

**FOREWORD**

**INTRODUCTION**

**1,1-DIFLUOROETHANE (HFC-152a)**

**CAS N°: 75-37-6**

## SIDS Initial Assessment Report

### For

### SIAM 22

Paris, France, 18-21 April 2006

- 1. Chemical Name:** 1,1-Difluoroethane (HFC-152a)
- 2. CAS Number:** 75-37-6
- 3. Sponsor Country:** Republic of Korea  
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- 4. Shared Partnership with:**
- 5. Roles/Responsibilities of the Partners:**
  - Name of industry sponsor /consortium DuPont
  - Process used Industry collected data and prepared the draft versions of the IUCLID dossier, SIAR, and SIAP.
- 6. Sponsorship History**
  - How was the chemical or category brought into the OECD HPV Chemicals Programme? This substance is sponsored by Korea under the ICCA Initiative and is submitted for the first discussion at SIAM 22.
- 7. Review Process Prior to the SIAM:** NIER, Korea reviewed the documents and added the use volume and exposure information.
- 8. Quality check process:** The quality of the existing data was reviewed against the OECD criteria as described in the Manual for Investigation of HPV Chemicals.
- 9. Date of Submission:** 20 January, 2006
- 10. Date of last Update:** 29 June 2006
- 11. Comments:**

**SIDS INITIAL ASSESSMENT PROFILE**

<b>CAS No.</b>	75-37-6
<b>Chemical Name</b>	1,1-Difluoroethane (HFC-152a)
<b>Structural Formula</b>	F <sub>2</sub> – HC – CH <sub>3</sub>

**SUMMARY CONCLUSIONS OF THE SIAR****Human Health**

No toxicokinetic data for HFC-152a were found.

HFC-152a has low acute inhalation toxicity, with a 4-hour rat approximate lethal concentration (ALC) of 383,000 ppm. No valid acute oral toxicity studies are available. Although no standard test results are available, the repeat dose studies show some potential for irritation.

As with most HFCs, HFC-152a has the potential to produce cardiac sensitization in dogs challenged simultaneously with high exposure concentrations and high doses of exogenous epinephrine. Marked responses, which included a cardiac arrhythmia were observed in 3 of 12 dogs at 150,000 ppm. No response was observed at 50,000 ppm. No sensitization studies were available.

HFC-152a has low repeated dose toxicity. HFC-152a had anesthetic properties at a 100,000 ppm exposure level during a 2-week repeated dose inhalation study in rats. No other clinical, haematological, blood chemistry or histopathology effects were observed during the 2-week inhalation study. No adverse effects were observed in rats following a 3-month inhalation exposure to 25,000 ppm HFC-152a.

HFC-152a was not mutagenic in the *in vitro* bacterial reverse mutation test (Ames test) in *Salmonella typhimurium* and *Escherichia coli* strains. However, HFC-152a showed evidence of weak clastogenicity in an *in vitro* human lymphocyte chromosome aberration test. Further evaluation of the chromosome aberration potential using an *in vivo* micronucleus test produced negative results.

In a 2-year bioassay, HFC-152a was not carcinogenic to rats at inhalation exposure levels up to 25,000 ppm.

In a developmental study, female rats were exposed via inhalation up to 50,000 ppm during days 6 to 15 of pregnancy for 6 hours per day. No compound related maternal and developmental effects were observed at any of the concentrations tested, hence, the NOEL is 50,000 ppm. No histopathological or weight effects on reproductive organs were observed in male and female rats exposed up to 25,000 ppm HFC-152a for 6 hours per day, 5 days per week for 3, 12 or 24 months.

**Environment**

On the basis of its physical properties HFC-152a may be expected, when released to the environment, to partition almost exclusively into the atmosphere as it is a gas, with a vapor pressure at 25°C of 6065.2 hPa, and it has a water solubility of 2.671 g/l at 25°C. Any HFC-152a, which might be present in aqueous waste streams discharged directly into rivers or lakes would be expected, by analogy with similar compounds, to have a half-life with respect to volatilization of days or at the very most a few weeks. HFC-152a is expected to exist solely in the vapor-phase in the ambient atmosphere.

Vapor-phase HFC-152a is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals with a lifetime of 1.4 years. The atmospheric lifetime of this chemical suggests that it will mix throughout the troposphere with a globally averaged concentration in 2003 of about 2.6 ppt. Because of its IR absorption, it will contribute a very small amount to climate change with a global warming potential (GWP) relative to CO<sub>2</sub> of 140 for a time horizon of 100 years.

In addition, some HFC-152a is expected to gradually diffuse into the stratosphere above the ozone layer where it

will slowly degrade due to reaction with hydroxyl radicals and direct photolysis from UV-C radiation. The ozone depletion potential (ODP) of HFC-152a has been determined to be negligible.

HFC-152a is not expected to adsorb to sediment or particulate matter. Bioconcentration is expected to be low based on an estimated BCF value of approximately 2 using the measured n-octanol/water partition coefficient (log value is 0.75). A Mackay Level III fugacity model (EPIWIN v.3.05) predicts that HFC-152a will partition mainly to the air (99.9%), with very little going to water (0.111%), and virtually none going to soil or sediment (0.01 and <0.01%, respectively).

Based on the ECOSAR predictions (96-hour LC<sub>50</sub> in fish of 733 mg/L 48-hour EC<sub>50</sub> in daphnids of 720 mg/L, and 96-hour EC<sub>50</sub> in algae of 419 mg/L), actual toxicity test data for the analog chemical HFC-134a (96-hour LC<sub>50</sub> in fish of 450 mg/L and 48-hour EC<sub>50</sub> in daphnids of 980 mg/L), and the high Henry's Law Constant for these compounds (0.02 atm-m<sup>3</sup>/mole for HFC-152a), the predicted toxicity of HFC-152a to aquatic organisms is low.

#### **Exposure**

The primary uses for HFC-152a are as an aerosol propellant and a foam expansion agent. Other potential uses include refrigeration blends and catalyst regeneration. Production capacities are confidential, but are in excess of 5000 metric tonnes per year. In Korea, it is also used in maintaining of a catalytic activity and estimated usage volume of 1,1-difluoroethane was 4.63, 4.85, and 3.14 tonnes/year in 2003, 2004, and 2005, respectively.

Emissions from HFC-152a manufacturing facilities are small. In the sponsor country, small amounts of HFC-152a are used in a closed system. HFC-152a is treated with steam and emitted to wastewater plant. Fluorine is below the detection limit (1 mg/L) in discharged water. There are no reported natural sources of HFC-152a. HFC-152a used in propellant and foaming applications will be emitted to the atmosphere.

Industrial hygiene monitoring data during manufacture and industrial use show exposure to be well under acceptable exposure limits. The current AIHA WEEL (Workplace Environmental Exposure Limit) and DuPont AEL (Acceptable Exposure Limit) are 1000 ppm, 8-hour TWA (time-weighted average). Though consumer exposure has not been measured directly, modeling based on measurement of similar uses shows consumer exposure to be minimal during intended uses.

#### **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. Its global warming potential is acknowledged and is being addressed by other programs.

## SIDS Initial Assessment Report

### 1 IDENTITY

#### 1.1 Identification of the Substance

CAS Number: 75-37-6  
IUPAC Name: 1,1-Difluoroethane  
Molecular Formula: C<sub>2</sub>H<sub>4</sub>F<sub>2</sub>  
Structural Formula: F<sub>2</sub> – HC – CH<sub>3</sub>  
Molecular Weight: 66.1  
Synonyms: Ethane, 1,1-difluoro-  
HFC-152a (name to be used throughout dossier)  
Freon<sup>®</sup> 152a  
Ethylidene fluoride  
Genetron<sup>®</sup> 152a  
Algofrene 67  
Dymel 152  
Dymel 152a  
F152A  
FC152a  
FKW 152a  
HFA 152a  
R 152a  
Ethylene fluoride  
Ethylidene difluoride  
Genetron 100 (CHEMLIST, 1999; HSDB; 2000).

Since solubility and physical characteristics are similar, data for analogous chemicals, 1,1,1,2,2-pentafluoroethane (HFC-125) and 1,1,1,2-tetrafluoroethane (HFC-134a), are used where data are lacking for 1,1-difluoroethane (HFC-152a) (DuPont, 2002a; 2003).

#### 1.2 Purity/Impurities/Additives

Purity: > 99.9 %

Impurities/Additives: Typical impurities in HFC-152a include low level (ppm) water, low level (ppb) residual HCl and/or HF acids (DuPont Co., 2006).

### 1.3 Physico-Chemical Properties

**Table 1 Summary of Physico-Chemical Properties**

Property	Value	
Physical state	Gas	
Melting point	-117 °C	Lewis, 1993
Boiling point	-24.7 °C	Lewis, 1993
Density	0.91 g/mL @ 21 °C	Kirk-Othmer, 1991
Vapour pressure	4,550 mmHg (6,065.2 hPa) @ 25 °C	Daubert and Danner, 1989a
Water solubility (calculated)	2.671 g/L @ 25 °C	Meylan and Howard, 1996
Partition coefficient n-octanol/water (log value) (measured)	0.75	Jow and Hansch, n.d.
Henry's law constant (calculated)	0.02 atm·m <sup>3</sup> /mole (2,026.5 Pa·m <sup>3</sup> /mole)	Daubert and Danner, 1989b Ruelle and Kesselring, 1997 SRC, n.d.
Flammability limits	3.7 % - 18 % (in air)	Sax and Lewis, 1987

## 2 GENERAL INFORMATION ON EXPOSURE

### 2.1 Production Volumes and Use Pattern

HFC-152a is produced in a closed system by catalytic reaction of vinyl chloride with hydrofluoric acid and is purified based on market specification. Production capacities are confidential, but are in excess of 5,000 metric tonne (10 million pounds) per year. In Korea, estimated usage volume of 1,1-difluoroethane was 4.63, 4.85, and 3.14 tonnes/year in 2003, 2004, and 2005, respectively (NIER, 2005).

Approximately 80 % of HFC-152a is used as an aerosol propellant and approximately 15 % is used as a foam expansion agent. The remaining 5 % of the HFC-152a is for other potential uses, which include refrigeration blends and catalyst regeneration. In Korea, it is also used in maintaining of a catalytic activity (NIER, 2005).

Because of its low vapor pressure, HFC-152a is handled as a liquefied gas during manufacture and shipping. Therefore, HFC-152a is handled in closed pressurize systems so that exposure typically does not occur in the manufacturing, except for during maintenance or an abnormal process situation, such as a leak (DuPont, 2004).

HFC-152a is used in aerosol consumer personal care and household products and is dispensed with the product during use. Typically there is no HFC-152a left in the container when it is disposed (DuPont, n.d.).

HFC-152a used to manufacture foam is contained within the foam, and remains in the foam for a long period of time. The HFC-152a will be disposed with the foam (DuPont, 2002b).

HFC-152a used in refrigerants is contained in the refrigeration system until such time as it is collected for recycle or disposal (DuPont, 2005).

## 2.2 Environmental Exposure and Fate

On the basis of its physical properties, HFC-152a may be expected, when released to the environment, to partition almost exclusively into the atmosphere as:

- it is a gas, with a vapour pressure at 25 °C of 4,550 mmHg.
- it has a limited water solubility of 2.7 g/L at 25 °C.

Any HFC-152a that might be present in aqueous waste streams discharged directly into rivers or lakes would be expected, by analogy with similar compounds, to have a half-life with respect to volatilisation of days or at the very most a few weeks. In the sponsor country, small amounts of HFC-152a are used in a closed system. HFC-152a is treated with steam and emitted to wastewater plant. Fluorine is below the detection limit in discharged water (NIER, 2005).

### 2.2.1 Sources of Environmental Exposure

There are no reported natural sources of HFC-152a. HFC-152a used in propellant and foaming applications will be emitted to the atmosphere.

### 2.2.2 Photodegradation

1,1-Difluoroethane (HFC-152a) is expected to exist solely in the vapor-phase in the ambient atmosphere. Vapor-phase HFC-152a is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals with an atmospheric lifetime of 1.4 years. The atmospheric lifetime of this chemical suggests that some HFC-152a is expected to gradually diffuse into the stratosphere above the ozone layer where it will degrade due to direct photolysis from UV-C radiation (Nimitz and Skaggs, 1992; SRC, n.d.).

The molecular breakdown to give CO, CO<sub>2</sub>, H<sub>2</sub>O, and C(O)F<sub>2</sub> proceeds via various free-radical intermediates. C(O)F<sub>2</sub> is incorporated into rain, cloud, or fog water and is hydrolyzed to form HF and CO<sub>2</sub> (AFEAS, 1989).

### 2.2.3 Stability in Water

HFC-152a is predicted to be stable in water under environmentally relevant conditions, and hydrolysis is not expected to occur, as indicated by HydroWin calculations.

### 2.2.4 Transport between Environmental Compartments

Mackay Level III fugacity model (EPIWIN v.3.05) predicts that HFC-152a will partition mainly to the air (99.9 %), with very little going to water (0.111 %), and virtually none going to soil or sediment (0.01 and < 0.01 %, respectively). The following input parameters were used: Molecular Weight: 66.05; Henry's Law Constant: 0.0203 atm·m<sup>3</sup>/mole; Vapor Pressure: 3.86 x 10<sup>3</sup>; log Kow: 0.75; Soil Koc: 2.31.

If released to water, HFC-152a is not expected to adsorb to sediment or particulate matter based upon the estimated Koc of 60 (SRC, n.d.). HFC-152a is expected to volatilize rapidly from water surfaces based upon this compound's estimated Henry's Law constant. Estimated half-lives for a model river and model lake are 2 and 77 hours, respectively (Lyman et al., 1990; SRC, n.d.).

### 2.2.5 Biodegradation

Modeling of several physical-chemical parameters and fate processes (Table 2) was conducted to help provide insight into the behavior in the environment of a homologous series of 4 fluorocarbon compounds (HFC-152a, HFC-134a, and HFC-125).

Syracuse Research Corporation models for estimating physical-chemical properties and fate processes were used to estimate  $\log_{10}$  Kow (Meylan and Howard, 1995), water solubility at 25 °C (Meylan and Howard, 1996), Henry's Law Constant (Meylan and Howard, 1991), and ultimate biodegradation (Boethling et al., 1994). The dominant fate process controlling distribution of these compounds in the environment is volatilisation (Mackay et al., 1996).

**Table 2 Environmental Fate Parameters**

Compound	$\log_{10}$ Kow (Estimated)	Water Solubility (Estimated)	Henry's Law Constant (Estimated)	Ultimate Degradation (Estimated)
HFC-152a (1,1-Difluoroethane) (C <sub>2</sub> H <sub>4</sub> F <sub>2</sub> )	1.13	2,671 mg/L	0.38 atm·m <sup>3</sup> /mole	Weeks
HFC-134a (1,1,1,2-Tetrafluoroethane) (C <sub>2</sub> H <sub>2</sub> F <sub>4</sub> )	1.68	768 mg/L	1.5 atm·m <sup>3</sup> /mole	Weeks-months
HFC-125 (1,1,1,2,2-Pentafluoroethane) (C <sub>2</sub> HF <sub>5</sub> )	1.55	867 mg/L	3.1 atm·m <sup>3</sup> /mole	Weeks-months

Highly chlorinated/fluorinated compounds are not expected to biodegrade rapidly (Boethling et al., 1994). Based on the expected lack of sorption to soil, sediment, or particulate matter from fugacity modeling and its high vapour pressure, biodegradation is not expected to be an important environmental fate process for HFC-152a (HSDB, 2000). In addition, biodegradation testing with similar compounds, e.g. difluoromethane (HFC-32), which was degraded 8 % after 28 days, and 1,1,1,2-tetrafluoroethane (HFC-134a), which was degraded 4 % after 28 days, has indicated that these types of compounds are not readily biodegradable (Tobeta 1989; 1992).

### 2.2.6 Bioaccumulation

Bioconcentration is expected to be low based upon an estimated BCF value of 2 (SRC, n.d.).

### 2.2.7 Other Information on Environmental Fate

Due to the absence of chlorine and bromine atoms in the molecule, and the ozone depletion potential of other hydrofluorocarbons (HFC's), the contribution of HFC-152a to atmospheric ozone depletion can be considered negligible.

Global Warming potential (GWP) values of 410, 120, and 37 relative to carbon dioxide (GWP = 1) were calculated for integration time horizons of 20, 100, and 500 years, respectively (IPCC TAR, 2001). An official value of 140 was adopted by the Kyoto Protocol (IPCC AAR, 1996) for at time horizon of 100 years, indicating a potential contribution to global warming.

The Advanced Global Atmospheric Gasses Experiment observed the tropospheric abundance of HFC-152a to be 2.6 ppt in 2003 (IPCC/TEAP, 2005).

### **2.3 Human Exposure**

HFC-152a is a gas at room temperature. Therefore, the main route of human exposure is via inhalation. On the basis of its physico-chemical properties, if released into the environment HFC-152a will partition mostly into the atmosphere.

#### **2.3.1 Occupational Exposure**

Emissions from DuPont HFC-152a manufacturing facilities are small and industrial hygiene monitoring data during manufacture and industrial use show exposure to be well under acceptable exposure limits. In the sponsor country, HFC-152a is handled in a closed system. Workers typically do not have a potential exposure to HFC-152a except for during maintenance or a leak. No industrial hygiene monitoring data were available (NIER, 2005).

The current AIHA WEEL (Workplace Environmental Exposure Limit) and DuPont AEL (Acceptable Exposure Limit) are 1000 ppm, 8-hour TWA (time-weighted average) (AIHA, 1994; DuPont Co., 1998).

#### **2.3.2 Consumer Exposure**

HFC-152a consumer exposures have been modeled based on similar use scenarios. The predicted aggregate exposure of the general public while using key products is minimal (DuPont, 2001a).

## **3 HUMAN HEALTH HAZARDS**

### **3.1 Effects on Human Health**

#### **3.1.1 Toxicokinetics, Metabolism and Distribution**

No kinetic, metabolism, and distribution studies in animals or humans were identified.

#### **3.1.2 Acute Toxicity**

##### Studies in Animals

##### *Inhalation*

The 4-hour inhalation ALC (approximate lethal concentration) in male rats was 383,000 ppm. Labored breathing, lethargy, and unresponsiveness to sound were observed during exposure, but no clinical signs were noted following exposure. No compound-related gross pathology changes were observed (DuPont Co., 1975). Acute inhalation studies are summarized in Table 3:

**Table 3 Acute Inhalation Studies in Animals**

Species	Duration of Exposure	Concentration (ppm)	Effect	Reference
Rat (ChR-CD®)	4 hours	66,400 175,200 319,000 383,000 437,500	ALC = 383,000 ppm	DuPont Co., 1975
Rat (strain not reported)	30 minutes	100,000 - 550,000	No postural reflex (200,000 ppm); no righting reflex (250,000 ppm); no corneal reflex (450,000 ppm); acute irritation of lungs ( $\geq 400,000$ ppm); lethality ( $\geq 500,000$ ppm)	Lester and Greenberg, 1950
Rat (strain not reported)	2 hours	74,000 100,000 200,000	Occasional trembling and incoordination	DuPont Co., 1951
Rat (ChR-CD)	15 minutes	1100 °C 1200 °C 1300 °C (pyrolysis products)	Ptosis ( $\geq 1100$ °C); apnea ( $\geq 1100$ °C); pale ears ( $\geq 1100$ °C); hyperemia ( $\geq 1100$ °C); dyspnea ( $\geq 1100$ °C); irregular respiration ( $\geq 1100$ °C); lacrimation ( $\geq 1100$ °C); chromodacryorrhea ( $\geq 1100$ °C); salivation ( $\geq 1100$ °C); gasping (1300 °C); convulsions (1300°C)	DuPont Co., 1966
Dog (Beagle)	Not Reported	500,000	Light surgical anesthesia; no change in EKG	Van Poznak and Artusio (1960).

*Dermal*

No acute dermal studies in animals were identified.

*Oral*

There was no reliable acute oral study.

Other Available Data

Cardiotoxicity studies in rats and dogs performed at levels up to 40 % HFC-152a showed varying effects listed in Table 4 below (Simaan and Aviado, 1975; Aviado and Belej, 1975). Male beagle dogs were exposed to 50,000 or 150,000 ppm HFC-152a in a cardiac sensitisation study. Marked responses, which included a cardiac arrhythmia that was considered to pose a serious threat to life, were observed in 3 of 12 dogs at 150,000 ppm. No response was observed at 50,000 ppm (DuPont Co., 1969; Reinhardt et al., 1971).

**Table 4** Cardiotoxicity Studies in Animals

Species	Concentration (ppm)	Effect	Reference
Dog (Mongrel)	200,000	Decrease in mean pulmonary arterial flow	Simaan and Aviado, 1975
Dog (strain not reported)	25,000 - 200,000	Depression of force of contraction ( $\geq 100,000$ ppm); displacement of ventricular function curve ( $\geq 100,000$ ppm)	Aviado and Belej, 1975

Studies in Humans*Inhalation*

No reliable inhalation studies in humans were identified.

*Dermal*

No dermal studies in humans were identified.

*Oral*

No oral studies in humans were identified.

*Other Routes of Exposure*

No additional studies were identified.

Conclusion

Although there is no standard studies available, information from a limited study indicates that HFC-152a is of low acute oral toxicity. HFC-152a has low acute inhalation toxicity, with a 4-hour rat ALC of 383,000 ppm. As with most HFCs, HFC-152a has the potential to produce cardiac sensitisation in dogs challenged simultaneously with high exposure concentrations (150,000 ppm) and high doses of exogenous epinephrine.

**3.1.3 Irritation**

In an acute-inhalation study in rats, there was considerable effusion of fluid from the respiratory tract, indicative of acute irritation of the lungs, at concentrations  $\geq 400,000$  ppm. When exposed at 100,000 ppm for 16 hours/day for 2 months, a mild diffuse infiltration of round cells (suggestive of mild chronic irritation) was the only finding noted (Lester and Greenberg, 1950). In a 2-year carcinogenicity study, nasal discharge in rats was reported (DuPont Co., 1982; 1992), suggesting that chronic low level nasal irritation occurred.

**3.1.4 Sensitisation**

No skin or respiratory tract sensitisation studies in animals or humans were identified.

### 3.1.5 Repeated Dose Toxicity

#### Studies in Animals

##### *Inhalation*

ChR-CD rats exposed to 100,000 ppm HFC-152a for 6 hours/day, 5 days/week for 2 weeks appeared to be anesthetized during exposure. Although there was a slight increase in urinary fluoride following the last exposure, no other effects were observed in clinical, haematological, blood chemistry, or histopathology endpoints (DuPont Co., 1976). When exposed at 100,000 ppm for 16 hours/day for 2 months, a mild diffuse infiltration of round cells in the lung (suggestive of mild chronic irritation) was the only finding noted (Lester and Greenberg, 1950). During a 2-year inhalation study in Crl:CD<sup>®</sup>Br rats, no adverse effects were observed at the 3-month interim evaluation point. The NOAEL was 25,000 ppm (67,500 mg/m<sup>3</sup>) (DuPont Co., 1982; 1992). Additional results of the 2-year inhalation study are detailed in section 3.1.7 Carcinogenicity – *in vivo* studies in animals.

##### *Dermal*

No dermal repeated dose studies in animals were identified.

##### *Oral*

No oral repeated dose studies in animals were identified.

#### Studies in Humans

No repeated dose inhalation, dermal, or oral studies in humans were identified.

#### Conclusion

HFC-152a has low repeated dose toxicity. Indications of respiratory tract irritation were observed acutely at concentrations  $\geq$  400,000 ppm and after repeated concentrations of 100,000 ppm. HFC-152a had anaesthetic properties at a 100,000-ppm exposure level during a 2-week repeated dose inhalation study in rats. No other clinical, haematological, blood chemistry, or histopathology effects were observed. No adverse effects were observed in rats following a 3-month inhalation exposure to 25,000 ppm HFC-152a.

### 3.1.6 Mutagenicity

#### Studies in Animals

##### *In vitro Studies*

HFC-152a was not mutagenic in the *in vitro* bacterial reverse mutation test (Ames test), following OECD Guideline 471, in *Salmonella typhimurium* and *Escherichia coli* strains, when tested with or without metabolic activation (DuPont Co., 2000a).

##### *In vivo Studies*

HFC-152a was negative in a rat *in vivo* micronucleus assay following OECD Guideline 474 (DuPont Co., 2001b), but was positive in the *Drosophila* SLRL test (Garrett and Fuerst, 1974).

### Studies in Humans

HFC-152a showed evidence of weak clastogenicity, only in the absence of metabolic activation, in an *in vitro* human lymphocyte chromosome aberration test following OECD Guideline 473 (DuPont, 2000b).

### Conclusion

HFC-152a was not mutagenic in the *in vitro* bacterial reverse mutation test (Ames test) in *Salmonella typhimurium* and *Escherichia coli* strains. However, HFC-152a showed evidence of weak clastogenicity in an *in vitro* human lymphocyte chromosome aberration test. Further evaluation of the chromosome aberration potential using an *in vivo* micronucleus test produced negative results.

## **3.1.7 Carcinogenicity**

### In vitro Studies

No *in vitro* carcinogenicity studies were identified.

### In vivo Studies in Animals

#### *Inhalation*

Male and female rats were exposed to 0, 2,000, 10,000, or 25,000 ppm HFC-152a for 6 hours per day, 5 days per week for 2 years. During the course of the study, no differences in body weights or body weight gains were observed. Clinical signs observed included ocular/nasal discharge, wet/stained perineum, stained body/face, and/or swollen ears.

Clinical chemistry effects noted throughout the study included increased mean corpuscular volumes, increased serum bilirubin, increased hematocrits, and/or increased urobilinogen. In the absence of any abnormalities in hematopoietic tissues or red blood cells or changes in serum bilirubin, these observations, which would be consistent with a haemolytic effect, provide inconclusive evidence of such a condition. A decrease in eosinophils and/or monocytes was observed. A dose-dependent increase in urinary fluoride concentration, but no fluorosis was observed. An increase in serum creatinine and urine volume, and a decrease in urine osmolality were observed in female rats.

At the end of the 2-year study, no treatment-related differences in organ weights were observed in male rats, but significant organ weight changes were observed in female rats at all concentrations with unclear biological significance. No treatment-related tumors were observed in male and female rats. Therefore, HFC-152a was not carcinogenic and did not produce life-shortening toxic effects (DuPont Co., 1982; 1992).

#### *Dermal*

No dermal carcinogenicity studies in animals were identified.

#### *Oral*

No oral carcinogenicity studies in animals were identified.

### Studies in Humans

No carcinogenicity studies in humans were identified.

## Conclusion

HFC-152a was not carcinogenic to rats.

### **3.1.8 Toxicity for Reproduction**

#### Studies in Animals

##### *Effects on Fertility*

Although no specific reproduction studies have been performed with HFC-152a, histopathology of reproductive organs was examined in a 2-year chronic and carcinogenicity study. No histopathological or weight effects on reproductive organs were observed in male and female rats exposed to HFC-152a via inhalation for 6 hours per day, 5 days per week for 2 years. The NOAEL was 25,000 ppm (DuPont Co., 1982).

##### *Developmental Toxicity*

Pregnant female rats were exposed to 0, 5,000, or 50,000 ppm HFC-152a for 6 hours per day on gestation days 6 - 15. No maternal or developmental toxicity was observed. The NOEL for maternal and developmental toxicity was 50,000 ppm, the highest level tested (DuPont Co., 1979).

#### Studies in Humans

##### *Effects on Fertility*

No reproduction studies in humans were identified.

##### *Developmental Toxicity*

No developmental toxicity studies in humans were identified.

## Conclusion

HFC-152a was not a developmental toxin in rats. No histopathological or weight effects on reproductive organs were observed in male and female rats exposed to HFC-152a for 6 hours per day, 5 days per week for 2 years.

### **3.2 Initial Assessment for Human Health**

HFC-152a has a very low potential for producing adverse health effects in workers or the general population. HFC-152a has low acute inhalation toxicity, with a rat 4-hour approximate lethal concentration of 383,000 ppm. Male beagle dogs treated with exogenous epinephrine were exposed to 50,000 or 150,000 ppm HFC-152a in a cardiac sensitisation study. Marked responses, which included a cardiac arrhythmia, were observed in 3 of 12 dogs at 150,000 ppm. No response was observed at 50,000 ppm. Although significant organ weight changes were observed at all concentrations tested after 90 days of exposure, the biological significance is unclear. The NOAEL for developmental toxicity was 50,000 ppm (the highest dose tested), and no adverse effects on reproductive organ weight were observed following 3 months of exposure to 25,000 ppm. HFC-152a was not mutagenic in the in vitro bacterial reverse mutation test (Ames test) in *Salmonella typhimurium* and *Escherichia coli* strains. However, HFC-152a showed evidence of weak clastogenicity in an in vitro human lymphocyte chromosome aberration test. Further evaluation of the chromosome aberration potential using an in vivo micronucleus test produced negative results. As no significant increase in tumors were observed, HFC-152a was not carcinogenic and did not produce life-shortening toxic effects at doses ranging from 2,000 to 25,000 ppm.

## 4 HAZARDS TO THE ENVIRONMENT

### 4.1 Aquatic Effects

#### Acute Toxicity Test Results

No ecotoxicological studies have been conducted with HFC-152a and there is very little or no ecotoxicology data for similar non-chlorinated, fluorocarbon compounds. The related compounds HFC-134a (1,1,1,2-tetrafluoroethane) and HFC-125 (1,1,1,2,2-pentafluoroethane) have been included here for comparison with HFC-152a as they are both fluorinated ethane substances, and test data for HFC134a are available. ECOSAR was used to predict the aquatic toxicity of these fluorocarbons to green algae, daphnids (planktonic freshwater crustaceans), and fish (Table 5). ECOSAR predictions are based on actual toxicity test data for classes of compounds with similar modes of action, i.e., narcosis in the case of fluorocarbons. Predicted  $\log_{10}$  Kow values were used as input for the ECOSAR model. To help gauge the sensitivity of the prediction to this parameter, ECOSAR predictions were made using 2 Kow values. The initial Kow value was based on the estimated value from the Syracuse Research Corporation model except for the measured value of 0.75 for HFC-152a (Jow and Hansch, n.d.). The second Kow value was empirically selected to be approximately  $\log_{10}$  0.5 greater than the initial measured or estimated value.

**Table 5 Aquatic Toxicity Values**

Compound	$\log_{10}$ Kow (Estimated)	Algae, 96-hr EC <sub>50</sub> (Estimated) (mg/L)	Daphnid, 48-hr EC <sub>50</sub> (Estimated) (mg/L)	Fish, 96-hr LC <sub>50</sub> (Estimated) (mg/L)
HFC-152a (1,1-Difluoroethane) (C <sub>2</sub> H <sub>4</sub> F <sub>2</sub> )	0.75* 1.5	419 91	720 150	733 145
HFC-134a (1,1,1,2-Tetrafluoroethane) (C <sub>2</sub> H <sub>2</sub> F <sub>4</sub> )	1.5 2.0	140 51	231 81	223 76
HFC-125 (1,1,1,2,2-Pentafluoroethane) (C <sub>2</sub> HF <sub>5</sub> )	1.5 2.0	165 60	272 95	263 89
* measured value				

The only test data available are for HFC-134a. Results of aquatic testing of HFC-134a with daphnids and fish indicated that the daphnid 48-hour EC<sub>50</sub> was 980 mg/L and the 96-hour fish LC<sub>50</sub> was 450 mg/L (Stewart and Thompson, 1991; Thompson, 1991). The lower measured log Kow of 0.75 would lead to estimated toxicity values that would be even closer to the actual data. Based on the ECOSAR predictions, the actual toxicity test data, and the high Henry's Law Constant for these compounds, HFC-152a is considered a low hazard to aquatic organisms.

#### Chronic Toxicity Test Results

No chronic toxicity studies were identified.

#### Toxicity to Microorganisms

No toxicity studies to microorganisms were identified.

## **4.2 Terrestrial Effects**

### Acute Toxicity Test Results

No acute toxicity studies were identified.

### Chronic Toxicity Test Results

No chronic toxicity studies were identified.

## **4.3 Other Environmental Effects**

No additional data were identified.

## **4.4 Initial Assessment for the Environment**

HFC-152a is expected to exist solely in the vapour-phase in the ambient atmosphere. Vapour-phase HFC-152a is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals with an atmospheric half-life of about 472 days. The long atmospheric lifetime of this chemical suggests that some HFC-152a is expected to gradually diffuse into the stratosphere above the ozone layer, where it will slowly degrade due to direct photolysis from UV-C radiation (Nimitz and Skaggs, 1992; SRC, n.d.). HFC-152a is not expected to adsorb to sediment or particulate matter. Bioconcentration is expected to be low based on an estimated BCF value of approximately 2. The predicted toxicity of HFC-152a to aquatic organisms is low.

## **5 RECOMMENDATIONS**

The chemical is currently of low priority for further work, due to its low hazard profile. Its global warming potential is acknowledged and is being addressed by other programmes.

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# SIDS

## Dossier

**Existing Chemical** : ID: 75-37-6  
**CAS No.** : 75-37-6  
**Substance name** : Ethane, 1,1-difluoro  
**Synonym** : HFC-152a

### Producer related part

**Company** : E. I. du Pont de Nemours and Company  
**Creation date** : 15.01.2003

### Substance related part

**Company** : E. I. du Pont de Nemours and Company  
**Creation date** : 15.01.2003

**Status** :  
**Memo** :

**Printing date** : 29.06.2006  
**Revision date** :  
**Date of last update** : 29.06.2006

**Number of pages** : 80

**Chapter (profile)** : Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10  
**Reliability (profile)** : Reliability: without reliability, 1, 2, 3, 4  
**Flags (profile)** : Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

**1.0.1 APPLICANT AND COMPANY INFORMATION**

**Type** : manufacturer  
**Name** : E. I. du Pont de Nemours and Company  
**Contact person** :  
**Date** :  
**Street** : 1007 Market Street  
**Town** : 19898 Wilmington, Delaware  
**Country** : United States  
**Phone** :  
**Telefax** :  
**Telex** :  
**Cedex** :  
**Email** :  
**Homepage** :  
22.09.2005

**1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR**

**Type** : manufacturer  
**Name of plant** : DuPont- Corpus Christi  
**Street** :  
**Town** : Corpus Christi  
**Country** : United States  
**Phone** :  
**Telefax** :  
**Telex** :  
**Cedex** :  
**Email** :  
**Homepage** :  
22.09.2005

**1.0.3 IDENTITY OF RECIPIENTS****1.0.4 DETAILS ON CATEGORY/TEMPLATE****1.1.0 SUBSTANCE IDENTIFICATION**

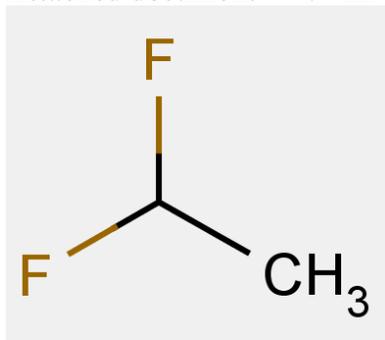
**IUPAC Name** : 1,1-Difluoroethane  
**Smiles Code** : FC(F)C  
**Molecular formula** : C<sub>2</sub>H<sub>4</sub>F<sub>2</sub>  
**Molecular weight** : 66.05  
**Petrol class** :  
29.06.2006

(10) (41)

**1.1.1 GENERAL SUBSTANCE INFORMATION**

**Purity type** : typical for marketed substance  
**Substance type** : organic  
**Physical status** : gaseous  
**Purity** : > 99.9 % w/w  
**Colour** : Clear, colorless  
**Odour** : Slight ethereal odor

**Attached document** : HFC-152a structure.bmp

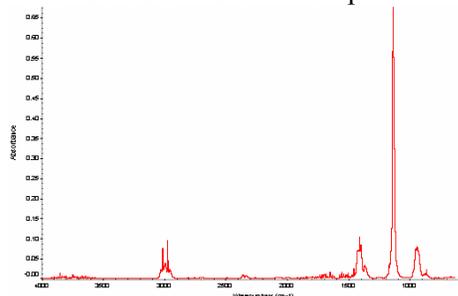


31.03.2006

(26)

**1.1.2 SPECTRA**

**Type of spectra** : other  
**Attached document** : spectra.bmp

**1.2 SYNONYMS AND TRADENAMES**

**Algofrene 67**  
15.01.2003

**Dymel 152**  
15.01.2003

**Dymel 152a**

15.01.2003

**Ethylene fluoride**

15.01.2003

**Ethylidene difluoride**

15.01.2003

**Ethylidene fluoride**

15.01.2003

**F152A**

15.01.2003

**FC152a**

15.01.2003

**FKW 152a**

15.01.2003

**Freon(R) 152a**

15.01.2003

**Genetron 100**

15.01.2003

**Genetron(R) 152a**

15.01.2003

**HFA 152a**

15.01.2003

**HFC-152a (name to be used throughout dossier)**

23.03.2006

**R 152a**

30.05.2006

(10) (41)

### 1.3 IMPURITIES

**Remark** : Typical impurities in HFC-152a include low level (ppm) water, low level (ppb) residual HCl and/or HF acids.

29.06.2006

(33)

### 1.4 ADDITIVES

**Remark** : None.

14.06.2005

**1.5 TOTAL QUANTITY**

**Remark** : Production capacities are confidential, but are in excess of 5,000 metric tones (10 million pounds) per year.

29.06.2006 (34)

**Remark** : In Korea, estimated usage volume of 1,1-difluoroethane was 4.63, 4.85, and 3.14 tonnes/year in 2003, 2004, and 2005, respectively.

30.05.2006 (55)

**1.6.1 LABELLING**

**Remark** : Flammable gas.

30.05.2006 (25) (26)

**1.6.2 CLASSIFICATION****1.6.3 PACKAGING**

**Memo** : HFC-152a is sold in small packages (steel reusable cylinders ranging from 95 lbs to 2,000 lbs), and in bulk containers (ISO tanks, tank trailers, and rail cars).

29.06.2006 (31)

**1.7 USE PATTERN**

**Remark** : Approximately 80 % of HFC-152a is used as a propellant in aerosol products. It is present in the aerosol container, liquified under pressure as part of the aerosol formulation. The vapor pressure of the 152a provides the driving force for dispensing the product.

Approximately 15 % of HFC-152a is used as a foam expansion agent. In foam manufacture HFC-152a is the formulation ingredient used to foam the polymer. It is stored as an ingredient and feed to the foaming process directly. The HFC-152a is contained in process equipment and the closed-cell foam product, so that exposure to workers and consumer is negligible.

Approximately 5 % of HFC-152a is used for other potential uses, which include catalyst regeneration, as well as HFC-152a being blended with other fluorocarbons for use as in refrigeration systems.

The refrigerant blends are contained in closed pressurized containers and refrigeration systems. Potential for exposures would occur only during servicing or an abnormal situation such as a leak.

29.06.2006 (14) (30) (31)

**Remark** : In Korea, it is used in maintaining of a catalytic activity.  
10.03.2006 (55)

### 1.7.1 DETAILED USE PATTERN

### 1.7.2 METHODS OF MANUFACTURE

**Origin of substance** : other  
**Type** :  
**Remark** : HFC-152a is produced by catalytic reaction of vinyl chloride with hydrofluoric acid.  
30.05.2006 (54)

## 1.8 REGULATORY MEASURES

### 1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

**Type of limit** : other: AIHA WEEL 8-hour TWA  
**Limit value** : 1,000 other: ppm  
30.05.2006 (1)

**Type of limit** : other: DuPont Acceptable Exposure Limit (AEL) 8-hour TWA  
**Limit value** : 1,000 other: ppm  
30.05.2006 (25) (26)

### 1.8.2 ACCEPTABLE RESIDUES LEVELS

**Proposed residues level** : HFC-152a is volatile and generally leaves no residue.  
**Maximum residue level** : mg/kg  
29.06.2006 (41)

### 1.8.3 WATER POLLUTION

**Remark** : None.  
14.06.2005

**1.8.4 MAJOR ACCIDENT HAZARDS**

**Remark** : Hazards include pressure, flammability, and potential for liquid exposure to cause frostbite.  
30.05.2006 (25) (26)

**1.8.5 AIR POLLUTION**

**Remark** : HFC-152a has no ozone depletion potential, low global warming potential, and is not regulated as a volatile organic compound.  
29.06.2006 (14)

**1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES**

**Type** : EINECS  
**Additional information** : EINECS Inventory  
CAS RN: 75-37-6  
Name: 1,1-Difluoroethane  
EINECS Inventory Number: 200-866-1  
30.05.2006 (10)

**1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS**

**Remark** : Hydrogen Fluoride.  
23.03.2006 (25) (26)

**Remark** : The atmospheric degradation of hydrofluorocarbons (HFCs) have been extensively studied through different research programmes from industry (AFEAS) and from EU (Step halocside project (STEP-HALOCSIDE/AFEAS, 1993) and were reported in the different WMO-UNEP scientific assessments on stratospheric ozone (WMO, 1989; 1991; 1994)  
30.05.2006 (67) (68)

**1.9.2 COMPONENTS****1.10 SOURCE OF EXPOSURE**

**Source of exposure** : Human: exposure by production  
**Exposure to the** :  
**Remark** : As a liquefied gas HFC-152a has to be handled in closed pressurize

29.06.2006 systems so that exposure typically does not occur in the manufacturing, except for during maintenance or an abnormal process situations, such as a leak. (31)

**Source of exposure** : Human: exposure by production  
**Exposure to the** :  
**Remark** : HFC-152a used to manufacture foam is contained within the foam, and remains in the foam for a long period of time. The HFC-152a will be disposed with the foam.

29.06.2006 (30)

**Source of exposure** : Human: exposure of the consumer/bystander  
**Exposure to the** :  
**Remark** : HFC-152a is used in aerosol consumer personal care and household products and is dispensed with the product during use. Typically there is no 152a left in the container when it is disposed.

29.06.2006 (14)

**Source of exposure** : other  
**Exposure to the** :  
**Remark** : HFC-152a used in refrigerants is contained in the refrigeration system until such time as it is collected for recycle or disposal.

29.06.2006 (32)

### 1.11 ADDITIONAL REMARKS

### 1.12 LAST LITERATURE SEARCH

### 1.13 REVIEWS

**2.1 MELTING POINT**

<b>Value</b>	: -117 °C	
<b>Decomposition</b>	: no, at °C	
<b>Sublimation</b>	:	
<b>Method</b>	:	
<b>Year</b>	: 1993	
<b>GLP</b>	: no data	
<b>Test substance</b>	: as prescribed by 1.1 - 1.4	
<b>Reliability</b>	: (2) valid with restrictions 2g. Data from handbook or collection of data.	
<b>Flag</b>	: Critical study for SIDS endpoint	
14.06.2005		(47)

**2.2 BOILING POINT**

<b>Value</b>	: -24.7 °C at	
<b>Decomposition</b>	:	
<b>Method</b>	:	
<b>Year</b>	: 1993	
<b>GLP</b>	: no data	
<b>Test substance</b>	: as prescribed by 1.1 - 1.4	
<b>Reliability</b>	: (2) valid with restrictions 2g. Data from handbook or collection of data.	
<b>Flag</b>	: Critical study for SIDS endpoint	
14.06.2005		(47)

<b>Value</b>	: -25 °C at	
<b>Decomposition</b>	:	
<b>Method</b>	:	
<b>Year</b>	:	
<b>GLP</b>	:	
<b>Test substance</b>	: as prescribed by 1.1 - 1.4	
<b>Reliability</b>	: (4) not assignable 4b. Secondary literature.	
24.03.2006		(26)

**2.3 DENSITY**

<b>Type</b>	:	
<b>Value</b>	: .91 at 21 °C	
<b>Method</b>	:	
<b>Year</b>	: 1991	
<b>GLP</b>	: no data	
<b>Test substance</b>	: as prescribed by 1.1 - 1.4	
<b>Result</b>	: Density is 0.91 g/mL at 21°C.	
<b>Reliability</b>	: (2) valid with restrictions	

	2g. Data from handbook or collection of data.	
<b>Flag</b>	: Critical study for SIDS endpoint	
24.03.2006		(44)
<b>Type</b>	:	
<b>Value</b>	: .9 at 25 °C	
<b>Method</b>	:	
<b>Year</b>	: 1998	
<b>GLP</b>	: no data	
<b>Test substance</b>	: as prescribed by 1.1 - 1.4	
<b>Remark</b>	: Density was determined for liquid density, units are in mg/L.	
<b>Reliability</b>	: (4) not assignable 4b. Secondary literature.	
24.03.2006		(25)

### 2.3.1 GRANULOMETRY

### 2.4 VAPOUR PRESSURE

<b>Value</b>	: 6,065.2 hPa at 25 °C	
<b>Decomposition</b>	:	
<b>Method</b>	: other (measured)	
<b>Year</b>	: 1989	
<b>GLP</b>	: no data	
<b>Test substance</b>	: as prescribed by 1.1 - 1.4	
<b>Reliability</b>	: (2) valid with restrictions 2g. Data from handbook or collection of data.	
<b>Flag</b>	: Critical study for SIDS endpoint	
31.03.2006		(12)
<b>Value</b>	: 5,998.5 hPa at 25 °C	
<b>Decomposition</b>	:	
<b>Method</b>	:	
<b>Year</b>	:	
<b>GLP</b>	:	
<b>Test substance</b>	: as prescribed by 1.1 - 1.4	
<b>Remark</b>	: Vapor pressure was reported as 87 psia at 25°C	
<b>Reliability</b>	: (4) not assignable 4b. Secondary literature.	
09.01.2006		(26)
<b>Value</b>	: 4,343.7 hPa at 20 °C	
<b>Decomposition</b>	:	
<b>Method</b>	:	
<b>Year</b>	: 1975	
<b>GLP</b>	: no data	

**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Vapor pressure was listed as 63 psig.  
**Reliability** : (4) not assignable  
 4e. Documentation insufficient for assessment.  
 23.03.2006 (5)

**Value** : 5,146.2 hPa at 25 °C  
**Decomposition** :  
**Method** : other (calculated)  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Reliability** : (2) valid with restrictions  
 2f. Accepted calculation method.  
 30.03.2006 (37)

## 2.5 PARTITION COEFFICIENT

**Partition coefficient** : octanol-water  
**Log pow** : .75 at °C  
**pH value** :  
**Method** : other (measured)  
**Year** :  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Reliability** : (2) valid with restrictions  
 2g. Data from handbook or collection of data.  
**Flag** : Critical study for SIDS endpoint  
 23.03.2006 (43)

**Partition coefficient** : octanol-water  
**Log pow** : 1.13 at °C  
**pH value** :  
**Method** : other (calculated)  
**Year** : 1995  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Reliability** : (2) valid with restrictions  
 2f. Accepted calculation method.  
 24.03.2006 (52)

### 2.6.1 SOLUBILITY IN DIFFERENT MEDIA

**Solubility in** :  
**Value** : 2,671 mg/l at 25 °C  
**pH value** :  
**concentration** : at °C

**Temperature effects** :  
**Examine different** :  
**pol.**  
**pKa** : at 25 °C  
**Description** :  
**Stable** :  
**Deg. product** :  
**Method** : other: Estimated  
**Year** : 1996  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Method** : The method used is a new mew calculation method that outperformed other widely used general-purpose equations based on log Kow.

The program uses the following equation if a melting point is available:

$$\log S = 0.693 - 0.96 \log Kow - 0.0092(Tm-25) - 0.00314(MW) + \text{summation of fl}$$

The program uses the following equation if no melting point is available:

$$\log S = 0.796 - 0.854 \log Kow - 0.00728(MW) + \text{summation of fl}$$

where:

S= water solubility in moles/L

Kow = n-octanol:water partition coefficient

Tm = melting temperature in °C

Summation of fl = summation of all correction factors applicable to a given compound

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

**Flag** : Critical study for SIDS endpoint

24.03.2006

(53)

**Solubility in** : Water  
**Value** : 17.8 g/l at 25 °C  
**pH value** :  
**concentration** : at °C  
**Temperature effects** :  
**Examine different** :  
**pol.**  
**pKa** : at 25 °C  
**Description** :  
**Stable** :  
**Deg. product** :  
**Method** :  
**Year** : 1997

**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Reliability** : (2) valid with restrictions  
 2f. Accepted calculation method.  
 11.01.2006 (57)

**Solubility in** : Water  
**Value** : 2.8 g/l at 25 °C  
**pH value** :  
**concentration** : at °C  
**Temperature effects** :  
**Examine different** :  
**pol.**  
**pKa** : at 25 °C  
**Description** :  
**Stable** :  
**Deg. product** :  
**Method** :  
**Year** : 1998  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Reliability** : (4) not assignable  
 4b. Secondary literature.  
 09.01.2006 (25)

**Solubility in** : Water  
**Value** : 3,200 mg/l at 20 °C  
**pH value** :  
**concentration** : at °C  
**Temperature effects** :  
**Examine different** :  
**pol.**  
**pKa** : at 25 °C  
**Description** :  
**Stable** :  
**Deg. product** :  
**Method** : other: experimental  
**Year** : 1982  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
  
**Test substance** : HFC-152a, purity not reported  
**Reliability** : (4) not assignable  
 4b. Secondary literature.  
 30.03.2006 (40)

## 2.6.2 SURFACE TENSION

**2.7 FLASH POINT**

**Value** : < -50 °C  
**Type** : open cup  
**Method** :  
**Year** : 1998  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Reliability** : (4) not assignable  
4b. Secondary literature.

09.01.2006

(25)

**2.8 AUTO FLAMMABILITY****2.9 FLAMMABILITY**

**Result** : other: 3.7 % - 18 % (in air)  
**Method** :  
**Year** : 1987  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Reliability** : (2) valid with restrictions  
2g. Data from handbook or collection of data.

14.06.2005

(58)

**Result** : other: 3.9 % - 16.9 % (in air)  
**Method** :  
**Year** : 1998  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Reliability** : (4) not assignable  
4b. Secondary literature.

09.01.2006

(25)

**2.10 EXPLOSIVE PROPERTIES****2.11 OXIDIZING PROPERTIES****2.12 DISSOCIATION CONSTANT****2.13 VISCOSITY****2.14 ADDITIONAL REMARKS**

**3.1.1 PHOTODEGRADATION**

<b>Type</b>	: other: modeled
<b>Light source</b>	:
<b>Light spectrum</b>	: nm
<b>Relative intensity</b>	: based on intensity of sunlight
<b>Deg. product</b>	:
<b>Method</b>	: other (calculated)
<b>Year</b>	:
<b>GLP</b>	:
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Method</b>	: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere (Bidleman TF (1988). Atmospheric processes. Environ. Sci. Technol., 22:361 - 367 (HSDB/5205), 1,1-difluoroethane is expected to exist solely as a vapor in the ambient atmosphere.
<b>Result</b>	: The rate constant of $3.4E+14$ cm <sup>3</sup> /molecule-sec corresponds to an atmospheric half-life of about 472 days at an atmospheric concentration of $5E+5$ hydroxyl radicals per cm <sup>3</sup> Atkinson R (1989). J. Phys. and Chem. Reference Data (HSDB/5205).
	<p>The long atmospheric lifetime of this chemical suggests some 1,1-difluoroethane is expected to gradually diffuse into the stratosphere above the ozone layer where it will slowly degrade due to direct photolysis from UV-radiation (Nimitz JS and Skaggs SR (1992). Estimating tropospheric lifetimes and ozone-depletion potentials of one- and two-carbon hydrofluorocarbons and hydrochlorofluorocarbons. Environ. Sci. Technol., 26:739 - 44 (HSDB/5205); SRC (Syracuse Research Corporation) (n.d.). (HSDB/5205).</p>
	<p>1,1-Difluoroethane is not expected to undergo hydrolysis or direct photolysis in the troposphere due to the lack of functional groups to hydrolyze or absorb UV light at environmentally significant wavelengths (SRC (Syracuse Research Corporation) (n.d.). (HSDB/5205).</p>
<b>Reliability</b>	: (2) valid with restrictions 2g. Data from handbook or collection of data.
<b>Flag</b>	: Critical study for SIDS endpoint
04.04.2006	(41)
<b>Deg. product</b>	:
<b>Method</b>	: other (calculated)
<b>Year</b>	: 1997
<b>GLP</b>	:
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Remark</b>	: Using the AER (Atmospheric and Environmental Research) model, the lifetime global warming potential value for HFC-152a was calculated to be 1.5 years.

**Reliability** : (2) valid with restrictions  
2f. Accepted calculation method.  
11.01.2006 (45)

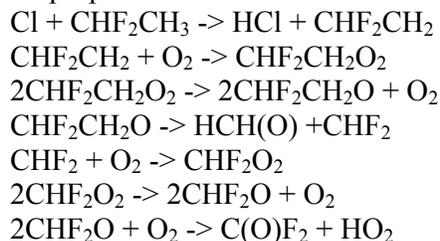
**Type** : air  
**Light source** :  
**Light spectrum** : nm  
**Relative intensity** : based on intensity of sunlight  
**Deg. product** :  
**Method** :  
**Year** : 1992  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**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 HFC-152a with Cl<sub>2</sub> for 20 minutes gave C(O)F<sub>2</sub> as product, with a yield of 100 %.

The proposed mechanism was:



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

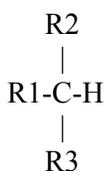
**Flag** : Critical study for SIDS endpoint  
31.03.2006 (36)

**Deg. product** :  
**Method** : other (calculated): AOPWIN v1.91  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** : Overall OH Rate Constant = 0.0348E-12 cm<sup>3</sup>/molecule-sec

Half-life = 307.163 days (12-hour day; 1.56E+6 OH/cm<sup>3</sup>).  
**Reliability** : (2) valid with restrictions  
2f. Accepted calculation method.  
23.03.2006 (37)

**3.1.2 STABILITY IN WATER**

**Deg. product** :  
**Method** : other (calculated): HYDROWIN v1.67  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** :



X: -F (leaving halogen in R1)

R1: -CH-F2

R2: -H

R3: -H

Kb hydrolysis at atom #4: 1.157E-13 L/mol-sec

Total Kb for pH > 8 at 25 °C: 1.157E-13 L/mol-sec

Kb half-Life at pH 8: 1.898E+11 years

Kb Half-Life at pH 7: 1.898E+12 years

The rate constant estimated for the Alkyl Halide DOES NOT include the neutral hydrolysis rate constant! For some alkyl halides, the neutral rate constant is the dominant hydrolysis rate at environmental pHs. If the neutral rate constant is important, the HYDRO estimated rate will under estimate the actual rate.

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

08.03.2006

(37)

**3.1.3 STABILITY IN SOIL****3.2.1 MONITORING DATA****3.2.2 FIELD STUDIES****3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS**

**Type** : fugacity model level III

<b>Media</b>	: other: air-water-soil-sediment
<b>Air</b>	: % (Fugacity Model Level I)
<b>Water</b>	: % (Fugacity Model Level I)
<b>Soil</b>	: % (Fugacity Model Level I)
<b>Biota</b>	: % (Fugacity Model Level II/III)
<b>Soil</b>	: % (Fugacity Model Level II/III)
<b>Method</b>	: other: Mackay, Level III Fugacity Model
<b>Year</b>	:
<b>Method</b>	: Calculated according to Mackay, Level III, Syracuse Research Corporation Epiwin Version 3.05 Emissions to Air (1,000 kg/hr) EPA Model Defaults.

## Data Used:

Molecular Weight: 66.05

Henry's Law Constant: 0.0203 atm-m<sup>3</sup>/mole (Henry database)

Vapor Pressure: 4,550 mmHg at 25 °C (user entered)

Log Kow: 0.75 (Jow and Hansch, n.d.)

Soil Koc: 2.31 (calculated by model)

<b>Result</b>	: Distributions:
	Air 99.9 %
	Water 0.111 %
	Soil 0.0113 %
	Sediment 0.000214 %

<b>Reliability</b>	: (2) valid with restrictions
	2f. Accepted calculation method.

30.03.2006

(43) (49) (50) (51)

<b>Type</b>	:
<b>Media</b>	:
<b>Air</b>	: % (Fugacity Model Level I)
<b>Water</b>	: % (Fugacity Model Level I)
<b>Soil</b>	: % (Fugacity Model Level I)
<b>Biota</b>	: % (Fugacity Model Level II/III)
<b>Soil</b>	: % (Fugacity Model Level II/III)
<b>Method</b>	: other: modeled
<b>Year</b>	:

<b>Result</b>	: Estimated half-lives for a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) and model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) are 2 and 77 hours, respectively (Lyman et al., 1990; SRC, n.d.). Based on a recommended classification scheme (Swann et al., 1983), an estimated Koc value of 60 (SRC, n.d.), determined from a measured log Kow of 0.75 (Jow and Hansch, n.d.) and a recommended regression-derived equation (Lyman et al., 1990), 1,1-difluoroethane is not expected to adsorb to suspended solids and sediment in water (SRC, n.d.). 1,1-Difluoroethane is expected to volatilize rapidly from water surfaces (Lyman et al., 1990; SRC, n.d.) based on an estimated Henry's Law constant of 0.02 atm-m <sup>3</sup> /mole (Daubert and Danner, 1989); Ruelle and Kesselring, 1997; SRC, n.d.).
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## References for modeling:

Lyman WJ, Reehl WF, and Rosenblatt DH (1990). Handbook of Chemical Property Estimation Methods, pp. 4 - 9, 5 - 4, 5 - 10, 15 - 1 to 15 - 29, Amer. Chem. Soc., Washington, DC (HSDB/5205)

SRC (Syracuse Research Corporation) (n.d.). (HSDB/5205).

Swann RL, Laskowski DA, McCall PJ, Vander Kuy K, and Dishburger HJ (1983). A rapid method for the estimation of the environmental parameters octanol/water partition coefficient, soil sorption constant, water to air ratio, and water solubility. Res. Rev., 85:23 (HSDB/5205).

Jow P and Hansch C (n.d.). Pomona College, unpublished analysis (cited in Hansch C and Leo A (1995). Exploring QSAR Fundamentals and Applications in Chemistry and Biology, Amer. Chem. Soc., Washington, DC (HSDB/5205).

Daubert TE and Danner RP (1989). Physical and Thermodynamic Properties of Pure Chemicals Data Compilation, Amer. Inst. Chem. Eng., Hemisphere Pub. Corp., New York (HSDB/5205).

Ruelle P and Kesselring UW (1997). Aqueous solubility prediction of environmentally important chemicals from the mobile order thermodynamics. Chemosphere, 34:275 - 298 (also cited in HSDB/5205).

**Reliability** : (2) valid with restrictions  
2f. Accepted calculation method.  
30.03.2006 (41)

**3.3.2 DISTRIBUTION**

**Method** : Determined from a measured log Kow of 0.75.  
**Remark** : Estimated Koc = 60  
**Reliability** : (2) valid with restrictions  
2f. Accepted calculation method.  
11.01.2006 (60)

**Remark** : Estimated Henry's Law constant = 0.02 atm-m<sup>3</sup>/mole (2026.5 Pa-m<sup>3</sup>/mol), determined from a vapor pressure of 4,550 mmHg and water solubility of 17,800 mg/L.  
**Reliability** : (2) valid with restrictions  
2f. Accepted calculation method.  
04.04.2006 (11) (57) (60)

**Method** : PCKOC v1.66

**Remark** : Estimated Koc = 35  
**Reliability** : (2) valid with restrictions  
 2f. Accepted calculation method.  
 30.03.2006 (37)

### 3.4 MODE OF DEGRADATION IN ACTUAL USE

### 3.5 BIODEGRADATION

**Type** : aerobic  
**Inoculum** : other: filtered sample of secondary effluent from a sewage plant  
**Contact time** :  
**Degradation** : 4 (±) % after 28 day(s)  
**Result** : other: not readily biodegradable  
**Deg. product** :  
**Method** : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"  
**Year** : 1989  
**GLP** : no data  
**Test substance** : other TS  
**Method** : The test was performed in accordance with OECD guideline 301D and EEC guideline C.6. A solution of the test substance in mineral medium was inoculated with a filtered sample of secondary effluent from a sewage plant. The initial test substance concentration was 1.44 mg/L. Bottles were completely filled, closed, and incubated in the dark for a period of 28 days at  $20 \pm 1$  °C. The decrease of the oxygen content in the medium over a period of 28 days was used to calculate the percentage of aerobic biodegradation. To correct for the endogenous oxygen consumption of the inoculum, blanks with secondary effluent but without test substance were included in the test.

The biodegradation was also based on the gas chromatographic analysis of the test substance in the solutions at the end of the study. Measured concentrations in bottles with mineral medium and test substance were compared with concentrations in bottles with mineral medium, test substance, and inoculum. The biodegradation was determined using the difference in the measured concentration. To verify the procedures used, the biodegradability of a reference compound (sodium n-dodecylsulfate) was measured.

**Result** : The TOD (based on biomass integral) was 0.7. The measured decrease of oxygen content was 0.03 mg/L.  
**Test substance** : other TS: HFC-134a (1,1,1,2-tetrafluoroethane), purity not specified  
**Reliability** : (1) valid without restriction  
 1a. GLP guideline study.  
 30.03.2006 (63)

<b>Type</b>	: aerobic
<b>Inoculum</b>	: other: filtered sample of secondary effluent from a sewage plant
<b>Contact time</b>	:
<b>Degradation</b>	: 8 (±) % after 28 day(s)
<b>Result</b>	: other: not readily biodegradable
<b>Deg. product</b>	:
<b>Method</b>	: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
<b>Year</b>	: 1992
<b>GLP</b>	: no data
<b>Test substance</b>	: other TS
<b>Method</b>	: The test was performed in accordance with OECD guideline 301D and EEC guideline C.6. A solution of the test substance in mineral medium was inoculated with a filtered sample of secondary effluent from a sewage plant. The initial test substance concentration was 3.38 mg/L. Bottles were completely filled, closed, and incubated in the dark for a period of 28 days at 20 ± 1 °C. The decrease of the oxygen content in the medium over a period of 28 days was used to calculate the percentage of aerobic biodegradation. To correct for the endogenous oxygen consumption of the inoculum, blanks with secondary effluent but without test substance were included in the test.
	<p>The biodegradation was also based on the gas chromatographic analysis of the test substance in the solutions at the end of the study. Measured concentrations in bottles with mineral medium and test substance were compared with concentrations in bottles with mineral medium, test substance, and inoculum. The biodegradation was determined using the difference in the measured concentration. To verify the procedures used, the biodegradability of a reference compound (sodium n-dodecylsulfate) was measured.</p>
<b>Result</b>	: The TOD (based on biomass integral) was 2.1. The measured decrease of oxygen content was 0.16 mg/L.
<b>Test substance</b>	: other TS: HFC-32 (difluoromethane), purity not specified
<b>Reliability</b>	: (1) valid without restriction 1a. GLP guideline study.
30.03.2006	(64)

### 3.6 BOD5, COD OR BOD5/COD RATIO

### 3.7 BIOACCUMULATION

<b>BCF</b>	: 2
<b>Elimination</b>	:
<b>Method</b>	: other: Modeled
<b>Year</b>	:
<b>GLP</b>	:

- Test substance** : as prescribed by 1.1 - 1.4
- Method** : BCF was determined using a measured log Kow of 0.75 (Jow P and Hansch C (n.d.). Pomona College, unpublished analysis (cited in Hansch C and Leo A (1995). Exploring QSAR Fundamentals and Applications in Chemistry and Biology, Amer. Chem. Soc., Washington, DC)) and a recommended regression-derived equation (Lyman WJ, Reehl WF, and Rosenblatt DH (1990). Handbook of Chemical Property Estimation Methods, pp. 4 - 9, 5 - 4, 5 - 10, 15 - 1 to 15 - 29, Amer. Chem. Soc., Washington, DC (HSDB/5205)).
- Result** : According to a classification scheme (Franke C, Studinger G, Berger G, Böhling S, Bruckmann U, Cohors-Fresenborg U, and Jöhncke U (1994). The assessment of bioaccumulation. Chemosphere, 29:1501-1514 (HSDB/5205)), the estimated BCF value of 2 suggests that bioconcentration in aquatic organisms is low SRC (Syracuse Research Corporation) (n.d.). (HSDB/5205).
- Reliability** : (2) valid with restrictions  
2f. Accepted calculation method.

09.01.2006

(41)

### 3.8 ADDITIONAL REMARKS

#### 4.1 ACUTE/PROLONGED TOXICITY TO FISH

**Type** : other: Modeled  
**Species** : other: Fish  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC<sub>50</sub>** : 733  
**Method** : other: calculated ECOSAR v0.99h  
**Year** :  
**GLP** :  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : log<sub>10</sub> Kow of 0.75  
**Reliability** : (2) valid with restrictions  
 2f. Accepted calculation method.  
**Flag** : Critical study for SIDS endpoint  
 09.01.2006

(35)

**Type** : semistatic  
**Species** : Oncorhynchus mykiss (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC<sub>50</sub>** : 450  
**Limit test** :  
**Analytical monitoring** : yes  
**Method** : Directive 84/449/EEC, C.1 "Acute toxicity for fish"  
**Year** : 1991  
**GLP** : yes  
**Test substance** : other TS  
**Method** : To prevent loss of the substance from the solutions, closed vessels were used. The test was conducted under semistatic conditions with daily renewal of the test solutions. Chemical analyses of the test solutions were performed to check the exposure of the organisms to the test chemical. If the difference between nominal and mean measured concentrations was more than 20 %, the endpoint of the test was based on mean measured concentrations.

Saturated solutions were prepared. HFC-134a was bubbled for 60 minutes through medium via a sintered glass diffuser. This solution was diluted with oxygen saturated solutions to restore the amount of oxygen in the test solutions.

The EC<sub>50</sub> value was determined using the method of Stephan, 1977 (Stephan, C. E. (1977). Methods for calculating an LC<sub>50</sub>. Proceedings first annual symposium on aquatic toxicology. In: Mayer, F. L. and J. L. Hamelink (eds). Aquatic toxicology and hazard evaluation, ASTM STP 634:65-84).

**Remark** : Data provided on analog chemical (similar non-chlorinated fluorocarbon) to strengthen the use of ECOSAR to characterize the toxicity of HFC-152a.

<b>Result</b>	: No mortality was found after 96 hours of exposure at mean measured concentrations of 180 and 300 mg/L, but symptoms of toxicity were observed at these concentrations (dark discoloration, quiescence, and sounding behavior). No symptoms of toxicity occurred at a mean measured concentration of 87 mg/L.
<b>Test substance</b>	: other TS: HFC-134a (1,1,1,2-tetrafluoroethane), purity not specified
<b>Reliability</b>	: (2) valid with restrictions 2a. Guideline study without detailed documentation.
<b>Flag</b>	: Critical study for SIDS endpoint
04.04.2006	(62)

#### 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

<b>Type</b>	: other: Modeled
<b>Species</b>	: other: Daphnid
<b>Exposure period</b>	: 48 hour(s)
<b>Unit</b>	: mg/l
<b>EC<sub>50</sub></b>	: 720
<b>Method</b>	: other: calculated ECOSAR v0.99h
<b>Year</b>	:
<b>GLP</b>	:
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Remark</b>	: log <sub>10</sub> Kow of 0.75
<b>Reliability</b>	: (2) valid with restrictions 2f. Accepted calculation method.
<b>Flag</b>	: Critical study for SIDS endpoint
23.03.2006	(35)

<b>Type</b>	: static
<b>Species</b>	: Daphnia magna (Crustacea)
<b>Exposure period</b>	: 48 hour(s)
<b>Unit</b>	: mg/l
<b>EC<sub>50</sub></b>	: 980
<b>Analytical monitoring</b>	: yes
<b>Method</b>	: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
<b>Year</b>	: 1991
<b>GLP</b>	: yes
<b>Test substance</b>	: other TS
<b>Method</b>	: To prevent loss of the substance from the solutions, closed vessels were used. The test was conducted under static conditions. Chemical analyses of the test solutions were performed to check the exposure of the organisms to the test chemical. If the difference between nominal and mean measured concentrations was more than 20 %, the endpoint of the test was based on mean measured concentrations.

Saturated solutions were prepared. HFC-134a was bubbled for 60 minutes through medium via a sintered glass diffuser. This solution was diluted with oxygen saturated solutions to restore the amount of

oxygen in the test solutions.

The EC<sub>50</sub> value was determined using the method of Stephan, 1977 (Stephan, C. E. (1977). Methods for calculating an LC<sub>50</sub>. Proceedings first annual symposium on aquatic toxicology. In: Mayer, F. L. and J. L. Hamelink (eds). Aquatic toxicology and hazard evaluation, ASTM STP 634:65 - 84).

<b>Remark</b>	: Data provided on analog chemical (similar non-chlorinated fluorocarbon) to strengthen the use of ECOSAR to characterize the toxicity of HFC-152a.
<b>Result</b>	: The acute test with <i>Daphnia magna</i> showed a steep concentration-immobility curve. At mean measured concentrations of 870 and 1,100 mg/L the immobility after 48 hours was 0 and 100 %, respectively.
<b>Test substance</b>	: other TS: HFC-134a (1,1,1,2-tetrafluoroethane), purity not specified
<b>Reliability</b>	: (2) valid with restrictions 2a. Guideline study without detailed documentation.
<b>Flag</b>	: Critical study for SIDS endpoint
04.04.2006	(61)

#### 4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

<b>Species</b>	: other algae
<b>Endpoint</b>	: other: Modeled: Inhibition of growth measured as number of cells
<b>Exposure period</b>	: 96 hour(s)
<b>Unit</b>	: mg/l
<b>EC<sub>50</sub></b>	: 419
<b>Method</b>	: other: calculated ECOSAR v0.99h
<b>Year</b>	:
<b>GLP</b>	:
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Remark</b>	: log <sub>10</sub> Kow of 0.75
<b>Reliability</b>	: (2) valid with restrictions 2f. Accepted calculation method.
<b>Flag</b>	: Critical study for SIDS endpoint
09.01.2006	(35)

#### 4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

##### 4.5.1 CHRONIC TOXICITY TO FISH

##### 4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

**4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS****4.6.2 TOXICITY TO TERRESTRIAL PLANTS****4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS****4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES****4.7 BIOLOGICAL EFFECTS MONITORING****4.8 BIOTRANSFORMATION AND KINETICS****4.9 ADDITIONAL REMARKS**

## 5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

### 5.1.1 ACUTE ORAL TOXICITY

<b>Type</b>	: other: Approximate Lethal Dose (ALD)
<b>Value</b>	: > 1,500 mg/kg bw
<b>Species</b>	: rat
<b>Strain</b>	: other: CrI:CD(R)BR
<b>Sex</b>	: male
<b>Number of animals</b>	: 6
<b>Vehicle</b>	: other: corn oil
<b>Doses</b>	: 200, 300, 450, 670, 1,000, 1,500 mg/kg
<b>Method</b>	: other
<b>Year</b>	: 1990
<b>GLP</b>	: yes
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Method</b>	: Food and water were available to the rats ad libitum. Rats were approximately 7 weeks old upon arrival. HFC-152a was dissolved in corn oil (23 or 46 mg/mL) and kept under pressure in aerosol cans that were maintained in an ice bath. The cans were fitted with a septum from which the dosing solution was withdrawn. One rat per dose group was administered the compound by gavage. Dose levels were 200, 300, 450, 670, 1,000, or 1,500 mg/kg. Doses of 450 mg/kg and above were administered in 2 portions about 15 minutes apart. A dose of 1,500 mg/kg was the maximum feasible dose. Rats were observed for mortality, clinical signs, and body weight over a 14-day period.
<b>Result</b>	: No mortality occurred at any dose level. Immediately after dosing, abdominal distention related to gas evolution was evident in all rats. Lethargy was observed at 1,000 and 1,500 mg/kg. High carriage, wet and yellow stained perineum, and diarrhea were observed in all rats 1 to 2 days post-dosing. No other toxicologically significant effects occurred.
<b>Test substance</b>	: HFC-152a, purity 99.9 %
<b>Reliability</b>	: (3) invalid 3c. Unsuitable test system.
09.01.2006	(23)

### 5.1.2 ACUTE INHALATION TOXICITY

<b>Type</b>	: other: Approximate Lethal Concentration (ALC)
<b>Value</b>	: 383,000 ppm
<b>Species</b>	: rat
<b>Strain</b>	: other: ChR-CD(R)
<b>Sex</b>	: male
<b>Number of animals</b>	: 30
<b>Vehicle</b>	:

<b>Doses</b>	: 66,400, 175,200, 319,000, 383,000, 437,500 ppm
<b>Exposure time</b>	: 4 hour(s)
<b>Method</b>	: other
<b>Year</b>	: 1975
<b>GLP</b>	: no
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Method</b>	: Groups of 6 rats were exposed whole-body to 66,400, 175,200, 319,000, 383,000, and 437,500 ppm. The age of the rats was not specified, however, the initial body weight of the rats was 240 - 297 grams. The gas was regulated through a calibrated flowmeter into a mixing chamber. Regulated flows of air and/or oxygen were used as the carrier gas from the mixing chamber to the exposure chamber. At the 66,400 ppm level, air was used as the carrier gas. At 175,200 ppm, chamber concentrations were 16 – 17 %. Oxygen level was maintained at about 20 % for the exposure concentrations at or above 319,000 ppm. Chamber atmospheres were sampled at 30-minute intervals and analyzed by thermal conductivity gas chromatography. Clinical observations were recorded during the exposure and post-exposure. Gross pathology was performed on surviving rats after a 14-day observation period.
<b>Remark</b>	: Reliability: High because a scientifically defensible or guideline method was used.
<b>Result</b>	: Mortality ratio of 1/6 occurred at 383,000 ppm and 2/6 occurred at 437,500 ppm. Labored breathing, lethargy, and unresponsiveness to sound were observed during exposure. No clinical signs were noted following exposure. No compound-related gross pathology changes were observed.
<b>Test substance</b>	: HFC-152a, purity 99.9 %
<b>Reliability</b>	: (1) valid without restriction 1d. Test procedure in accordance with generally accepted scientific standards and described in sufficient detail.
<b>Flag</b>	: Critical study for SIDS endpoint
09.01.2006	(18)
<b>Type</b>	: other: Cardiac Sensitization
<b>Value</b>	: 150,000 ppm
<b>Species</b>	: dog
<b>Strain</b>	: Beagle
<b>Sex</b>	: male
<b>Number of animals</b>	: 24
<b>Vehicle</b>	:
<b>Doses</b>	: 50,000, 150,000 ppm
<b>Exposure time</b>	: 5 minute(s)
<b>Method</b>	: other
<b>Year</b>	: 1969
<b>GLP</b>	: no
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Method</b>	: Beagle dogs (12/group) were exposed to 50,000 or 150,000 ppm for 5 minutes. The age of the dogs was not specified. The dogs received a control injection of epinephrine (0.008 mg/kg) intravenously, prior to

exposure and a challenge injection (same dosage) after breathing the test material for 5 minutes. The desired concentrations (calculated) were achieved by delivering a metered volume of the vapor or gas from the pressured cylinder containing the test substance and diluting it with a known volume of air. The flow meter used for monitoring the test compound had been previously calibrated with the compound by a dry gas test meter.

The dogs were trained to maintain a standing position while lightly supported by a cloth sling with a hole for each leg, to wear a mask over their snout, and to accept a venupuncture. An electrocardiogram was recorded continuously during the experimental procedure.

**Result** : Marked responses (a cardiac arrhythmia which was considered to pose a serious threat to life) were observed in 3 of the 12 dogs at the 150,000 ppm level. No response was seen at the 50,000 ppm level.

**Test substance** : HFC-152a, purity 99.99 %

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

**Flag** : Critical study for SIDS endpoint

24.03.2006

(17) (56)

**Type** : other

**Value** :

**Species** : rat

**Strain** : other: albino

**Sex** : no data

**Number of animals** :

**Vehicle** :

**Doses** : ranged from 100,000 to 550,000 ppm

**Exposure time** : 30 minute(s)

**Method** : other

**Year** : 1950

**GLP** : no

**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Rats were exposed for a maximum of 30 minutes to concentrations ranging from 100,000 to 550,000 ppm.

**Result** : The postural reflex was lost at 200,000 ppm, righting reflex was lost at 250,000 ppm, and the corneal reflex was lost at 450,000 ppm. Exposure to concentrations > 500,000 ppm was lethal in 10 - 25 minutes. At concentrations of 400,000 ppm or higher, there was considerable effusion of fluid from the respiratory tract, indicative of acute irritation of the lungs.

**Test substance** : HFC-152a, purity not reported

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

04.04.2006

(46)

**Type** : other

**Value** :  
**Species** : rat  
**Strain** : no data  
**Sex** : no data  
**Number of animals** : 2  
**Vehicle** :  
**Doses** : 74,000, 100,000, or 200,000 ppm  
**Exposure time** : 2 hour(s)  
**Method** : other  
**Year** : 1952  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** : Occasional trembling and incoordination were observed during the exposure. No gross or pathological changes were found in the rats 4 – 7 days post-exposure.  
**Test substance** : HFC-152, purity not specified  
**Reliability** : (2) valid with restrictions  
 2e. Study well documented, meets generally accepted scientific principles, acceptable for assessment.

11.01.2006 (15)

**Type** : other: Approximate Lethal Concentration (ALC) (Lethality in 2 - 4 of 6 rats)  
**Value** : 64,000 ppm  
**Species** : rat  
**Strain** : Sherman  
**Sex** : male/female  
**Number of animals** : 6  
**Vehicle** :  
**Doses** :  
**Exposure time** : 4 hour(s)  
**Method** : other  
**Year** : 1949  
**GLP** : no  
**Test substance** : as prescribed by 1.1 – 1.4  
**Result** : Inhalation of 64,000 ppm HFC-152a for 4 hours killed 2/6, 3/6, or 4/6 rats.  
**Test substance** : HFC-152a, purity not reported  
**Reliability** : (2) valid with restrictions  
 3a. Documentation insufficient for assessment.

04.04.2006 (9)

**Type** : LC<sub>50</sub>  
**Value** : 977,200 ppm  
**Species** : mouse  
**Strain** : no data  
**Sex** : no data  
**Number of animals** :  
**Vehicle** :  
**Doses** :

**Exposure time** : 2 hour(s)  
**Method** : other  
**Year** : 1982  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** : The LC<sub>50</sub> was 977,200 ppm (896,000 - 1,065,000 ppm). Narcotic effects were observed at the LC<sub>50</sub>.  
**Test substance** : HFC-152a, purity not reported  
**Reliability** : (4) not assignable  
 4b. Secondary literature.

24.03.2006

(42)

**Type** : other  
**Value** :  
**Species** : dog  
**Strain** : no data  
**Sex** : no data  
**Number of animals** : 3  
**Vehicle** :  
**Doses** : 500,000 ppm  
**Exposure time** :  
**Method** : other  
**Year** : 1960  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Method** : Three dogs inhaled HFC-152a at a concentration of 500,000 ppm. Two dogs also received atropine and succinylcholine intravenously.  
**Result** : Light surgical anesthesia, with no change in EKG, resulted.  
**Test substance** : HFC-152a, purity not reported  
**Reliability** : (2) valid with restrictions  
 2e. Study well documented, meets generally accepted scientific principles, acceptable for assessment.

11.01.2006

(65)

**Type** : other  
**Value** :  
**Species** : human  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Doses** : 50,000 ppm  
**Exposure time** :  
**Method** : other  
**Year** : 1960  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** : HFC-152a was inhaled briefly by several volunteers, who noted good analgesia and impending loss of consciousness.  
**Test substance** : HFC-152a, purity not reported

<b>Reliability</b>	: (3) invalid 3a. Documentation insufficient for assessment.	
11.01.2006		(65)
<b>Type</b>	: other: Acute Inhalation Toxicity of Pyrolysis Products	
<b>Value</b>	:	
<b>Species</b>	: rat	
<b>Strain</b>	: other: CHR-CD	
<b>Sex</b>	: male	
<b>Number of animals</b>	:	
<b>Vehicle</b>	:	
<b>Doses</b>	: various temperatures (1,100, 1,200, and 1,300 °C)	
<b>Exposure time</b>	: 15 minute(s)	
<b>Method</b>	:	
<b>Year</b>	: 1966	
<b>GLP</b>	: no	
<b>Test substance</b>	: as prescribed by 1.1 - 1.4	
<b>Method</b>	: Rats were exposed for 15 minutes to vapors produced by heating HFC-152a to various temperatures (1,100, 1,200, and 1,300 °C).	
<b>Result</b>	: No mortality was observed in the study. Clinical signs observed at all three temperatures included ptosis, apnea, pale ears followed by hyperemia, marked dyspnea followed by rapid irregular respiration, lacrimation, chromodacryorrhea, salivation, and moderate responsiveness. Rats exposed at 1,300 °C also exhibited gasping and mild convulsions.	
<b>Test substance</b>	: HFC-152a, purity not reported	
<b>Reliability</b>	: (2) valid with restrictions 2e. Study well documented, meets generally accepted scientific principles, acceptable for assessment.	
11.01.2006		(16)
<b>Type</b>	: other: Cardiac Sensitization	
<b>Value</b>	:	
<b>Species</b>	: rat	
<b>Strain</b>	: Wistar	
<b>Sex</b>	: female	
<b>Number of animals</b>	: 50	
<b>Vehicle</b>	:	
<b>Doses</b>	: 25,000, 50,000, 100,000, 200,000, 400,000 ppm	
<b>Exposure time</b>	:	
<b>Method</b>	: other	
<b>Year</b>	: 1975	
<b>GLP</b>	: no data	
<b>Test substance</b>	: as prescribed by 1.1 - 1.4	
<b>Method</b>	: Female rats were anesthetized.	
<b>Result</b>	: Administration of 100,000 ppm HFC-152a caused slowing of the heart rate whereas 50,000 ppm provoked abnormalities of the electrocardiographic patterns (prolongation of the P-R interval, elevation of the S-T segment, and widening of the T-wave).	
<b>Test substance</b>	: HFC-152a, purity not reported	

**Reliability** : (3) invalid  
3b. Significant methodological deficiencies.  
24.03.2006 (13)

**Type** : other: Cardiac Sensitization  
**Value** :  
**Species** : mouse  
**Strain** : Swiss  
**Sex** : male  
**Number of animals** :  
**Vehicle** :  
**Doses** : 200,000, 400,000 ppm  
**Exposure time** : 6 minute(s)  
**Method** : other  
**Year** : 1974  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Method** : Exposure was to anesthetized mice  
**Result** : Exposure did not sensitize the heart to epinephrine. No cardiac arrhythmias were observed.  
**Test substance** : HFC-152a, purity not reported  
**Reliability** : (3) invalid  
3b. Significant methodological deficiencies.  
11.01.2006 (3)

**Type** : other: Cardiac Sensitization  
**Value** :  
**Species** : mouse  
**Strain** : Swiss  
**Sex** : male  
**Number of animals** :  
**Vehicle** :  
**Doses** : up to 400,000 ppm  
**Exposure time** : 4 minute(s)  
**Method** : other  
**Year** : 1974  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Method** : Male mice were anesthetized.  
**Result** : Mice exhibited reduction in respiratory rate, tidal volume, respiratory minute volume, decreased pulmonary compliance, and increased pulmonary resistance. HFC-152a did not produce arrhythmias nor did it sensitize the heart to epinephrine. Inhalation of HFC-152a caused sensitization of the heart to epinephrine in mice that had experimentally induced bronchopulmonary lesions following intratracheal injection of papain.  
**Test substance** : HFC-152a, purity not reported  
**Reliability** : (3) invalid  
3b. Significant methodological deficiencies.  
11.01.2006 (8)

**Type** : other: Cardiotoxicity  
**Value** :  
**Species** : rat  
**Strain** : Wistar  
**Sex** : male  
**Number of animals** :  
**Vehicle** :  
**Doses** : 2.5, 5, 10, 20, 40 %  
**Exposure time** :  
**Method** : other  
**Year** : 1975  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 – 1.4  
**Result** : There were no observations relating to the effect of HFC-152a on the respiratory system. In anesthetized rat, abnormalities in the electrocardiogram were produced at 40 % HFC-152a.  
**Test substance** : HFC-152a, purity not specified  
**Reliability** : (3) invalid  
 3b. Significant methodological deficiencies.  
 24.03.2006 (66)

**Type** : other: Cardiotoxicity  
**Value** :  
**Species** : dog  
**Strain** : other: Mongrel  
**Sex** : male/female  
**Number of animals** : 13  
**Vehicle** :  
**Doses** : 20 %  
**Exposure time** : 5 minute(s)  
**Method** : other  
**Year** : 1975  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Method** : Hemodynamic effects of fluorocarbon propellants on the systemic and pulmonary components of the cardiovascular system were studied, with special attention to effects on cardiac output as reflected by mean pulmonary arterial flow, total systemic vascular resistance, and pulmonary vascular resistance.  
**Result** : HFC-152a administered at a maximal concentration of 20 %, except for a decrease in mean pulmonary arterial flow of 7 %, was without effect on the studied parameters.  
**Test substance** : HFC-152a, purity not specified  
**Reliability** : (2) valid with restrictions  
 2e. Study well documented, meets generally accepted scientific principles, acceptable for assessment.  
 24.03.2006 (59)

**Type** : other: Cardiotoxicity

**Value** :  
**Species** : dog  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Doses** : 2.5, 5, 10, 20 %  
**Exposure time** :  
**Method** : other  
**Year** : 1975  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 – 1.4  
**Result** : HFC-152a administered in 10 or 20 % concentration caused depression of the force of contraction and a displacement of the ventricular function curve.  
**Test substance** : HFC-152a, purity not specified  
**Reliability** : (2) valid with restrictions  
 2e. Study well documented, meets generally accepted scientific principles, acceptable for assessment.  
 24.03.2006 (4)

**Type** : other: Cardiotoxicity  
**Value** :  
**Species** : dog  
**Strain** : other: Mogrel  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Doses** : up to 20 %  
**Exposure time** : 5 minute(s)  
**Method** : other  
**Year** : 1975  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** : HFC-152a did not influence the cardiovascular system when inhaled at a concentration of 20 %. However, at a concentration of 10 %, there was a stimulation of respiration and an increase in pulmonary resistance.  
**Test substance** : HFC-152a, purity not specified  
**Reliability** : (3) invalid  
 3b. Significant methodological deficiencies.  
 24.03.2006 (6)

**Type** : other: Cardiotoxicity  
**Value** :  
**Species** : monkey  
**Strain** : other: Macaca mulatta  
**Sex** :  
**Number of animals** : 30  
**Vehicle** :

**Doses** : 2.5, 5, 10, 20 %  
**Exposure time** : 5 minute(s)  
**Method** : other  
**Year** : 1974  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** : HFC-152a did not influence cardiac rhythm, heart rate, contractility, aortic blood pressure, left atrial pressure, or pulmonary arterial pressure. In concentrations as high as 20 %, HFC-152a can be regarded as inactive in the cardiovascular system.  
**Test substance** : HFC-152a, purity not specified  
**Reliability** : (3) invalid  
 3b. Significant methodological deficiencies.  
 24.03.2006 (7)

**Type** : other: Cardiotoxicity  
**Value** :  
**Species** : monkey  
**Strain** : other: Rhesus  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Doses** : up to 20 %  
**Exposure time** :  
**Method** : other  
**Year** : 1975  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** : HFC-152a did not influence respiration or circulation, even when inhaled in levels up to 20 % concentration.  
**Test substance** : HFC-152a, purity not specified  
**Reliability** : (3) invalid  
 3b. Significant methodological deficiencies.  
 24.03.2006 (5)

### 5.1.3 ACUTE DERMAL TOXICITY

### 5.1.4 ACUTE TOXICITY, OTHER ROUTES

#### 5.2.1 SKIN IRRITATION

#### 5.2.2 EYE IRRITATION

### 5.3 SENSITIZATION

### 5.4 REPEATED DOSE TOXICITY

<b>Type</b>	: Sub-acute
<b>Species</b>	: rat
<b>Sex</b>	: male
<b>Strain</b>	: other: ChR-CD
<b>Route of admin.</b>	: inhalation
<b>Exposure period</b>	: 2 weeks
<b>Frequency of treatm.</b>	: 6 hours/day, 5 days/week
<b>Post exposure period</b>	: 14-day recovery period
<b>Doses</b>	: 100,000 ppm
<b>Control group</b>	: yes
<b>Method</b>	: other
<b>Year</b>	: 1976
<b>GLP</b>	: no
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Method</b>	: Ten rats/concentration were exposed. Control animals were exposed to house-line air. Five rats/group were sacrificed for gross and histopathologic examination after the last exposure. The remaining rats were sacrificed after a 14-day recovery period. At both sacrifice intervals, hematological, urine analytical, and biochemical indices were also measured in all rats.
<b>Result</b>	: No clinical, hematological, blood chemistry or histopathological evidence of effect was seen. There was a slight increase in urinary fluoride following the last exposure. During the exposure the rats appeared to be anesthetized as indicated by sleeping and unresponsiveness to sound.
<b>Test substance</b>	: HFC-152a, purity 99.9+%
<b>Reliability</b>	: (2) valid with restrictions 2e. Study well documented, meets generally accepted scientific principles, acceptable for assessment.

04.04.2006

(19)

<b>Type</b>	:
<b>Species</b>	: rat
<b>Sex</b>	: no data
<b>Strain</b>	: other: albino
<b>Route of admin.</b>	: inhalation
<b>Exposure period</b>	: 2 months
<b>Frequency of treatm.</b>	: 16 hours/day
<b>Post exposure period</b>	:
<b>Doses</b>	: 100,000 ppm
<b>Control group</b>	:
<b>Method</b>	: other
<b>Year</b>	: 1950
<b>GLP</b>	: no data
<b>Test substance</b>	: as prescribed by 1.1 - 1.4

<b>Method</b>	: Eight rats were exposed to 10 % HFC-152a for 16 hours per day for 2 months. At the conclusion of the repeated exposures, surviving animals were sacrificed and examined for gross pathological changes. Sections of lung and liver were examined microscopically.
<b>Result</b>	: No signs of ill health were apparent at any time. Gross examination at autopsy revealed no changes. Microscopic examination revealed a mild diffuse infiltration of small and large round cells in the lung suggestive of mild chronic irritation.
<b>Test substance</b>	: HFC-152a, purity not reported
<b>Reliability</b>	: (2) valid with restrictions 2e. Study well documented, meets generally accepted scientific principles, acceptable for assessment.
04.04.2006	(46)

### 5.5 GENETIC TOXICITY 'IN VITRO'

<b>Type</b>	: Bacterial reverse mutation assay
<b>System of testing</b>	: Salmonella typhimurium strains TA97a, TA98, TA100, and TA1535 and Escherichia coli strain WP2uvrA (pKM101)
<b>Test concentration</b>	: 0, 20, 30, 40, 50, 75 %
<b>Cytotoxic concentr.</b>	:
<b>Metabolic activation</b>	: with and without
<b>Result</b>	: negative
<b>Method</b>	: OECD Guide-line 471
<b>Year</b>	: 2000
<b>GLP</b>	: yes
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Method</b>	: This study also followed the U.S. EPA Health Effects Test Guideline OPPTS 799.9510 (1989) and Commission Directive 92/69/EEC, EEC Method B.12.

The study consisted of 2 independent trials with and without a metabolic activation system (Aroclor®-induced rat liver S-9). Three replicates were plated for each tester strain, test concentration, and condition. Positive and negative controls were included in all assays. The reaction mixture (S-9 mix) contained glucose 6-phosphate, NADP, NaH<sub>2</sub>PO<sub>4</sub>, KCl, MgCl<sub>2</sub>, distilled water, and S-9. Treatments with activation were conducted by adding 0.5 mL of S-9 mix, and 0.1 mL of an overnight culture to 2 mL of top agar. These components were briefly mixed and poured onto a minimal glucose agar plate. Treatments in the absence of the metabolic activation system were identical to those with activation with the exception that 0.5 mL of sterile buffer was used as a replacement for the S-9.

Plates were exposed to dilutions of the test gas in 6-L glass chambers. The test substance and filtered air flows were regulated using individual rotameters, and mixed prior to entry into the chambers. Chambers were placed into an incubator at 37 °C for approximately 48 hours. Gas chromatographic analysis was used to confirm the

concentration of test atmospheres.

Bacterial background lawns were evaluated for evidence of test substance toxicity and precipitation. Revertant colonies for a given tester strain and condition were counted by an automated colony counter.

Positive control substances tested in this study included 2-nitrofluorene, N-ethyl-N-nitro-N-nitroguanidine, sodium azide, ICR 191 acridine mutagen, 9,10-dimethyl-1,2-benzanthracene, and 2-aminoanthracene.

Filtered house-line air was the test substance diluent and negative control.

A test substance was classified as positive if the mean number of revertants in any strain (except *S. typhimurium* TA1535) at any concentration was at least 2 times greater than the mean number of revertants of the concurrent negative control, and there was a concentration-related increase in the mean number of revertants per plate in that same strain. For *S. typhimurium* TA1535, there must be no test substance concentration with a mean number of revertants that is at least 3 times greater than the mean number of revertants of its concurrent negative control and a concentration-related increase in the mean number of revertants per plate. A test substance was classified as negative if all positive classification criteria for all strains were not met.

Data for each tester strain were evaluated independently. For each tester strain, the mean number of revertants and the standard deviation at each concentration in the presence and absence of the exogenous metabolic system were calculated.

**Result**

- : The actual concentrations for the first trial were 0, 20.4, 33.5, 42.0, 55.5, and 82.7 % in the absence of S-9 and 0, 21.7, 33.4, 43.6, 56.1, and 84.4 % in the presence of S-9. No test substance-related precipitate was observed at any concentration level. Test substance-related toxicity, evidenced by the concentration-dependent reduction in the mean number of revertants per plate, was observed in the first trial in *S. typhimurium* strains TA97a (-S-9) and TA1535 (+S-9), and in the *E. coli* strain (+S-9, -S-9).

The actual concentrations for the second trial were 0, 20.5, 30.9, 41.4, 53.9, and 85.1 % in the absence of S-9 and 0, 20.8, 31.7, 41.9, 55.3, and 81.4 % in the presence of S-9. Test substance-related toxicity, evidenced by the concentration-dependent reduction in the mean number of revertants per plate, was observed in the first second in *S. typhimurium* strains TA97a (-S-9) and TA98 (+S-9, -S-9), and in the *E. coli* strain (+S-9, -S-9).

All acceptability criteria were met in this test. All tester strains

exhibited appropriate phenotypic characteristics. No test substance-related precipitate was observed. The mean number of revertants in the negative control for each strain was within the prescribed acceptable historical control range. Mean positive control values for the tester strains exhibited greater than a 3-fold increase over the means of the respective negative controls in both trials. Differences between targeted and actual doses in both analyses were acceptable for the purposes of this assay and in no way impacted the integrity or validity of this study.

**Test substance** : HFC-152a, purity 99.99 %  
**Reliability** : (1) valid without restriction  
 1a. GLP guideline study.  
**Flag** : Critical study for SIDS endpoint  
 09.01.2006 (28)

**Type** : Chromosomal aberration test  
**System of testing** : Human lymphocytes  
**Test concentration** : Test 1 (3-hour exposure with and without S-9): 0, 35, 50, 70 %  
 Test 2 (3-hour exposure with S-9): 0, 35, 50, 70 %  
 Test 2 (19-hour exposure without S-9): 0, 35, 50, 70 %  
 Test 3 (19-hour exposure without S-9): 0, 50, 60, 70 %  
**Cytotoxic concentr.** :  
**Metabolic activation** : with and without  
**Result** :  
**Method** : OECD Guide-line 473  
**Year** : 2000  
**GLP** : yes  
**Test substance** : as prescribed by 1.1 - 1.4  
**Method** : This study also followed the U.S. EPA Health Effects Test Guidelines OPPTS 870.5375 (1998).

Human lymphocytes, in whole blood culture, were stimulated to divide by addition of phytohaemagglutinin, and duplicate cultures were exposed to the test substance. Treatment atmospheres of the test substance were prepared in sterile glass bottles with septum caps. Negative and positive control cultures were also prepared. Mitomycin C and cyclophosphamide were used as positive control substances. Air was used as the negative control substance.

The test substance was sampled from the cylinder into a gas-sampling bag. Air was withdrawn from each pre-warmed (37 °C) bottle and then an appropriate volume of test substance gas was introduced from the sampling bag, inserted through the septum cap, and the atmosphere was equilibrated at 37 °C. After injection of the lymphocyte culture, air was allowed to enter each bottle through a hollow needle to produce the required concentration at atmospheric pressure. After approximately 48 hours, the cultures in duplicate were injected into the sterile glass bottles. The culture bottles were incubated on their sides at 37 °C in a roller apparatus which rotated the bottles once every 8 minutes.

Test 1 included a 3-hour treatment with and without S-9 mix and 16 hours of recovery. Test 2 included a 3-hour treatment with S-9 mix and 16 hours of recovery, and a 19-hour continuous treatment without S-9.

Following the results of the second test, a third test was performed for a continuous treatment time, in the absence of S-9 only, to demonstrate reproducibility.

Two hours before the end of the incubation period, cell division was arrested using Colcemid(R), the cells harvested and slides prepared, so that metaphase cells could be examined for numerical (polyploidy) and structural chromosomal damage.

In order to assess the toxicity to cultured lymphocytes, the mitotic index was calculated for all cultures treated with the test substance and the negative control. The highest dose level scored for chromosomal damage was, whenever possible, selected as the dose level causing a relative depression in mitotic index of at least 50 %.

The test substance was considered to cause a positive response if the following conditions were met:

Statistically significant increases ( $p < 0.01$ ) in the frequency of metaphases with aberrant chromosomes (excluding gaps) were observed at one or more test concentration.

The increases exceeded the negative control range of this laboratory, taken at the 99 % confidence limit.

The increases were reproducible between replicate cultures.

The increases were not associated with large changes in osmolality of the treatment medium or extreme toxicity.

Evidence of a dose-relationship was considered to support the conclusion.

A negative response was claimed if no statistically significant increases in the number of aberrant cells above concurrent control frequencies were observed, at any dose level.

The numbers of aberrant and polyploid metaphase figures in each treatment group were compared with the negative control value using a one-tailed Fisher's test.

**Result** : No substantial toxicity (greater than or equal to 50 % mitotic inhibition) was observed at any dose level under any testing condition.

In the first test, after 3-hour exposure in the absence or presence of S-9, the test substance caused no biologically relevant statistically significant increases in the proportion of cells with chromosomal aberrations at any dose level.

In the second test, after 19-hour exposure in the absence of S-9, the test substance caused statistically significant increases in the proportion of metaphase figures containing chromosomal aberrations at the 70 % dose levels both including and excluding gap-type aberrations. A trend test analysis also recorded a statistically significant dose-response. The observed increased chromosome aberration frequencies were outside the upper 99 % confidence limits of the historical control range. In the presence of S-9, the test substance caused no statistically significant increase in the proportion of metaphase figures containing chromosomal aberrations at any dose level.

In the third test, after a confirmatory 19-hour exposure in the absence of S-9, the test substance caused a statistically significant increase in the proportion of cells with chromosomal aberrations only at the 60 % dose level, excluding gap-type aberrations only. There was, however, no recording of a statistically significant dose-response. Cultures treated with the test substance at 50 and 70 % did not show any statistically significant chromosome aberration increases.

A quantitative analysis for polyploidy was made in cultures treated with the negative control and highest dose level. No increases in the proportion of polyploid cells were seen in any test.

All positive control compounds caused large, statistically significant increases in the proportion of aberrant cells, demonstrating the sensitivity of the test system and the efficacy of the S-9 mix.

It was concluded that the test substance showed statistically significant evidence of clastogenic activity in this test system only after continuous 19-hour treatment in the absence of S-9. However, the observed positive responses were weak and considered to be of marginal biological relevance.

<b>Test substance</b>	: HFC-152a, purity 99.99 %	
<b>Conclusion</b>	: Weakly positive	
<b>Reliability</b>	: (1) valid without restriction 1a. GLP guideline study.	
<b>Flag</b>	: Critical study for SIDS endpoint	
09.01.2006		(27)
<b>Type</b>	: Bacterial reverse mutation assay	
<b>System of testing</b>	: Salmonella typhimurium strains TA98, TA97, TA100, and TA1537 or in Escherichia coli WP2 uvrA	
<b>Test concentration</b>	:	
<b>Cycotoxic concentr.</b>	:	

**Metabolic activation** : with and without  
**Result** : negative  
**Method** : other  
**Year** : 1994  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Test substance** : HFC-152a, purity not reported  
**Reliability** : (4) not assignable  
 4a. Abstract.

23.03.2006 (2)

**Type** : Bacterial reverse mutation assay  
**System of testing** : Salmonella typhimurium strains TA1535, TA1537, TA98, and TA100  
**Test concentration** : 0, 20, 35, 50 %  
**Cycotoxic concentr.** :  
**Metabolic activation** : with and without  
**Result** : negative  
**Method** : other  
**Year** : 1977  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Test substance** : HFC-152a, purity 99.9+ %  
**Reliability** : (4) not assignable  
 4a. Abstract.

09.01.2006 (20)

**Type** : Bacterial reverse mutation assay  
**System of testing** : Salmonella typhimurium strains TA1535 and TA100  
**Test concentration** :  
**Cycotoxic concentr.** :  
**Metabolic activation** : with  
**Result** : negative  
**Method** : other  
**Year** : 1984  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4  
**Test substance** : HFC-152a, purity not reported  
**Reliability** : (4) not assignable  
 4a. Abstract.

09.01.2006 (48)

## 5.6 GENETIC TOXICITY 'IN VIVO'

**Type** : Micronucleus assay  
**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation

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<b>Exposure period</b>	: 6 hours
<b>Doses</b>	: 0, 4875, 9750, 19,500 ppm
<b>Result</b>	: negative
<b>Method</b>	: OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
<b>Year</b>	: 2001
<b>GLP</b>	: yes
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Method</b>	: The procedures used in the test were also based on the recommendations of the EC Commission Directive 2000/32/EC Annex 4C - B.12. Mutagenicity - In vivo mammalian erythrocyte micronucleus test. No. L 136/50 and US EPA (1998) Health Effects Test Guidelines; OPPTS 870.5395 Mammalian erythrocyte micronucleus test. EPA 712-C-98-226.

Animals were treated for a single 6-hour period of whole body inhalation exposure to nominal concentrations of 4,875, 9,750, and 19,500 ppm. The negative control group received clean air only. The positive control group was dosed, orally, by gastric intubation, with cyclophosphamide at 20 mg/kg body weight. Rats weighed between 140 and 149 grams on dispatch from the supplier. Each group of animals was kept, with sexes separate, in cages and maintained in a controlled environment. Temperatures recorded throughout the test were in the range  $21 \pm 2$  °C. Relative humidity was recorded in the range 34 - 56 %. Although the lower limit was outside the normal range for this species ( $55 \pm 10$  %), no adverse effects were recorded for any animal throughout the test and was not considered to have any affect on the integrity of the study. The room was illuminated by artificial light for 12 hours per day. Animals were provided with food and tap water ad libitum except during the period of inhalation exposure.

Animals were exposed in whole-body exposure chambers constructed from stainless steel and glass. The internal volume of each chamber was approximately 750 litres. Air was introduced into each exposure chamber at a total rate of 150 litres per minute. The flow through each chamber was approximately 12 air changes an hour; normally sufficient to maintain oxygen concentration above 19 % v/v, temperature approximately  $22 (\pm 1)$  °C and relative humidity between 40 – 60 %. The exposure chamber was maintained 1 - 10 mm H<sub>2</sub>O below ambient pressure. Animals were housed singly in stainless steel mesh compartments during exposure.

The test atmosphere was produced by diluting the gaseous test substance with air. Adjustments were made to the gaseous test substance supply to each chamber during exposures in order to maintain the desired concentrations. The dilutions of gaseous test substance with air were determined during preliminary generation trials. During exposure the chamber atmosphere was sampled to determine the concentration of test vapor on at least six occasions during each exposure. The nominal concentration of test substance

was calculated by recording the amount of test substance delivered to the generation system during the exposure. The usage over the six hours exposure was divided by the total airflow through the chamber. Any losses during the generation process were quantified and included in the calculation of the nominal concentration. Airflow, chamber temperature, and humidity were monitored continuously and recorded at approximately 30-minute intervals.

Following dosing, the animals were examined regularly and any observed mortality or adverse clinical signs were recorded. Five males and five females were sacrificed from the negative control and each of the test substance groups 24 hours after completion of the exposure period and from the positive control group 24 hours after dosing. In addition 5 male and 5 female animals were sacrificed from the negative control and high level treatment groups 48 hours after completion of the exposure period.

The animals were killed by cervical dislocation following carbon dioxide inhalation and both femurs dissected out from each animal. The femurs were cleared of tissue and the proximal epiphysis removed from each bone. The bone marrow of both femurs from each animal was flushed out and pooled in a total volume of 10 mL Hanks' balanced salts solution by aspiration. The resulting cell suspensions were centrifuged at 1,000 rpm (150 x g) for 5 minutes and the supernatant discarded. Each resulting cell pellet was resuspended in 2 mL of filtered foetal calf serum before being sedimented by centrifugation. The supernatant was discarded and the final cell pellet was resuspended in a small volume of foetal calf serum to facilitate smearing in the conventional manner on glass microscope slides. Several smears were prepared from each femur.

Due to the presence of mast cell granules in rat bone smears, which appear identical to micronuclei when stained using the Romanowsky methods, a modified Feulgen staining method was employed. This method specifically stains DNA-containing bodies deep purple while leaving mast cell granules unstained. The method also allows reasonable differentiation of mature and immature erythrocytes and produces permanent preparations. The stained smears were examined (under code) by light microscopy to determine the incidence of micronucleated cells per 2000 immature erythrocytes (polychromatic erythrocytes, PCE) per animal. The proportion of PCEs was assessed by examination of at least 1000 erythrocytes from each animal.

The results for each treatment group were compared with the results for the concurrent control group using non-parametric statistics. For incidences of micronucleated immature erythrocytes, exact one-sided P-values were calculated by permutation. Comparison of several dose levels was made with the concurrent control using the Linear by Linear Association test for trend, in a step-down fashion if significance was detected. For individual inter-group comparisons

<b>Result</b>	<p>(i.e. the positive control group), this procedure simplified to a straightforward permutation test. For assessment of effects on the proportion of immature erythrocytes, equivalent permutation tests based on rank scores were used, i.e. exact versions of Wilcoxon's sum of ranks test and Jonckheere's test for trend.</p> <p>: The exposure mean concentrations of the test material were 5,031, 9,413, and 19,030 ppm compared with target levels of 4,875, 9,750, and 19,500 ppm, respectively, expressed in terms of volume of test substance vapour per unit volume of atmosphere.</p> <p>Neither mortality nor adverse clinical signs was observed in the micronucleus test for any animal in any dose group over the duration of the test.</p> <p>No statistically significant increases in the frequency of micronucleated PCEs and no substantial decrease in the proportion of PCEs were observed in rats treated with the test substance and killed 24 or 48 hours, compared to negative control values.</p> <p>The positive control compound, cyclophosphamide, produced large, highly significant increases in the frequency of micronucleated PCEs and a decrease in the proportion of PCEs.</p> <p>It was concluded that the test substance did not show any evidence of causing chromosome damage or bone marrow cell toxicity when administered by whole body inhalation exposure in this in vivo test procedure.</p>
<b>Test substance</b>	: HFC-152a, purity 99.99 %
<b>Reliability</b>	: (1) valid without restriction 1a. GLP guideline study.
<b>Flag</b> 09.01.2006	: Critical study for SIDS endpoint (29)
<b>Type</b>	: Drosophila SLRL test
<b>Species</b>	: Drosophila melanogaster
<b>Sex</b>	: male/female
<b>Strain</b>	: other: Canton-S
<b>Route of admin.</b>	:
<b>Exposure period</b>	: 5 minutes
<b>Doses</b>	: 100 %; flow rate of 10 mL/min
<b>Result</b>	: positive
<b>Method</b>	: other
<b>Year</b>	: 1974
<b>GLP</b>	: no
<b>Test substance</b>	: as prescribed by 1.1 - 1.4
<b>Method</b>	: The Canton-Special (Canton-S) strain was obtained from the laboratory of Dr. Luolin Browning of Houston Texas. The cultures were kept under standard laboratory conditions in an air conditioned room at approximately 22 °C. Newly hatched (< 12 hours old) unetherized virgin flies were used.

A Turner bulb apparatus was used. The gas was passed through a cotton trap and from there into a dry gassing chamber that contained the flies. From this Turner bulb, tubing connected with the inlet of a second Turner bulb, which contained 15 mL of water, into which the gas was bubbled. In this way,  $100 \pm 5$  bubbles per minute could easily be counted. The rate of gas flow in mL/min, as determined by bubble count, was also measured by water displacement. The gassing time was 5 minutes with a flow rate of 10 mL/min, with the flies remaining in the gaseous atmosphere another 5 minutes. The treated flies were then placed in a clean container and observed. Upon recovery, the flies were lightly etherized and the males placed in 1/2 pint culture bottles. The females were discarded. Using the Basc technique, untreated Muller-5 virgin females were placed with Canton-S treated males. The Basc technique was used for scoring sex-linked recessive lethal mutations that arose in the germ line of the treated paternal male. The protocol for scoring semilethal (mosaic lethal) recessive mutations was to further test any F2 culture having a ratio of at least 10 heterozygous females, or 11 Basc males, to 1 normal male, and if this ratio continued in the F3 generation, to score the culture as a semilethal mutation.

The significance of the mutation rate induced was determined by t-test comparison to the control rate.

**Result** : Individual lethal tests of 276 F1 females gave 1 lethal and 8 semi-lethal, each scored as 0.5 lethal, giving a lethal count of 5/276 chromosomes. A lethal mutation frequency of 1.5 % was calculated; this value was corrected for a spontaneous frequency of 0.23 %. A number of developmental type abnormalities were noted among F2 progeny. One heterozygous female had ocelli in place of proboscis and no proboscis was present. Eye color mutants transmitted were white, apricot, and a deep orange.

**Test substance** : HFC-152a, purity > 98 %

**Reliability** : (4) not assignable

4e. Documentation insufficient for assessment.

09.01.2006

(38)

**Type** : Drosophila SLRL test

**Species** : Drosophila melanogaster

**Sex** :

**Strain** : other: Canton-S and Muller-5

**Route of admin.** :

**Exposure period** : 6 minutes

**Doses** :

**Result** : positive

**Method** : other

**Year** : 1974

**GLP** : no data

**Test substance** : as prescribed by 1.1 - 1.4

**Result** : HFC-152a was mutagenic to Drosophila melanogaster as determined

by the Basc technique for the detection of sex-linked lethal recessive mutations. Treatment with HFC-152a produced a mutation rate of  $1.31 \pm 0.05$ .

**Test substance** : HFC-152a, purity 99.5 - 99.9 %  
**Reliability** : (2) valid with restrictions  
2d. Test procedure in accordance with national standard methods with acceptable restrictions.

09.01.2006 (39)

## 5.7 CARCINOGENICITY

**Species** : rat  
**Sex** : male/female  
**Strain** : other:CrI:CD(R)Br  
**Route of admin.** : inhalation  
**Exposure period** : 2 years  
**Frequency of treatm.** : 6 hours/day, 5 days/week (excluding holidays)  
**Post exposure period** :  
**Doses** : 0, 2,000, 10,000, 25,000 ppm  
**Result** : negative  
**Control group** : yes  
**Method** : other  
**Year** : 1982  
**GLP** : yes  
**Test substance** : as prescribed by 1.1 - 1.4  
**Method** : Food and water were available to the rats ad libitum except during exposures. Thirty rats per sex per concentration (54 days of age at the time of the first exposure) were exposed whole-body to the vapor. During exposures, chamber temperature and relative humidity were maintained at approximately  $24 \pm 5$  °C and  $50 \pm 10$  %, respectively. Chamber atmospheres were generated by metering HFC-152a vapors from 1-ton cylinders of liquid HFC-152a, maintained at room temperature, through rotometers into the chamber air flow. The control chamber received dilution air only. Chamber atmospheres were quantitatively analyzed for HFC-152a by gas chromatography.

Body weights were recorded twice monthly for the first 14 weeks, and then once monthly for the remainder of the study. All animals were observed for abnormal behavior and clinical signs of toxicity twice daily during the work week. On weekends and holidays, all cages were observed daily for animals that had died.

Ten rats/sex/group were subjected to clinical pathology evaluation at 1, 3, 6, 12, 18, and 24 months on test. Twelve hematological and 8 clinical chemistry parameters were measured or calculated. On the day prior to each bleeding time, an overnight urine specimen was collected and 12 urine parameters were measured or calculated.

Ten rats/sex/group were sacrificed and necropsied at 3 and 12

months. All surviving rats at 24 months were sacrificed and necropsied. Gross examinations were conducted on all rats and 38 tissues were saved for microscopic examination. Organ weights were recorded for 10 of the organs. Histopathological examinations were conducted on the control and high-exposure groups and on any animals that died or were sacrificed in extremis. In addition, kidneys and nasal tissues at the 3-month and 24-month final sacrifices, respectively, from all intermediate- and low-exposure rats received histological evaluation.

Clinical measurements were subjected to partially-nested and crossed analysis of variance. Organ weight and final body weight data were subjected to one-way analysis of variance and Dunnett's test. The least significant differences from control values were calculated whenever the ratio of variances indicated that differences existed among the study groups. Body weight data were subjected to one-way analysis of variance. Significance was judged at the  $p = 0.05$  level of significance. The results of histopathologic examination were analyzed by the Fisher's Exact Test for differences between control and exposed groups and by the Mantel-Haenszel Test for a dose-related trend.

**Result**

- : Overall means and standard deviations of the weekly average exposure concentrations were  $2,000 \pm 100$ ,  $10,000 \pm 500$ , and  $25,000 \pm 600$  ppm HFC-152a.

Mean body weights and body weight gains of male and female rats were comparable or superior to their respective controls. Ocular/nasal discharges (25,000 ppm males and females), wet/stained perinea (25,000 ppm males and females), and stained body/face (25,000 females) were observed. Dose-response trends were apparent for the latter two signs. Swollen ears were significantly elevated in the 2000 ppm male and the 25,000 ppm males and females with a dose-related trend apparent in the females. Incidence of the clinical signs noted above are presented in the table below:

Exposure (ppm)	0	2,000	10,000	25,000
<b>Males</b>				
Ocular/nasal discharges	19 <sup>a</sup>	27	21	31
Wet/stained perineum	10	4	12	25
Swollen ears	11	30	16	31
<b>Females</b>				
Ocular/nasal discharges	13	16	15	24
Wet/stained perineum	30	18	36	50
Stained body/face	3	6	9	21
Swollen ears	4	5	4	16

a Incidence is the total number of rats affected throughout the study.

At the time of final sacrifice, mortality ratios of male rats were 48/100, 51/100, 49/100, and 51/100 in the 0, 2,000, 10,000 and 25,000 ppm groups, respectively. Mortality ratios in female rats were 54/100, 61/100, 47/100, and 47/100 in the 0, 2,000, 10,000 and 25,000 ppm groups, respectively.

Over the duration of the study, female rats exhibited increased mean corpuscular volumes (10,000 and 25,000 ppm) and increased serum bilirubin (all treatment groups), while male rats exhibited increased hematocrits (10,000 and 25,000 ppm), increased mean corpuscular volumes (10,000 and 25,000 ppm), and increased urobilinogen (25,000 ppm). In the absence of any abnormalities in hematopoietic tissues or red blood cell counts among either males or females or of changes in serum bilirubin in males, the above observations, which would be consistent with a hemolytic effect, provide inconclusive evidence of such a condition. While significantly lower than control values for all treated female groups when analyzed as relative numbers, eosinophils were significantly low only for the 10,000 ppm female group when analyzed as absolute numbers. Monocytes were significantly lower than control values for all treated male groups when analyzed as either relative or absolute numbers. The depression in monocytes, however, is of unknown clinical or biological significance.

A dose-related increase in urinary fluoride concentration and excretion was observed in the 10,000 and 25,000 ppm male and female rats and in the 2,000 ppm males when evaluated over the entire study. Urine fluoride concentrations ( $\mu\text{g}$ ) are listed in the tables below.

Months on Test (males) 1 3 6 12 18 24

Concentration (ppm)	Urine Fluoride (ppm)					
0	1.7	1.4	3.7	3.4	10.9	2.5
2,000	2.9	1.9	6.9	7.1	38.9	4.2
10,000	6.5	5.6	13.7	16.4	44.8	8.5
25,000	8.1	11.8	19.2	30.9	88.4	13.0

Months on Test (females): 1 3 6 12 18 24

Concentration (ppm)	Urine Fluoride (ppm)					
0	4.2	2.3	3.5	2.8	10.8	2.2
2,000	5.3	2.4	5.3	4.5	17.0	4.1
10,000	9.4	4.9	11.8	12.5	32.0	13.5
25,000	9.6	5.3	14.2	14.6	42.8	10.5

Serum creatinine was significantly elevated in both the 10,000 and 25,000 ppm female groups. The latter also exhibited increased urine volume and a decrease in urine osmolality.

At the 3-month sacrifice, statistically significant differences in the following organ weights were noted: increased absolute heart, stomach, and adrenal weights (2000 ppm males); decreased absolute liver and spleen weights (25,000 ppm males); decreased relative liver and spleen weights (10,000 and 25,000 ppm males); decreased relative lung weights (2,000 and 25,000 ppm males); decreased relative testes weights (10,000 ppm males); decreased relative pituitary weights (2,000 ppm males); increased absolute stomach weights (2,000 ppm females); increased adrenal weights (2,000 and 10,000 ppm females); decreased absolute brain weights (25,000 females); decreased relative brain weights (2,000 and 25,000 ppm females); decreased absolute heart weight (25,000 females); decreased relative heart weights (all treated female groups); decreased absolute lung weights (10,000 and 25,000 ppm females); decreased absolute spleen weights (25,000 ppm females); decreased relative spleen weights (all treated females); increased absolute pituitary weights (all treated females); increased relative pituitary weights (10,000 and 25,000 ppm females); and decreased relative liver weights (25,000 ppm females). Renal tubular changes were noted in females at the 3-month sacrifice. The changes consisted of slight cytoplasmic vacuolation, luminal dilation, and presence of occasional vesiculated nuclei in 4/10 males and 7/10 females in the 25,000 ppm group. Similar lesions were not seen in rats from the 2,000 or 10,000 ppm groups. A pathological peer review of the study by Pathology Associates revealed no distinct evidence of HFC-152a-induced toxicity or carcinogenicity in any tissue examined. Preparation of additional kidney sections indicated that renal tubular changes recorded by the original pathologist in female rats sacrificed after 3 months exposure were the result of tissue processing artifact rather than treatment-related nephrotoxicity.

At the 12-month sacrifice, no differences in macroscopic lesions were detected between the treated and control groups. No compound-related neoplastic or non-neoplastic lesions were observed. Differences in mean absolute and relative organ weights of animals sacrificed at 12 months consisted of: increased absolute lung weights (10,000 ppm males); decreased absolute thymus weights (2,000 ppm males); decreased relative thymus weights (2,000 and 10,000 ppm males); increased relative heart and stomach weights (25,000 ppm males); decreased absolute pituitary weights (2,000 and 10,000 ppm females); decreased relative pituitary weights (all treated females); and decreased relative liver weights (25,000 ppm females).

No statistically significant difference in mean absolute or relative organ weights were noted between treated and control male rats sacrificed at 24 months. However, treated female rats presented the following differences from control in organ weights: increased absolute and relative lung weights (2,000 and 10,000 ppm), increased absolute stomach weight (25,000 ppm), increased relative stomach

weight (all treated females), increased relative heart weight (2000 ppm), and increased relative liver weight (25,000 ppm).

Female Exposure (ppm)	0	2,000	10,000	25,000
Absolute lung weight (g)	1.9939	2.1244	2.1166	2.0562
Relative lung weight (g)	0.3870	0.4447	0.4415	0.4115
Absolute stomach weight (g)	2.5302	2.6428	2.6200	2.7792
Relative stomach weight (g)	0.4857	0.5494	0.5446	0.5448
Relative heart weight (g)	0.2570	0.3176	0.2966	0.2917
Relative liver weight (g)	3.3324	3.4723	3.6701	3.8151

Atrophy of the nasal olfactory epithelium was noted at the 2-year sacrifice in some rats from all but the intermediate-exposure females. Incidences of the lesions are provided in the table below. The incidence of focal mucosal metaplasia in all treated groups were clearly not dose-related. The increased incidence of mucosal atrophy was statistically significant in the 2,000 and 25,000 ppm male and female groups, although an analysis for dose-related trend was significant only in the males.

Exposure (ppm)	0	2,000	10,000	25,000
<b>Males</b>				
No. of nasal tissues examined	97	87	92	89
Focal mucosal metaplasia	57	21	21	21
Mucosal atrophy	0	5	2	8
<b>Females</b>				
No. of nasal tissues examined	95	88	91	95
Focal mucosal metaplasia	22	17	6	23
Mucosal atrophy	0	9	0	17

Atrophy of the olfactory epithelium was confirmed by the peer review to be present in small numbers of females exposed for 2 years. These nasal changes, however, usually were unilateral in distribution and were entirely consistent with olfactory lesions, which have been described as spontaneous alterations in aging rats. Further, group incidence trends for olfactory atrophy were inconsistent with exposure concentration gradients. Olfactory changes, therefore, were not regarded as treatment related.

A nasal adenoma in 1 male and 1 female from the 25,000 ppm groups and osteomas originating from the skull in 3 males from the 25,000

ppm group were observed at the final sacrifice. These tumor types did not occur in the concurrent controls. The incidence of neither tumor was statistically significant and each was considered to be of unclear biological significance.

FC-152a was not carcinogenic and produced no life-shortening toxic effects.

**Test substance** : HFC-152a, purity > 99.9 %  
**Reliability** : (1) valid without restriction  
 1b. Comparable to guideline study.  
**Flag** : Critical study for SIDS endpoint

04.04.2006

(22) (24)

### 5.8.1 TOXICITY TO FERTILITY

### 5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

**Species** : rat  
**Sex** : female  
**Strain** : other: Charles River CD(R)  
**Route of admin.** : inhalation  
**Exposure period** : Days 6 - 15 of gestation  
**Frequency of treatm.** : Daily  
**Duration of test** : 6 hours/day  
**Doses** : 0, 5,000, 50,000 ppm  
**Control group** : yes, concurrent vehicle  
**NOAEL maternal tox.** : 50.000 ppm  
**NOAEL teratogen.** : 50.000 ppm  
**Method** : other  
**Year** : 1979  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Method** : The rats were bred by the supplier (Charles River). The morning when sperm were found in the vaginal smear was counted as Day 1 of gestation. Animals (young adults weighing approximately 185 grams) were delivered at either 4 or 2 days pregnant. Food and water were available ad libitum except during inhalation exposures.

Pregnant female rats (27 rats/group) were exposed to nominal concentrations of 0, 5,000, or 50,000 ppm HFC-152a for 6 hours per day on days 6 - 15 of gestation. Desired exposure concentrations were generated by metering the vapors of HFC-152a from the cylinder into 1.4 m<sup>3</sup> stainless steel and glass chambers operating under dynamic airflow conditions. Chamber atmospheres were monitored every 30 minutes via gas chromatograph (GC). The GC was calibrated daily with gaseous standards. Control animals were exposed to room air in

identical chambers. Animals were observed daily for signs of toxicity and weighed periodically throughout the study. Dams were euthanized on Day 21 and organs of the thoracic and abdominal cavities were examined and the uterine weight was recorded. Corpora lutea, implantation sites, live and dead fetuses, resorptions, fetal weight, crown-rump length of live fetuses, and a gross external fetal examination were recorded. Half of the fetuses from each litter were examined for skeletal abnormalities. The remaining fetuses were examined for visceral and neural anomalies (via the Wilson method with modification described by Barrow and Taylor).

For statistical evaluation of the data, the litter was considered the experimental unit of treatment and observation. The Fisher Exact probability test was used to evaluate the incidence of resorptions and abnormalities among litters. Maternal and fetal body weights and fetal crown-rump measurements were treated statistically by analysis of variance and least significant difference (LSD) tests. The number of corpora lutea, implantations, and live fetuses per litter were analyzed by the Wilcoxon rank sum test. In all cases, two-tailed significance tests were performed and significance was judged at the 0.05 probability level.

**Result**

- : The daily average analytical exposure levels during the entire 10-day exposure period were  $5,300 \pm 1,200$  and  $45,300 \pm 4,900$  ppm.

No compound-related clinical signs of maternal toxicity or body weight changes were observed. No gross pathological abnormalities were observed in ovaries, uterine horns, vital organs, or tissues of treated animals.

Pregnancy ratios were 22/27, 21/27, and 19/27 at 0, 5,000, and 50,000 ppm, respectively. A summary of other reproductive outcomes (means/litter) are provided in the table below:

Concentration (ppm)	0	5000	50,000
Corpora lutea:	11.6	11.3	12.2
Implantations:	10.0	9.4	10.5
No. of Resorptions:	1.5	1.4	1.2
Total No. of Fetuses:	9.3	8.8	9.9
Total No. of Live Fetuses:	9.3	8.8	9.9
Mean Fetal Weight (g):	4.3	4.4	4.3
Sex Ratio:	NR	NR	NR

NR = Fetal sex was not recorded; therefore, sex ratios could not be calculated.

The number of corpora lutea, implantation sites, and live fetuses per litter were similar in all groups. The post-implantation death of

fertilized ova in exposed females indicated by early and late resorptions and dead fetuses was not different from that of the control group. Fetal body measurements, i.e. mean weight and crown-rump length in groups were not different from controls.

The HFC-152a treatment did not affect embryonal development as measured by gross external, visceral, and skeletal examinations. Petechial hemorrhages and small subcutaneous hematomas on various parts of the body and the number of runts among litters and fetuses were similar in all groups. Apparent hydronephrosis, transposition of the viscera, liver peliosis, and internal hemorrhage were detected; however, none of these findings were considered to be treatment-related. No statistically significant differences in the frequency of minor skeletal anomalies or variants were observed.

A summary of gross, soft tissue, and skeletal anomalies are provided in the table below. Data are presented as number of litters (fetuses) affected.

Concentration (ppm)	0	5,000	50,000
Gross External, Number examined:	22(205)	20(184)	19(188)
Petechial hemorrhages	4(4)	5(5)	3(5)
Hematoma	10(12)	6(7)	8(14)
Runts	2(2)	1(1)	1(1)
Soft Tissue, Number examined:	22(105)	20(93)	19(90)
Hydronephrosis (apparent)	1(1)	3(4)	2(2)
Situs inversus	0	0	1(1)
Liver peliosis	0	0	3(3)
Internal hemorrhage	1(1)	0	0
Skeletal, Number examined:	22(100)	20(91)	19(98)
14th rudimentary rib	16(51)	16(53)	19(69)
Wavy ribs	8(17)	6(8)	5(7)
Sternebrae unossified	10(14)	9(16)	12(23)
Bipartite centra	3(3)	0	2(2)
Hyoid unossified	2(3)	0	4(6)

The NOEL for maternal and developmental toxicity was 50,000 ppm, the highest level tested.

- Test substance** : HFC-152a, purity > 99.9 %  
**Reliability** : (2) valid with restrictions  
 2e. Study well documented, meets generally accepted scientific

**Flag** : principles, acceptable for assessment.  
: Critical study for SIDS endpoint  
30.05.2006 (21)

### 5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

**Type** : other: 2-year Chronic and Carcinogenicity Study  
**In vitro/in vivo** : In vivo  
**Species** : rat  
**Sex** : male/female  
**Strain** : other: Rats/Crl:CD(R)BR  
**Route of admin.** : inhalation  
**Exposure period** : 2 years  
**Frequency of treatm.** : 6 hours/day, 5 days/week (excluding holidays)  
**Duration of test** :  
**Doses** : 0, 2,000, 10,000, 25,000 ppm  
**Control group** : yes, concurrent vehicle  
**Result** : No histopathological or weight effects on reproductive organs of either male or female rats were observed.  
**Method** : other  
**Year** : 1982  
**GLP** : yes  
**Test substance** : as prescribed by 1.1 - 1.4  
**Method** : Refer to 2-year carcinogenicity study in Section 5.7 for methods.  
**Result** : Additional information can be found in the Carcinogenicity Section (Section 5.7).  
**Test substance** : HFC-152a, purity > 99.9 %  
**Reliability** : (2) valid with restrictions  
 2e. Study well documented, meets generally accepted scientific principles, acceptable for assessment.  
**Flag** : Critical study for SIDS endpoint  
 09.01.2006 (22)

### 5.9 SPECIFIC INVESTIGATIONS

### 5.10 EXPOSURE EXPERIENCE

### 5.11 ADDITIONAL REMARKS

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