 6.4
Method : OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year : 1992
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4

Remark : A stock solution of the test substance was prepared by introducing the HFC-125 gas through a silicon septum into a vacuum tube containing 1-octanol saturated with water. 0.1 ml of the stock solution was added in an equilibrium vessel previously injected with determined volumes of 1-octanol and water. The equilibrium vessel was shaken and 1-octanol and water samples were prepared for the GC analysis. HFC-125 concentration was determined in 1-octanol and in water samples and used for Kow determination.
Source : du Pont-Mitui fluorochemicals
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
05.09.2003 (29)

Partition coefficient : octanol-water
Log pow : = 1.55 at °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance :

Remark : Estimated value - EPIWIN calculation (KOWWIN v1.66):
Input: MW 120.02 g/mol
Reliability : (2) valid with restrictions
2f Accepted calculation method
24.10.2003 (16)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : = 908.5 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :

Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Estimation. Value calculated by EPIWIN using the chemical structure formula.
Reliability : (2) valid with restrictions
2f Accepted calculation method
Flag : Critical study for SIDS endpoint
13.06.2005 (16)

Solubility in : Water
Value : = 432 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Authors reported that the Ostwald solubility coefficient (log Lw) in water was calculated from the experimentally-determined Henry's Law Constant of HFC-125 at 25°C. Lw represents the gas volume solubilised at atmospheric pressure in one liter of water.
The value reported is log Lw = -1.059, corresponding to a gas volume of 0.0875 liter HFC-125/liter of water. The volumes of solute dissolved can be converted in mmoles by applying the equation: n =PV/RT (where P is atmospheric pressure, Pa, T = 298 °K, R = gas constant and V is the solute volume, expressed in liters) and then expressed in mg/l by multiplying mmoles for the molecular weight of the solute.
Thus:
w.s. = 120.02 x (101325 x 0.0875)/(8.31 x 298) = 432 mg/l

this value represents the water solubility at 25°C and atmospheric pressure.
Reliability : (2) valid with restrictions
2f accepted calculation method
Flag : Critical study for SIDS endpoint
13.06.2005 (1)

Solubility in : Water
Value : = 970 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Value listed in ECETOC JACC Report no. 24, 1994. Solubility at atmospheric pressure
Reliability : (2) valid with restrictions
2g Data from handbook or collection of data
13.06.2005 (13)

Solubility in : Water
Value : = 1071 mg/l at 25 °C
pH value :

concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Estimation - calculated using the measured Log Kow value
Input:
MW 120.02 g/mol
Log Kow 1.48
Reliability : (2) valid with restrictions
2f Accepted calculation method
Flag : Critical study for SIDS endpoint
09.12.2003 (16)

Solubility in : Water
Value : = 5970 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Water solubility at saturated vapour pressure.
Calculated from Henry's Law Constant:

W.s. = (v.p./HLC)*M.W. = (1399860/28180)*120.02= 5970 g/m3
Reliability : (2) valid with restrictions
2f accepted calculation method
Flag : Critical study for SIDS endpoint
09.12.2003 (38)

Solubility in : Water
Value : = 4500 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : DuPont measured the mutual solubility of HFC-125 and water under saturation condition at 25°C. The experimental conditions considered the solubility of HFC-125 in water in the presence of a saturated atmosphere at equilibrium, in which the partial pressure of HFC-125 corresponds to its vapour pressure. Under this conditions, about 4500 mg/l HFC-125 were measured in water. This value may be considered approximately as the water solubility of HFC-125 at equilibrium.
Reliability : (2) valid with restrictions
2g data from handbook or collection of data
13.06.2005 (11)

2.6.2 SURFACE TENSION

Test type : Other
Value : at °C

Concentration :

Remark : HFC-125 is a gas at atmospheric pressure and ambient temperature. Surface tension is not relevant

04.11.2003

2.7 FLASH POINT

Value : °C
Type : Other

Remark : Non-flammable
04.11.2003

2.8 AUTO FLAMMABILITY

Method : other
Year :
GLP :
Test substance :

Remark : Non-flammable
04.11.2003

2.9 FLAMMABILITY

Result : non flammable

09.10.2003

2.10 EXPLOSIVE PROPERTIES

Result : other: HFC-125 is not explosive per se. Contact with alkaline and earth-alkaline metals may provoke violent reactions or explosions

10.12.2003

2.11 OXIDIZING PROPERTIES

Result : no oxidizing properties

Remark : No data available. HFC-125 is not expected to have oxidising properties.
10.12.2003

2.12 DISSOCIATION CONSTANT

Acid-base constant : not determined
Method : OECD Guide-line 112
Year : 1992
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Dissociation of HFC-125 in water solution was evaluated by means of specific electric conductivity measurements.
stock water solutions were prepared by adding 50 ml of distilled water in a 1000 ml vacuum tube and saturating the vacuum tube with test substance. 2 dilution were prepared from the stock solution at dilution ratio of 7.4 and 74. Electric conductivity of the 2 test solution was measured. Concentration of test substance into the test solutions was determined by gas chromatography.

Results:
the measures of electric conductivity were below 2.00 uS/cm, (in the range of conductivity of purified water) and showed no concentration dependency.
HFC-125 is considered not dissociated in water solution. Dissociation constant, thus, was not determined.

Reliability : (1) valid without restriction
1a GLP guideline study

10.11.2003 (41)

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Memo : Henry's Law Constant

Remark : The HLC constant may be calculated from the equation below

Ls = R x T x /(HLC x MW)
Where Ls is the Ostwald coefficient for water (Log Ls = -1.059), R is the universal gas constant (8.31 J K-1 mol), T is the temperature (298.15 K), and MW are the water density (1 x 106 g/m3) and Molecular weight (18 uma), respectively.
HLC (per unit mole fraction) = 1,559 MPa
Which can be converted to HLC [Pa m3/mol] by dividing for the conversion factor 55323, thus:
HLC = 28,180 Pa m3/mol

Reliability : (2) valid with restrictions
2f accepted calculation method

04.11.2003 (1)

Memo : Henry's Law Constant

Remark : Estimation at 25°C (HENRYWIN v3.10):

Results:

Bond estimation: 3.05 atm*m3/mol (3.09x10^5 Pa m^3/mol)
Group estimation: 0.05 atm*m3/mol (5.07x10^3 Pa m^3/mol)

Reliability : (2) valid with restrictions
2f accepted calculation method

04.11.2003 (16)

3.1.1 PHOTODEGRADATION

Type	:	Air
Light source	:	
Light spectrum	:	Nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	cm^3/(molecule*sec)
Degradation	:	% after
Remark	:	The rate constants for the reaction of HFC-125, HFC-32, HFC-143a and HCFC-141b with hydroxyl radicals were determined at various temperatures (in the range 220-364 °K). All experiments were carried out under pseudo-first order conditions for OH radicals (i.e. [OH]<<[HFC] or [HCFC]). Hydroxyl radical concentration was measured by using two different techniques: Discharge flow-laser magnetic resonance and pulsed photolysis-pulsed laser-induced fluorescence. The second order kinetic constants were calculated from the measured pseudo-first order constants at each temperature. Arrhenius coefficients and E/R were calculated by plotting the second order rate constants (on logaritmic scale) vs 1/T. RESULTS: Arrhenius coefficient: A= 5.41 +/- 0.83 x 10^-13 cm3/molecule/s E/R = 1700 +/- 100 1/K The second order rate constant at 298 °K, calculated with the equation of Arrhenius was k(298) = 5.41 x 10^-13 * e^-(1700/298) = 1.90 +/- 0.27 x 10^-15 cm3/molecules/s. CONCLUSION: HFC-125 is slowly subjected to indirect photolysis by OH radicals. The authors estimated a photochemical atmospheric lifetime of 48 years.
Reliability	:	(2) valid with restrictions 2e Study well documented, meets generally accepted scientific principles, acceptable for assessment
Flag	:	Critical study for SIDS endpoint

09.12.2003 (37)

Type	:	Air
Light source	:	
Light spectrum	:	Nm
Relative intensity	:	based on intensity of sunlight
Remark	:	Arrhenius espression of the constant of reaction of HFC-125 with OH radicals listed in JPL reposrt is: k = 6 x 10^-13 * e^-(1700/T) cm3/molecule/sec as a result of a combined fit of different experimental data. the relative constant of reaction at 298 °K is 2 x 10^-15 cm3/molecule/sec.
Reliability	:	(2) valid with restrictions

2g Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
13.06.2005 (28)

Type : Air
Light source :
Light spectrum : Nm
Relative intensity : based on intensity of sunlight
DIRECT PHOTOLYSIS
Halflife t1/2 : = 8788 day(s)
Degradation : % after
Quantum yield :
Deg. product :
Method : other (calculated)
Year :
GLP : no
Test substance :

Remark : QSAR result (AOP program v1.90). EPIWINN calculation:

Rate constant=1.2x10^-15 cm^3/molecule/sec
half-life=8788 days (24 years), considering 12hours/day and 1.5x10^6 molecule OH radical/cm^3.
Reliability : (2) valid with restrictions
2f Accepted calculation method
27.11.2003 (16)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight

Remark : Reaction of several HFCs and HCFCs with Cl radicals were studied. concentration of reagents and products were monitored by a FT-IR absorption spectrometer. Chlorine radicals were used in order to study the degradation pathways, as a surrogate of OH radicals.

RESULTS:
Reaction of 4.5 ppm HFC-125 with 298 ppm Cl2 for 30 minutes gave C(O)F2 as main product, with a yeld of 109%. Minor production of CF3OOCF3 was also observed, but its quantitative yeld was not measured. The presence of this product is probably due to the high concentration of substrate in the experimental conditions and CF3COOCF3 is not expected to be formed in the atmosphere.

The proposed mechanism was:
Cl + CF3CHF2 -> HCl + CF3CF2
CF3CF2 + O2 -> CF3CF2O2
2CF3CF2O2 -> 2CF3CF2O + O2
CF3CF2O -> CF3 + C(O)F2
Reliability : (2) valid with restrictions
2e Study well documented, meets generally accepted scientific principles, acceptable for assessment
09.12.2003 (14)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight

Remark : Reaction of several HFCs and HCFCs with Cl radicals were studied.

concentration of reagents and products were monitored by a FT-IR absorption spectrometer.

RESULTS:
HFC-125 reaction with Cl radicals showed 10 and 17% of reagent losses after 33 and 60 minutes, respectively. Infra-red spectrum of the product of reaction showed the presence of C(O)F2 as main product. the yeld of production of C(O)F2 was estimated to be approximately 100%. Minor production of CF3OOOCF3 was also observed, but its quantitative yeld was not measured.

Reliability : (2) valid with restrictions
2e Study well documented, meets generally accepted scientific principles, acceptable for assessment

27.11.2003 (42)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight

Remark : The reaction of HFC-125 with fluorine radicals was studied by FTIR spectroscopy.

RESULTS:
The second order rate constant for the reaction of HFC-125 with F atoms in atmosphere is reported to be = 3.6x10^-13 cm^3/molecule/s. The yelds of reaction indicate the formation of C(O)F2 as main degradation product.

The study confirmed the degradation pathway of HFC-125 with OH radicals.

Reliability : (2) valid with restrictions
2e Study well documented, meets generally accepted scientific principles, acceptable for assessment

09.12.2003 (25)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight

Remark : Ozone-forming potential.

The Photochemical Ozone Creating Potential (POCP) of HFC-125 was calculated considering an annual emission term of 10 kt/50x50km2 and a life-time of 36.5 years.

Result:
the POCP of HFC-125 relative to ethylene is below 0.1 (ethylene POCP = 100).

Comment:
Due to the low reactivity of HFC-125 with OH radicals, its contribution to ozone tropospheric formation is negligible.

Reliability : (2) valid with restrictions
2f Accepted calculation method
Flag : Critical study for SIDS endpoint
27.11.2003 (26)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	= 3 year at 25 °C
t1/2 pH9	:	at °C
Deg. product	:	
Method	:	other (calculated)
Year	:	
GLP	:	no
Test substance	:	
Remark	:	QSAR result (HYDROWIN v1.67) EPIWIN calculation: basic hydrolysis (pH>8) rate at 25°C=0.069 l/mol/sec half-life at pH 8= 117 days half-life at pH 7= 3 years The rate constant estimation does not include the neutral hydrolysis. For some alkyl halides the neutral hydrolysis is the dominant reaction at anvironmental pH. In this case the calculated rate could underestimate the actual rate.
Reliability	:	(2) valid with restrictions 2f Accepted calculation method
Flag	:	Critical study for SIDS endpoint

24.10.2003 (16)

3.1.3 STABILITY IN SOIL

Type	:	other
Radiolabel	:	
Concentration	:	
Soil temperature	:	°C
Soil humidity	:	
Soil classification	:	
Year	:	
Remark	:	No data are available. However, due to the low Log Kow (1.48) and to the high vapour pressure, HFC-125 is not expected to be significantly adsorbed into soil compartment.

27.11.2003

3.2.1 MONITORING DATA

Type of measurement	:	background concentration
Media	:	air
Concentration	:	
Method	:	
Remark	:	Mixing ratios for HFC-125 were detected in 2 laboratories by AGAGE from 1998 to 2000 (Mace Head, Ireland, 53 N; 10 W and Cape Grim, Tasmania, 41 S; 145 E). Environmental Concentrations measured by means of a gas-chromatographic method were 0.92 and 1.4 ppt in 1998 and 2000, respectively, each of which is an average of the data from Ireland and Tasmania, with an estimated growth rate of 0.3 ppt/year.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

13.06.2005 (43)

Type of measurement : other
Media :
Concentration :
Method :

Remark : AFEAS (2004) estimated a global release of about 3,500 tonnes HFC-125 in 2002, principally due to HFC-125 already present in the market. Fugitive emissions related to the 2002 production (16,400 tonnes), occurring during transport and transfer operations have been estimated to be less than 10 tonnes (AFEAS 2004). These estimations have been carried out by using the HFC-134a emission function and are considered provisional values.
Flag : Critical study for SIDS endpoint
13.06.2005 (2)

Type of measurement : other
Media :
Concentration :
Method :

Remark : The IPCC special report mixing scenarios calculated a mixing ratio of 30-60 ppt and 60-140 ppt in 2050 and 2100, respectively
13.06.2005 (27)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : volatility
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :

Remark : EPIWIN calculation
Input:
MW 120.02 g/mol
Water solubility 432 mg/l
Vapour pressure 1.05 x 10^4 mm Hg
Henry's Law Constant: 0.276 atm x m3/mol

	River	Lake
Water depth (m)	1	1
Wind velocity (m/sec)	5	0.5
Current velocity (m/sec)	1	0.05

Results:

	River	Lake
Half-life (h)	1.123	104.1
Half-life (days)	0.05	4.34

Due to high values of vapour pressure (1.05 x 10^4 mm Hg) and of Henry's Law Constant (0.276 atm x m3/mol), volatilisation is the main process of removal of HFC-125 from water compartment, and biotic and abiotic degradation can be considered not significant processes.
Reliability : (2) valid with restrictions

2f accepted calculation method
Flag : Critical study for SIDS endpoint
23.06.2005 (16)

Type : fugacity model level III
Media :
Air : 100 % (Fugacity Model Level I)
Water : .002 % (Fugacity Model Level I)
Soil : .004 % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : EPA OPPTS 835.1110
Year :

Remark : Fugacity-based Multimedia Environmental Model Level III (v2.70).
Simulation made using EQC standard environmental parameters.
Input Parameters:

M.W. 120.02 g/mol
Data Temperature 25 °C
Water Solubility 5970 g/m3
Vapour Pressure 1399860 Pa
Log Kow 1.48
Melting Point -103 °C
Reaction Half-life: air 100000 h (calculated*)
water 26280 h (EPIWIN data)
other compartments 1 E+11 (negligible)
Emission 3000 kg/h (air)
*calculated from the second order constant of reaction = 2 x 10^-15 cm3/molecule/sec (NASA JPL, 2003) and a [OH]= 10^6 molecules/cm3.

Results:

	Fugacity (Pa)	Reaction (%)	Advection (%)	Mass Amount (%)
Air	6.2x10^-5	0.07	99.9	100
Water	4.4x10^-5	3x10^-5	0.0012	0.012
Soil	6.2x10^-5	3x10^-12	-	0.005

Residence time
Advection 100 h
Reaction 1.4x10^+5 h
Total 100 h

CONCLUSION:
According to Mackay level III model, HFC-125, released at the rate 3000 kg/h in atmosphere, will not partition significantly into water and soil compartments.
The removal of the substance from the EQC-environment will occur mainly via advection, due to the low atmospheric degradation rate of HFC-125.
Reliability : (2) valid with restrictions
2f Accepted calculation method
Flag : Critical study for SIDS endpoint
23.06.2005 (17)

3.3.2 DISTRIBUTION

Media : water – soil
Method : other (calculation)
Year :

Remark : EPIWIN calculation (PKOCWIN v1.66):
Input:
MW 120.02 g/mol

Estimated Koc = 154 l/Kg

Calculated Koc can be defined as "the ratio of the amount of chemical adsorbed per unit weight of organic carbon (oc) in the soil or sediment to the concentration of the chemical in solution at equilibrium"
Koc = (ug adsorbed/g organic carbon) / (ug/mL solution)

Reliability : (2) valid with restrictions
2f accepted calculation method

05.11.2003 (16)

3.4 MODE OF DEGRADATION IN ACTUAL USE

Memo : Volatilisation

Remark : According to Mackay Level III simulation, advection from atmosphere is the main process of removal HFC-125 following its emission into air compartment.

27.11.2003

3.5 BIODEGRADATION

Type : Aerobic
Inoculum : activated sludge, domestic
Concentration : 2.99 mg/l related to Test substance
related to
Contact time : 28 day(s)
Degradation : = 5 (±) % after 28 day(s)
Result : under test conditions no biodegradation observed
Kinetic of testsubst. : 5 day(s) = 2 %
15 day(s) = 5 %
28 day(s) = 5 %
%
%
Control substance : Laurylsulfonate
Kinetic : 5 day(s) = 30 %
28 day(s) = 92 %
Deg. product : No
Method : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year : 1992
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4

Remark : The sludge was sampled from a city sewage plant and filtered. The activated sludge contained 2.8 x 10^8 bacteria/ml. One drop was added to one liter of final test solution.
A stock solution of the test substance was prepared by adding gaseous HFC-125 to a vacuum tube containing water until saturation (ca. 0.5 g/l). 600 ul of the stock solution were added to 100 ml of mineral medium containing the inoculum. Sodium laurylsulfate was used as positive control

The test was run at a temperature of 20 ± 1 °C.

Biodegradation of tested substance was measured by gas chromatography

and biochemical oxygen demand methods.
Degradation of 2, 5 and 5% was calculated after 5, 15 and 28 days of incubation of the test substance with the inoculum by measuring the BOD. a biodegradation of 30, 57 and 92% was measured for the positive control after 5, 15 and 28 days, respectively.

Reliability : (1) valid without restriction
1a GLP guideline study

Flag : Critical study for SIDS endpoint

13.06.2005 (40)

Remark : EPIWIN estimations (BIOWIN v4.00):

Model	Result (biodegr. prob.)	Comment
Linear	0.17	Does not biodegr. fast
Non-linear	0.0126	Does not biodegr. fast
Survey(ultimate)	2.4	Weeks-Months
Survey(primary)	3.4	Days-Weeks
Miti linear	0.39	Does not biodegr. fast
Miti non-linear	0.00	Does not biodegr. Fast

Reliability : (2) valid with restrictions
2f Accepted calculation method

24.10.2003 (16)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species : Other
Exposure period : at °C
Concentration :
BCF : = 2.75

Remark : .
QSAR result (Bcfwin v2.14) EPIWIN calculation:

logBCF = 0.77 logKow - 0.70 = 0.44

BCF = 2.752

Reliability : (2) valid with restrictions
2f accepted calculation method

Flag : Critical study for SIDS endpoint

04.11.2003 (16)

3.8 ADDITIONAL REMARKS

Memo : Global warming potential (GWP)

Remark : The HFC-125 calculated global warming potential (GWP), relative to CO2 (GWP=1) for three different time horizons (TH) is:

GWP	TH (years)
5970	20
3450	100
1110	500

the radiative efficiency is 0.23 W/m2/ppb

Conclusion:
Due to its long atmospheric lifetime (29 years) and radiative efficiency, HFC-125 could contribute to global warming effect.

Reliability : (2) valid with restrictions
2f accepted calculation method

Flag : Critical study for SIDS endpoint

09.12.2003 (43)

Memo : Ozone depletion potential (ODP)

Remark : The HFC-125 ozone depletion potential (ODP) was calculated with WMO (1999) model (relative to CFC-11):

Result

ODP HFC-125 < 3x10^-5 (ODP CFC-11 = 1)

Conclusion:
due to the absence of chlorine and bromine atoms, HFC-125 will not contribute to atmospheric ozone depletion

Reliability : (2) valid with restrictions
2e Study well documented, meets generally accepted scientific principles, acceptable for assessment

09.12.2003 (45)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	Semistatic
Species	:	Poecilia reticulate (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	
Limit test	:	
Analytical monitoring	:	Yes
Method	:	other: OECD Method 203 (April 1984) and EPA guidelines 72-1 (1982)
Year	:	1990
GLP	:	Yes
Test substance	:	other TS: 1-chloro-1,1-difluoroethane (CAS no. 75-68-3; HCFC-142b), purity>99.99%
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 300 mg/l) Test temperature range: 22 +/- 1 °C. Results: Nominal concentrations (mg/l): 0, 30, 53, 94, 170, 300 Measured concentrations (mg/l): 0, 33, 56, 106, 189, 321 (mean measured concentrations) EC50 = 220 mg/l at 96 hours based on the mean measured concentrations NOEC = 110 mg/l based on the mean measured concetrations Statistical results: 95% confidence interval 190-310 mg/l Mortality of guppies Control 1/8 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 within 5 hours) Conclusion: based on this key study, 1-chloro-1,1-difluoroethane (HCFC-142b) is of low toxicity for the fish
Reliability	:	(2) valid with restrictions 2e (4 fish used instead of 5 and low oxygen content at high test concentration).
Flag	:	Critical study for SIDS endpoint

15.06.2005 (20)

Type	:	other: QSAR
Species	:	
Exposure period	:	
Unit	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: 1-chloro-1,1-difluoroethane (CAS no. 75-68-3; HCFC-142b), purity>99.99%

Remark	:	QSAR results (ECOSAR v0.99g) EPIWIN calculation: Used data: MW = 100.50 g/mol Log Kow = 1.64 Melting point =-130.8 °C Water solubility = 1.400 mg/l Results - Fish parameter duration predicted (mg/l) LC50 96-hr 162
Reliability	:	(2) valid with restrictions 2f accepted calculation method

15.06.2005 (16)

Type	:	Static
Species	:	Brachydanio rerio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 126 measured
Method	:	other: OECD Method 203 (April 1984) and ECCDirective 84/449, Method C1
Year	:	1989
GLP	:	Yes
Test substance	:	other TS: 1,1-dichloro-1-fluoroethane (CAS no. 1717-00-6; HCFC-141b), purity>99.5%.
Remark	:	Groups of 20 fish and nominal test concentrations of 60, 120 and 264 mg/l were used. Survival was noted at 24, 48, 72 and 96 hoursfrom 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 hours was estimated using gas chromatography. Highest non-lethal level at 24 hours - 96 mg/l and at 48-96 hours <60 mg/l. Estimated LC50 for 24 hours - 276 mg/l, 48 hours - 192 mg/l, 72 hours - 174 mg/l and 96 hours - 126 mg/l. The actual concentrations measured at 96 hours were 66.8 (nominal 60), 100.8 (nominal 120) and 200.4 mg/l (nominal 264).
Source	:	.
Reliability	:	(2) Valid with restrictions
Flag	:	Critical study for SIDS endpoint

15.06.2005 (5)

Type	:	other: QSAR
Species	:	
Exposure period	:	
Unit	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: 1,1-dichloro-1-fluoroethane (CAS no. 1717-00-6; HCFC-141b), purity>99.5%.
Remark	:	QSAR results (ECOSAR v0.99g) EPIWIN calculation: Used data: MW = 116.95 g/mol Log Kow = 2.3 Melting point =-103.5 °C Water solubility = 4000 mg/l Results - Fish

parameter	duration	predicted (mg/l)
LC50	96-hr	45

Reliability : (2) valid with restrictions
2f accepted calculation method
15.06.2005 (16)

Type : other: QSAR
Species :
Exposure period :
Unit :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Remark : QSAR results (ECOSAR v0.99g) EPIWIN calculation:
Used data:
MW = 120.02 g/mol
Log Kow = 1.48
Melting point =-103 °C
Water solubility = 432 mg/l

Results - Fish

parameter	duration	predicted (mg/l)
LC50	96-hr	274

Reliability : (2) valid with restrictions
2f Accepted calculation method
Flag : Critical study for SIDS endpoint
23.06.2005 (16)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : Static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 31.2 measured
Method : other: OECD Method 202 (April 1984) and ECC Directive 84/449, Method C
Year : 1989
GLP : Yes
Test substance : other TS: 1,1-dichloro-1-fluoroethane (HCFC 141b; CAS no 1717-00-6), purity >99.5%.

Remark : Four replicates containing 5 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 hours 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 : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
23.06.2005 (6)

Type : Static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 160 measured
Analytical monitoring : Yes

Method : other: OECD Method 202 (April 1984) and EPA guidelines 72-2 (1982)
Year : 1990
GLP : Yes
Test substance : other TS: 1-chloro-1,1-difluoroethane (HCFC 142b; CAS no 75-68-3), purity >99.9%

Remark : Test design: 30 daphnia per concentration using 3 replicates of 10.
Immobilisation was checked after 15 minutes, 24 hours and 48 hours.
Test flask were completely filled and tightly closed with aluminum stopper with rubber septum. No aeration, no solution renewal.
Method of calculating mean measured concentrations: arithmetic mean measured concentrations in 1 hour sample
Exposure period: 48 hours.
Analytical monitoring: GC 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 of calibration)

Results:
Test condition:
Temperature 20 +/- 1 C;
pH variations from 6.8 to 8 (after 48 hrs);
dissolved oxygen variations from 7.9 to 9 mg/l

Nominal concentrations: 30, 53, 94, 170, 300 mg/l.
Measured concentrations: 33, 58, 106, 197, 348 mg/l (in 1 hour sample)
EC50: 160 mg/l at 48 hours
NOEC: 106 mg/l
Statistical results: 95%
Confidence interval: 70-200
Biological observations

	N. tested daphnids	immobility at 48 hrs (%)
Control	32	22
33 mg/l	30	37
58 mg/l	28	25
106 mg/l	27	41
197 mg/l	28	75
348 mg/l	30	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, HCFC 142b is of low toxicity to Daphnia.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
23.06.2005 (19)

Type : Static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Method : Other: OECD Method 202 (April 1984) and EPA guidelines 72-2 (1982)
Year : 1989
GLP : Yes
Test substance : other TS: 1-chloro-1,1-difluoroethane (HCFC 142b; CAS no 75-68-3), purity >99.9%as prescribed by 1.1 - 1.4

Remark : Test design: 20 Daphnids per concentration using 2 replicates of 10.
Immobilisation was cehcked after 24 and 48 hours

Method of calculating mean measured concentration: no immobilisation observed during the test.
Exposure period: 48 hours.
Analytical monitoring: GC using head space analysis.

Result : Nominal concentrations: no indications.
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

Source : .

Reliability : (2) valid with restrictions
2e not enough documented

27.11.2003 (12)

Type : other: QSAR
Species :
Exposure period :
Unit :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Remark : QSAR results (ECOSAR v0.99g) EPIWIN calculation:
Used data:
MW = 120.02 g/mol
Log Kow = 1.48
Melting point = -103 °C
Water solubility = 432 mg/l

Results - Daphnid

parameter	duration	predicted (mg/l)
EC50	48-hr	283

Reliability : (2) valid with restrictions
2f Accepted calculation method

23.06.2005 (16)

Type : other: QSAR
Species :
Exposure period :
Unit :
Method :
Year :
GLP :
Test substance : other TS: 1,1-dichloro-1-fluoroethane (HCFC 141b; CAS no 1717-00-6), purity >99.5%.

Remark : QSAR results (ECOSAR v0.99g) EPIWIN calculation:
Used data:
MW = 116.95 g/mol
Log Kow = 2.3
Melting point = -103.5 °C
Water solubility = 4000 mg/l

Results - Daphnid

parameter	duration	predicted (mg/l)
EC50	48-hr	49

Reliability : (2) valid with restrictions
2f accepted calculation method

15.06.2005 (16)

Type : other: QSAR

Species	:	
Exposure period	:	
Unit	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: 1-chloro-1,1-difluoroethane (HCFC 142b; CAS no 75-68-3), purity >99.9%
Remark	:	QSAR results (ECOSAR v0.99g) EPIWIN calculation: Used data: MW = 100.50 g/mol Log Kow = 1.64 Melting point = -130.8 °C Water solubility = 1400 mg/l Results - Daphnid parameter duration predicted (mg/l) EC50 48-hr 170
Reliability	:	(2) valid with restrictions 2f accepted calculation method

15.06.2005 (16)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	
Exposure period	:	72 hour(s)
Unit	:	mg/l
Method	:	other: OECD Method 201 (April 1984) and EPA guideline 40 cfr part 797 & 1060 (1989)
Year	:	1991
GLP	:	Yes
Test substance	:	other TS: 1,1-dichloro-1-fluoroethane (HCFC 141b; CAS no 1717-00-6), purity >99.9%
Remark	:	The toxicity of HCFC-141b to the alga S. capricornutum was tested in a series of sealed glass containers with nominal test concentrations of 0, 250, 500 and 1000 l/l test substance. Samples of the test solutions were taken at test initiation and each 24 hrs and analysed by gas-chromatography. pH and temperature were measured at the test initiation and each 24 hrs. Biomass growth was determined by measuring the spectrometric absorption at 680 nm at day 0,1, 2, 3 and 4 of exposure. RESULTS: pH variations from 7.1 to 9.7 Temperature 25 +/-1 C Measured concentrations ranged from 16 to 35 l/l, resulting 10-50 times lower than nominal concentrations. This was caused by the volatility of the test substance and by the head space in the test vessels, necessary for the supply of CO2to the algae. An algae growth lower than usual was observed, likely due to low CO2 levels in the test vessels. No growth inhibition or biomass inhibition were recorded in the test substance samples if compared with concurrent control. The EC50 of the study was considered to be > maximal measured concentration (35 l/l or 44 mg/l)
Result	:	The 72-hours no-observed effect concentration for both growth rate and biomass for algae was >44 mg/l.
Source	:	.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
15.06.2005 (21)

Method : other: calculated
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Remark : QSAR results (ECOSAR v0.99g) EPIWIN calculation:
Used data:
MW = 120.02 g/mol
Log Kow = 1.48
Melting point = -103 °C
Water solubility = 432 mg/l

Results - Green algae

parameter	duration	predicted (mg/l)
EC50	96-hr	172

Reliability : (2) valid with restrictions
2f Accepted calculation method
Flag : Critical study for SIDS endpoint
15.06.2005 (16)

Method :
Year :
GLP :
Test substance : other TS: 1,1-dichloro-1-fluoroethane (HCFC 141b; CAS no 1717-00-6), purity >99.9%

Remark : QSAR results (ECOSAR v0.99g) EPIWIN calculation:
Used data:
MW = 116.95 g/mol
Log Kow = 2.3
Melting point = -103.5 °C
Water solubility = 4000 mg/l

Results - Green algae

parameter	duration	predicted (mg/l)
EC50	96-hr	31

Reliability : (2) valid with restrictions
2f accepted calculation method
15.06.2005 (16)

Method :
Year :
GLP :
Test substance : other TS: 1-chloro-1,1-difluoroethane (HCFC 142b; CAS no 75-68-3), purity >99.9%as prescribed by 1.1 - 1.4

Remark : QSAR results (ECOSAR v0.99g) EPIWIN calculation:
Used data:
MW = 100.50 g/mol
Log Kow = 1.64
Melting point = -130.8 °C
Water solubility = 1400 mg/l

Results - Green algae

parameter	duration	predicted (mg/l)
EC50	96-hr	104

Reliability : (2) valid with restrictions

2f accepted calculation method
15.06.2005 (16)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : Other
Species :
Exposure period :
Unit :
Remark : No data are available
27.11.2003

4.5.1 CHRONIC TOXICITY TO FISH

Species : Other
Endpoint :
Exposure period :
Unit :
Remark : No data are available
27.11.2003

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : Other
Endpoint :
Exposure period :
Unit :
Remark : No data are available
27.11.2003

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

Species : Other
Endpoint :
Exposure period :
Unit :
Remark : No data are available
27.11.2003

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species : other terrestrial plant
Endpoint :
Exposure period :
Unit :
Remark : No data are available
27.11.2003

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

Type : artificial soil
Species :

Endpoint :
Exposure period :
Unit :

Remark : QSAR results (ECOSAR v0.99g) EPIWIN calculation:
Used data:
MW = 120.02 g/mol
Log Kow = 1.48
Melting point =-103 °C
Water solubility = 432 mg/l

Results - Earthworm

parameter	duration	predicted (mg/kg dry wt)
LC50	14-day	1068

Reliability : (2) valid with restrictions
2f acceptable calculation method

23.06.2005 (16)

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

Species : Other
Endpoint :
Exposure period :
Unit :
Remark : No data are available
27.11.2003

4.7 BIOLOGICAL EFFECTS MONITORING

Memo : No data are available
27.11.2003

4.8 BIOTRANSFORMATION AND KINETICS

Type : other
Deg. product :
Remark : No data are available
27.11.2003

4.9 ADDITIONAL REMARKS

Memo : see remark
Remark : Aquatic and terrestrial toxicity tests were not performed for HFC-125. The test compound is a gas with a low water solubility (432 mg/l) and a high Henry's law constant (28k Pa m3/mol) at environmental condition. Mackay Level III model predicted a negligible partitioning of 0.028 and 0.006% in water and soil compartments, following emission of HFC-125 injto the atmosphere. Moreover, the test conditions that should be used in ecotoxicity tests (semistatic conditions, sealed apparatus) are not representative of natural environmental conditions.

23.06.2005

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo	:	In vivo
Type	:	Metabolism
Species	:	rat
Number of animals		
Males	:	6
Females	:	
Doses		
Males	:	1%
Females	:	
Vehicle	:	other: air
Route of administration	:	inhalation
Exposure time	:	6 hour(s)
Product type guidance	:	
Decision on results on acute tox. tests	:	
Adverse effects on prolonged exposure	:	
Half-lives	:	1st.: 2nd.: 3rd.:
Toxic behaviour	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	

Remark : The goal of the study was the determination of relative potential for different halogenated-penthanes to form trifluoroacetylated-hepatic proteins. This feature is related to the hepatic metabolisation pathway of these substances and is linked to trifluoroacetic acid (TFA) urinary excretion.

Male Fisher rats were used: in the same study rats were exposed to halotane (1.1%, n=6), HCFC-124 (1%, n=6), HFC-125 (0.97%, n=6), HCFC-123 (1.1%, n=6) and HFC-134a (1%, n=3). Chamber halocarbon concentrations were monitored periodically during exposure by means of GC-MS analysis. Chamber oxygen depleted during the exposure was supplemented . At the end of the 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 after the exposure period, animals were sacrificed, liver was homogenized and cytosolic and microsomal fractions prepared. Protein of the subcellular fractions were separated by SDS-PAGE and immunoblotted with anti-TFA-protein serum.

Results:
The semi-quantitative analysis of immunoblotted TFA-proteins indicated a decreasing potential to form TFA-proteins, in this order:

Halotane>=HCFC-123>>HCFC-124>HFC-125.

No quantitative analysis of TFA-protein amount was carried out.
TFA-proteins were not detected in samples from rats exposed to HFC-134a.

19F-NMR analysis of urinary TFA excretion after 12 hrs from the end of exposure confirmed the previous data:

Halocarbon	TFA excretion (umol/kg)

halotane	65 +/- 16
HCFC-123	82 +/- 20
HCFC-124	16 +-/ 2
HFC-125	1.7 +/- 1.7

Comment:
The proposed metabolic pathway for TFA production involves the initial H abstraction, mediated by cytochrome P450, leading to the formation of a carbon-based radical. This is considered the rate determinant step of the process. The radical is then hydroxilated and the trifluoroacetyl halide is formed by the exit of hydrogen halide. Trifluoroacetyl halide can react with water to give TFA or with a nucleofilic protein moiety to give a protein adduct.

The increased fluorination on dihalomethyl group (-CX2H) decreases the metabolism of these compounds in vivo.
HFC-125 showed a low potential to form TFA in liver, compared to other halogenated ethanes.

Reliability : (2) valid with restrictions
2e Study well documented, meets generally accepted scientific principles, acceptable for assessment

01.12.2003 (24)

In Vitro/in vivo : In vivo
Type : Toxicokinetics
Species :
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :

Remark : Male Sprague-Dawley rats were individually exposed to 1000, 5000 and 50000 ppm HFC-125 for 6 hours. Chamber concentrations were measured every 10 minutes during the exposure period. Absorption of test material was measured by measuring the decrease of chamber concentration throughout the exposure.

Results:
A little uptake was observed for the 3 test concentration at the end of the 6 hr-exposure. Inspection of the gas-uptake data did not show any first order-attributable absorption and distribution of HFC-125 within the body.
The uptake of HFC-125 was too low to compute kinetic constants of uptake and metabolism with physiologically-based pharmacokinetic models.

Reliability : (3) invalid
Documentation insufficient for the assessment

01.12.2003 (3)

5.1.1 ACUTE ORAL TOXICITY

Type : Other
Value :
Species :
Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Remark : HFC-125 is a gas. Oral intake is not a relevant route of exposure.
27.11.2003

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LCLo
Value	:	> 800000 ppm
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	20
Vehicle	:	
Doses	:	800000 ppm; 4 g/l
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	1992
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Group of 5 male and 5 female rats was exposed to 80% HFC-125 and 20% oxygen atmosphere for 4 hrs. Control Group of 5 male and 5 female rats was exposed to normal air. Animals were exposed by whole body exposure in chamber.Chamber concentration of HFC-125 was monitored by gas-chromatography analysis.

Parameter evaluated:
Observation of clinical signs and mortality were carried out during the exposure period, 1, 3 and 6 hours after the end of exposure and more than once a day for 14 days.
Body weights were measured prior the exposure and on day 1, 3, 7, 10 and 14.
Gross pathology examinations were carried out at the end of exposure period.

Results:

No mortality was observed during the study.
During the exposure clinical signs such as ataxic gait, and abnormal respiration were observed in all exposed rats. The clinical signs disappeared one hour after the exposure.
There was a slight decrease in mean body weight of exposed males in comparison to control value.
No remarkable findings were observed during pathology examinations.

Reliability : (1) valid without restriction
1a GLP Guideline study

Flag : Critical study for SIDS endpoint
29.10.2003 (34)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	Other
Value	:	
Species	:	
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	

Doses :

Remark : HFC-125 is a gas. dermal uptake is not a relevant route of exposure.
27.11.2003

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species :
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result :
Classification :
Method : other
Year :
GLP :
Test substance :

Remark : There are no skin irritation studies available. No signs of dermal irritation were observed during whole-body exposure in acute or repeated-dose inhalation studies.
27.11.2003

5.2.2 EYE IRRITATION

Species :
Concentration :
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result :
Classification :
Method : other
Year :
GLP :
Test substance :

Remark : There are no eye irritation studies available. No signs of ocular irritation were observed during whole-body exposure in acute or repeated-dose inhalation studies.
27.11.2003

5.3 SENSITIZATION

Number of animals :
Vehicle :
Result :
Classification :

Method	:	other
Year	:	
GLP	:	
Test substance	:	
Remark	:	There are no sensitisation studies available. No sensitisation responses were observed during whole-body exposure in repeated-dose inhalation studies.

22.06.2005

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-acute
Species	:	Rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	Inhalation
Exposure period	:	4 weeks
Frequency of treatm.	:	6 hrs/day, 5 days/week
Post exposure period	:	
Doses	:	5000, 15000 and 50000 ppm
Control group	:	Yes
NOAEL	:	>= 50000 ppm
Method	:	OECD Guide-line 412 "Repeated Dose Inhalation Toxicity: 28-day or 14-day Study"
Year	:	1992
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4

Remark :

Groups of 10 male and 10 female rats were exposed to 0, 5000, 15000 and 50000 ppm HFC-125 for 28 days (6 hrs/day, 5 days/week). 2 recovery groups of 10 male and 10 female rats were exposed to 0 and 50000 ppm HFC-125 (2 weeks of recovery). The animals were exposed by whole body exposure in chamber. 2 1060 l chambers (1250x950 mm for 20 rats) and 2 2140 l chambers (2500x950 mm for 40 rats) were used in the study. Chamber concentration of HFC-125 was monitored by gas-chromatography analysis.

PARAMETER EVALUATED:
Clinical observations were carried out daily.
Body weights were measured prior the exposure and on day 1, 2 and 5 during the first week. All rats were weighed once a week after the second week of exposure, during the observation period and on the day before termination.
Food consumption of all rats were measured once a week during the exposure and observation period.
Haematology, blood chemistry and urinalysis examinations were carried out at the end of the exposure period.
Liver samples were collected at the end of the study to determinate peroxisomal proliferation.
At the end of the exposure/recovery period, all the animals were sacrificed and examined grossly.
Organ weight: brain, lungs, liver, spleen heart, kidneys, adrenals, testes, ovaries and thymus were weighed at necropsy.

Histopathologic examinations:
The following organs/tissues were collected from all rats and were further processed, fixed and examined microscopically:
" Skin
" Nasal cavity

" Nasopharynx
" Larynx
" Trachea
" Lung
" Bone marrow
" Lymph node
" Thymus
" Spleen
" Heart
" Tongue
" Salivary glands
" Esophagus
" Stomach
" Small intesitne
" Large intestine
" Liver
" Pancreas
" Kidneys
" Urinary bladder
" Pituitary
" Thyroid-parathyroid
" Adrenals
" Testes
" Epididymis
" Seminal vesicles
" Prostate
" Ovaries
" Uterus
" Vagina
" Mammary gland
" Brain (medulla/pons, cerebellar cortex, cerebral cortex)
" Spinal Cord
" Peripheral nerve (sciatic)
" Eyes
" Harderian glands
" Muscle (thigh)
" Bone (femur)

STATISTICAL METHODS:
Dunnett's test was used for determining the significant difference of test values of bodyweight, food consumption, blood chemistry, haematology and organ weight. The X2 test was used for determining the significant differences of urinary test values. T-test was used for the statistical analysis of the recovery groups parameters and for determining the significant differences in urinary volume, urine specific gravity and peroxysomal beta-oxidation activity.

RESULTS:

Chamber concentrations:
The overall mean concentrations of HFC-125 during the study were 0, 5040, 15277, 50630 ppm. Mean daily chamber concentrations were within 99-105% of the nominal concentrations, with a standard deviation ranged between 0.9-1.2% of the mean value.
Mean daily chamber temperature and humidity ranged between 21.6-24.7 °C and 54.2-74.4%, respectively.

Clinical observation:
No mortality was observed at any dose.
skin ulcer was observed for one female of high-dose group during treatment and recovery period. No other clinical signs were observed.

Body weights and food consumption:
There were no differences in body weight and food consumption among the treated groups and the control group.

Haematology, blood biochemistry and urinalysis:
A statistically higher mean corpuscolar haemoglobin concentration (MCHC) was measured in the males of high dose group, compared to control. however no dose dependence was observed. No hematological changes were observed in treated animals in comparison to controls at the end of the recovery period.
Males of high-dose group had a statistically higher concentration of plasma phospholipids compared to control.
Males exposed to 5000 and 15000, but not 50000 ppm had a lower albumine content.
Males of the exposed recovery group had a statistically higher plasma albumine and total protein values compared to control recovery group.

-Findings in haematology and blood chemistry in males-

	MCHC(g/dl)	Albumin(g/dl)	Phopsholipid(mg/dl)
control	34.0+/-0.3	3.8+/-0.1	98+/-14
5000 ppm	34.8+/-0.3	3.7+/-0.1*	98+/-10
15000 ppm	34.5+/-0.3	3.7+/-0.1*	103+/-12
50000 ppm	34.5+/-0.4**	3.8+/-0.1	113+/-14*
RECOVERY			
control	34.8+/-1.3	6.1+/-0.2	115+/-14
50000 ppm	34.2+/-0.4	6.3+/-0.2*	114+/-22

**=p<0.01; *=p<0.05.

No treatment related findings were observed in urinalysis

Organ weight:
No treatment related findings were observed.

Gross pathology:
No dose-related changes were observed in treated animals at the end of exposure and recovery period.

Peroxisomal beta-oxidation activity:
A higher activity was measured in liver samples of male high-dose group, respect to control. However the female high-dose group had a lower activity compared to control.

Histology:
No compound related changes were found at the end of exposure and recovery periods.

50000 ppm was considered the NOAEL of the study.

Reliability : (1) valid without restriction
(1a) GLP Guideline study

22.06.2005 (36)

Type : Sub-chronic
Species : Rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : Inhalation
Exposure period : 13 weeks
Frequency of treatm. : 6 hrs/day, 5 days/week
Post exposure period : 4 weeks

Doses	:	5000, 15000 and 50000 ppm
Control group	:	Yes
NOAEL	:	>= 50000 ppm
Method	:	OECD Guide-line 413 "Subchronic Inhalation Toxicity: 90-day Study"
Year	:	1993
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Groups of 10 male and 10 female rats were exposed to 0, 5000, 15000 and 50000 ppm HFC-125 for 13 weeks (6 hrs/day, 5 days/week). Additional groups of 10 male and 10 female rats/concentration (0, 5000, 15000, and 50000 ppm) were designated for a 4-week recovery period. The animals were exposed by whole body exposure in chamber. 4 2140 l chambers (2500x950 mm for 40 rats) were used in the study. Chamber concentration of HFC-125 was monitored by gas-chromatography analysis.

PARAMETER EVALUATED:
Clinical observations were carried out daily.
Body weights were measured before the start of the dosing, on day 1, 2 and 5 during the first week of exposure and weekly throughout the exposure period and the recovery period. Food consumption was measured weekly during the exposure and the recovery period.
Haematology, blood chemistry and urinalysis examinations were carried out at the 7th week and at end of the exposure period.
Liver samples were collected at the end of the study to determine the peroxisome proliferation.
At the end of the exposure/recovery period, all the animals were sacrificed and examined grossly.
Organ weight: brain, lungs, liver, spleen heart, kidneys, adrenals, testes, ovaries and thymus were weighed at necropsy.

Histopathologic examinations:
The following organs/tissues were collected from all rats and were further processed, fixed and examined microscopically:
" Skin
" Nasal cavity
" Nasopharynx
" Larynx
" Trachea
" Lung
" Bone marrow
" Lymph node
" Thymus
" Spleen
" Heart
" Tongue
" Salivary glands
" Esophagus
" Stomach
" Small intesitne
" Large intestine
" Liver
" Pancreas
" Kidneys
" Urinary bladder
" Pituitary
" Thyroid-parathyroid
" Adrenals
" Testes
" Epididymis
" Seminal vesicles

" Prostate
" Ovaries
" Uterus
" Vagina
" Mammary gland
" Brain (medulla/pons, cerebellar cortex, cerebral cortex)
" Spinal Cord
" Peripheral nerve (sciatic)
" Eyes
" Harderian glands
" Muscle (thigh)
" Bone (femur).

STATISTICALL METHODS:
Dunnett's test was used for determining the significant difference of test values of bodyweight, food consumption, blood chemistry, haematology and organ weight. The X2 test was used for determining the significant differences of urinary test values. T-test was used for the statistical analysis of the recovery groups parameters and for determining the significant differences in urinary volume, urine specific gravity and peroxysomal beta-oxidation

RESULTS:
Chamber concentrations:
The overall mean concentration of HFC-125 during the study were 0, 4995, 14891, 50113 ppm. Mean daily chamber concentration were within 90-106% of the nominal concentrations, with a standard deviation ranged between 1.5-2.1% of the mean values.
Mean daily chamber temperature and humidity ranged between 20.6-24.5 °C and 50.1-69.9%, respectively.

Clinical observation:
No mortality was found at any dose.
No clinical signs were observed throughout the study.

Body weight and food consumption:
There were no differences in body weight and food consumption among the treated and the control groups.

Haematology, blood biochemistry and urinalysis:
No statistical differences were observed in hematology, blood biochemistry and urinalysis among the treated and the control groups.

Organ weight:
No significant differences were observed among exposed and control groups.

Peroxisomal beta-oxidation activity in liver:
No statistically significant differences were measured among the treated and the control groups.

Gross pathology:
No treatment-related findings were observed.
White patch in the liver of one male and cyst in the kidney of another male dosed at 50000 ppm were observed. Thick of the ear of one female in 5000 ppm group, one in 50000 ppm group and one in the control group were observed. Enlargement of the lymph node in one female and cyst in the ovary in another female of the 50,000 ppm recovery group were observed. these findings were considered incidental.

Histology:

No compound-related changes were found at the end of treatment period.

50000 ppm was considered the NOAEL for the study.

Reliability : (1) valid without restriction
1a GLP Guideline study
Flag : Critical study for SIDS endpoint
22.06.2005 (35)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Salmonella typhimurium reverse mutation assay
System of testing : Salmonella typhimurium and Escherichia coli
Test concentration : 20%, 40%, 60%, 80%, 100% v/v atmospheric concentrations (nominal)
Cycotoxic concentr. : 100%
Metabolic activation : with and without
Result : Negative
Method : OECD Guide-line 471
Year : 1992
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Mutagenic activity of HFC-125 was evaluated by using 5 histidine dependent strains of Salmonella typhimurium (TA 98, TA 1538, TA 100, TA 1535 and TA 1537) and one tryptophan-dependent strain of Escherichia coli (WP2 uvrA). Preliminary toxicity tests were carried out to select the maximal concentration for the main test.
Tests were carried out in presence and in absence of Rat liver derived S-9 mix activation system. Cells were incubated with 20%, 40%, 60%, 80%, 100% v/v HFC-125 for 48 hours at 37°C.
Suitable positive controls were used in the presence (2-aminoanthracene and benzo-alfa-pyrene) and in the absence (Sodium azide, aminoacridine and 2-nitrofluorene) of S-9 mix. In addiction to the positive controls listed above, dichloromethane 7.5% v/v was used as positive control and tested under the same conditions of HFC-125.

Results:
HFC-125 was found to be toxic at 100% in the presence and in the absence of S-9 mix.
HFC-125 produced no significant changes in mutant numbers compared to negative control values, in any of the strains, with or without the enzimatic activation.

Reliability : (1) valid without restriction
1a GLP Guideline study
07.10.2003 (33)

Type : Cytogenetic assay
System of testing : Chinese Hamster Ovary (CHO) cells
Test concentration : 4 hrs exposure: 15%, 30% and 70% v/v
24 and 48 hrs: 15, 30 and 60% v/v
Cycotoxic concentr. : 4 hrs exposure in the presence of S-9 mix: 40% (reduction 21% of mitotic activity)
24 hrs exposure in the absence of S-9 mix: 30% (reduction 42% of mitotic activity)
Metabolic activation : with and without
Result :
Method : OECD Guide-line 473
Year : 1992
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4

Remark : CHO cells were exposed to 15%, 30% and 70% v/v HFC-125 in atmosphere for 4 hrs, in the presence and in the absence of S-9 mix, and to 15%, 30% and 60% v/v HFC-125 in atmosphere for 24 and 48 hrs, in the absence of S-9 mix. The highest doses were chosen by a preliminary toxicity test.
Positive controls containing cyclophosphamide and mitomycin-C were incorporated in the main tests.
2 hrs prior to the end of the exposure, cell division was arrested by preincubation with 0.4 ug/ml colcemid.
Clastogenic potential was assessed by the analysis of 100 cells/slide in metaphase. 2 slides /culture were analysed. Mitotic index (% cells in metaphase) was calculated by examination of 1000 cells/culture.
The following character were recorded:
-chromosome number
-presence of aberrant chromosomes
-types and number of aberrations
Presence of polyploid cells was recorded

Statistical analysis:
Fisher Exact Probability test

Results:

HFC-125	Mitotic index	Chromosomal aberrations
4 hrs with S-9 mix		
0	/	3.5%
15%	-35%	5.5%
30%	-33%	5.5%
70%	-18%	7.5%
4 hrs without S-9 mix		
0	/	5.0%
15%	-42%	7.0%
30%	-52%	2.5%
70%	-47%	5.5%
24 hrs		
0	/	2.5%
15%	/	2.0%
30%	/	3.5%
60%	/	1.5%
48 hrs		
0	/	4.0%
15%	/	6.5%
30%	-15%	6.5%
60%	-45%	11.0%**

** = p<0.01

A statistically significant increase in chromosomal aberration and in number of polyploid cells was observed in cultures exposed to HFC-125 60% for 48 hrs. However, these findings were related to clear evidences of cellular toxicity (-45% of mitotic index) and were considered not a specific clastogenic effect of the tested substance.

No clear evidence of clastogenic activity was observed in this study.

Reliability : (1) valid without restriction
1a GLP Guideline study

27.11.2003 (8)

Type : Chromosomal aberration test
System of testing : human lymphocytes
Test concentration : 17.5%, 35% and 70% v/v in atmosphere
Cycotoxic concentr. :

Metabolic activation : with and without
Result : Negative
Method : OECD Guide-line 473
Year : 1992
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Human lymphocytes were exposed to 17.5%, 35% and 70% v/v HFC-125 in atmosphere for 3 hrs, in the presence and in the absence of S-9 mix and for 24 and 48 hrs in hte absence of S-9 mix. The highest doses were chosen by a preliminary toxicity test.
Positive controls containing cyclophosphamide and chlorambucil were incorporated in the main tests.
2 hrs prior to the end of the exposure, cell division was arrested by preincubation with 0.4 ug/ml colcemid.
Clastogenic potential was assessed by the analysis of 100 cells/slide in metaphase. 2 slides /culture were analysed. Mitotic index (% cells in metaphase) was calculated by examination of 1000 cells/culture.
The following character were recorded:
-chromosome number
-presence of aberrant chromosomes
-types and number of aberrations
Presence of polyploid cells was recorded

Statistical analysis:
Fisher Exact Probability test.

Results:

HFC-125	Mitotic index	Chromosomal aberrations
3 hrs with S-9 mix		
0	/	1.5%
17.5%	/	3.5%
35%	/	6.5%**
70%	/	3.5%
3 hrs without S-9 mix		
0	/	2.5%
17.5%	/	2.5%
35%	/	5.5%
70%	/	7.0%*
24 hrs without S-9 mix		
0	/	2.5%
17.5%	/	3.5%
35%	/	4.5%
70%	/	3.0%
48 hrs without S-9 mix		
0	/	5.0%
17.5%	14%	4.0%
35%	35%	6.0%
70%	19%	7.0%

* = p<0.05; ** = p<0.01.
No increases in the incidence of polyploid cells was observed. The statistically significant increases of chromosomal aberrations observed at 3 hrs are not considered biologically relevant, since the values are within the limits of the historical control range for this culture and the effect is not dose and time-related.
HFC-125 showed no clastogenic potential in this test.

Reliability : (1) valid without restriction
1a GLP Guideline study

07.10.2003 (9)

Type : Ames test

System of testing	:	
Test concentration	:	
Cycotoxic concentr.	:	
Metabolic activation	:	
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Remark	:	A Salmonella reverse mutation test was carried out in two strains of S. typhimurium, TA1535 and TA100. cells were incubated for 72 hrs to a maximal concentration of 20 % HFC-125, with or without metabolic activation (S9 mix). The seeded dishes were exposed to the test gas by incubation at 37°C inside a glass reraction vessel. The mutation frequency was measured by counting the number of histidine-revertant colonies. The mutation frequency ratio was calculated between cultures exposed to HFC-125 and control samples and the substance was considered to give a positive response with a mutation frequency ratio > 2. No positive response was observed for HFC-125 up to 20%.
Reliability	:	(2) valid with restrictions 2e Study well documented, meets generally accepted scientific principles, acceptable for the assessment
Flag	:	Critical study for SIDS endpoint

23.06.2005 (31)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	Mouse
Sex	:	male/female
Strain	:	CD-1
Route of admin.	:	Inhalation
Exposure period	:	6 hrs
Doses	:	2.4%, 12% and 60% v/v in atmosphere
Result	:	Negative
Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	1992
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Groups of male and female rats were exposed to 2.4, 12 and 60% v/v HFC-125 in atmosphere. 5 male and 5 female mice per group were killed 24 hrs, 48 hrs and 72 hrs after the exposure. A preliminary toxicity test was carried out. Concurrent negative and positive control groups were exposed to air or administered 30 mg/kg chlorambucil, respectively. Bone marrow smears on glass slides were made from each animal. A total of at least 2000 erythrocytes/animal was examined for the presence of micronuclei. Calculated number of micronuclei per 1000 polychromatic erythrocytes were analysed. The ratio of polychromated:mature cells was also determined as an indicator of cytotoxicity. Statistical analysis: The frequency of micronucleated cells were analysed by the Mann-Withney U procedure. Result:

mice exposed to HFC-125 60% showed clinical signs of toxicity (hunced posture, tremors, slow respiration). All mice killed 24 hrs after the exposure had lost weight.

No statistically significant increased frequency of micronucleated erythrocytes was observed in any group treated with HFC-125, in comparison to negative control.
Chlorambucil treatment significantly increased the number of micronucleated cells in comparison to control ($p<0.01$).

No significant changes were observed in the ratio polychromated:mature cells, among the control groups, the groups treated with HFC-125 and the chlorambucil-treated groups.

Conclusion:
Under the conditions of test, HFC-125 did not induce any chromosomal damage or other clastogenic effect leading to micronuclei formation in polychromatic murine erythrocytes.

Reliability : (1) valid without restriction
1a GLP Guideline study

28.11.2003 (15)

5.7 CARCINOGENICITY

Species	:	
Sex	:	
Strain	:	
Route of admin.	:	Other
Exposure period	:	
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	
Result	:	
Control group	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	

Remark : No data
10.10.2003

5.8.1 TOXICITY TO FERTILITY

Type	:	Other
Species	:	
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Frequency of treatm.	:	
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	

Control group :

Remark : not available
27.11.2003

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	Rat
Sex	:	Female
Strain	:	other: Crl: CD (SD)BR VAF/plus strain
Route of admin.	:	Inhalation
Exposure period	:	day 6-15 post-coitum
Frequency of treatm.	:	6 hrs/day
Duration of test	:	
Doses	:	5000, 15000, 50000 ppm (0.5, 1.5 and 5%)
Control group	:	yes, concurrent no treatment
NOAEL maternal tox.	:	>= 50000 ppm
NOAEL teratogen.	:	>= 50000 ppm
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	1992
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Groups 40 mated female rats were exposed to 5000, 15000 and 50000 ppm HFC-125 in the day 6-15 of pregnancy for 6 hrs/day. Animals were exposed whole body in exposure chambers. Concentration of HFC-125 in atmosphere was measured at 1 hour intervals during exposure.

EXAMINED PARAMETERS:
Adult females:
All animals were subjected to daily examination for clinical signs of toxicity. Body weight gain and food consumption were measured regularly during exposure.
On day 20 of pregnancy the animals were killed and examined for pathological changes.

Litter and foetuses:
developmental and teratogenic potential of HFC-125 was assessed by examination of the typical parameters:
-number of corpora lutea
-number and distribution of live young
-number and distribution of embryofoetal deaths
-individual and litter foetal weight
-foetal abnormalities.

STATISTICAL METHODS:
Analysis of variance followed by Williams' test and Kursal-Wallis test followed by Shirley's test were used to analyse parametric and non-parametric data, respectively.
For Litter data and foetal changes the litter was considered the basic sample unit and non-parametric analyses were routinely used.
Where 75% or more of the values for a given variable are the same, a Fisher's exact test was used, when considered necessary.

RESULTS:

Chamber conditions:
The overall mean concentrations of HFC-125 during the study were 0, 4995, 14433, 49207 ppm. Mean daily chamber concentrations were within 96% of the nominal concentrations.

Mean daily chamber temperature and humidity ranged between 21.0-22.2 °C and 34.3-44.3%, respectively.

Adult females:
Animals of high dose group showed unsteady gait during exposure period, related to anaesthetic properties of the test material. there were no mortalities and no other clinical signs.
No statistically significant differences were observed in body weight gain and food consumption among the treated and the control groups. No treatment related findings were observed at terminal autopsy.

Litters:
No treatment-related findings were observed in litter size, embryofoetal loss and litter and foetal weight among the treated and the control groups. The incidence of foetal malformations was 1/317, 2/341, 11/342 and 5/366 (litter affected: 1/25, 2/27, 3/29 and 3/29) in control group, 5000, 15000 and 50000 ppm HFC-125, respectively. 2 litters (6 and 4 foetuses) in the 15000 ppm-group and 1 litter (3 foetuses) in the 50000 ppm-group were affected by bilateral forelimb flexure associated with distorted ribcage and thickened ribs. This syndrome, that typically occurs in more foetuses in the same litter, is considered spontaneous and not related to treatment.

There was no evidence of any morphological changes attributable to HFC-125.
No statistically significant differences in the incidence of anomalies and variants were observed during visceral and skeletal examination of foetuses among the control and the treated groups.

The maternal and the foetal NOAEL for this study were considered 50000 ppm.

Reliability : (1) valid without restriction
1a GLP Guideline study

Flag : Critical study for SIDS endpoint

22.06.2005 (32)

Species	:	Rabbit
Sex	:	Female
Strain	:	New Zealand white
Route of admin.	:	Inhalation
Exposure period	:	day 6-18 of pregnancy
Frequency of treatm.	:	6 hrs/day
Duration of test	:	
Doses	:	5000, 15000, 50000 ppm v/v HFC-125 in atmosphere
Control group	:	yes, concurrent no treatment
NOAEL maternal tox.	:	>= 50000 ppm
NOAEL teratogen.	:	>= 50000 ppm
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	1992
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Groups 24 mated female rabbits were exposed to 5000, 15000 and 50000 ppm HFC-125 in the day 6-18 of pregnancy for 6 hrs/day. Animals were housed individually in metal cages and exposed whole body in chambers. HFC-125 concentration was monitored at 1 hour intervals during the exposure.

EXAMINED PARAMETHERS:
Adult females:
All animals were subjected to daily examination for clinical signs of toxicity. Body weight gain and food consumption were measured regularly during

exposure.
On day 20 of pregnancy the animals were killed and examined for pathological changes.

Litter and foetuses:
developmental and teratogenic potential of HFC-125 was assessed by examination of the typical parameters:
-number of corpora lutea
-number and distribution of live young
-number and distribution of embryofoetal deaths
-individual and litter foetal weight
-foetal abnormalities.

STATISTICAL METHODS:
Analysis of variance followed by Williams' test and Kursal-Wallis test followed by Shirley's test were used to analyse parametric and non-parametric data, respectively.
For Litter data and foetal changes the litter was considered the basic sample unit and non-parametric analyses were routinely used.
Where 75% or more of the values for a given variable are the same, a Fisher's exact test was used, when considered necessary.

RESULTS:
Chamber conditions:
The overall mean concentrations of HFC-125 during the study were 0, 5032, 15131, 50383 ppm. Mean daily chamber concentrations were within 101% of the nominal concentrations.
Mean daily chamber temperature and humidity ranged between 19.7-21.2 °C and 33.2-40.0%, respectively.

Adult females:
One animal of control group and one of 5000 ppm groups were killed due to poor condition. One animal of control group produced a litter on day 29 of pregnancy and was excluded from the study. One animal of 5000 ppm group showed weight loss and aborted on days 20/21 of pregnancy. No other instances of abortion were present in the study.
Incidence of animals showing cold ears during the exposure period was higher in all the treated groups, in comparison with control group. This finding was considered a response to stress, not directly related to exposure.
Statistically significant reduction in food consumption of animals of 50000 ppm-group was observed during the exposure period. However any difference in food consumptions was observed between the 5000 and the 15000 ppm groups and the control group, and the effect was considered no treatment-related. No differences were observed in body weight among the treated and the control groups. No treatment-related findings were observed at terminal autopsy.

Litters:
No treatment-related findings were observed in litter size, embryofoetal loss and litter and foetal weight in the 5000 ppm- and 15000 ppm-groups. A slightly increased incidence of early and late in utero deaths was observed in the 50000 ppm-group, in comparison to control. However, the in utero loss incidence at 50000 ppm felt within the historical range and was not conclusively considered treatment-related. At lower concentrations there was no related effect on post-implantation losses or litter size.
The incidence of embryonic deaths occurred within the study and the comparison with the background control range available for 9 other studies carried out by the same laboratory in 1991 are reported in the table below.

	Litter size	N. corpora lutea	Implants	Pre-implant loss (%)	Embryonic deaths			Post-implant loss (%)	Live young
					early	late	total		
Control	21	11.4	8.7	22.2	0.4	0.4	0.8	9.0	7.9
5,000 ppm	21	11.2	10.2	10.9	0.6	0.4	1.0	9.9	9.2
15,000 ppm	24	11.5	9.9	13.0	0.5	0.4	1.0	8.4	9.0
50,000 ppm	21	11.8	9.5	18.6	0.7	0.8	1.5	15.8	8.1
Background control range#					0.4-0.8	0.1-0.9	0.7-1.4		

from 9 studies perfomed in 1991

Although the mean incidence of both early and late in utero deaths at 50,000 ppm falls within concurrent background, the total number of in utero deaths
at this concentration is slightly greater than expected.
There were no significant effects on litter weights or mean foetal weights.
The incidence of foetal malformations was 2/165, 1/193, 7/215 and 2/169 in control group, 5000, 15000 and 50000 ppm HFC-125, respectively.

No statistically significant differences in the incidence of anomalies and variants were observed during visceral and skeletal examination of foetuses among control and treated groups.

Attached document : Litte data.doc
Reliability : (1) valid without restriction
1a GLP Guideline study
Flag : Critical study for SIDS endpoint
22.06.2005 (7)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type : other
In vitro/in vivo :
Species :
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :
Duration of test :
Doses :
Control group :

Remark : There are no data available
28.11.2003

5.9 SPECIFIC INVESTIGATIONS

Endpoint	:	other: Cardiac sensitisation
Study descr. in chapter	:	
Reference	:	
Type	:	
Species	:	dog
Sex	:	male
Strain	:	Beagle
Route of admin.	:	Inhalation
No. of animals	:	12
Vehicle	:	other: air
Exposure period	:	5 minute(s)
Frequency of treatm.	:	
Doses	:	7.5, 10, 15, 20, 25, 30%
Control group	:	
Observation period	:	
Result	:	
Method	:	other: Reinhardt et al. (1971), Arch. Env. Health, 22, 265-279
Year	:	1992
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Remark : In this study the cardiac sensitisation potentials of HFC-125 and Halon 13B1, following adrenaline intravenous injection, were compared.
12 pure-bred male beagle dogs 6-7 months old were used for the study.
The animals were exposed via face mask to the test materials. The test atmospheres were continously analysed by an infra-red gas analyser.
ECG recording was carried out for each animal during the experiment with the following protocol:

Time from start (minutes)	
0	Start ECG recording
2	Adrenaline injection
7	Inhalation of test gas
12	Adrenaline injection
17	Stop ECG recording

Adrenaline solutions were given at a rate of 0.1 ml/sec.
The study was carried out in 3 stages:
1. each animal was tested with various concentrations of adrenaline solutions, in order to establish the response of adrenaline alone.
2. 2 dogs out of 12 were selected and exposed to the well known cardiac sensitiser CFC-11 (2-2.5% in atmosphere) to have a positive control.
3. 6 dogs out of 12 were selected and tested according to the experimental procedure, using the following concentrations:

Exp. session	Halon 13B1 (% in air)	HFC-125 (% in air)
1	-	-
2	5	-
3	-	10
4	10	-
5	-	15
6	15	-
7	-	20
8	20	-
9	-	25
10	25	-
11	-	30
12	-	7.5

The criterion to evaluate positive response in the study was the

appearance of 5 or more apparently multifocal ventricular ectopic beats or ventricular fibrillation.
When a clear positive response was observed in a dog, it was no longer exposed to that gas (but it was still used for the other gas).
If a dog died during earlier experimental sessions, it was replaced by a dog from the remaining animals available.
This approach is based on the idea that if a dog gives a positive response at a certain concentration, it is considered as a positive response also at higher concentrations.

RESULTS:
Stage 1.
on the ground of the initial study of the cardiac response with adrenaline alone the 12 dogs were divided in 3 groups:
a-high responsivity (response at 1-2 ug/kg adrenaline)
b-low responsivity (response at 4-8 ug/kg)
c-very low responsivity (response at 12 ug/kg)

Stage 2.
one dog from group a and 1 from group c were exposed to 2-2.5% CFC-11. Positive responses (fatal ventricular fibrillation and multiple ectopic beats) were observed in the two dogs.

Stage 3.
No positive responses were observed when animals were administered to adrenaline and exposed to air only.

Halon 13B1 (% in air)	Positive response	% Positive response
5	0/6	0
10	0/6	0
15	0/6	0
20	2/6	33
25	3/6	50

1 dog exposed to 25% Halon 13B1 showed fatal ventricular fibrillation

HFC-125 (% in air)	Positive response	% Positive response
7.5	0/6	0
10	1/6	17
15	4/6	67
20	5/6	83
25	5/6	83
30	6/6	100

2 dogs exposed to 20 and 30% HFC-125 showed fatal ventricular fibrillation.

CONCLUSION:
The result of the study showed that the concentration of gas at which 50% of exposed animals gave positive response to cardiac sensitisation was 25% for Halon 13B1 and between 10 and 15% for HFC-125.
The NOEC for HFC-125 is 7.5%

Reliability : (1) valid without restriction
1d Test procedure in accordance wtih generally accepted scientific standards and described in sufficient detail

Flag : Critical study for SIDS endpoint
22.06.2005 (23)

Endpoint : other: Cardiac sensitisation
Study descr. in chapter :
Reference :

Type :
Species : Dog
Sex : Male
Strain : Beagle
Route of admin. : Inhalation
No. of animals :
Method : other: Reinhardt et al. (1971), Arch. Env. Health, 22, 265-279
Year :
GLP :
Test substance :

Remark : In this study the cardiac sensitisation potential of HFC-23 (trifluoromethane) following adrenaline intravenous injection. CFC-11 (chloro-trifluoromethane) and Halon 13B1, were compared used as positive controls and cardiac sensitisation potential of a mixture HFC-23/HFC-125 (36.5/63.5% v/v) was assessed.
9 pure-bred male beagle dogs 6-7 months old were used for the study. The animals were exposed via face mask to the test materials. The test atmospheres were continously analysed by an infra-red gas analyser.
ECG recording was carried out for each animal during the experiment with the following protocol:

Time from start (minutes)	
0	Start ECG recording
2	Adrenaline injection
7	Inhalation of test gas
12	Adrenaline injection
17	Stop ECG recording

Adrenaline solutions were given at a rate of 0.1 ml/sec.
The study was carried out in 3 stages:
1. each animal was tested with various concentrations of adrenaline solutions, in order to establish the response of adrenaline alone.
2. 2 dogs out of 9 were selected and exposed to the well known cardiac sensitiser CFC-11 (2% in atmosphere) to have a positive control.
3. 6 dogs out of 12 were selected and tested according to the experimental procedure, using the following concentrations:

Exp. session	Halon 13B1 (% in air)	HFC-23 (% in air)	HFC-125/HFC-23 (% in air)
1	-	-	-
2	5	-	-
3	-	10	-
4	10	-	-
5	-	15	-
6	15	-	-
7	-	20	-
8	20	-	-
9	-	25	-
10	25	-	-
11	-	30	-
12	-	50*	-
13	-	-	10

* auxiliary oxygen added

The criterion to evaluate positive response in the study was the appearance of 5 or more apparently multifocal ventricular ectopic beats or ventricular fibrillation.
When a clear positive response was observed in any animal, no further experiments were carried out on the dog with that tested gas (the animal was assumed to gave positive responses at higher exposure levels).

If a dog died during earlier experimental sessions, it was replaced by a do from the remaining animals available.

RESULTS:
Stage 1.
on the ground of the initial study of the cardiac response with adrenaline alone the 9 dogs were divided in 3 groups:
a-high responsivity (response at 2 ug/kg adrenaline)
b-low responsivity (response at 2-4 ug/kg)
c-very low responsivity (response at 4-12 ug/kg)

Stage 2.
2 dogs were randomly selected and exposed to 2% CFC-11. Positive responses (fatal ventricular fibrillation and multiple ectopic beats) were observed in the two dogs.

Stage 3.
No positive responses were observed when animals were administered to adrenaline and exposed to air only.
50% of ppositive respones were observed in dogs exposed to 25% halon 13B1. There were no positive responses for HFC-23 up to 50% in atmosphere.
1/6 dog exposed to HFC-23/HFC125 mixture showed a positive response (fatal ventricular fibrillation).

CONCLUSION:
The result of the study showed that the concentration of gas at which 50% of exposed animals gave positive response to cardiac sensitisation was 25% for Halon. The tested dose of 10% in air of the mixture HFC-23/HFC-125 (36.5%/63.5% v/v) gave a positive response and was considered a LOEC.

Reliability : (1) valid without restriction
1d Test procedure in accordance wtih generally accepted scientific standards and described in sufficient detail

22.06.2005 (22)

5.10 EXPOSURE EXPERIENCE

Type of experience : other: Occupational exposure

Remark : Occupational exposure to halogenated refrigerants was measured during 30 maintenance/repair operations in refrigeration systems. Exposure of 22 refrigeration repair workers to HCFC-22, HFC-134a and to a mixture of HFC-134a, HFC-143a and HFC-125 (52, 4 and 44%, respectively) was monitored through personal sampling (sampling in tubes in Carboxen 1000 followed by gaschromatographic analysis) and workroom air direct measurements (photoacustic IR gas analyser).

Results:
Concentrations of halogenated refrigerants measured with personal sampling were generally low, varying from a value of 1 mg/m3 (3.4 ppm) for HFC-143a to a value of 2171 mg/m3 (600 ppm) for HCFC-22.

Sampling	n	time (min)	Concentration (mg/m3)
HCFC-22	12	6-390	10.6 - 2171
HFC-134a	8	20-120	12.5 - 442
HFC-125 (mix.)	10	20-210	4.9 - 182
HFC-134a (mix)	10	20-210	1.3 - 513
HFC-143a (mix)	10	20-210	1.0 - 210

Direct reading measurements showed periods of peak of concentration in workroom air.

Peaks	n	time (min)	Concentration (mg/m3)
HCFC-22	32	1-21	39 - 42434
HFC-134a	22	1-11	133 - 5842
HFC-125 (mix.)	36	3-18	64 - 5891
HFC-134a (mix)	31	1-16	6.3 - 1448
HFC-143a (mix)	36	3-18	38 - 4950

Conclusion:
According to the study results, occupational exposures to halogenated refrigerants during maintenance/repair operations is moderate

Reliability : (2) valid with restrictions
2e Study well documented, meets generally accepted scientific principles, acceptable for assessment

Flag : Critical study for SIDS endpoint

02.12.2003 (18)

Type of experience : other: Occupational exposure

Remark : 6 male workers employed in large scale repair works on refrigerators were selected. ECG monitoring was performed for 24 hours on the day of exposure and on a control day. 6 plumbers were chosen as controls. the number of ventricular ectopic beats on the day of exposure was recorded and compared with that of the control day and with that of the control group (plumbers). The concentrations of HCFC-22 and FC-12 were measured in 3 and 1 cases, respectively and performed by personal sampling followed by IR analysis.

Results:
There was no clear correlation between the exposure to halogenated hydrocarbons and cardiac arrhythmias in exposed workers.
Average concentration of FC-12 was 202 ppm during 48 minutes of exposure, with a peak value of 2800 ppm.
Average concentrations of HCFC-22 felt in the range 170-815 ppm during 70-150 minutes of exposure, with peak values comprised between 1300-10000 ppm. The duration of peak period had a range of 2-35 minutes.

Reliability : (3) invalid
3b Significant methodological deficiencies including monitoring of only 6 workers, concentrations measured only four times in a period of more than a year, and alcohol use as a potential confounding factor.

02.12.2003 (4)

Type of experience : other: workplace monitoring data

Remark : due to HFC-125 low toxicity and its production and processing are carried out in closed systems, no monitoring activities are performed in the workplace.

20.01.2004

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

Test substance : HFC -125
Method :

Remark : Gas chromatograph Shimadzu GC-8AIF equipped with flame ionization detector.

Column:
3m x 3mm I.D. stainless steel packed with 20% DC-200 liquid phase on a 60/80 mesh chromosorb W (acid washed and dimethyldichlorosilane treated) solid phase.

Condition:
Samples were chromatographed isothermally at

Source : Dupont-Mitui fluorochemicals
Reliability : (1) valid without restriction
28.10.2003 (34)

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

Safe handling : Carry out all operation in closed piping circuits and equipment.
Prevent product vapours decomposition from contacting hot spots.
Keep away from heat sources.
Use equipment and materials which are compatible with the products.

Fire/exp. protection : Contact with alkaline and alkaline-earth metals may provoke violent reactions or explosions.

Storage requirement : Store in a ventilated cool area.
Keep away from heat sources.
Keep away from alkaline metals and their alloys.

Common storage :

Container : Ordinary steel

Unsuitable container :

Add. information :

Transport code : UN Number 3220
IATA class 2.2

Source : Solkane 125 MSDS
10.12.2003

8.2 FIRE GUIDANCE

Hazards : Non-flammable. Formation of dangerous vapours in case of decomposition.

Protective equipment : Self-contained breathing apparatus, full protective acid resistant suite.

Extinguishing medium : In case of fire in close proximity, all means of extinguishing are suitable.

Unsuit. exting. medium : No restrictions

Add. information :

Fire class :

Products arising : Hydrogen fluoride, fluorophosgene

Source : Solkane 125 MSDS
10.12.2003

8.3 EMERGENCY MEASURES

Type : accidental spillage

Remark : Accidental release measures:

Self-contained breathing apparatus in case of large uncontrolled emissions.
Keep away heat sources and alkaline metals.
Vapours heavier than air. Possible oxygen depletion.
10.12.2003

Type : injury to persons (skin)

Remark : Apron/boots of neoprene if risk of splashing.
First aid measures:
Allow evaporation of the product.
Rinse with running water.
10.12.2003

Type : injury to persons (eye)

Remark : Wear protective goggles for all industrial operations.
First aid measures:
Allow evaporation of the product
Flush eyes with running water

10.12.2003

Type : injury to persons (oral)

Remark : Not possible

10.12.2003

Type : injury to persons (inhalation)

Remark : Self-contained breathing apparatus in medium confinement/insufficient oxygen/ini case of uncontrolled emissions.
First aid measures:
Oxygen or cardiopulmonary resuscitation if necessary
Consult with a physician in case of respiratoryand nervous symptoms

10.12.2003

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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