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1-CHLORO-1,1-DIFLUOROETHANE

CAS N°: 75-68-3

SIDS INITIAL ASSESSMENT REPORT**for****SIAM 12**

(Paris, 27-29 June 2001)

Chemical Name : 1-chloro-1,1-difluoroethane
CAS No.: 75-68-3

Sponsor Country: France

National SIDS Contact Point in Sponsor County:

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History:

Comments: The national peer review consisted of a presentation and critical discussion at a national panel of experts in toxicology and ecotoxicology from administration, university and industry and nominated by the ministry of environment. In parallel, a review was performed by the national institute on environmental and industrial risk (INERIS) by request from the ministry of environment.

Deadline for Circulation: 30 March 2001

Date of Circulation: 30 March 2001

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	75-68-3
Chemical Name	1-chloro-1,1-difluoroethane
Structural Formula	$\text{ClF}_2\text{C} - \text{CH}_3$
RECOMMENDATIONS	
<p>The chemical is currently of low priority for further work as it is subject to withdrawal under international activity (Montreal protocol).</p>	
SUMMARY CONCLUSIONS OF THE SIAR	
Human Health	
<p>1-chloro-1,1-difluoroethane is a colourless gas with slight ethereal odour:</p> <p>Acute toxicity of 1-chloro-1,1-difluoroethane is low ($\text{LC}_{50}/6\text{h} > 1,640,000 \text{ mg/m}^3$ (400,000ppm) in rats). Inhalation of high concentrations induced signs of lung irritation and Central Nervous System depressing effects of anesthetic type in rats and cardiac sensitisation in dogs. Consequently, 1-chloro-1,1-difluoroethane may be hazardous to humans in case of accidental exposure to high concentrations occurring in confined area where replacement of air by the gas could at the same time reduce oxygen in the atmosphere. In repeated inhalation exposure studies, 1-chloro-1,1-difluoroethane did not induce specific chronic toxicity in rats and dogs exposed 6 h/d, 5 d/week during several months (no target organs identified ; the no observed adverse effects were higher than 41 000 mg/m³ (10,000ppm) in dogs exposed during 3 months and higher than 82 000mg/m³ (20,000ppm) in rats exposed for their lifetime). There was no carcinogenic effect in rats exposed for their life time (6h/d, 5d/week at concentrations up to 82 000 mg/m³ (20,000ppm)). In genotoxicity studies, 1-chloro-1,1-difluoroethane was mutagenic <i>in vitro</i> on bacteria (Ames test) and gave equivocal results in a cell neoplastic transformation assay. However, in <i>in vivo</i> mutagenicity studies it was inactive (in a Dominant lethal assay and in a Bone Marrow cytogenetic assay in rats exposed by inhalation during 15 and 13 weeks respectively). Overall, these results suggest that 1-chloro-1,1-difluoroethane does not pose a significant genotoxic hazard to humans. In the reproduction field, 1-chloro-1,1-difluoroethane did not induce adverse effect on fertility of male mice exposed up to 82 000 mg/m³ (20,000ppm) (in a Dominant lethal assay) and did not induce male and female lesions of sexual organs in rats and dogs exposed for several months. Also the gas did not induce teratogenic or embryo/foetotoxicity effect and no maternal toxicity in two inhalation developmental toxicity studies where rats were exposed during pregnancy up to 41000 mg/m³ (10,000ppm).</p>	
Environment	
<p>Based on its physico-chemical properties, the air compartment is the preferred target one for 1-chloro-1,1-difluoroethane. The global atmospheric lifetime of 142b is 18.5 years corresponding to a 1/2 -lifetime of 12.8 years. The tropospheric lifetime due to removal by reaction with OH is 19.5 years.</p> <p>Atmospheric degradation products are essentially the aldehyde form of 142b which further degrade to form $\text{CF}_2(=\text{O})$ which will hydrolyse in atmospheric water to form HF (also in the OECD HPV Chemicals Programme) and CO_2.</p> <p>The ozone depletion potential (ODP) of 1-chloro-1,1-difluoroethane is the main concern of this substance. Due to its ODP value of 0.065, it is considered as an ozone depleting substance. The calculated Global Warming Potential of 1-chloro-1,1-difluoroethane is 1800 (IPCC 1995) for an integration horizon of 100 years. Its contribution to the Greenhouse effect is small i.e. 0.00108 W/m² from IPCC 1995 data.</p>	

In water, 1-chloro-1,1-difluoroethane is not readily biodegradable under aerobic condition (about 5 % of biodegradation after 28 days). It is not expected to bioaccumulate ($\log K_{ow} = 1.64 - 2.05$).

1-chloro-1,1-difluoroethane has a low acute toxicity to fish and daphnia. The lowest available LC 50 being higher than 100mg/liter. No acute toxicity tests are available for algae. Algae appear to be more sensitive than fish and daphnids to 1-chloro-1,1-difluoroethane with a calculated 96h EC50 of 45mg/l.

From these results, a PNEC of 45 $\mu\text{g/l}$ is proposed applying a factor of 1000 to the lowest figure obtained from the QSAR for algae (45 mg/l).

Exposure

The expected production volume of 1-chloro-1,1-difluoroethane in year 2000 is 36,000 tonnes in Europe, 42,000 tonnes in the USA and an amount of 84,000 tonnes for the total world. Its main uses are as a chemical intermediate to produce fluoropolymers and as a blowing agent. A small portion is used as a component of refrigerant fluids.

Because of its ODP, the production and consumption of 1-chloro-1,1-difluoroethane are covered by the Montreal Protocol. In the case of developed countries, a phase-out of 1-chloro-1,1-difluoroethane and other hydrochlorofluorocarbons (HCFCs) is scheduled as follows: 35% in 2004, 65% in 2010, 90% in 2015, 99.5% in 2020. A total phase-out is scheduled in 2030. For developing countries, a freeze of the production is scheduled in 2016 and a total phase-out in 2040.

In the European Union, the phase-out of ozone depleting substances is scheduled more rapidly than that required by the Montreal protocol. The total ban of hydrochlorofluorocarbons (HCFCs) is required on January 1, 2010, the use as blowing agent for expanded polystyrene being prohibited from January 1, 2002.

NATURE OF FURTHER WORK RECOMMENDED

None recommended.

Due to be phased out under the Montreal protocol.

FULL SIDS SUMMARY

CAS NO: 75-68-3		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			-130.8 °C
2.2	Boiling Point			-9.2 °C
2.3	Density			
2.4	Vapour Pressure			339,000 Pa at 20°C
2.5	Partition Coefficient (Log Pow)		Calculated	1.64 - 2.05
2.6 A.	Water Solubility			1,900 mg/l at 25°C
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		calculated	Overall atmospheric lifetime :18.5 years 1/2 lifetime: 12.8 years
3.1.2	Ozone depleting potential (ODP)		Calculated	0.065
3.1.3	Global Warming potential (GWP)		Calculated	1800
3.2	Stability in Water		N.D.	
3.3	Transport and Distribution		Calculated (fugacity model level 1 of Mackay)	Air : 99.98 Water : 0.02 Soil : 0.6 10 ⁻⁴ Sediments : 0.5 10 ⁻⁴
3.5	Biodegradation		Modified Sturm adapted to gas substance	5% after 28 days
ECOTOXICOLOGY				
4.1	Acute Toxicity to Fish	<i>Poecilia reticulata</i> (guppy)	OECD 203	96 h LC50 = 220 mg/l
4.2	Acute Toxicity to Aquatic Invertebrates (<i>Daphnia</i>)	<i>Daphnia magna</i>	OECD 202 (2 tests)	48h EC50 = 160 mg/l 48h EC50 > 190mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	Green algae	Estimated (ECOSAR)	96 h EC 50 = 45 mg/l
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	exposure during 6 hours	No data, test chemical is a gas LC50: higher than 1,640,000 mg/m ³
5.1.2	Acute Inhalation Toxicity	Dog	Cardiac sensitization , exposure during 5 minutes	EC50: 2,050,000 mg/m ³
5.1.3	Acute Dermal Toxicity			No data, test chemical is a gas:
5.2.1	Skin Irritation			No data, test chemical is a gas
5.2.2	Eye Irritation			No data, test chemical is a gas

CAS NO: 75-68-3		SPECIES	PROTOCOL	RESULTS
5.4	Repeated Dose Toxicity	Rat	90-day exposure, 6h/d, 5d/w	NOAEL: higher than 41,000 mg/m ³
		Dog	90-day exposure, 6h/d, 5d/w	NOAEL: higher than 41,000 mg/m ³
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	Salmonella typhimurium	Gas exposure strains TA 1535, 1537, 1538, 98, 100	Positive with and without metabolic activation in TA 1535 and TA 100
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)			No data
C.	Cell transformation assays	BHK21	Liquid exposure	Positive
		BALB/3T3	Gas exposure	Negative
5.6	Genetic Toxicity In Vivo	Rat	Dominant lethal assay /inhalation exposure 15 w 6h/d, 5d/w	Negative
		Rat	Chromosomal aberration assay /inhalation exposure 13w, 6h/d, 5d/w	Negative
5.8	Toxicity to Reproduction	Rat	Dominant lethal assay /inhalation exposure 15 w 6h/d, 5d/w	NOAEL on male fertility: higher than 82,000 mg/m ³
		Rat	13-week and 104-week exposure, 6h/d, 5d/w	NOAEL on male and female sexual organs: higher than 82,000 mg/m ³
		Dog	13-week and 104-week exposure, 6h/d, 5d/w	NOAEL on male and female sexual organs: higher than 82,000 mg/m ³
5.9	Developmental Toxicity/ Teratogenicity	Rat	Inhalation exposure from day 3 to 15 of pregnancy, 6h/d	NOAEL maternal toxicity: higher than 41,000 mg/m ³ NOAEL developmental toxicity : higher than 41,000 mg/m ³
5.10	Carcinogenicity	Rat	2-year Inhalation, 6h/d, 5d/w	No increase of cancer incidences at all tested concentrations (up to 82,000 mg/m ³)
5.11	Experience with Human Exposure			No data available
HUMAN EXPOSURE				
6.1	Workers	Work area	Using HCFC 141b as a surrogate	8h OEL = 4,200 mg/m ³ less than 410 mg/m ³
6.2	Consumers	Rigid foams	Gas diffusion out of foams	0.004 mg/m ³
6.3	Indirect via the environment	Global average in atmosphere	Observed in 1998 Expected in 2015	0.000045 mg/m ³ 0.000143 mg/m ³

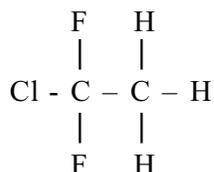
SIDS INITIAL ASSESSMENT REPORT

1 GENERAL INFORMATION:

1.1 IDENTITY:

CAS Number: 75-68-3
Name (IUPAC) : 1-chloro-1,1-difluoroethane
Common Name: HCFC 142b

EINECS n°: 200-891-8
Molecular Weight: 100.5
Empirical Formula: C₂H₃ClF₂
Structural Formula:



1.2 PHYSICO-CHEMICAL PROPERTIES

Form: colorless gas
Odor : slightly ethereal
Melting Point: -131.0°C
Boiling Point: - 9.2° C
Vapor Pressure: 339 kPa at 20° C
Solubility in Water: 1.9 g/l at 25° C
Flammability: flammable gas
Explosive limit
Lower 9 % in volume
Higher 14.8 % in volume
log kow : 1.6 - 2.05

1 ppm (v/v) = 4.1 mg/m³ ; 1 mg/m³ = 0.24 ppm (v/v)

1.3 PURITY : > 99.85 %

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION VOLUME/USES :

The expected production volume of 1-chloro-1,1-difluoroethane in year 2000 is 36,000 tonnes/year in Europe, 42,000 tonnes/year in the USA and an amount of 84,000 tonnes/year for the total world.

The producers and locations are listed below:

United States : ATOFINA, AUSIMONT, HONEYWELL

Europe: ATOFINA (France), SOLVAY (France)

Asia: DAIKIN (Japan)

2.2 USES AND FUNCTIONS :

The main uses of 1-chloro-1,1-difluoroethane are as a chemical intermediate to produce fluoropolymers and as a blowing agent. A small portion is used as a refrigerant fluid .

The breakdown of the various uses for the year 2000 is given below :

	Europe	North America	ROW
Polymers (France 100 %)	20 KT	25 KT	2 KT
Blowing Agents	11 KT	17 KT	6 KT
Refrigeration	3 KT	-	-

2.3 REGULATORY CONTROLS

An international agreement, known as the **Montreal Protocol**, controls the production and consumption of substances that can cause Ozone Depletion

Regarding **hydrochlorofluorocarbons** (HCFCs), in case of developed countries, the Montreal Protocol implies a freeze of their production in 1996 to the baseline level calculated for each country using the following formula: 2.8 percent of Ozone Depletion Potential (ODP) weighted production in 1989 of chlorofluorocarbons (CFCs) augmented by 100 percent of ODP weighted production in 1989 of HCFCs.

Furthermore, time limits for consumption were also given by authorizing 100 percent of maximum value of consumption (calculated as above) until January 1, 2004 and then applying every five years a decreasing threshold to this authorized maximum:

65% as from January 1, 2004

35% as from January 1, 2010

10% as from January 1, 2015

0.5% as from January 1, 2020

A total ban on HCFCs (including 142b) is planned for 2030 for developed countries.

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

In the European Union (EU), the Phase out of ozone depleting substances is scheduled more rapidly than that required by the Montreal protocol. The total ban of hydrochlorofluorocarbons (HCFCs) is required on January 1, 2010. Regarding the use of 1-chloro-1,1-difluoroethane as blowing agent for expanded polystyrene, it will be prohibited in the EU as from January 1, 2002, in Japan in 2004 and in the US in 2010.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 General Discussion:

Due to its high vapor pressure, 339 kPa at 20° C, and relatively low water solubility, 1.9 g/l, 1-chloro-1,1-difluoroethane will partition mostly into the atmosphere. Using the fugacity model level 1 of Mackay and Paterson (1981) a theoretical distribution can be calculated indicating that 99.98 % of 1-chloro-1,1-difluoroethane released into the environment will enter the atmosphere

Its overall atmospheric lifetime is estimated to be 18.5 years and its ozone depleting potential, relative to CFC11 = 1.0, is 0.065

3.1.2 Fate in Waste Water Treatment Plants

In waste water treatment plants, 1-chloro-1,1-difluoroethane will be mainly eliminated by stripping to the air. For example, the model SIMPLETREAT (Struijs et al. 1991) estimates that 94 % are stripped to air and 1% adsorbed to sewage sludge, the remaining 5 % being released with the effluent into the receiving surface water.

3.1.3 Distribution in Air, Water and Soil

Any 1-chloro-1,1-difluoroethane which might be present in aqueous waste streams discharged directly into rivers and lakes would be expected to have a half-life of days or at the very most a few weeks. 1-chloro-1,1-difluoroethane present in surface or ground waters would have little tendency to partition onto solids as the $\log K_{ow}$ is 1.6 - 2.05, indicating little potential for accumulation in soil.

3.1.4 Abiotic and Biotic Degredation in Air, Water and Soil

3.1.4.1 Atmospheric life time

The tropospheric lifetime of 1-chloro-1,1-difluoroethane due to removal by reaction with OH is 19.5 years and the stratospheric lifetime is 372 years (WMO 1998). The global atmospheric lifetime is 18.5 years as a result of tropospheric and stratospheric degradation of the substance. The corresponding global 1/2-lifetime is 12.8 years. Note that by definition the atmospheric lifetime of a substance refers to the time needed for the concentration to be divided by 2.718 whereas the 1/2 lifetime refers to the time required for the concentration to be divided by 2. The atmospheric lifetime is the value mostly used in the scientific literature

3.1.4.2 Atmospheric degradation.

Atmospheric degradation products are essentially the aldehyde form of 1-chloro-1,1-difluoroethane which further degrade to form $CF_2(=O)$ which will hydrolyze in atmospheric water to form HF and CO_2 .

Because of the very low atmospheric concentration (11 parts per trillion by volume (pptv)) of 1-chloro-1,1-difluoroethane and of its very slow rate of degradation, the

concentration of the degradation products will represent fraction of pptv and the impact of HF on acid rain will be negligible.

3.1.4.3 Ozone depleting potential

The accepted value for the Montreal Protocol is 0.065(CFC11=1) based on a semi-empirical calculation approach which consists in calculating the amount of chlorine atoms released in the stratosphere by the substance on the basis of measured atmospheric concentration profiles or inferred atmospheric concentration profiles for the locations where data are lacking. These results are weighted for the observed ozone depletion and integrated spatially and temporally over the stratosphere (WMO 1991, 1998).

3.1.4.4 Global Warming potential and contribution to the greenhouse effect:

The global warming potential relative to CO₂ and calculated with an integration horizon of 100 years is 1800 (IPCC 1995). The absolute contribution of 142b to the greenhouse effect is 0,02 w/m² (IPCC 2001) calculated on the basis of its atmospheric concentration of 11 pptv in 1998 (see section 3.1.6). It can be compared with the absolute contribution of anthropogenic CO₂ which is 1.46 w/m² (IPCC 2001).

3.1.4.5 Biodegradation

The biodegradability of 1-chloro-1,1-difluoroethane was determined using a modified Sturm test (OECD 301 B). Because of the volatility of the substance, glass bottles closed with a plastic screw cap were used. A glass vial containing the CO₂ absorbing fluid was suspended from the screw caps of the bottles. The initial concentrations in the test medium were estimated from the calculated Henry constant of the substance. Before inoculation, the test substance was equilibrated between water and headspace by shaking the closed flasks overnight. Under these test conditions, the substance was found not readily biodegradable (about 5 percent of biodegradation after 28 days) (Matla, Y.A. and Blom A.J.M., 1991) (2e).

3.1.5 Bioaccumulation

1-Chloro-1,1-difluoroethane has a calculated log K_{ow} of 1.64 - 2.05 (Hansch and Leo, 1979; SRC). It is therefore not expected to bio-accumulate to any significant degree.

3.1.6 Predicted Environmental Concentration

1-chloro-1,1-difluoroethane is produced in a relatively small scale (in year 2000 : 36,000 tonnes in Europe, 42,000 tonnes in the USA and an amount of 84,000 tonnes for the total world). More than the half is consumed as a chemical intermediate. As it is used in closed system, the release into the environment from the production of fluoropolymers is expected to be low.

Information on atmospheric concentrations at the vicinity of production and fluoropolymer production sites are not available.

More important emissions are expected from the plants using 1-chloro-1,1-difluoroethane as blowing agent for expanded polystyrene. In the vicinity of industrial sites using the substance as a blowing agent, high atmospheric concentrations could occur. No information on measured concentrations are available.

It has to be recalled that this use will be prohibited in the EU by the end of 2001 and in the US in 2010.

The global average observed atmospheric concentration of 142b is 11 pptv in 1998. (IPCC 2001). This atmospheric concentration is the average value derived from observations worldwide by existing monitoring networks and sampling experiments i.e. flask sampling by Montzka et al and ALE/GAGE/AGAGE experiments which first started in 1978. These observations which have been documenting the long term evolution of atmospheric concentration of CFCs, HCFCs and HFCs are summarized in the main scientific assessments of stratospheric ozone and climate change.(WMO 1998, IPCC 2001)

Using data from the 1998 UNEP report on scientific ozone depletion chapter11 (halocarbons atmospheric emission scenario A1) the maximum predicted atmospheric concentration for 142b is 35 pptv for the year 2015. (IPCC 2001).

1-Chloro-1,1-difluoroethane is expected to be present in surface water at very small concentrations because it partitions mainly to air.

The main intermediate decomposition product of 1-chloro-1,1-difluoroethane is $C(O)F_2$ which further decomposes in the atmosphere to HF and CO_2 through hydrolysis in atmospheric water. In view of the very low concentrations of 1-chloro-1,1-difluoroethane measured in the atmosphere, its decomposition end-products are expected to be generated in the atmosphere at pptv levels.

3.2 EFFECTS ON THE ENVIRONMENT

Giving the physical nature of 1-chloro-1,1-difluoroethane and due to the difficulty to test it meaningfully, very few experimental aquatic results are available.

3.2.1 Aquatic Effects

3.2.1.1 Acute toxicity to fish

The acute toxicity of 1-chloro-1,1-difluoroethane to fish (*Poecilia reticulata*) was carried out according to OECD guideline 203. Because of the volatility of the substance, a semi-static method (renewal each 24 h) with a closed system was used.

The results of the test showed a low toxicity of 1-chloro-1,1-difluoroethane to *Poecilia reticulata* : 96h LC 50 = 220mg/l based on measured concentrations (Groeneveld A.H.C. and Kuijpers L.A.M.,1990) (2e)

3.2.1.2 Acute toxicity to daphnia

Two daphnia tests were conducted in closed glass containers without renewal or aeration of the test solution.

The results of the tests summarized in the following table show that 1-chloro-1,1-difluoroethane is of low toxicity to daphnia:

Species	duration	Results mg/l	Remarks	References	Reliability
<i>Daphnia magna</i>	48h	EC50 = 160	OECD 202 static test, no renewal, no aeration, sealed glass containers, measured concentrations. Mortality in the control: 22 %	Groeneveld A.H.C., Kuijpers L.A.M., 1990	2e (due to mortality in the control)
<i>Daphnia magna</i>	48h	EC50 > 190	Static unaerated conditions, sealed vessels, no immobilisation over 48h	Haskell laboratory, 1989	2e (not enough documented)

3.2.1.3 Acute toxicity to algae:

There are no acute toxicity tests available for algae. QSAR methods have been used to estimate the algae toxicity of 1-chloro- 1,1-difluoroethane.

A 96h EC50 of 45 mg/l is predicted using the ECOSAR program.

To evaluate the accuracy of the predicted values versus measured values, ECOSAR was used to predict the aquatic toxicity of other HCFCs and hydrofluorocarbons. The ECOSAR predictions were compared to the available measured values for these compounds.

The results are given in the following table:

Substance	Log Kow	Fish 96h LC50 mg/l		Daphnid 48h EC50 mg/l		Algae 96 h EC50 mg/l	
		QSAR	measured	QSAR	measured	QSAR	Measured
F 142b (C2C1F2)	2.05	67	220	72	160->190	45	-
F 141b (C2C12F)	2.3	45.3	158	49.5	31.2	31.5	> 44 (72h EC0)
F 134a (C2H2F4)	1.5	578	450	581	980	344	
F 125 (C2HF5)	1.5	263		272		172	
F 152a (C2H4F2)	1	322		325		193	
F 143a (C2H3F3)	1.5	188	> 40	194	300	118	
F 123 (C2H2F3)	2.8	19	55.3	22	17.3	14.2	

3.2.2 PNEC for the aquatic environment

From the aquatic toxicity results reported above, it can be seen that the QSAR results predict that 1-chloro- 1,1-difluoroethane is more toxic than might be expected from the experimental data.

Therefore, it is proposed to base the PNEC on the lowest figure obtained from the QSAR, which is 45 mg/l for 96 h exposure to algae.

As only short term toxicity values at three trophic levels are available, an assessment factor of 1000 is applied to this figure. The derived PNEC for fresh water is 45 µg/l.

It has to be noticed that the aqueous concentration of 1-chloro-1,1-difluoroethane that can be sustained in equilibrium with the current atmospheric concentration of 11 pptv (paragraph 3.1.6.) is extremely small (about $4 \cdot 10^{-6}$ µg/l). Furthermore, the aqueous solution at near the solubility limit of 2g/l is only sustainable under atmosphere of pure 1-chloro-1,1-difluoroethane.

3.2.3 Terrestrial Effects

No data are available on 1-chloro-1,1-difluoroethane

4 HUMAN HEALTH

4.1 HUMAN EXPOSURE

1-chloro-1,1-difluoroethane is a colorless gas with slight ethereal odour:

1 ppm (v/v) = 4.1 mg/m³ ; 1 mg/m³ = 0.24 ppm (v/v)

4.1.1 Occupational Exposure

Potential Exposures to 1-chloro-1,1-difluoroethane can occur as a result of loading / unloading, use as blowing agent for foams and, use as a refrigerant fluid. There are no reported data on measured occupational exposure concentrations on 1-chloro-1,1-difluoroethane. However limited survey of production and use in these application exposures with a closely related material, 1,1-dichloro-1-fluoroethane, were below 100 ppm (corresponding to 410 mg/m³ of 1,1-chloro-1,1-difluoroethane). This compares favorably with the occupational exposure guideline recommended by the American Industrial Hygiene Association and the German MAK of 1000 ppm (4200 mg/m³) as an 8-hr time weighted average for 1-chloro-1,1-difluoroethane.

4.1.2 Consumer Exposure

Other than its use in rigid foam insulation 1-chloro-1,1-difluoroethane is not used in consumer products. In rigid foam, loss is limited to a very slow diffusion resulting in levels below 1 ppb (0,004 mg/m³) and may lead to some very low human exposure.

4.1.3 Indirect Exposure via the Environment

1-chloro-1,1-difluoroethane does not accumulate in water as evidenced by its relatively low water solubility of 1.9 g/l and high vapor pressure of 339 kPa. It also has a low affinity for soil and with a $\log P_{ow}$ of 1.6- 2.05 would not be expected to show significant bioconcentration. It will thus partition into the air. Measured levels of 1-chloro-1,1-difluoroethane in the atmosphere were in the order of 11 pptv in 1998 (IPCC 2001). As 1-chloro-1,1-difluoroethane is scheduled for phase out beginning in 2003, even these levels will drop in the near future. Compared to its toxicity, these levels would not represent any concern. The highest exposure to humans via the environment is probably to be expected via air in the vicinity of industrial sites using the substance as a blowing agent.

4.2 EFFECTS ON HUMAN HEALTH

4.2.1 Mechanism of action and Toxicokinetics :

Studies in rats exposed by inhalation show that 1-chloro-1,1-difluoroethane is rapidly absorbed by the lungs. Analysis of selected tissues from rats and dogs exposed by inhalation for 13 weeks did not reveal the presence of 1-chloro-1,1-difluoroethane and no significant increase in inorganic fluoride in the urine was

observed (Kelly and Trochimowicz, 1976). This is consistent with a low metabolism of the molecule as indicated by physiologically based pharmacokinetics of uptake by inhalation in rats (Loizou et al, 1996). However Van Dyke (1977) observed a slight dechlorination *in vitro* after incubation of 1-chloro-1,1-difluoroethane with rat hepatic microsomes.

4.2.2 Acute Toxicity

With a rat 6h-LC50 higher than 400,000 ppm (>1,640,000 mg/m³), the acute toxicity of 1-chloro-1,1-difluoroethane is low (see following table). As 1-chloro-1,1-difluoroethane is a gas at ambient temperature no oral or dermal acute toxicity were determined.

Species	Exposure Duration	Exposure Concentration	Mortality	LC 50	Reference	Reliability
Rat	30 minutes	150,000 ppm 200,000 ppm 300,000 ppm 400,000 ppm 500,000 ppm	0/1 0/1 0/1 0/1 1/1	>400,000 ppm (>1,640,000 mg/m ³)	Lester and Greenberg, 1950	2d
Rat	4 hours	128,000 ppm	(2/6 to 4/6)	Approx 128,000 ppm (525,000 mg/m ³)	Carpenter et al, 1949	2d
Rat	6 hours	200,000 ppm 400,000 ppm	0/10 2/10	>400,000 ppm (>1,640,000 mg/m ³)	Mecler and Knapinski, 1978	1d

The target organs are the lungs with signs of irritation at autopsy observations, and the central nervous system, with anesthesia-like symptoms which are rapidly reversible after the end of exposure ((Lester and Greenberg, 1950; Mecler and Knapinski, 1978)

The CNS effects (loss of starting reflex) appear above 150,000 ppm (615,000 mg/m³) for a 30 minutes exposure. (Lester and Greenberg, 1950).

ACUTE CARDIAC SENSITIZATION:

Acute cardiac sensitization to the arrhythmogenic effects of adrenaline has been shown in an assay in unanesthetized dogs exposed during 5 minutes by inhalation, followed by an IV injection of adrenaline. The threshold concentration of 1-chloro-1,1-difluoroethane for cardiac arrhythmia induction by adrenaline was 25,000 ppm (102,500 mg/m³). The EC50 was about 50,000 ppm (205,000 mg/m³) (Reinhardt *et al*, 1971)(2e)

4.2.3 Skin irritation

There are no data available. However 1-chloro-1,1-difluoroethane is a gas at ambient temperature and testing it on skin is not relevant.

4.2.4 Eye irritation

In a study done by Brittelli (1976) on rabbit's eye undiluted liquified 1-chloro-1,1-difluoroethane did not induce effects on the cornea or iris but induced slight conjunctival swelling with some discharge. However, because the liquid boiled out of the eye immediately due to the so low boiling point (-9°C), the relevance of the result to human as 1-chloro-1,1-difluoroethane is poor.

4.2.5 Skin sensitization

There are no data available. However 1-chloro-1,1-difluoroethane is a gas at ambient temperature and testing it on skin is not relevant.

4.2.6 Effects in Animals Resulting from Repeat Exposures

Male and female rats and male dogs whole body exposed to atmosphere of 1-chloro-1,1-difluoroethane at concentrations of 1000 and 10000 ppm (4,100 and 41,000 mg/m³) for 6 h/d, 5 d/w, during 13 weeks, showed no treatment-related effects upon mortality, body weight, hematology, clinical chemistry, urinalysis or histopathological evaluation of selected tissues (Kelly and Trochimowicz, 1976) (1c).

Rats receiving exposures to atmosphere of 1-chloro-1,1-difluoroethane at concentrations up to 20000 ppm (82,000 mg/m³) for 6 h/d, 5 d/w during 104 weeks, showed no treatment-related effects upon mortality, body weight, hematology, clinical chemistry, urinalysis and opthalmological examinations, histopathological evaluation of selected tissues, or statistical analysis of neoplasms incidences. Non-neoplastic microscopic pathology findings at final sacrifices were similar in treated and control groups and were confined to degenerative lesions typical of old rats of the strain used in the study (Seckar et al, 1986) (1b).

Overall the NOAEL for repeat toxicity is higher than 10000 ppm (41,000 mg/m³) in dogs exposed for a period of 3 months and higher than 20000 ppm (82,000 mg/m³) in rats exposed for a period of 2 years.

4.2.7 Effects in Animals on Reproductive Capabilities

There are no standard reproductive toxicity tests available on 1-chloro-1,1-difluoroethane. However direct effects on the male and female organs were examined in three different studies where animals were repeatedly exposed by inhalation to high concentrations of this substance. Results from these 3 studies have shown that 1-chloro-1,1-difluoroethane tested by inhalation at concentrations ranging from 1000 to 20000 ppm (4,100 to 82,000 mg/m³) has no effect on the fertility of male rats repeatedly exposed during 15 weeks up to 20000 ppm (82,000 mg/m³) in a Dominant Lethal assay (Schroeder and Reinhardt, 1980) (2e); it has not induced any lesion to any of the reproduction-related tissues of male dogs repeatedly exposed during 13 weeks up to 10000 ppm (41,000 mg/m³) in a sub-chronic toxicity study (Kelly and Trochimowicz, 1976) (1c); and it has not induced any lesion to any of the reproduction-related tissues of male and female rats repeatedly exposed during two years up to 20000 ppm (82,000 mg/m³) in a two-year chronic toxicity study (Seckar et al, 1986) (1b).

The overall conclusion is that the experimental evidence available for 1-chloro-1,1-difluoroethane does not indicate effects on reproductive organs. However, no experimental data on reproductive/fertility effects has been located except for a negative dominant lethal assay in rats. As 1-chloro-1,1-difluoroethane was also tested for developmental toxicity in rats (see section 4.2.4), it appears that the “reproductive toxicity” of this substance has been adequately covered and does not need specific standard testing.

4.2.8 Effect in Animals on Developmental Toxicity

Two developmental toxicity studies have been performed and reported in the initial assessment report. Pregnant female rats were exposed 6 h/d, from day 3 to 15 or 6 to 15 of pregnancy, to airborne concentrations of 1-chloro 1,1-difluoroethane at concentrations ranging from 1000 (4,100 mg/m³) to 10000 ppm (41,000 mg/m³). No treatment related effects were reported on the pregnant dams at all test levels. In one study (Damske et al, 1978 – 2g), an increased incidence of delayed ossification of supraoccipital bone in both exposure levels was seen. The authors considered these findings as usual in the strain of rats used in their laboratory and concluded that they were not compound-induced. Furthermore such finding was not observed in the second study (Cullik and Kelly, 1976 – 1b). In both studies there was no evidence of teratogenesis or embryotoxicity or inhibition of fetal growth and development. Consequently NOAEL for developmental toxicity and maternal toxicity were higher than 10,000 ppm (41,000mg/m³).

4.2.9 Genotoxicity

4.2.9.1 Genotoxicity and cell transformation *in vitro*

in vitro testing

Assay	Result	Testing conditions for positive result	Reference	Reliability
Ames test	-S9: positive +S9: positive	TA 1535 and TA100 Conc. 100 % in air/1 h-72 h (4,100,000 mg/m ³)	Jaganath and Brusik, 1977	2c
Ames test	-S9: negative +S9: negative	TA 98, TA100, 1535, TA 1537, TA 1538 Conc. Up 40 % in air/6 h (1,640,000 mg/m ³)	Barsky and Buterworth, 1976	2c
Ames test	-S9: positive +S9: positive	TA 1535 Conc. 30 % in air/48 h (1,230,000 mg/m ³)	Koops and Krahn, 1977	2c
Ames test	-S9: positive +S9: positive	TA 1535 and TA100 Conc. 50 % in air/24 h (2,050,000 mg/m ³)	Longstaff et al, 1984	2c
BHK21 cell transformation	Positive	Liquid phase exposure Conc. Not stated	Longstaff et al, 1984	2c
BALB/3T3 cell transformation	Negative	Gaseous phase exposure Conc. Not stated	Matheson and Brusik, 1978	2c

The results of 4 separate Ames tests conducted on 1-chloro-1,1-difluoroethane vapors indicate that the material produced a mutagenic activity in Salmonella Typhimurium TA 1535 and TA 100 strains with, as well as without metabolic activation by S9 mix rat

microsomes. Concentrations as high as 30 % or more of the gas in air and a sufficient time exposure (24 hours or more) were generally needed to get positive effects. The increase in revertant colony number over the control values remained small with TA 100 (never more than 3 times control value, even with 100% gas exposure – 4,100,000 mg/m³). With TA 1535 values tended to remain low (less than 4 times control value) up to 50% gas exposure (2,050,000 mg/m³); only the 100% (4,100,000 mg/m³) concentration exposure gave large excess of revertant colony number over the control (44 times control value).

In addition two cell transformation assays were conducted on 1-chloro-1,1-difluoroethane. One was poorly reported and gave a positive result (exposure in liquid phase). The other gave a negative result (exposure in gaseous phase). Overall, it is not possible to derive any firm conclusion about the cell transforming potential of the compound.

4.2. 9.2 Genotoxic Effects in Animals

In vivo testing

Assay	Result	Testing conditions for positive result	Reference	Reliability
Bone marrow chromosome aberration in rats	Negative	90 day inhalation exposure 6 h/d, 5 d/w up to 20000 ppm (82,000 mg/m ³)	Rusch and Hogan, 1983; Seckar et al, 1985	1a
Dominant Lethal assay in rats	Negative	15 week inhalation exposure 6 h/d, 5 d/w up to 20000 ppm (82,000 mg/m ³)	Schroeder and Reinhardt, 1980	1a

1-Chloro-1,1-difluoroethane did not demonstrate statistically significant chromosomal aberration activity in a 90 day-inhalation bone marrow cytogenic study in male rats exposed to airborne concentrations ranging from 1000 (4,100 mg/m³) to 20000 ppm (82,000 mg/m³), 6 h/d, 5 d/w. A slight, but not statistically significant, increase in the mitotic rate was noted but was not considered to be an exposure-related adverse response. There were no increases in the numbers of chromosome gaps. Increased numbers of chromosome breaks were seen at all exposure levels and were accompanied by an increased incidence of acentric fragments at the 20,000 ppm exposure level. These intergroup differences were neither statistically significant nor dose-related.

In a Dominant Lethal assay, male rats were exposed by inhalation to 1-chloro-1,1-difluoroethane at concentrations of 1000, 10000 and 20000 ppm (4,100 , 41,000 and 82,000 mg/m³ respectively) for a 15 week-treatment period and subsequently mated with untreated females. The results were considered to show negative dominant lethal mutagenicity.

4.2. 9.3 Genotoxicity overall conclusion

1-Chloro-1,1-difluoroethane has shown positive effect in the Ames test on *Salmonella typhimurium* TA 1535 and TA 100 with as well as without metabolic activation and gave equivocal results in cell transformation assays. However 1-chloro-1,1-difluoroethane has shown two negative *in vivo* assays in a Dominant Lethal and in a Bone Marrow Cytogenetic assay in rats exposed during 15 and 13 weeks respectively.

It should be noticed that such a genotoxicity picture is common to other 1,1,1 trihaloethanes. Indeed 1,1-dichloro-1-fluoroethane – HCFC 141b- (IPCS 1992; Millischer *et al* 1995) and 1,1,1-trichloroethane – T-111- (ATSDR, 1995) also show:

- occasional positive Ames test in *Salmonella typhimurium TA 1535 and TA 100* with, as well as without metabolic activation,
- negative *in vivo* mutagenicity tests,
- and no induction of malignant tumours in long term rat studies.

4.2.10 Carcinogenic Effects in Experimental Animals

Rats exposed by inhalation in a lifetime study to concentrations of 0, 1000, 10000 and 20000 ppm (4,100 , 41,000 and 82,000 mg/m³ respectively) 6 h/day 5 days/wk showed no treatment-related effects upon mortality, body weight, hematology, clinical chemistry, urinalysis and opthalmological examinations, histopathological evaluation of selected tissues, or statistical analysis of neoplasms incidences. Neoplastic findings in animals that died during the study or in survivors to termination were similar in control and all exposed groups, and comprised predominantly tumors of the mammary and subcutaneous tissues in females, and pituitary and adrenal adenomas in both sexes. No treatment-related increases in tumors of the respiratory tract were noted. (Terril and Hogan, 1983) (1b) (Seckar et al, 1986 (1b)

5 CONCLUSIONS AND RECOMMENDATIONS

5.1 CONCLUSIONS

Environment

The majority of 1-chloro-1,1-difluoroethane will enter the air compartment. It will then be broken down in the lower atmosphere by hydroxyl radicals to yield fluorhydric acid and carbon dioxide. The global atmospheric lifetime of 1-chloro-1,1-difluoroethane is 18.5 years corresponding to a 1/2-lifetime of 12.8 years. It has a stratospheric ozone depletion of 0.065, a global warming potential of 1800. Its Contribution to the greenhouse effect is extremely small i.e. 0.00108 W/m² from IPCC 1995 data.

In water, 1-chloro-1,1-difluoroethane is not readily biodegradable under aerobic condition (about 5 % of biodegradation after 28 days). Bioaccumulation is not a concern because of its low log K_{ow} of 1.64- 2.05.

1-Chloro-1,1-difluoroethane has a low acute toxicity to fish and daphnia, the lowest available LC 50 being higher than 100 mg/liter. No acute toxicity tests are available for algae. Algae appear to be more sensitive than fish and daphnids to 1-chloro-1,1-difluoroethane with a calculated 96h EC₅₀ of 45mg/l.

From this results, a PNEC of 45 µg/l is proposed applying a factor of 1000 to the lowest figure obtained from the QSAR for algae (45 mg/l).

Human Health

Acute toxicity of 1-chloro-1,1-difluoroethane is low in rats. However high sub-lethal concentrations can induce pulmonary irritation and reversible Central Nervous System depressing effects of anesthetic type in rats. It can also induce reversible cardiac sensitization in dogs. Consequently, 1-chloro-1,1-difluoroethane may be hazardous to humans in case of accidental exposure to high concentrations occurring in confined area where replacement of air by the gas could at the same time reduce oxygen in the atmosphere.

In repeated inhalation exposure studies, 1-chloro-1,1-difluoroethane did not induce specific chronic toxicity in rats and dogs. No target organs were identified and the NOAELs were higher than 10,000 ppm (41,000 mg/m³) in dogs (90 day study) and higher than 20,000 ppm (82,000 mg/m³) in rats (2 year study) which were the highest tested concentrations.

In a combined inhalation lifetime chronic toxicity/carcinogenicity study 1-chloro-1,1-difluoroethane did not show any carcinogenic effect. In genotoxicity studies, 1-chloro-1,1-difluoroethane has shown positive results in the Ames test and equivocal results in a cell transformation assay. However, a dominant lethal assay and a Bone Marrow cytogenetic assay in rats were negative suggesting that 1-chloro-1,1-difluoroethane does not present a genotoxic hazard to man. No effect on male fertility has been shown in the Dominant Lethal assay and no toxic effects have been seen in sexual organs of male dogs, and male and female rats exposed repeatedly to 1-chloro-1,1-difluoroethane. Also the gas did not induce teratogenic or embryo/foetotoxicity effect in the rat and no maternal toxicity.

5.2 RECOMMENDATIONS

Environment

Low Priority for further work. It is subject to withdrawal under international activity (Montreal protocol).

Human Health

Low priority for further work. It is subject to withdrawal under international activity (Montreal protocol).

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1-CHLORO-1,1-DIFLUOROETHANE
CAS Reg no. 75-68-3

1. PHYSICAL/CHEMICAL PROPERTIES

1.1 MELTING POINT

TEST SUBSTANCE

- Identity : **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method/guideline followed (include calculated as one of the possible methods) : NR
- GLP (Y/N) : NR
- Year (study performed) : NR
- Remarks field for Test Conditions (Detail and discuss any significant protocol deviations.)

RESULTS

- Melting point value in °C (include <0°C as an acceptable answer) : **- 130.8**
- Decomposition
- Sublimation: NA (gas)
- Remarks field for Results (Describe additional information that may be needed to confirm data reliability and relevance)

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag for key study) : **2g**

REFERENCES

ECETOC: JACC 17, chlorodifluoromethane (1-chloro-1, difluoroethane; HFA 142b)(February 1991).

Handbook of environmental fate and exposure data for organic chemicals (volume II): Howard P.H., (1990), 110.

1.2 BOILING POINT

TEST SUBSTANCE

- Identity : **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method/guideline followed (include calculated as one of the possible methods) : NR
- GLP (Y/N) : NR
- Year (study performed) : NR
- Remarks field for Test Conditions (Detail and discuss any significant protocol deviations.)

RESULTS

- Boiling point value in °C : **- 9.2**
- Pressure : *1030hPa*
- Decomposition (yes/ no /ambiguous)

- Remarks field for Results (Describe additional information that may be needed to confirm data reliability and relevance)

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag for key study) : **2g**

- Remarks field for Data Reliability

REFERENCES

ECETOC : JACC 17, chlorodifluoromethane (1-chloro-1, difluoroethane; HFA 142b) (February 1991).

Handbook of environmental fate and exposure data for organic chemicals (volume II) : Howard P.H., (1990), 110.

1.3 VAPOUR PRESSURE

TEST SUBSTANCE

- Identity : **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method/guideline followed (include calculated as one of the possible methods) : NR
- GLP (Y/N) : NR
- Year (study performed) : NR
- Remarks field for Test Conditions (Detail and discuss any significant protocol deviations.)

RESULTS

- Vapor Pressure value (include $<1 \times 10^{-5}$ kPa as an acceptable answer) : **339 kPa**
- Temperature °C : 20
- Decomposition (yes/no/ambiguous)
- Remarks field for Results (Describe additional information that may be needed to adequately)

CONCLUSIONS

- Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag for key study) : **2g**
- Remarks field for Data Reliability key

REFERENCES

ECETOC : JACC 17, chlorodifluoromethane (1-chloro-1, difluoroethane; HFA 142b) (February 1991).

Handbook of environmental fate and exposure data for organic chemicals (volume II) : Howard P.H., (1990), 110.

1.4 PARTITION COEFFICIENT**1.4.1**

TEST SUBSTANCE

- Identity : **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method/guideline followed (include calculated as one of the possible methods) : *calculated according to Hansch and Leo, AJ method*
- Remarks field for Test Conditions (Detail and discuss any significant protocol deviations.)

RESULTS

- Log K_{ow} : **1.64**
- Temperature °C
- Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use. In particular note if compound is surface active, dissociative, insoluble in water, etc.)

CONCLUSIONS

- Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag for key study)
- Remarks field for Data Reliability key

REFERENCES : Hansch, C., and Leo, A.J. 1979 (1979) Substituent Constants for correlation Analysis in Chemistry and biology.

1.4.2

TEST SUBSTANCE

- Identity : **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

Method/guideline followed (include calculated as one of the possible methods) : *calculated using KOWWIN program (Syracuse Research Corporation)*

SMILES : FC(F)(CL)C
 CHEM : Ethane, 1-chloro-1,1-difluoro-
 MOL FOR: C2 H3 CL1 F2
 MOL WT : 100.50

TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	-CH3 [aliphatic carbon]	0.5473	0.5473
Frag	1	C [aliphatic carbon - No H, not tert]	0.9723	0.9723
Frag	1	-CL [chlorine, aliphatic attach]	0.3102	0.3102
Frag	2	-F [fluorine, aliphatic attach]	-0.0031	-0.0062
Const		Equation Constant		0.2290
			Log Kow =	2.0526

RESULTS

- LogKow : 2.05

1.5 WATER SOLUBILITY

TEST SUBSTANCE

- Identity: **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method/guideline followed (include calculated as one of the possible methods) : NR
- GLP (Y/N)
- Year (study performed)
- Remarks field for Test Conditions (Detail and discuss any significant protocol deviations.)

RESULTS

- Value (mg/L) at 25°C : **1900**
at 20°C : **1400**
- Description of solubility (e.g., miscible to soluble to not soluble)
- pH value : NA
- pKa value at 25 °C NA
- Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use.)

CONCLUSIONS

- Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag for key study) : **2g**
- Remarks field for Data Reliability key

REFERENCES

ECETOC: JACC 17, chlorodifluoromethane (1-chloro-1, difluoroethane; HFA 142b) (February 1991).

Handbook of environmental fate and exposure data for organic chemicals (volume II) : Howard P.H., (1990), 110.

2. ENVIRONMENTAL FATE AND PATHWAY

2.1 PHOTODEGRADATION

TEST SUBSTANCE

- Identity: 1-chloro, 1,1-difluoroethane (cas n° 75-68-3)

2.1.1 REACTION WITH THE ATMOSPHERIC OH RADICALS.

METHOD

- Principle of the method: OH radicals are generated from the photolysis of a precursor which can be H₂O, H₂O₂ or HNO₃. The concentration of the substance (i.e. 142b) is put in excess and considered constant during the experiment. The rate constant can be inferred from the rate of disappearance of the OH radical. In this experiment (Gierczak et al) OH is produced by photolysis of H₂O by a Xenon flash lamp in the 165-185 nm region or using 248 nm laser pulse photolysis of H₂O₂ or HNO₃. The temporal observation of the OH concentration is done by induced fluorescence from a pulse laser and follow up of the fluorescence signal from OH with a photomultiplier.

RESULTS:

- Rate constant of the reaction OH + 1-chloro-1,1-difluoroethane :

$$k = 2.95 \pm 0.25 \cdot 10^{-15} \text{ cm}^3 \text{ mol}^{-1} \text{ S}^{-1} \text{ at } 298 \text{ K}$$

$$k(T) = 1.14 \pm 0.26^{0.35} \cdot 10^{-12} \text{ Exp } (-1750 \pm 75/T)$$

OTHER EXPERIMENTAL WORK:

- Several other experimental studies have been carried out using different or similar techniques:
(R. Atkinson, 1994)

Preferred value :

$$k = 3.3 \cdot 10^{-15} \text{ cm}^3 \text{ mol}^{-1} \text{ S}^{-1} \text{ at } 298 \text{ K}$$

$$k(T) = 1.4 \cdot 10^{-12} \text{ Exp } (-1800 \pm 200/T) \text{ (NASA, JPL, 1992)}$$

2.1.2 ATMOSPHERIC LIFETIME OF 1-CHLORO-1,1-DIFLUOROETHANE.

METHOD OF DETERMINATION:

- **Tropospheric lifetime:**

The lifetime of 142b is calculated by scaling to the lifetime of methylchloroform i.e. 5.9 years for OH tropospheric removal on the basis of the rate constant with OH at 277 K. (WMO 1998).

- **Stratospheric lifetime:**

Inferred from a 2 dimensions atmospheric model using photolysis rate constant for 142b. (WMO 1991, 1994, 1998)

RESULTS:

- tropospheric lifetime = 19.5 years. (WMO 1998)
- Stratospheric lifetime = 372 years. (WMO 1998)
- Overall atmospheric lifetime = 18.5 years (WMO 1998).
corresponding to a 1/2 lifetime of 12.8 years.

2.1.3 ATMOSPHERIC DEGRADATION PRODUCTS OF 1-CHLORO-1,1-DIFLUOROETHANE.

METHOD

- Atmospheric chamber.

The substance is introduced in a chamber which can be flexible (teflon bag) or rigid (glass cylinder) of a volume from a few hundred liters to several cubic meters. After checking the absence of wall effects by monitoring the concentration of the substance in the dark, the chamber is submitted to UV light at wavelength higher than 300 nm. Depending on the reactivity of the substance, the oxidation can be started by reaction with chlorine atoms produced by photolysis of Cl_2 or by the OH radical. The degradation products are identified using FTIR (Fourier Transformed Infrared Spectroscopy) and Mass spectrometry.

RESULTS:

- The intermediate compounds identified are (Tuazon et al, 1994):

1st oxidation step: The aldehyde form of 142b: $\text{CF}_2\text{ClC}(=\text{O})\text{H}$

2nd oxidation step: $\text{C}(=\text{O})\text{F}_2$.

OTHER STUDIES.

- These results have been confirmed by other laboratory studies and methods. (Mörs et al, WMO 1991, 1994).

The fate of $\text{C}(=\text{O})\text{F}_2$ is known to undergo hydrolysis in atmospheric water to form HF and CO_2 . (WMO 1994 and 1998).

2.1.4 REACTION WITH STRATOSPHERIC OZONE.

METHOD:

- Atmospheric Modelling.

The chemical kinetic rate constant of the substance are introduced in a state of the art 2 dimension atmospheric model which reproduces atmospheric transport and atmospheric chemical processes in the stratosphere. A potential of the substance for ozone depletion is calculated by comparison of its impact on ozone with CFC11.

- Semi-Empirical calculation approach.

It consists in calculating the amount of chlorine atoms released in the stratosphere by the substance on the basis of measured atmospheric concentration profiles or inferred atmospheric concentration profiles for the locations where data are lacking. These results are weighted for the observed ozone depletion and integrated spatially and temporally over the stratosphere.

A potential for ozone depletion (ODP) is calculated by comparison with CFC11 (ODP CFC11=1).

RESULTS:

Model: ODP= 0.043 (WMO 1998)
 Semi-empirical: ODP= 0.066 (WMO 1998)
 Accepted value for the Montreal protocol: Semi-empirical ODP = 0.065 (WMO 1991)

2.1.5 CONTRIBUTION TO THE GREENHOUSE EFFECT.

METHOD:

- The contribution to the greenhouse effect can be calculated from atmospheric concentration and the radiative forcing properties of the substance inferred from an atmospheric radiative transfer model using the infra red absorption bands of the substance. The result is expressed in W/m^2 .
- The contribution to the greenhouse effect can also be calculated by multiplying quantities emitted to the atmosphere of a substance by its global warming potential (GWP). The global warming potential is calculated by comparing the integrated radiative forcing on a period of 100 years due to 1 kg of a substance emitted to the atmosphere with a similar calculation done with CO_2 which is the accepted reference. (IPCC 1990, 1995) The result is expressed in GWP.tonnes.

RESULTS:

- Contribution from atmospheric concentration in 1992: $0.00108 W/m^2$ to be compared with $1.52 w/m^2$ for CO_2 . (value from IPCC 1995)
- GWP (100) = 1800 (IPCC 1995)
 Production of 142b in 1996 = 38 Kt (AFEAS, 1996)
- Contribution of 142b to global warming: $6.8 \cdot 10^7$ GWP.tonnes to be compared with $2.6 \cdot 10^{10}$ GWP.tonnes for CO_2 (IPCC 1995)
- GWP values from IPCC 1995 are the accepted values for the Kyoto Protocol (Décision 2/CP.3 Methodological issues related to the Kyoto Protocol, FCCC/CP/1997/7/Add.1)

CONCLUSION.

The atmospheric fate of 142b has been vastly studied in the context of the Montreal Protocol and IPCC. The results above are a brief summary of those studies.

DATA QUALITY.

Those data correspond to the best existing scientific information and methods.

REFERENCES (for all section 2.1)

AFEAS, Production, Sales and Atmospheric Release of Fluorocarbons Through 1996.

Gierczak et al, Journal of Geophysical Research, Vol. 96, N°. D3; P. 5001-5011, March 20, 1991.

IPCC 1990, Climate Change 1990, The Science of Climate Change, Contribution of Working Group I to the second Assessment Report of the Intergovernmental Panel on Climate Change.

IPCC 1995, Climate Change 1995, The Science of Climate Change, Contribution of Working Group I to the second Assessment Report of the Intergovernmental Panel on Climate Change.

Mörs. V et al, Time resolved studies of intermediate products in the oxidation of HCFCs, Ber.Bunsenges. Phys. Chem. 100, 540-552 (1996) N°2.

R.Atkinson Gas phase Tropospheric Chemistry of Organic compounds J.Phys.chem. Monography N° 2, 1994

Tuazon, E.C., and Atkinson R, Products of the tropospheric reactions of hydrochlorofluorocarbons (HCFCs-225ca -225cb -141b and -142b, Env.Science and Technology, 1994.

WMO 1991, scientific assessment of Ozone Depletion, World Meteorological Organization, Global Ozone Research and Monitoring Project- Report N°. 27.

WMO 1994 Scientific assessment of Ozone Depletion, World Meteorological Organization, Global Ozone Research and Monitoring Project- Report N°. 37.

WMO 1998, scientific assessment of Ozone Depletion, World Meteorological Organization, Global Ozone Research and Monitoring Project- Report N°. 44.

Research and Monitoring Project- Report N°. 44.

2.2 STABILITY IN WATER

- No studies located

2.3 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

2.3.1

- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Test (test type) : *Fugacity model level 1 of Mackay ()*
- Detail the model used (title, version and date) : *Nord base*
- input parameters (chemical-specific, environmental conditions) as necessary :
 temperature : 25°C
 molecular weight : 100,47
 Vapor pressure (Pa) : 339000
 Solubility (g/m³) : 1900
 Henry's law constant (Pa.m³/mol) : 17925.96
 LogPow : 1.64
 Amount of chemical (mole) : 1

RESULTS

Estimated distribution between environmental compartment

Compartment	%
Air	99.98
Water	0.02
Soil	0.5610-4
Sediment	0.5 10-4

CONCLUSIONS

When released to the atmosphere, 1-chloro, 1,1-difluoroethane will partition almost exclusively into the atmosphere

REFERENCES: ATOFINA 2001 (unpublished internal report)

2.3.2

TEST SUBSTANCE

- Identity : **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**

METHOD

- Test (test type) : *Fugacity model level 1 of Mackay ()*
- Detail the model used (title, version and date) : *Nord base*
- input parameters (chemical-specific, environmental conditions) as necessary :
 - temperature : 25°C
 - molecular weight : 100,47
 - Vapor pressure (Pa) : 339000
 - Solubility (g/m³) : 1900
 - Henry's law constant (Pa.m³/mol) : 17925.96
 - Log Kow: 2;05
 - Amount of chemical (mole) : 1

RESULTS

Estimated distribution between environmental compartment

Compartment	%
Air	99.98
Water	0.02
Soil	0.14 10 ⁻³
Sediment	0.13 10 ⁻³

CONCLUSIONS

When released to the atmosphere, 1-chloro, 1,1-difluoroethane will partition almost exclusively into the atmosphere

REFERENCES: ATOFINA 2001 (unpublished internal report)

2.4 BIODEGRADATION

TEST SUBSTANCE

- Identity: **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Purity: 99,9%

METHOD

- Method/guideline followed: *OECD 301 B (modified Sturm test)*
- Test Type (test type/aerobic/anaerobic) : *aerobic*
- GLP (Y/N) : *Yes*
- Year (study performed) : *1990*
- Contact time (units): *42 days*
- Inoculum :
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations
Due to the volatility of the substance, 2 liter glass bottles closed with a plastic screw cap were used for the test. A 20 ml glass vial containing the CO₂ absorbing fluid was suspended from the screw cap in each bottle
- Inoculum (concentration and source) : *30 mg of solid substance per liter*

Fresh activated sludge: from an oxidation ditch used to treat domestic sewage

- Concentration of test chemical: 25 and 50 mg/l (nominal concentration)
- Temperature of incubation: 20± 2°C
- Dosing procedure :
- Sampling frequency : CO₂ absorption vials were replaced by fresh ones after 7, 14, 21, 28 and 42 days
- Appropriate controls and blank system used: Triplicate control bottles containing Sturm and ISO medium but no test substance were used to determine the background CO₂ production by the inoculum.
The inoculum activity was tested using sodium acetate.
The possible toxic effect of the substance to the inoculum was also tested in bottle containing both the test substance and sodium acetate.
- Analytical method used to measure biodegradation : titration of CO₂ with 0.1M HCl.
- Method of calculating measured concentrations ., arithmetic mean, geometric mean, etc.)

RESULTS

- Degradation : 5.6 and 4.4 % after 28 days for the low and high concentration respectively
- Kinetic (for sample, positive and negative controls)
- For each time period %
- Breakdown products (yes/no) If yes describe breakdown products and whether they were transient or stable in the Remarks field for Results.
- Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use, e.g. lag time, observed inhibition, excessive biodegradation, excessive standard deviation, kinetics, time required for 10% degradation and total degradation at the end of the test.)

CONCLUSIONS

- Under the above experimental conditions, 1-chloro, 1,1-difluoroethane was not readily biodegradable.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : **2e** (some reservation on the choice of the protocol : too high quantity of microorganism in the non aerated closed tests flasks)
- Remarks field for Data Reliability

REFERENCES

Matla, Y.A. and Blom A.J.M, (1991) Biodegradability of FC 142b according to OECD 301B (modified Sturm test). Report N° 90/307 DUPHAR B.V.

3. ECOTOXICITY PROPERTIES

3.1 ACUTE TOXICITY TO FISH

TEST SUBSTANCE

- Identity: **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Purity: > 99.99 %
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method/guideline followed (experimental): *OECD guideline 203 (1984) and EPA guidelines 72-1 (1982)*
- Type (test type) : *Acute toxicity to fish*

GLP (Y/N) : Y

- Year (study performed) : *1990*
- Species/Strain/Supplier: *Poecilia reticulata*
- Analytical monitoring: *yes*
- Exposure period (unit) : *96 hours*
- Statistical methods: *probit analysis model (program PROBIT of SPSS-X, version 2.2,1986)*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations, and detail differences from the guideline followed including the following as appropriate:
Because of the volatility of the substance, sealed glass containers were used.
A few deviations of the experimental protocol were observed during the study:
 - *A 22 liter aluminium bag was used to prepare the stock solution instead of a 20 liter bag as stated in the protocol*
 - *The analyses were conducted within 24 hours but not on the same day*
 - *As not enough fish of the appropriate size were available only 4 fish per test vessel were used instead of 5*
 - *The mean measured test concentrations were based on the samples of 1, 24, 48, 72 and 96 hours. According to the protocol they should have been based on samples of 24, 48, 72 and 96 hours.*
- Test fish (Age/length/weight, loading, pretreatment): *guppies (Poecilia reticulata) 2 to 3 cm long with a mean weight of 0.6 gram, fed with Tetramine, hold in 2 aquaria containing 36 liter of ISO water continuously filtered and aerated.*
- Details of test (static, semi-static, flow-through) : *semi-static (renewal each 24 hours)*
- Dilution water source: *ISO water*
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity) :
Hardness (CaCO₃): 250 mg/l
pH : 7.8
- Stock and test solution and how they are prepared: Concentrations dosing rate, flow-through rate, in what medium:
A stock solution containing 1059 mg of HCFC 142b per liter ISO water was prepared in a 22 liter aluminium bag coated with teflon at the inside
- stability of the test chemical solutions
- Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment) :
3200 ml
test flasks completely filled with ISO water and tightly closed with aluminium stoppers with rubber septum.
Renewal of the test solutions each 24 hours

- Number of replicates, fish per replicate: *8 fish per concentration using 2 replicates of 4.*
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed
pH variations : around 7 over 28 days in the control and test samples
Dissolved oxygen: below 5 mg/l at high concentrations (170 et 300mg/l)
- Test temperature range: $22 \pm 1^\circ\text{C}$

RESULTS

- Nominal concentrations (as mg/L) : 0, 30, 53, 94, 170, 300
- Measured concentrations (as mg/L) : 0, 33, 56, 106, 189, 321 (*mean measured concentrations*)
- Unit (results expressed in what unit) : mg/l
EC50 = 220 mg/l at 96 hours based on the mean measured concentrations
NOEC = 110 mg/l based on the mean measured concentrations
- Statistical results: *95 % confident interval: 190 - 310 mg/l*
- Remarks field for Results. Discuss if element effect concentration is greater than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:

- *Biological observations**Mortality of guppies:*

Nominal test concentration mg/l	Measured test concentrations mg/l	N° dead guppies per test vessel				N° guppies tested	Mortality (%) at 96 hours
		24	48	72	96		
Control	Control	0	0	0	1	8	13
30	33	0	0	0	0	4	0
53	56	0	0	0	0	8	0
94	106	0	0	0	0	8	0
170	189	1 ¹⁾	0	0	0 ³⁾		13
300	321	8 ²⁾	0	0		8	100

1) One fish showed uncontrolled movement

2) Four fish were dead within 5 hours after initiation

3) Two fish showed loss of equilibrium

CONCLUSIONS

Based on this key study, 1-chloro, 1,1-difluoroethane is of low toxicity to fish.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') 2e (4 fish instead of 5 ; too low oxygen concentration at high dose tested) **Key study**

REFERENCES

Groeneveld, A.H.C. and Kuijpers, L.A.M., (1990) The Acute Toxicity of 1-chloro-1,1-difluoroethane (HCFC 142b) to the Guppy *Poecilia Reticulata*. Report N° 56635/33/90 DUPHAR B.V.

3.2 TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

TEST SUBSTANCE

- Identity : **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
No experimental data are available

METHOD

A 96h EC 50 of 45 mg/l has been estimated using the ECOSAR program.

SMILES : CC(F)(CL)F
 CHEM : F142b
 CAS Num: 75-68-3
 MOL FOR: C2 H3 CL1 F2
 MOL WT : 100.50
 Log Kow: 2.05 (User entered)
 Wat Sol: 397.3 mg/L (calculated)

RESULTS

ECOSAR Class(es) Found

 Neutral Organics

Predicted

ECOSAR Class	Organism	Duration	End Pt	mg/L (ppm)
Konemann Equation	: Fish (guppy)	14-day	LC50	122.067
Neutral Organics	: Daphnid	48-hr	LC50	71.887
Neutral Organics	: Daphnid	16-day	LC50	9.123
Neutral Organics	: Daphnid	16-day	EC50	3.768
Neutral Organics	: Fish	14-day	LC50	122.067
Neutral Organics	: Fish (SW)	96-hr	LC50	15.691
Neutral Organics	: Fish	96-hr	LC50	66.857
Neutral Organics	: Fish		ChV	8.683
Neutral Organics	: Green Algae	96-hr	EC50	45.071
Neutral Organics	: Green Algae		ChV	4.639
Neutral Organics	: Mysid Shrimp	96-hr	LC50	18.606
Neutral Organics	: Earthworm	14-day	LC50	596.690 *

Note: * = asterick designates: No Effect at Saturation.

CONCLUSION

This QSAR result shows a moderate toxicity of 1-chloro, 1,1-difluoroethane to the algae.

REFERENCES : ATOFINA 2001 : unpublished internal report

3.3 ACUTE TOXICITY TO AQUATIC INVERTEBRATES (E.G., DAPHNIA)**3.3.1 Acute toxicity to *Daphnia* : DUPHAR study****TEST SUBSTANCE**

- Identity : 1-chloro, 1,1-difluoroethane (cas n° 75-68-3)
- Purity : > 99.9 %

METHOD

- Method/guideline followed (experimental/calculated) : OECD guideline 202(1984) and EPA Guideline 72-2 (EPA, 1982).
- Test type : *Daphnia* acute toxicity 48h
- GLP (Y/N) : Y

- Year (study performed) : 1990
 - Analytical procedures : *Gas Chromatography*
 - Species/Strain : *Daphnia magna*
 - Test details (static, semi-static, dosing rate, flow-through rate, etc.) : *static*
 - Statistical methods: *program PROBIT of SPSS-X, version 2.2 (SPSS, 1986)*
- ⇒ Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate: *Because of the volatility of the substance, sealed glass containers were used. A few deviations of the Guidelines were necessary:*
- *preparation of test solutions*
 - *the immobile daphnids were not removed after 24 h because the flasks had to remain closed to avoid disappearance of the substance.*
 - *the pH and dissolved oxygen concentrations were measured in the ISO-water only and not in the tests substance for the same reason.*
- Test organisms source, supplier, any pretreatment, breeding method: *DUPHAR*
- B.V. laboratory culture in reconstituted water (ISO+). Daphnids are fed an algal suspension of chlorella pyrenoidosa and a yeast/Mikromin suspension*
- . Age at study initiation: *0-24 hours*
- Test conditions
- . Stock solutions preparation (vehicle, solvent, concentrations) and stability of the substance : *a stock solution containing 1059 mg of HCFC 142b per liter ISO was water prepared.*
 - . Test temperature range : *20 ± 1°C*
 - . Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): *320ml glass test flasks completely filled and tightly closed with aluminium stopper with rubber septum*
No aeration, no renewal of the test solutions.
 - . Dilution water source: *ISO*
 - . Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio)
pH : 7.8
hardness (CaCO₃) : 250 mg/l
 - . Lighting (quality, intensity and periodicity) : *16 hours a day with fluorescent lamps.*
 - . Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed
pH variations from 6.5 to 8 (at 48 h)
Dissolved oxygen : variations from 7.9 to 9 mg/l
- Element (unit) basis (i.e. immobilization) : *immobilisation*
 - Test design (number of replicates, individuals per replicate, concentrations): *30 daphnids per concentration using 3 replicates of 10. Immobilisation was checked after 15 minutes, 24 hours and 48 hours*
 - Method of calculating mean measured concentrations : *arithmetic mean measured concentrations*
In 1hour sample
 - Exposure period : *48 h*
 - Analytical monitoring : *Gas Chromatography with flame ionisation detector*
The mean response factor of all calibration was 1.85 with a coefficient of variation of 7 % (n=40 ; 3 calibration levels).

RESULTS

- Nominal concentrations : 30, 53, 94 , 170, 300 mg/l
- Measured concentrations : 33, 58, 106, 197, 348 mg/l (in 1h samples)
- Unit : mg/l
- EC50 : 160 at 48 hours
- NOEC : 106
- Statistical results : 95 % Confidence Interval : 70 – 200

- Biological observations

- Number immobilized as compared to the number exposed :

Nominal test Concentration mg/l	Measured test concentration mg/l	Number daphnids tested	Immobility at 48h %
		Control 32	22
		Test substance	
30	33	30	37
53	58	28	25
94	106	27	41
170	197	28	75
300	348	30	100

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

CONCLUSION

On the basis of this key study, 1-chloro,1,1-difluoroethane is of low toxicity to daphnia

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : **2e (because of the control mortality) Key study**

REFERENCES (Free Text)

Groeneveld, A.H.C. and Kuijpers, L.A.M., (1990) The Acute Toxicity of 1-chloro-1,1difluoroethane (HCFC 142b) to Daphnia Magna. Report N° 56635/32/90 DUPHAR B.V.

3.3.2 Acute toxicity to Daphnia : Haskell laboratory study

TEST SUBSTANCE

- Identity : **1-chloro, 1,1-difluoroethane (cas n° 75-68-3)**
- Purity : > 99.9 %

METHOD

- Method/guideline followed : *OECD guideline 202(1984) and EPA Guideline 72-2 (EPA,1982).*

- Test type : *Daphnia acute toxicity 48h*
 - GLP (Y/N) : Y
 - Year (study performed) : 1989
 - Analytical procedures : *Gas Chromatography*
 - Species/Strain : *Daphnia magna*
 - Test details (static, semi-static, dosing rate, flow-through rate, etc.) : *static*
 - Statistical methods: no *immobilisation at the highest concentration tested*
- ⇒ Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
Because of the volatility of the substance, sealed glass containers were used.
- preparation of test solutions
 - Test organisms
 - . source, supplier, any pretreatment, breeding method : *Haskell laboratory-bred stock*
 - . Age at study initiation: *0-24 hours*
 - Test conditions
 - . stock solutions preparation (vehicle, solvent, concentrations) and stability : *a stock solution containing 350 mg/l was prepared by bubbling the gas through the water.*
 - . Test temperature range : *19.7 to 19.8 °C*
 - . Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment):
250 ml glass test flasks filled with 200ml solution and sealed with Mininert caps. No aeration, no renewal of the test solutions.
 - . Dilution water source:
 - . Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio)
pH : 7.2
hardness (CaCO₃) : 83 mg/l
 - . Lighting (quality, intensity and periodicity) : *16 hours a day.*
 - . Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed
pH variations : from 7.2 to 7.8
Dissolved oxygen : variations from 6.7 to 8.6 mg/l
D.O. and pH were measured in H₂O control and in the low, medium and high concentrations at the beginning, at 24 hours and at the end of the exposure.
 - Element (unit) basis (i.e. immobilization) : *immobilisation*
 - Test design (number of replicates, individuals per replicate, concentrations) : 20 daphnids per concentration using 2 replicates of 10. Immobilisation was checked after 24 hours and 48 hours
 - Method of calculating mean measured concentrations: *no immobilisation observed during the test*
 - Exposure period: *48 h*
 - Analytical monitoring: *Gas Chromatography using head space analysis*

RESULTS

- Nominal concentrations: no indication
- Measured concentrations (at the beginning and at the end of the test): *8, 14, 20, 40, 69, 110, 190 mg/l*
- EC₅₀ : *at 48 hours no immobilisation up to 190 mg/l.*
- Statistical results: -

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : **2e** (not enough documented)

REFERENCES

E.I. du Pont de Nemours and Company, Inc. (1989) Static Acute 48-hour EC50 of chlorodifluoroethane to Daphnia magna. Report N° 542-89 Haskell Laboratory for Toxicology and Industrial Medicine Newark, Delaware

4. HEALTH PROPERTIES

4.1 ACUTE TOXICITY

4.1.1 Acute inhalation toxicity :

4.1.1.1 Acute inhalation toxicity : Mecler and Knapinski study

TEST SUBSTANCE

- Identity

1-chloro 1,1-difluoroethane

CAS : 75-68-3

→ Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks)

The test material was « Aerosol Grade Isotron 142b » from Penwalt Corporation, presented as compressed form in a gas cylinder. Purity >99.5%

METHOD

- Method/guideline followed (experimental/calculated) : *experimental*
- Test type : *Acute inhalation toxicity*
- GLP : *No*
- Year (study performed) : *1978*
- Species/Strain : *Rat / Charles River CD*
- Sex : *males and females*
- No. Of animals per sex per dose : *5*
- Vehicle : *air*
- Route of administration (if inhalation – aerosol, vapor, gas, particulate) : *inhalation (gas)*

REMARKS field for Test conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate

- Age : *adult*
- Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail) : *200,000 ppm and 400,000 ppm (20% and 40% in air volume/volume respectively) = (820 mg/l and 1640 mg/l respectively)*
- Doses per time period : *dynamic exposure in a 27 liter glass exposure chamber*
- Volume administered or concentration : *20% and 40% in air volume/volume (820 mg/l and 1640 mg/l respectively)*
- Post dose observation period : *14 days*
- Exposure duration (for inhalation studies) : *6 hours*

RESULTS

- Value (LD50 or LC50) with confidence limits if calculated: *LC50/6h >400,000 ppm (>1640 mg/l)*
 - Number of death at each dose level:
 - *200,000 ppm : no death in males and females*
 - *400,000 ppm : male = 1/5 death ; female = 1/5 death*
- Remarks field for results. Describe additional information that may be needed to adequately assess data for reliability and use, including the following if available :
- Time of death (provide individual animal time if less than 24 hours after dosing):
death after 5h of exposure
 - Description, severity, time of onset and duration of clinical signs at each dose level :
 - *200,000 ppm : no signs*
 - *400,000 ppm : lethargy and labored breathing during exposure in all animals ; signs disappeared soon after discontinuing exposure*
 - Necropsy findings, included doses affected, severity and number of animals affected :
 - *200,000 ppm : dark and red mottling in all lobes of the lung in one male and one female*
 - *400,000 ppm : the 2 dead rats had dark red lungs and pale livers ; all surviving rats had dark red mottled lungs ; 3 rats had mottled kidney and one red spots in thymus*
 - Potential target organs (if identified in the report) : *lung,*
 - If both sex tested, results should be compared : *similar findings in males and females*

CONCLUSIONS

Exposure of rats for 6 hours to a test atmosphere of 200,000 of 1-chloro 1,1-difluoroethane produces no gross signs of toxicity or death. Three animals on necropsy showed signs of lung damage. Exposure of rats for 6 hours to a test atmosphere of 400,000 ppm of 1-chloro 1,1-difluoroethane produced lethargy, labored respiration and death in 20% of the exposed population. All animals on necropsy showed signs of lung damage. The LC50/6h was >400,000 ppm

Based on this key study, 1-chloro 1,1-difluoroethane is of low acute toxicity.

DATA QUALITY

Reliability (Klimisch Code, if used, possibly a flag if « key study ») : **1d -, Key study**
Well conducted study carried out by Litton Bionetics, Inc, Kensington, Ma, USA

→ Remark field for data availability

REFERENCES (Free text)

FJ Mecler and PJ Knapinski . « Acute inhalation toxicity study in rats. Isotron 142b ». Final report. Submitted to Penwalt Corporation, King of Prussia, Pennsylvania, 19406. Submitted by Litton Bionetics, Inc. Kensington, Maryland, 20795. LBI project NO 20888, February 1978

4.1.1.2 Acute inhalation toxicity : Lester and Greengerg study

TEST SUBSTANCE

- Identity

1-chloro 1,1-difluoroethane

CAS : 75-68-3

→ Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks)

There is no information on test material origin

METHOD

- Method/guideline followed (experimental/calculated)
experimental – screening method
- Test type: *Acute inhalation toxicity*
- GLP: *No*
- Year (study performed) : *1950*
- Species/Strain : *white rat (Strain not specified)*
- Sex: *not specified*
- No. Of animals per sex per dose : *1*
- Vehicle: *air/oxygen*
- Route of administration (if inhalation – aerosol, vapor, gas, particulate) : *gas*

REMARKS field for Test conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate

- Age: *adult*
- Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail) : *15, 20, 25, 30, 40, 50, 60, 70 ,80%*
- Doses per time period : *1l liter glass chamber ; static exposure*
- Volume administered or concentration : *15, 20, 25, 30, 40, 50, 60, 70 ,80%*
- Post dose observation period : *a few minutes*
- Exposure duration (for inhalation studies) : *30 minutes*

RESULTS

- Value (LD50 or LC50) with confidence limits if calculated: *>40%*
- Number of death at each dose level: *death occurred at concentration of 50% and above (single animal per test-concentration)*

→Remarks field for results. Describe additional information that may be needed to adequately assess data for reliability and use, including the following if available :

- Time of death (provide individual animal time if less than 24 hours after dosing) : *death occurred during the 30 minute exposure period*
- Description, severity, time of onset and duration of clinical signs at each dose level : *signs observed just after the 30 minute exposure period : lost of postural reflex at concentration of 20% ; lost of righting reflex at 25% ; lost of corneal reflex at 30%.*
- Necropsy findings, included doses affected, severity and number of animals affected: *effusion of fluid from the respiratory tract at 30%*
- Potential target organs (if identified in the report) : *lungs*
- If both sex tested, results should be compared : *not appropriate*

CONCLUSIONS

Rats exposed for 30 minutes by inhalation died at 1-chloro 1,1-difluoroethane concentrations of 50% and above. Signs of Central Nervous System depression were observed at concentration of 20% and above. Signs of lung irritation started at concentration of 30%.

These results, although not coming from a key-study, confirm the low acute toxicity of 1-chloro 1,1-difluoroethane as demonstrated in the Mecler and Napinski study – see above-.

DATA QUALITY

Reliability (Klimisch Code, if used, possibly a flag if « key study ») : *2d*

→ Remark filed for data availability

REFERENCES

Lester D and Greenberg LA (1950) – Acute and chronic toxicity of some halogenated derivatives of methane and ethane. Arch. Indust. Hyg. Occup. Med., 2, 335-344.

4.1.1.3 Acute inhalation toxicity : Carpenter *et al* study

TEST SUBSTANCE

- Identity

1-chloro 1,1-difluoroethane

CAS : 75-68-3

→ Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks)

There is no information on test material origin

METHOD

- Method/guideline followed (experimental/calculated)
experimental- screening method
- Test type : *Acute inhalation toxicity*
- GLP : *No*
- Year (study performed) : *1949*
- Species/Strain : *rat (Sherman strain)*
- Sex : *male or female*
- No. Of animals per sex per dose : *6*
- Vehicle : *air*
- Route of administration (if inhalation – aerosol, vapor, gas, particulate) : *gas*

REMARKS field for Test conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate

- Age : *young adult*
- Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail) : *128,000 ppm (12.8% in air)*
- Doses per time period : *9 liter glass chamber ; static exposure*
- Volume administered or concentration : *128,000 ppm (12.8% in air)*
- Post dose observation period : *14 days*
- Exposure duration (for inhalation studies) : *4 hours*

RESULTS

- Value (LD50 or LC50) with confidence limits if calculated : *ca 12.8% %*
- Number of death at each dose level : *the tested concentration of 12.8% induced either 2, 3 or 4 death among the six rats (exact number not stated)*

- Remarks field for results. Describe additional information that may be needed to adequately assess data for reliability and use, including the following if available :
- Time of death (provide individual animal time if less than 24 hours after dosing) :
time to death not stated
 - Description, severity, time of onset and duration of clinical signs at each dose

level : *signs not stated*

- Necropsy findings, included doses affected, severity and number of animals affected : *not stated*
- Potential target organs (if identified in the report) : ?
- If both sex tested, results should be compared: *not appropriate*

CONCLUSIONS

A 4 hour inhalation exposure at the concentration of 12.8 % of 1-chloro 1,1-difluoroethane induced mortality to rats ranging from 2/6 to 4/6. Based on this screening acute toxicity information, the authors classified 1-chloro 1,1-difluoroethane in their category « slightly toxic ».

These results, although not coming from a key-study, confirm the low acute toxicity of 1-chloro 1,1-difluoroethane as demonstrated in the Mecler and Napinski study – see above-.

DATA QUALITY

Reliability (Klimisch Code, if used, possibly a flag if « key study ») : 2d

→ Remark filed for data availability

REFERENCES

Carpenter CP, Smyth HF and Pozzani UC (1949) – The assay of acute vapor toxicity, and the grading and interpretation of results on 96 chemical compounds.

Journal of Industrial Hygiene and Toxicology, 31, 343-346.

4.1.1.4 Acute inhalation toxicity : Cardiac sensitisation study in dogs : Reinhardt *et al* study

TEST SUBSTANCE

- Identity

1-chloro 1,1-difluoroethane

CAS : 75-68-3

→ Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks)

The test material was of "commercial grade" from El DuPont de Nemours and Co. Purity >99.5%

METHOD

- Method/guideline followed (experimental/calculated) : *experimental*
- Test type : *Acute inhalation toxicity (dog cardiac sensitization assay)*
- GLP : *No*
- Year (study performed) : *1971*
- Species/Strain : *Dogs Beagle*
- Sex : *males*
- No. Of animals per sex per dose : *6 to 12*
- Vehicle : *air*
- Route of administration (if inhalation – aerosol, vapor, gas , particulate) : *inhalation (gas)*

REMARKS field for Test conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate

- Age : *adult – 18 to 26 month old*
- Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail) : *25,000 ppm, 50,000ppm and 100,000 ppm (2.5% , 5% and 10% in air volume/volume respectively) = (102 mg/l, 205 mg/l and 410 mg/l respectively)*

- Doses per time period : *dynamic exposure through gas mask in conscious trained dogs during 5 minutes before IV injection of 0.008 mg/kg adrenaline*
- Volume administered or concentration : *2.5% , 5% and 10% in air volume/volume*
- Post dose observation period : *continuous ECG recording during exposure and adrenaline injection*
- Exposure duration (for inhalation studies) : *5 minutes*

RESULTS

- Value (LD50 or LC50) with confidence limits if calculated : *threshold for cardiac arrhythmia induction = 25,000 ppm (102 mg/l)*
- EC50 = *about 50,000 ppm (205 mg/l)*
- Number of death at each dose level: *not applicable*
- Remarks field for results. Describe additional information that may be needed to adequately assess data for reliability and use, including the following if available:
 - Time of death (provide individual animal time if less than 24 hours after dosing): *no death at any concentration*
 - Description, severity, time of onset and duration of clinical signs at each dose level : *no signs at any concentration*
 - Necropsy findings, included doses affected, severity and number of animals affected : *not applicable*
 - Potential target organs (if identified in the report) : : *not applicable*
 - If both sex tested, results should be compared : : *not applicable*

CONCLUSIONS

Exposure of dogs for 5 minutes prior to adrenaline injection to a test atmosphere of 1-chloro-1,1-difluoroethane produced cardiac sensitization with a threshold concentration of 25,000 ppm (102 mg/l) and an EC50 of about 50,000 ppm (205 mg/l)

DATA QUALITY

Reliability (Klimisch Code, if used, possibly a flag if « key study ») : *1d -*,

→ Remark field for data availability

REFERENCES (Free text)

Reinhardt CF, Azar A, Maxfield ME, Smith PE and Mullin LS – "Cardiac arrhythmias and aerosol sniffing" Arch Environ. Health, 22, 265-279, 1971

4.1.2 Acute dermal toxicity :

As HCFC 142b is a gas at room temperature, testing by dermal route would be of poor relevance. Furthermore, such testing would pose practical difficulties for the administration to the animals. Dosing animals with the gas dissolved under pressure in a solvent or in the compressed liquified form would generate results of doubtful significance and, consequently, of poor practical usefulness.

Acute toxicity of HCFC 142b is already adequately qualified by the inhalation route testing (see above).

4.1.3 Acute oral toxicity:

As HCFC 142b is a gas at room temperature, testing by oral route would be of poor relevance. Furthermore, such testing would pose practical difficulties for the administration to the animals. Dosing animals with the gas dissolved under pressure in a solvent would generate results of doubtful significance and, consequently, of poor practical usefulness.

Acute toxicity of HCFC 142b is already adequately qualified by the inhalation route testing (see above).

4.2 SKIN IRRITATION

There are no data available on skin irritation.

As HCFC 142b is a gas at room temperature, skin application testing would be of poor relevance. Furthermore, such testing would pose practical difficulties for the administration to the animals. Dosing animals with the gas dissolved under pressure in a solvent or with the compressed liquified form would generate results of doubtful significance and, consequently, of poor practical usefulness.

4.3 EYE IRRITATION

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3

→ Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks)
The purity of the test material was 99.9 %

METHOD

- Method/guideline followed: experimental; *Draize type*
- GLP: *No*
- Year (study performed): *1976*
- Species/Strain: *Albino rabbit*
- Sex : *no stated*
- No. Of animals per sex per dose: *2*
- Vehicle: *none, undiluted liquified material*
- Route of administration: *deposition in the right conjunctival sac*

REMARKS

- Doses: *0.1 ml*
- Post dose observation period: *at 1 and 4 h , then at days one, two and five*
- Exposure duration: 20 seconds
- Procedure: *One treated eye not washed; one treated eye washed with 0.9% saline for one minute*

RESULTS

- Classification: *not irritant*
- Remarks field for results: *There were no effects on the cornea and on the iris. On the conjunctiva , minimal swelling at 1h and slight transient discharge observed in unwashed (1h-1d) as well as in washed eye (1d)
The substance produced practically no ocular effect in either the unwashed and the washed rabbit's eye. This could be due to the fact that the compound is so low boiling (-9°C) that it did not stay in the eye (compound boiled out of eye immediately).*

CONCLUSIONS

The substance is practically not irritating to the rabbit'eye

DATA QUALITY

Reliability (Klimisch Code, if used, possibly a flag if “ study »): 2c -,

REFERENCES (Free text)

Brittelli MR (1976) – Ethane, chlorodifluoro-(FC-142b) – Eye irritation test in rabbits.
EI – Du Pont de Nemours and Company, Haskel Laboratory Report N° 752-75, MR N° 2223-001, january 21, 1976

Source: Atofina, Paris La Defense, France.

4.4 SKIN SENSITIZATION

There are no data available on skin sensitization.

As HCFC 142b is a gas at room temperature, skin application testing would be of poor relevance. Furthermore, such testing would pose practical difficulties for the administration to the animals. Dosing animals with the gas dissolved under pressure in a solvent or with the compressed liquified form would generate results of doubtful significance and, consequently, of poor practical usefulness

4.5 GENETIC TOXICITY ELEMENTS

4.5.1 Genetic toxicity and related testing *in vitro*

4.5.1.1 Genetic toxicity *in vitro* : Litton Bionetics study

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3

- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
The test-material was presented as compressed form in a gas cylinder. The purity level was not stated.

METHOD

- Method/guideline followed *Ames / Salmonella mutation Plate assay*
- Type : *Reverse mutation assay*
- System of testing : *bacterial*
- GLP : *yes*
- Year : *1977*
- Strain : *Salmonella Typhimurium TA 98, TA100, TA1535, TA 1537 and TA 1538*
- Metabolic activation : *S9 Mix from Aroclor 1254 induced rat liver microsomes*
- Concentrations tested : *neat gas (although not stated, concentration was presumably 100% of the gaseous test material in special air tight chambers)*
- Statistical Methods : *not applicable*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate:

- Test Design

- Number of replicates : *one*
- Frequency of Dosing : *different plates exposed during variable periods : 1, 24, 48 and 72 hours*
- Positive and negative control groups and treatment : *yes*
- Solvent : *not applicable*
- Description of follow up repeat study : *not applicable*
- Criteria for evaluating results : *result positive if at least twice the control number of revertant Colonies in at least 3 time exposure periods*

RESULTS

- Result: *positive*

- Without metabolic activation: *positive in TA 1535 and TA 100*

Strain	TA1535	TA100
<i>Control</i>	<i>16</i>	<i>203</i>
<i>1h</i>	<i>29</i>	<i>214</i>
<i>24h</i>	<i>107</i>	<i>316</i>
<i>48h</i>	<i>700</i>	<i>490</i>
<i>72h</i>	<i>160</i>	<i>351</i>

- With metabolic activation : : *positive in TA 1535 and TA 100*

Strain	TA1535	TA100
<i>Control</i>	<i>30</i>	<i>235</i>
<i>1h</i>	<i>116</i>	<i>409</i>
<i>24h</i>	<i>322</i>	<i>484</i>
<i>48h</i>	<i>>1000</i>	<i>714</i>
<i>72h</i>	<i>434</i>	<i>672</i>

Remarks : *only one single concentration tested and test material concentration not measured, although presumed to be 100 %. The indicator organisms were exposed to the gas for different time periods such that there was either quantitative or qualitative evidence of some chemically induced physiological effect at the longest time period.*

CONCLUSIONS

Compound positive in the Salmonella/microsome Plate Assay at very high concentration.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : *Reliability code = 2c*
- Remarks field for Data Reliability:

REFERENCES (Free Text)

Jaganath DR and Brusick DJ – « Mutagenicity evaluation of Isotron 142b. Final Report ». Submitted to Penwalt Corporation , Buffalo, NY 14240, by Litton Bionetics, Inc, 5516 Nicholson Lane, Kensington, Maryland 20838, December, 1977

4.5.1.2 –Genetic toxicity *in vitro* : DuPont Haskell Lab.study**TEST SUBSTANCE**

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
No data. Purity level not stated.

METHOD

- Method/guideline followed *Ames / Salmonella mutation Plate assay*
- Type : *Reverse mutation assay*
- System of testing : *bacterial*
- GLP : *not stated*
- Year : *1976*
- Strain : *Salmonella Typhimurium TA 98, TA100, TA1535, TA 1537 and TA 1538*
- Metabolic activation : *S9 Mix from induced rat liver microsomes*
- Concentrations tested: *20 and 40% in air; measured by gas chromatography*
- Statistical Methods: *not applicable*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations.
Detail differences from the guideline followed including the following as appropriate: *exposure in a 9-litter gas chamber*

- Test Design

- Number of replicates: *one*
- Frequency of Dosing: *single 6 hours exposure*
- Positive and negative control groups and treatment: *yes*
- Solvent: *not applicable*
- Description of follow up repeat study: *not applicable*
- Criteria for evaluating results: *result positive if at least twice the control number of revertant Colonies*

RESULTS

- **Result** : *negative*
- With metabolic activation: *negative in all strains*
- Without metabolic activation: *negative in all strains*

Remarks: Prior to testing for mutagenicity, the tester strains were exposed to the test gas to determine any toxic effects. Exposure levels of 20% and 40% were chosen because they did not inhibit bacterial growth.

CONCLUSIONS

Compound negative in the Salmonella/microsome Plate Assay in strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 at concentrations of 20 and 40% in air with a 6 hour exposure..

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): *Reliability code = 2c*
- Remarks field for Data Reliability:

REFERENCES (Free Text)

Barsky, FC and Buterworth, BE – « In vitro microbial mutagenicity studies of ethane-chlorodifluoro. Report N° 322-76, Haskell Laboratory, DuPont de Nemours and Company April 26, 1976

4.5.1.3 –Genetic toxicity *in vitro* : Study by DuPont Haskell Lab 1977

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3

- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
No data. Purity level not stated.

METHOD

- Method/guideline followed *Ames / Salmonella mutation Plate assay*
- Type: *Reverse mutation assay*
- System of testing: *bacterial*
- GLP: *not stated*
- Year: *1977*
- Strain: *Salmonella Typhimurium TA 98, TA100, TA1535, TA 1537 and TA 1538*
- Metabolic activation: *S9 Mix from induced rat liver microsomes*
- Concentrations tested: *15, 30 an 50% in air; measured by gas chromatography)*
- Statistical Methods: *not applicable*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate:
exposure in 9-liter glass chambers
- Test Design
 - Number of replicates: *one*
 - Frequency of Dosing: *plates exposed during 48 hours*
 - Positive and negative control groups and treatment: *yes*
 - Solvent: *not applicable*
 - Description of follow up repeat study: *not applicable*
 - Criteria for evaluating results: *result positive if at least twice the control number of revertant Colonies*

RESULTS

- Result: *positive*

- With metabolic activation: *positive in TA 1535 ; negative in all other strains*

Test material concentration in air	TA1535, first trial Number of revertent colonies	TA 1535, second trial Number of revertent colonies
Control	15	15
15%	26	21
30%	36	32
50%	42	42

- Without metabolic activation: *positive in TA 1535, negative in all other strains*

Test material concentration in air	TA1535, first trial Number of revertent colonies	TA 1535, second trial Number of revertent colonies
Control	13	9
15%	15	14
30%	17	18
50%	27	29

Remarks : *Prior to testing for mutagenicity, the tester strain TA 1535 was exposed to the test gas to determine the general toxic range for all tester strains. Exposure in atmosphere that contains up to 50% of the compound did not inhibit bacterial growth.*

CONCLUSIONS

Compound is positive in strain TA 1535 in the Salmonella/microsome Plate Assay at a concentration of 30% to 50% and with 24h to 48h exposures.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : *Reliability code = 2c*
- Remarks field for Data Reliability:

REFERENCES (Free Text)

Koops A and Krahn DF – « Mutagenic activity of ethane-chlorodifluoro in the Salmonella/microsome assay ». Report N° 578-77, Haskell Laboratory, DuPont de Nemours and Company, August 5, 1977

4.5.1.4 –Genetic toxicity *in vitro* : Study by Longstaff *et al.*

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
No dat. Purity not stated

METHOD

- Method/guideline followed *Ames / Salmonella mutation Plate assay*
- Type: *Reverse mutation assay*
- System of testing: bacterial
- GLP: *not stated*
- Year: *1984*
- Strain: *Salmonella Typhimurium TA 98, TA100, TA1535 and TA 1538*
- Metabolic activation: *S9 Mix from Aroclor 1254 induced rat liver microsomes*
- Concentrations tested: *50% in air*

- Statistical Methods: *not applicable*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate: :
exposure in 1 or 5-liter glass reaction vessels

- Test Design

- Number of replicates: *not stated*
- Frequency of Dosing: *single 24 hours exposure*
- Positive and negative control groups and treatment: *yes*
- Solvent: *not applicable*
- Description of follow up repeat study: *not applicable*
- Criteria for evaluating results: *result positive if at least twice the control number of revertant Colonies*

RESULTS

- Result: *positive*
- With metabolic activation: *positive in TA 1535 (3.4 times control value) and TA 100 (2.8 control Value)*
- Without metabolic activation: *result not stated but presumably negative (see remark in Reference Section)*

Remarks: *only one single concentration reported; no data on test material concentration analysis. Cytotoxicity information was not provided.*

CONCLUSIONS

Compound is positive with metabolic activation in strains TA 1535 and TA 100 in the Salmonella/microsome Plate Assay at a high concentration (50%) after 24h exposure. It is negative without metabolic activation

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): *Reliability code = 2c*
- Remarks field for Data Reliability:

REFERENCES (Free Text)

Longstaff E, Robinson M, Brassbrook C, Styles JA and Purchase IF. « Genotoxicity and Carcinogenicity of Fluorocarbons : Assessment by Short-term in vitro Tests and Chronic Exposure in Rats » *Tox and Appl Pharmacol.*, 72, 15-31, 1984

Remark: *The results mentioned by Longstaff et al 1984 on 1-chloro-1, 1difluoroethane are apparently drawn from a testing report dated 1976 by Mc Gregor DB "Mutagenicity testing with Salmonella Tithgymurium strains on plates and gases, liquids and solids". Edimburgh, Inversek Research International (Report N° 513). That report was not available to us but was mentioned in the IPCS EHC N° 139 "Partially halogenated chlorofluorocarbons (ethane derivatives)", WHO Geneva, 1992. This IPCS document states on page 72 that the result of the Ames test without metabolic activation is **negative** under the reference Mc Gregor, 1976. Data shown under reference Mc Gregor, 1976 and under Longstaff et al, 1984 are strictly identical.*

4.5.1.5 Cell transformation *in vitro*: BHK21 Cell transformation assay

TEST SUBSTANCE

- Identity

1-chloro 1,1-difluoroethane

CAS : 75-68-3

- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

No data. Purity not stated

METHOD

- Method/guideline followed *Cell transformation (Styles) assay*
- System of testing: *Baby hamster kidney fibroblasts*
- GLP: *not stated*
- Year: *1984*
- Metabolic activation: *not stated*
- Concentrations tested: *not stated*
- Statistical Methods: *not applicable*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate: *exposure in liquid phase. No other details available*

- Test Design

- Number of replicates: *not stated*
- Frequency of Dosing: *not stated*
- Positive and negative control groups and treatment: *yes*
- Solvent: *not applicable*
- Description of follow up repeat study: *not applicable*
- Criteria for evaluating results: *result positive if transformation frequency is five fold in excess to control at the point where 50% cells are inhibited from growth*

RESULTS

- Result: *positive*

- With metabolic activation: *no stated*

- Without metabolic activation: : *not stated*

Remarks: the *published paper does not give any detail*

CONCLUSIONS

Compound is positive in the BHK 21 cell transformation assay under poorly described test conditions

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): *Reliability code = 3a*
- Remarks field for Data Reliability:

REFERENCES (Free Text)

Longstaff E, Robinson M, Brassbrook C, Styles JA and Purchase IF. « Genotoxicity and Carcinogenicity of Fluorocarbons: Assessment by Short-term *in vitro* Tests and Chronic Exposure in Rats » *Tox and Appl Pharmacol.*, 72, 15-31, 1984

4.5.1.6 Cell transformation *in vitro*: BALB/3T3 Cell transformation assay

TEST SUBSTANCE

- Identity

1-chloro 1,1-difluoroethane

CAS : 75-68-3

- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

No data. Purity not stated

METHOD

- Method/guideline followed *in vitro Cell transformation (Styles) assay*
- System of testing: *BALB/3T3 cell line*
- GLP: *yes*
- Year: *1978*
- Metabolic activation: *no*
- Concentrations tested: *neat gas (although not stated, concentration was presumably 100% of the gaseous test material in the gas flasks)*
- Statistical Methods: *not stated*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate: *exposure in gaseous phase. No other details available*

- Test Design

- Number of replicates: *10*
- Frequency of Dosing: *1, 2, 4, 6 and 24 hours*
- Positive and negative control groups and treatment: *yes*
- Solvent: *not applicable*
- Description of follow up repeat study: *not applicable*
- Criteria for evaluating results: *number of foci per set of replicate plates for each time exposure*

RESULTS

- Result: *negative*

Remarks: *lower than expected transforming effect with the positive control (3-methylcholanthrene)*

CONCLUSIONS

Compound was not active in this BALB/3T3 cell transformation assay as it did not produce any significant increase in the transformed clones compared to the untreated control .

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): *Reliability code = 2c*
- Remarks field for Data Reliability:

REFERENCES (Free Text)

Matheson DW and Brusick D. « Mutagenicity evaluation of Isotron 142B in the *in vitro* Transformation of BALB 3T3 cells assay». Final report Submitted to Penwalt Corporation King of Prussia Pennsylvania 19406, by Litton Bionetics, Inc, 5516 Nicholson Lane, Kensington, Maryland 20838,

4.5.2 Genetic toxicity *in vivo*

4.5.2.1 Genetic toxicity *in vivo* : Rat bone Marrow Cytogenetics Assay

TEST SUBSTANCE

- Identity

1-chloro 1,1-difluoroethane

CAS : 75-68-3

- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

The test-material was presented as compressed form in 8 gas cylinders and has a purity level of 99.9%

METHOD

- Method/guideline followed: *experimental*
- Type (test type): *in vivo bone-marrow cytogenetic assay*
- GLP (Y/N): *Yes*
- Year (study performed): *1980*
- Species: *rat*
- Strain: *Sprague-Dawley –CD Charles River*
- Sex: *male*
- Route of administration: *inhalation (gas) (dynamic exposure) (whole body exposure)*
- Doses/concentration levels: *0, 1000, 10000 and 20000 ppm*
- Exposure period: *13 weeks*
- Statistical methods: *for cytogenetic evaluation: Student's t-test and standard one way analysis of variance*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
 - Age at study initiation: *7 weeks*
 - No. of animals per dose : *10*
Vehicle : *air*
 - Duration of test : *13 week exposure*
 - Frequency of treatment : *6hours /day, 5 days /week*
 - Sampling times and number of samples : *within the 24h after the last exposure, Colcemid (4 mg/kg) was injected IP and bone marrow cells harvested 2 to 4 hours after the injection and processed for cytogenetic evaluation.*
 - Control groups and treatment: *0 (control) and 1000, 10000, 20000 ppm (treatment) 50 Metaphase scored by animal*
 - Clinical observations performed (clinical pathology, functional observations, etc.) : *mortality, clinical signs, body weights*
 - Organs examined at necropsy (macroscopic and microscopic) : *gross necropsy on main organs/tissues; microscopic examens on bone-marrow from femur*
 - Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test) : *at least 50 metaphases of bone marrow cells scored per Animal*
 - Criteria for selection of M.T.D. : *animals were simultaneously exposed with animals in a two-year inhalation chronicity/carcinogenicity study those MTD was selected on the basis of a previous 90 day-sub-chronic toxicity study which had shown no treatment related effect at a concentration of 10,000 ppm (6h/d, 5d/w).*

RESULTS

- Chamber concentrations of the test material: *mean exposure concentrations as measured by gas chromatography were 1000, 10400 and 19800 ppm corresponding to the nominal*

concentrations of 1000, 10000 and 20000 ppm respectively.

- Effect on mitotic index or PCE/NCE ratio by dose level by sex: *slight increase in the percent mitotic rate in the mid and high level exposure groups*
- Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal) : *negative*
- NOAEL (NOEL) (C)/LOAEL (LOEL) (C): *not appropriate*
- Statistical results, as appropriate: *not appropriate*
- Remarks field for Results Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:
 - Mortality at each dose level by sex : *no mortality in any group*
 - Mutant/aberration/mPCE/polyploidy frequency, as appropriate : *there was no statistically significant difference between exposed groups and control group for aneuploidy, gaps, rearrangements and open breaks of chromosomes*
 - Description, severity, time of onset and duration of clinical signs at each dose level and sex : *no treatment-related effect at any concentration*
 - Body weight changes by dose and sex: *no statistical difference with control group*
 - Food/water consumption changes by dose and sex: *not measured*

CONCLUSIONS

1-chloro 1,1-difluoroethane did not demonstrate statistically significant chromosomal aberration activity in this 90 day-inhalation bone marrow cytogenic study in male rats.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): *Reliability code = 1a*
- Remarks field for Data Reliability: *key study*

REFERENCES (Free Text)

G.M. Rusch and G.K. Hogan « A study in the rat of the cytogenetic effect of inhalation of fluorocarbon 142b for 13 weeks » Report submitted to E.I. du Pont de Nemours Company and Penwalt Corporation. Project No. 79-7289. June 30, revised June 1983.

J.A. Seckar, H.J. Trochimowicz and GK Hogan. (1986) « Toxicological evaluation of hydrochlorofluorocarbon 142b. » Fd Chem. Toxic., 24, 237-240,

4.5.2.2 Genetic toxicity *in vivo* : Rat Dominant Lethal Assay

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
The test-material was presented as compressed form in 16 gas cylinders and has a purity level of 99.9%

METHOD

- Method/guideline followed: *experimental*
- Type (test type) : *dominant lethal assay in rats*

- GLP (Y/N) : Yes
- Year (study performed): 1980
- Species: rat
- Strain: *Sprague-Dawley – CD Charles River*
- Sex: *males and females*
- Route of administration: *inhalation (gas) (dynamic exposure) (whole body exposure)*
- Doses/concentration levels: 0, 1,000, 10,000 and 20,000 ppm
- Exposure period: 15 weeks
- Statistical methods: *for implantation data: Barlett's Test, ANOVA, Dunnet's Test, Kruskal-Wallis, Summed Rank Test, Regression analysis trend, lack of fit, Jonckheere's Statistic; for pregnancy rates: Chi square, Fischer exact Test, Bonferroni Inequality, Armitage's ; for implantation efficiency values and mutagenic ratio values : Barlett's Transformation, F-ratio test*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
 - Age at study initiation: *males: 7 weeks at initiation of treatment; females: 8-10 weeks at Initiation of mating*
 - No. of animals per group : *10 males and 160 females*
 - Vehicle: *air*
 - Duration of test: *exposure of male groups during 15 consecutive weeks*
 - Frequency of treatment: *6 hours /day, 5 days /week*
 - Sampling times and number of samples: *Mutagenicity was evaluated over an eight week post-treatment mating period. During each week of the mating period, each male was caged continuously with two untreated females per week for the 8 consecutive weeks. Subsequently, females were sacrificed and scored for corpora lutea and uterine implantation sites.*
 - Control groups and treatment: *chamber exposure to 0 (negative control) and 1000, 10000, 20000 ppm of the test material; in addition a positive control group received 0,5 mg/kg of triethylenemelamine intraperitoneally two hours prior to initiation of the mating period.*
 - Clinical observations performed (clinical pathology, functional observations, etc.) : *mortality, clinical signs, body weights*
 - Mutagenicity was evaluated on the basis of pregnancy rates, mean corpora lutea and implantation data, implantation efficiency ratios. These parameters were evaluated on a weekly basis for the 8-week mating period.
 - Criteria for selection of M.T.D.: *The male rat groups were simultaneously exposed with animals in a two-year inhalation chronic toxicity/carcinogenicity study those MTD was selected on the basis of a previous 90 day-sub -chronic toxicity study which had shown no treatment related effect at a concentration of 10,000 ppm (6h/d, 5d/w).*

RESULTS

- Chamber concentrations of the test material : *mean exposure concentrations as measured by gas chromatography were 1000, 10400 and 19700 ppm corresponding to the nominal concentrations of 1000, 10000 and 20000 ppm respectively.*
- Observed effects : *No statistically significant differences were seen in pregnancy rate data for females exposed to the treated males throughout the 8-week mating period. The mean number of corpora lutea, implantations, dead implants and the mean mutagenic ratios were comparable in exposed and negative control groups. A few statistically significant differences were observed in weeks 6 and 7 for some parameters. However they were not trend-related and were considered as isolated occurrence and not treatment-related. The dominant lethal mutagenicity observed on the positive control group was consistent with published literature for the effects of triethylenemelamine in the male rat. An increase in pre-implantation loss was evident during weeks 1-5 post-treatment and an increase in post-implantation loss was noted during weeks 1-6.*
- Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal) : *negative*

- Remarks field for Results Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:
 - Mortality at each dose level by sex: *no mortality in any group*
 - Description, severity, time of onset and duration of clinical signs at each dose level and sex: *no treatment-related effect at any concentration*
 - Body weight changes by dose and sex : *no difference with control group in low and mid level Concentration male groups. There was a tendency of lower bodyweight in the high concentration group, although not statistically significant*

CONCLUSIONS

1-chloro 1,1-difluoroethane administred via inhalation at dose levels of 1000, 10000 and 20000 ppm for a 15 week-treatment period was not considered mutagenic in the male rat by the dominant-lethal test.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): *Reliabilty code = 1a*
- Remarks field for Data Reliability *key study.*

REFERENCES (Free Text)

R.E. Schroeder and W.E. Rienhardt " A dominant lethal inhalation study with fluorocarbon 142b in rats. Final report » Report submitted to E.I. du Pont de Nemours Company Haskell Laboratory Wilmington, Delaware 19898. Submitted by Bio/dynamics Inc., East Millstone, New Jersey 08873. Project No. 79-7288. September 30, 1980.

J.A. Seckar, H.J. Trochimowicz and GK Hogan. (1986) « Toxicological evaluation of hydrochlorofluorocarbon 142b. » Fd Chem. Toxic., 24, 237-240,

4.6 REPEATED DOSE TOXICITY

4.6.1: Ninety-day rat and dog study

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3

- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
The test-material was presented as compressed form in several 125 lbs gas cylinders with a purity level of 99.7 %

METHOD

- Method/guideline followed: *experimental*
- Test type : *whole body inhalation repeated dose toxicity*
- GLP (Y/N) : *no*
- Year (study performed) : *1976*
- Species : *rat and dog*
- Strain *ChR-CD rats , and Beagle dogs*
- Route of administration : *inhalation (gas) (dynamic exposure)*
- Duration of test : *90 days*
- Doses/concentration levels : *1000 and 10000 ppm*
- Sex : *male and female rats , and male dogs*

- Exposure period : *90 days*
- Frequency of treatment : *6 hours per day, 5 days per week*
- Control group and treatment : *one air control group and two treatment groups per sex/species*
- Post exposure observation period : *none*
- Statistical methods : *not stated*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test Subjects

- Age at study initiation : *young adult rats , 10-12 months dogs*
- No. of animals per sex per dose : *groups of 54 rats (27/sex), and 4 dogs. Rats and dogs from the same dose level were exposed together in the same inhalation chamber*

- Study Design

- Vehicle : *air*
- Satellite groups and reasons they were added : *none*
- Clinical observations performed and frequency (clinical pathology, functional observations , etc.) : *daily weighting ; daily clinical signs observations ; at monthly intervals, all dogs and 10 rats/sex/level were subjected to usual basic exams for hematology, urinalysis and blood chemistry.*
- Organs examined at necropsy (macroscopic and microscopic) : *At the end of the exposure period, all animals were sacrificed and major organs of all animals were weighted and grossly examined; the following tissues of all rats and dogs treated at the high dose level were microscopically examined : trachea, lung, heart, aorta, bone marrow, lymph node, spleen, thymus, tonsil (dogs only), liver, kidney, urinary bladder (dogs only), testis, ovary, prostate (dogsonly), oviduct, uterus, epididymis, esophagus, intestine, stomach, pancreas (dogs only), salivary gland, exorbital lacrimal gland (rats only), adrenals, pituitary, thyroid, parathyroid, brain, spinal cord, peripheral nerve, eye and skin.*

RESULTS

- NOAEL : *higher than 10000 ppm in rats and in dogs*
 - Actual dose received by dose level by sex, if known, : *1000 and 9900 ppm (means)*
 - Toxic response/effects by dose level: *none*
 - Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.
- Body weight : *there were no compound-related effects, neither in rats nor in dogs*
- Description, severity, time of onset and duration of clinical signs: *there were no compound-related effects, neither in rats nor in dogs*
- Hematological findings incidence and severity: *there were no compound-related effects, neither in rats nor in dogs*
- Clinical biochemistry findings incidence and severity: *there were no compound-related effects on blood and urinary parameters, neither in rats nor in dogs. In addition there was no significant increase in urinary fluoride suggesting low order of metabolic transformation of the test-compound.*
- Mortality and time to death: *there were no compound-related effects, neither in rats nor in dogs*
- Gross pathology incidence and severity: *there were no compound-related effects, neither in rats nor in dogs*
- Organ weight changes : *there were no compound-related effects neither in rats nor in dogs*
- Histopathology incidence and severity: *there were no compound-related effects, neither in rats nor in dogs*

CONCLUSIONS

Male and female rats and male dogs whole body exposed to atmosphere of 1-chloro 1,1-difluoroethane at concentrations of 1000 and 10000 ppm for 6h/d, 5d/w, during 13 weeks, showed no treatment-related effects upon mortality, body weight, hematology, clinical chemistry, urinalysis or histopathological evaluation of selected tissues.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): *Reliability code = 1c*
- Remarks field for Data Reliability: *key study for repeated dose toxicity and for reproductive toxicity.*

REFERENCES (Free Text)

D.P. Kelly and H.J. Trochimowicz « Ninety-day inhalation exposure of rats and dogs to vapors of 1-chloro 1,1-difluoroethane (FC-142b) » . Du Pont de Nemours, Haskell Laboratory for Toxicology and Industrial Medicine. Report N° 469-76, Medical research Project N° 2222. June 28, 1976.

4.6.2 : Two-year rat study

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
The test-material was presented as compressed form in several 750 kg gas cylinders provided periodically by the supplier over the 2 year exposure periode, with a purity level ranging from 99.85 to 99.99 %

METHOD

- Method/guideline followed: *experimental*
 - Test type : *combined 2-year whole body inhalation chronic toxicity and carcinogenicity study*
 - GLP (Y/N) : *yes*
 - Year (study performed) : *1979 to 1982*
 - Species : *Rat*
 - Strain : *Sprague-Dawley (CD) Charles River*
 - Route of administration: *inhalation (gas) (dynamic exposure) (whole body)*
 - Duration of test: *2 years*
 - Doses/concentration levels: *0, 1000, 10000 and 20000 ppm*
 - Sex : *males and females*
 - Exposure period : *104 weeks*
 - Frequency of treatment : *6 hours per day, 5 days per week.*
 - Control group and treatment : *3 treatment groups and one negative air control group*
 - Post exposure observation period : *none*
 - Statistical methods : *parametric data : F distribution and Dunett's test ; non parametric data : Kruskal-Wallis and Dunn summed rank tests ; equality of variance : Bartlett's test ; neoplastic lesions and survival : NCI statistical programs.*
 - Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
- Test Subjects
- Age at study initiation : *7 weeks*
 - No. of animals per sex per dose : *110*

- Study Design

- Vehicle : *air*
- Satellite groups and reasons they were added: *none*
- Clinical observations performed and frequency (clinical pathology, functional observations, etc.): *mortality/gross signs (twice daily), bodyweight (weekly) ; physical exams (weekly) ; ophthalmoscopic exams (yearly) ; hematology, clinical chemistry and urinalysis (10 animals/sex/group at 12, 18 and 24 months of treatment).*
- Organs examined at necropsy (macroscopic and microscopic) : *sacrifices conducted on 10 animals/sex/group at 12 months and on all survivors at 24 months ; organs weighted : brain, pituitary, lungs, liver, kidneys, spleen, adrenals, gonads and thymus ; morphological exams : adipose tissue, abdominal aorta, adrenals, bone marrow, femur, brain (3 sections), Zymbal gland, oesophagus, eyes, optic nerve, lacrimal gland, ovaries, testes with epididymis, heart, whole intestine, kidneys, liver, lungs, lymph nodes, mammary gland, nasal turbinates, pancreas, pituitary, prostate, salivary glands, sciatic nerve, skeletal muscle, skin, spinal cord, spleen, thymus, trachea, thyroid, parathyroid, urinary bladder, uterus, all gross lesions and tissue masses (all these tissues preserved from all animals ; all rats from control and high dose groups examined microscopically).*

RESULTS

- NOAEL : *higher than 20000 ppm*
- Actual dose received by dose level by sex, if known : *1000, 10100 and 19500 ppm (corresponding to the nominal intended concentrations of 1000, 10000 and 20000 ppm respectively)*
- Toxic response/effects by dose level : *none*
- Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.
 - Body weight : *inter-group differences in body weight that occurred during the study did not indicate any exposure-related responses to 1-chloro 1,1-difluoroethane.*
 - Description, severity, time of onset and duration of clinical signs : *most significant signs were respiratory distress which were considered factors in several increases of mortality : control group males between weeks 48 and 72 and low dose female group between weeks 40 and 48 and between weeks 72 and 80. However adequate number of animals in these groups survived the 2-year period and the effect of this respiratory distress was considered to be insignificant as far as toxicological and oncogenic assessment of the test material is concerned.*
 - Ophthalmologic findings incidence and severity: *exams at weeks 52 and 104 did not indicate any responses to exposure.*
 - Hematological findings incidence and severity: *the mean hematology values for the treated males and females were comparable to the control animals at 12, 18 and 24 month intervals and were within normal biological limits.*
 - Clinical biochemistry findings incidence and severity: *in the low dose female group a statistically significant value of the mean creatinine phosphokinase value was observed at 12 months but not thereafter at 18 and 24 months. In addition there was no such increase in mid and high dose groups, at any time and the effect was considered not related to exposure. All other clinical chemistry values in both treated males and females were comparable to control animals and all parameters were considered within normal biological limits.*
 - Urinalysis : *there were no differences from control values in any of the urine parameters evaluated which were considered related to the administration of the test material. Fluoride levels were comparable between treated and control animals.*
 - Mortality and time to death : *The survivorship figures at termination of exposure did not show dose-related effect on mortality in the treated males or females throughout the study.*
 - Gross pathology incidence and severity: *findings at necropsy of decedents or those rats sacrificed after 12 or 24 months of treatment, as well as those dying spontaneously or sacrificed in a moribund condition throughout the study, were considered typical for rats of similar age and strain and no treatment-related effects were apparent.*

- Organ weight changes: *the values were considered within the range of normal expectation and there were no treatment related changes of absolute and relative organ weights.*
- Histopathology incidence and severity: *Non-neoplastic microscopic pathology findings at the interim and final sacrifices were similar in treated and control groups and were confined to degenerative lesions typical of rats of this strain and age. Neoplastic findings in animals that died during the study or in survivors to termination were similar in all groups and comprised predominantly tumours of the mammary and subcutaneous tissues in females, and pituitary and adrenal adenomas in both sexes. No treatment-related increases in tumours of the respiratory tract were noted.*

CONCLUSIONS

Rats receiving exposures to atmosphere of 1-chloro 1,1-difluoroethane at concentrations up to 20000 ppm for 6h/d, 5d/w during 104 weeks, showed no treatment-related effects upon mortality, body weight, hematology, clinical chemistry, urinalysis and ophthalmological examinations, histopathological evaluation of selected tissues, or statistical analysis of neoplasms incidences.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): *reliability code = 1b*
- Remarks field for Data Reliability: *key study for repeated dose toxicity and for reproductive toxicity.*

REFERENCES (Free Text)

J. Terril and G.K. Hogan « A two year inhalation toxicity study of fluorocarbon 142b in the rat. Final report » Submitted to : E.I. du Pont de Nemours Company, Wilmington, Delaware, and Penwalt Corporation, King of Prussia, Pennsylvania.. Submitted by Bio/dynamics Inc., East Millstone, and New Jersey 08873. Project N° 79-7287, May 31, 1983

J.A. Seckar, H.J. Trochimowicz and GK Hogan. (1986) "Toxicological evaluation of hydrochlorofluorocarbon 142b." *Fd Chem. Toxic.*, 24, 237-240

4.7 TOXICITY TO REPRODUCTION

There are no standard reproductive toxicity tests available on 1-chloro 1,1-difluoroethane. However direct effects on the male and female organs were examined in three different studies where animals were repeatedly exposed by inhalation to high concentrations of this substance. These studies were :

- 1) *The rat Dominant lethal assay reported in the « Genotoxicity in vivo » section*
- 2) *The 90-day repeated inhalation toxicity study in rats and dogs, and*
- 3) ***The Two-year inhalation combined chronic toxicity and carcinogenicity that were both reported in the « Repeated dose Toxicity » section.***

CONCLUSION :

Based on the 3 studies hereafter reported the following conclusions can be drawn : 1-chloro 1,1-difluoroethane tested by inhalation at concentrations ranging from 1000 to 20000 ppm :

- *has no effect on the fertility of male rats repeatedly exposed during 15 weeks up to 20000 ppm ;*
- *does not induce any lesion to any of the reproduction-related tissues of male dogs repeatedly exposed during 13 weeks up to 10000 ppm ;*
- *does not induce any lesion to any of the reproduction-related tissues of male and female rats repeatedly exposed during two years up to 20000 ppm.*

As : 1-chloro 1,1-difluoroethane was also tested for developmental toxicity in rats (see section “Developmental toxicity”), it appears that the “reproductive toxicity” of this substance has been adequately covered and does not need specific standard testing.

The overall conclusion is that 1-chloro 1,1-difluoroethane is not an experimental reproductive toxic material.

Test conditions and results relevant to reproductive toxicity from the three above mentioned studies are summarised thereafter :

4.7.1 Rat Dominant Lethal Assay:

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
The test-material was presented as compressed form in 16 gas cylinders and has a purity level of 99.9%

METHOD

- Method/guideline followed : *experimental*
- Type (test type) : *dominant lethal assay in rats*
- GLP (Y/N) : *Yes*
- Year (study performed) : *1980*
- Species : *rat*
- Strain : *Sprague-Dawley –CD Charles River*
- Sex : *males and females*
- Route of administration: *inhalation (gas) (dynamic exposure) (whole body)*
- Doses/concentration levels: *0, 1,000, 10,000 and 20,000 ppm*
- Premating exposure period for males: *15 weeks*
- Statistical methods: *for pregnancy rates: Chi-square, Fischer exact Test, Bonferroni Inequality.*

- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
 - Age at study initiation: *males: 7 weeks at initiation of treatment; females: 8-10 weeks at initiation of mating*
 - No. of animals per group : *10 males and 160 females*
 - Vehicle : *air*
 - Duration of test : *exposure of male groups during 15 consecutive weeks*
 - Frequency of treatment : *6hours /day, 5 days /week*
During each week of the mating period, each male was caged continuously with two untreated females per week for the 8 consecutive weeks. Subsequently, females were sacrificed and scored for corpora lutea and uterine implantation sites.
 - Control groups and treatment: *chamber exposure to 0 (negative control) and 1000, 10000, 20000 ppm of the test material; in addition a positive control group received 0,5 mg/kg of triethylenemelamine intraperitoneally two hours prior to initiation of the mating period.*
 - Clinical observations performed (clinical pathology, functional observations, etc.) : *mortality, clinical signs, body weights*
 - Fertility index (pregnancies/matings) : *Pregnancy rates were evaluated on a weekly basis for the 8-week mating period. This procedure allowed assessment of the fertility of the rats pre-exposed to the test compound during 15 weeks.*
 - Criteria for selection of M.T.D. : *The male rat groups were simultaneously exposed with animals in a two-year inhalation chronicity/carcinogenicity study those MTD was selected on the basis of a previous 90 day-sub-chronic toxicity study which had shown no treatment related effect at a concentration of 10,000 ppm (6h/d, 5d/w).*

RESULTS

- Chamber concentrations of the test material: *mean exposure concentrations as measured by gas chromatography were 1000, 10400 and 19700 ppm corresponding to the nominal concentrations of 1000, 10000 and 20000 ppm respectively.*
- Observed effects: *No statistically significant differences were seen in pregnancy rate data of females exposed to the treated males throughout the 8-week mating period as compared to females exposed to untreated control males.*
- Remarks field for Results Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:
 - Mortality at each dose level by sex: *no mortality in any group*
 - Description, severity, time of onset and duration of clinical signs at each dose level and sex: *no treatment-related effect at any concentration*
 - Body weight changes by dose and sex: *no difference with control group in low and mid level concentration male groups. There was a tendency of lower bodyweight in the high concentration group, although not statistically significant*

CONCLUSIONS

1-chloro 1,1-difluoroethane was administered to male rats via inhalation at dose levels of 1000, 10000 and 20000 ppm for a 15 week pre-treatment period. This treatment did not impair the fertility of the exposed male rats as assessed by the normal rates of pregnancy showed by the females mated with the pre-treated males each week over an eight week period.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : *Reliability code for reproductive toxicity = 2e*
- Remarks field for Data Reliability: *key study for reproductive toxicity*

REFERENCES (Free Text)

R.E. Schroeder and W.E. Rinehart « A dominant lethal inhalation study with fluorocarbon 142b in rats. Final report » Report submitted to E.I. du Pont de Nemours Company Haskell Laboratory Wilmington, Delaware 19898. Project No. 79-7288. September 30, 1980.

J.A. Seckar, H.J. Trochimowicz and GK Hogan. (1986) «Toxicological evaluation of hydrochlorofluorocarbon 142b.» Fd Chem. Toxic., 24, 237-240,

4.7.2 Ninety-day repeated toxicity study in rats and dogs

TEST SUBSTANCE

- Identity

1-chloro 1,1-difluoroethane

CAS : 75-68-3

- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
The test-material was presented as compressed form in several 125 lbs gas cylinders with a purity level of 99.7 %

METHOD

- Method/guideline followed : *experimental*
- Test type : *inhalation repeated dose toxicity*
- GLP (Y/N) : *no*
- Year (study performed) : *1976*
- Species : *rat and dog*
- Strain *Chr-CD rats , and Beagle dogs*
- Route of administration : *whole body inhalation (gas) (dynamic exposure*
- Duration of test : *90 days*
- Doses/concentration levels: *1000 and 10000 ppm*
- Sex : *male and female rats , and male dogs*
- Exposure period: *90 days*
- Frequency of treatment: *6 hours per day, 5 days per week*
- Control group and treatment: *one air control group and two treatment groups per sex/species*
- Post exposure observation period: *none*
- Statistical methods: *not stated*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test Subjects

- Age at study initiation: *young adult rats, 10-12 months dogs*
- No. of animals per sex per dose : *groups of 54 rats (27/sex), and 4 dogs*

- Study Design

- Vehicle : *air*
- Satellite groups and reasons they were added: *none*
- Clinical observations performed and frequency (clinical pathology, functional observations, etc.) : *daily weighting, clinical signs observations ; At monthly intervals, all dogs and 10 rats/sex/level were subjected to usual basic exams for hematology, urinalysis and blood chemistry.*
- Organs examined at necropsy (macroscopic and microscopic): *At the end of the exposure period, all animals were sacrificed and major organs of all animals were weighted and grossly examined; selected tissues of all rats and dogs treated at the high level were microscopically examined including the following reproduction-related ones: testis, ovary, prostate (dogs), oviduct, uterus, epididymis.*

RESULTS

- NOAEL : *higher than 10000 ppm in rats and in dogs*
- Actual dose received by dose level by sex, if known, : *1000 and 9000 ppm*
- Toxic response/effects by dose level : *there were no toxic effect including on reproduction-related tissues of male and female rats and of male dogs*
- Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.
 - Body weight : *there were no compound-related effects, neither in rats nor in dogs*
 - Description, severity, time of onset and duration of clinical signs : *there were no compound-related effects, neither in rats nor in dogs*
 - Hematological findings incidence and severity: *there were no compound-related effects, neither in rats nor in dogs*
 - Clinical biochemistry findings incidence and severity: *there were no compound-related effects on blood and urinary parameters, neither in rats nor in dogs. In addition there was no significant increase in urinary fluoride suggesting low order of metabolic transformation of the test-compound.*
 - Mortality and time to death: *there were no compound-related effects, neither in rats or in dogs*
 - Gross pathology incidence and severity: *there were no compound-related effects, neither in rats nor in dogs*
 - Organ weight changes: *there were no compound-related effects, neither in rats nor in dogs*
 - Histopathology incidence and severity: *there were no compound-related effects, neither in rats nor in dogs in any of the examined tissue including the reproduction-related tissues.*

CONCLUSIONS

Male and female rats and male dogs whole body exposed to atmosphere of 1-chloro 1,1-difluoroethane at concentrations of 1000 and 10000 ppm for 6h/d, 5d/w, during 13 weeks, showed no treatment related effects upon reproduction-related tissues on macroscopic and microscopic examinations (as well as upon mortality, body weight, hematology, clinical chemistry, urinalysis or histopathological evaluation of other selected tissues).

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : *2e for reproductive toxicity*
- Remarks field for Data Reliability: *key study for reproductive toxicity.*

REFERENCES (Free Text)

D.P. Kelly and H.J. Trochimowicz « Ninety-day inhalation exposure of rats and dogs to vapors of 1-chloro 1,1-difluoroethane (FC-142b) ». Du Pont de Nemours, Haskell Laboratory for Toxicology and Industrial Medicine. Report N° 469-76, Medical research Project N° 2222. June 28, 1976.

4.7.3 Two-year repeated toxicity study in rats

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
The test-material was presented as compressed form in several 750 kg gas cylinders provided periodically by the supplier over the 2 year exposure periode, with a purity level ranging from 99.85 to 99.99 %

METHOD

- Method/guideline followed: *experimental*
 - Test type: *combined 2-year whole body inhalation chronic toxicity and carcinogenicity study*
 - GLP (Y/N): *yes*
 - Year (study performed) : *1979 to 1982*
 - Species : *Rat*
 - Strain : *Sprague-Dawley (CD) Charles River*
 - Route of administration: *inhalation (gas) (dynamic exposure) (whole body)*
 - Duration of test: *2 years*
 - Doses/concentration levels: *0, 1000, 10000 and 20000 ppm*
 - Sex : *males and females*
 - Exposure period: *104 weeks*
 - Frequency of treatment: *6 hours per day, 5 days per week.*
 - Control group and treatment: *3 treatment groups and one negative air control group*
 - Post exposure observation period: *none*
 - Statistical methods: *parametric data: F distribution and Dunnett's test; non parametric data : Kruskal-Wallis and Dunn summed rank tests ; equality of variance : Bartlett's test ; neoplastic lesions and survival : NCI statistical programs.*
 - Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
- Test Subjects
- Age at study initiation: *7 weeks*
 - No. of animals per sex per dose : *110*
- Study Design
- Vehicle : *air*
 - Satellite groups and reasons they were added : *none*
 - Clinical observations performed and frequency (clinical pathology, functional observations, etc.) : *mortality/gross signs (twice daily), bodyweight (weekly) ; physical exams (weekly) ; ophthalmoscopic exams (yearly) ; hematology, clinical chemistry and urinalysis (10 animals/sex/group at 12, 18 and 24 months of treatment).*
 - Organs examined at necropsy (macroscopic and microscopic) : *sacrifices conducted on 10 animals/sex/group at 12 months and on all survivors at 24 months ; organs weighted : nine organs including gonads; morphological exams : 45 different tissues including ovaries, testes with epididymis., prostate and uterus (all the tissues preserved from all animals ; all rats from control and high dose groups examined microscopically).*

RESULTS

- NOAEL : *higher than 20000 ppm*
- Actual dose received by dose level by sex, if known: *means of measured concentrations were 1000, 10100 and 19500 ppm (corresponding to the nominal intended concentrations of 1000, 10000 and 20000 ppm respectively)*
- Toxic response/effects by dose level: *none including in reproduction-related tissues of males and females.*
- Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.
- Body weight : *inter-group differences in body weight that occurred during the study did not indicate any exposure-related responses to 1-chloro 1,1-difluoroethane.*
- Description, severity, time of onset and duration of clinical signs : *most significant signs were respiratory distress which were considered factor in several increases of mortality : control group males between weeks 48 and 72 and low dose female groups between weeks 40 and 48 and between weeks 72 and 80. However adequate number of animals in these groups survived the 2-year period and the effect of this respiratory distress was considered to be*

insignificant as far as toxicological and oncogenic assessment of the test material is concerned.

- Ophthalmologic findings incidence and severity: *exams at week 52 and 104 did not indicate any responses to exposure.*
- Hematological findings incidence and severity: *the mean hematology values for the treated males and females were comparable to the control animals at 12, 18 and 24 month intervals and were within normal biological limits.*
- Clinical biochemistry findings incidence and severity : *in the low dose female group a statistically significant value of the mean creatinine phosphokinase value was observed at 12 months but not thereafter at 18 and 24 months. In addition there was no such increase in mid and high dose groups, at any time and the effect was considered not related to exposure. All other clinical chemistry values in both treated males and females were comparable to control animals and all parameters were considered within normal biological limits.*
- Urinalysis : *there were no differences from control values in any of the urine parameters evaluated which were considered related to the administration of the test material. Fluoride levels were comparable between treated and control animals.*
- Mortality and time to death : *The survivorship figures at termination of exposure did not show dose-related effect on mortality in the treated males or females throughout the study.*
- Gross pathology incidence and severity : *findings at necropsy of decedents or those rats sacrificed after 12 or 24 months of treatment, as well as those dying spontaneously or sacrificed in a moribund condition throughout the study, were considered typical for rats of similar age and strain and no treatment-related effects were apparent.*
- Organ weight changes : *the values were considered within the range of normal expectation and **there were no treatment related changes of absolute and relative organ weights including ovaries and testes.***
- Histopathology incidence and severity : *Non-neoplastic microscopic pathology findings at the interim and final sacrifices **including reproduction-related tissues were similar in treated and control groups** and were confined to degenerative lesions typical of rats of this strain and age. Neoplastic findings in animals that died during the study or in survivors to termination were similar in all groups and comprised predominantly tumours of the mammary and subcutaneous tissues in females, and pituitary and adrenal adenomas in both sexes. No treatment related increases in tumours of the respiratory tract were noted.*

CONCLUSIONS

Rats receiving exposures to atmosphere of 1-chloro 1,1-difluoroethane at concentrations up to 20000 ppm for 6h/d, 5d/w during 104 weeks, showed no treatment related effects upon reproduction-related tissues on macroscopical and microscopical examinations (as well as upon mortality, body weight, hematology, clinical chemistry, urinalysis and ophthalmological examinations, histopathological evaluation of selected tissues, or statistical analysis of neoplasms incidences).

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : *Reliability code = 2e for reproductive toxicity*

- Remarks field for Data Reliability : *key study for reproductive toxicity.*

REFERENCES (Free Text)

J. Terril and G.K. Hogan « A two year inhalation toxicity study of fluorocarbon 142b in the rat. Final report » Submitted to : E.I. du Pont de Nemours Company, Wilmington, Delaware, and Penwalt Corporation, King of Prussia, Pennsylvania.. Submitted by Bio/dynamics Inc., East Millstone, New Jersey 08873. Project N° 79-7287, May 31, 1983

J.A. Seckar, H.J. Trochimowicz and GK Hogan. (1986) « Toxicological evaluation of hydrochlorofluorocarbon 142b. » *Fd Chem. Toxic.*, 24, 237-240

4.8 DEVELOPMENTAL TOXICITY/TERATOGENICITY

4.8.1 Litton Bionetics Developmental toxicity study in rats

TEST SUBSTANCE

• Identity

1-chloro 1,1-difluoroethane

CAS : 75-68-3

• Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

The test-material was presented as compressed form in 2 gas cylinders and was an « aerosol grade of Isotron 142b » (purity level not stated)

METHOD

- Method/guideline followed: *experimental – inhalation teratogenicity in rats*
- GLP (Y/N) : *yes*
- Year (study performed) : *1978*
- Species : *Rat*
- Strain : *Charles River [CRL : COBS CD (SD) BR]*
- Route of administration *inhalation (gas) (dynamic exposure) (whole body exposure)*
- Doses/concentration levels: *0, 2000 and 10000 ppm (nominal)*
- Sex : *female*
- Exposure period: *day 6 through day 15 of gestation*
- Frequency of treatment: *6 hours per day*
- Control group and treatment: *0 (control); 3259 and 9420 ppm (means of measured concentrations)*
- Duration of test: *from day zero to day 20 of gestation*
- Statistical methods: *Dunett's t-test (for difference between means with near-normal distribution) ; 2x2 contingency table with Yates correction (for ratios) ; Wilcoxon Rank Sum (for discontinuous parameters).*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
 - Age at study initiation : *10 weeks*
 - Number of animals per dose per sex : *20 mated females per group*
 - Vehicle : *air*
 - Clinical observations performed and frequency: *daily observation of general appearance, behavior and conditions of dams*
 - Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy) : *each female was paired with a sexually-mature male of the same strain. The females were examined daily for the presence of a copulatory plug. The presence of such a plug was taken as evidence of mating and designated as Day 0 of gestation*
 - Parameters assessed during study (maternal and fetal) : *maternal : body weight on Day 0, 6, 15 and 20 of gestation ; food consumption from day 0-6, 6-15 and 15-20 ; number of implantations and placement in the uterine horns ; resorption sites ; fetal : number of live and dead ; external examination for abnormalities, body weight ;*
 - Organs examined at necropsy (macroscopic and microscopic) : *maternal : visceral and thoracic organs ; fetal : one third of each litter fixed in Bouin's fluid and examined for soft tissues of the head, thoracic and visceral organs. The remaining of fetuses examined for skeletal abnormalities following staining with alizarin Red S*

RESULTS

- NOAEL maternal toxicity: *higher than 9420 ppm*
- NOAEL developmental toxicity: *higher than 9420 ppm*

- Actual dose received by dose level by sex if available: *mean measured values were 3259 and 9420 ppm (6h/d over 18d) corresponding to the nominal concentrations of 2000 and 10000 ppm respectively.*
- Maternal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen : *no treatment-related effect at any dose level.*
- Fetal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen. : *no treatment related effect at any dose level*
- Statistical results, as appropriate: *not appropriate*
- Remarks for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following when there are dose related effects if available: Maternal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen.

- Mortality and day of death : *none at both dose levels*
- Number pregnant per dose level : *15/20, 18/20, 20/20 for control, low and high dose group respectively*
- Number aborting : *none in all groups*
- Number of resorptions, early/late if available : *15, 8 and 31 for control low and high dose group respectively*
- Number of implantation sites : *106/106, 109/137 and 131/ 129 for control low and high dose group respectively (Left horn/Right horn)*
- Body weight : *no statistical difference with control*
- Food/water consumption : *no statistical difference with controls*
- Description, severity, time of onset and duration of clinical signs : *no statistical difference with controls*
- Gross pathology incidence and severity *no statistical difference with controls*
- Fetal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen
 - Litter size : *15/15 , 18/18 and 19/20 20 for control, low and high dose group respectively ; there were no statistically significant difference of the mean weight of fetuses between treated and control groups*
 - Number viable (number alive) : *197, 238 and 229 for control, low and high dose group respectively . There was no dead fetus in any group.*
 - Sex ratio : *no statistical difference between exposed and control group*
 - Grossly visible abnormalities : 1) external :*one pup in each of the two litters in both the control and the high dose groups had sub -cutaneous hematomas ., 2) soft tissue : none in any group ; and 3) skeletal abnormalities : 1, 1 and 2 fetuses with unusual skeletal variations for control, low and high dose group respectively ; there was also an increased incidence of delayed ossification of the supra-occipital bone in both exposure groups ; this effect was not observed in the control group. However the authors stated about a number of changes including the delayed ossification of supra-occipital bone, that, while not strictly normal, such findings are frequently observed in 20-day old rat fetuses of this strain and source in their laboratory. So they clearly concluded that there was no evidence of compound-induced embryotoxicity or inhibition of fetal growth and development.*

CONCLUSIONS

Exposure of pregnant female rats to average airborne concentrations of 1-dichloro 1,1difluoroethane at 3259 and 9420 ppm produced no effect on the pregnant dams. There was no evidence of compound-induced terata, variation in sex ratio, embryotoxicity or inhibition of fetal growth and development.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : *Reliability code = 1b*
- Remarks field for Data Reliability : *key study*

REFERENCES (Free Text)

D.R. Damske, Mecler F.J. and R.P. Beliles « Teratology study in rats. Isotron 142B Monochlorodifluoroethane. Final report. » Submitted to Penwalt Corporation, 900 First Avenue, King of Prussia, Pennsylvania 19406. Submitted by Litton Bionetics, Inc. 5516 Nicholson Lane, Kensington, Maryland 20795. LBI Project N° 20890, August 1978.

4.8.2 Haskell Laboratory Developmental Toxicity study in rats

TEST SUBSTANCE

- Identity
1-chloro 1,1-difluoroethane
CAS : 75-68-3
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
(purity level not stated)

METHOD

- Method/guideline followed : *experimental – inhalation teratogenicity in rats*
- GLP (Y/N) : *not stated*
- Year (study performed) : *1976*
- Species : *Rat*
- Strain : *Charles River CD Rats*
- Route of administration *inhalation (gas) (dynamic exposure) (whole body exposure)*
- Doses/concentration levels : *0, 1000 and 10000 ppm (nominal)*
- Sex : *female*
- Exposure period : *day 3 through day 15 of gestation*
- Frequency of treatment : *6 hours per day*
- Control group and treatment : *0 (control) ; 1000 and 10000 ppm (means of measured concentrations)*
- Duration of test : *from day zero to day 20 of gestation*
- Statistical methods : *Fisher exact probability test ; Mann-Whitney U-test ; analysis of variance and Least Significant Difference.*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
-Age at study initiation : *primigravida females*
- Number of animals per dose per sex : *25 pregnant females per group*
- Vehicle : *air*
- Clinical observations performed and frequency : *daily behavioral observations*
- Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy) : *pregnancy confirmed by finding sperm in the vaginal smear of females caged overnight with males*
- Parameters assessed during study (maternal and fetal) : *bodyweight, corpora lutea, implantation sites, live/dead fetuses, early and late resorption, crown-rump length of live fetuses, -Organs examined at necropsy (macroscopic and microscopic) : gross examination of external anomalies, skeletal (alizarin staining) anomalies ; microscopic visceral examination on Wilson cuts. ; uterus and ovaries of mothers.*

RESULTS

- NOAEL maternal toxicity : *higher than 10000 ppm*
- NOAEL developmental toxicity : *higher than 10000 ppm*
- Actual dose received by dose level by sex if available : *1000 +/-100 ppm and 10000 +/-600 ppm*
- Maternal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen : *no treatment-related effect at any dose level.*

- Fetal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen. : *no treatment related effect at any dose level*
- Statistical results, as appropriate: *not appropriate*
- Remarks for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following when there are dose related effects if available: Maternal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen.
 - Mortality and day of death : *none at both dose levels*
 - Number pregnant per dose level : *21 (control) 22 (1000 and 10000 ppm)*
 - Number aborting :
 - Number of resorptions, early/late if available :
 - Number of implantation sites: *mean per litter: 9.7 (control); 9.7 (1000 ppm); 9.5 (10000 ppm)*
 - Body weight: *no statistical difference with control*
 - Food/water consumption :
 - Description, severity, time of onset and duration of clinical signs : *no statistical difference with controls*
 - Gross pathology incidence and severity *no statistical difference with controls*
 - Fetal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen
 - Litter size: *8.7 (control); 9.0 (1000 ppm); 9.0 (10000 ppm)*
 - Number viable (number alive): *no statistical difference versus control.*
 - Sex ratio:
 - Grossly visible abnormalities: *no statistical difference versus control*

CONCLUSIONS

Exposure of pregnant female rats to airborne concentrations of 1-dichloro 1,1difluoroethane at 1000 and 10000 ppm produced no effect on the pregnant dams. There was no evidence of teratogenesis or embryotoxicity or inhibition of fetal growth and developement.

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): *Reliability code = 2g*
- Remarks field for Data Reliability: *key study*

REFERENCES (Free Text)

Culik, R and Kelly DP « Embryotoxic and Teratogenic studies in rats with inhaled chlorodifluoroethane » Haskell Lab report N° 700-76 DuPont de Nemours and Company, 1976.

4.9 CARCINOGENICITY

Two-year repeated toxicity study in rats

TEST SUBSTANCE

- Identity
1-chloro 1,1 -difluoroethane
CAS : 75-68-3
- Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)
The test-material was presented as compressed form in several 750 kg gas cylinders provided periodically by the supplier over the 2 year exposure periode, with a purity level ranging from 99.85 to 99.99 %

METHOD

- Method/guideline followed: *experimental*
- Test type: *combined 2-year whole body inhalation chronic toxicity and carcinogenicity study*
- GLP (Y/N): *yes*
- Year (study performed): *1979 to 1982*
- Species: *Rat*
- Strain: *Sprague-Dawley (CD) Charles River*
- Route of administration: *inhalation (gas) (dynamic exposure) (whole body)*
- Duration of test: *2 years*
- Doses/concentration levels: *0, 1000, 10000 and 20000 ppm*
- Sex: *males and females*
- Exposure period: *104 weeks*
- Frequency of treatment: *6 hours per day, 5 days per week.*
- Control group and treatment: *3 treatment groups and one negative air control group*
- Post exposure observation period: *none*
- Statistical methods: *parametric data : F distribution and Dunett's test ; non parametric data : Kruskal-Wallis and Dunn summed rank tests ; equality of variance : Bartlett's test ; neoplastic lesions and survival : NCI statistical programs.*
- Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test Subjects

- Age at study initiation: *7 weeks*
- No. of animals per sex per dose: *110*

- Study Design

- Vehicle: *air*
- Satellite groups and reasons they were added: *none*
- Clinical observations performed and frequency (clinical pathology, functional observations, etc.): *mortality/gross signs (twice daily), bodyweight (weekly); physical exams (weekly); ophthalmoscopic exams (yearly) ; hematology, clinical chemistry and urinalysis (10 animals/sex/group at 12, 18 and 24 months of treatment).*
- Organs examined at necropsy (macroscopic and microscopic) : *sacrifices conducted on 10 animals/sex/group at 12 months and on all survivors at 24 months ; organs weighted : nine organs including gonads ; morphological exams : 45 different tissues including ovaries, testes with epididymis, prostate and uterus (all the tissues preserved from all animals ; all rats from control and high dose groups examined microscopically).*

RESULTS

- NOAEL : *higher than 20000 ppm*
- Actual dose received by dose level by sex, if known: *means of measured concentrations were 1000, 10100 and 19500 ppm (corresponding to the nominal intended concentrations of 1000, 10000 and 20000 ppm respectively)*
- Toxic response/effects by dose level: *none including in reproduction-related tissues of males and females.*
- Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.
- Body weight : *inter-group differences in body weight that occurred during the study did not indicate any exposure-related responses to 1-chloro 1,1-difluoroethane.*
- Description, severity, time of onset and duration of clinical signs: *most significant signs were respiratory distress which were considered factor in several increases of mortality : control group males between weeks 48 and 72 and low dose female groups between weeks 40 and 48 and between weeks 72 and 80. However adequate number of animals in these groups survived the 2-year period and the effect of this respiratory distress was considered to be insignificant as far as toxicological and oncogenic assessment of the test material is*

concerned.

- Ophthalmologic findings incidence and severity: *exams at week 52 and 104 did not indicate any responses to exposure.*
- Hematological findings incidence and severity: *the mean hematology values for the treated males and females were comparable to the control animals at 12, 18 and 24 month intervals and were within normal biological limits.*
- Clinical biochemistry findings incidence and severity: *in the low dose female group a statistically significant value of the mean creatinine phosphokinase value was observed at 12 months but not thereafter at 18 and 24 months. In addition there was no such increase in mid and high dose groups, at any time and the effect was considered not related to exposure. All other clinical chemistry values in both treated males and females were comparable to control animals and all parameters were considered within normal biological limits.*
- Urinalysis: *there were no differences from control values in any of the urine parameters evaluated, which were considered related to the administration of the test material. Fluoride levels were comparable between treated and control animals.*
- Mortality and time to death: *The survivorship figures at termination of exposure did not show dose-related effect on mortality in the treated males or females throughout the study.*
- Gross pathology incidence and severity: *findings at necropsy of decedents or those rats sacrificed after 12 or 24 months of treatment, as well as those dying spontaneously or sacrificed in a moribund condition throughout the study, were considered typical for rats of similar age and strain and no treatment-related effects were apparent.*
- Organ weight changes: *the values were considered within the range of normal expectation and there were no treatment related changes of absolute and relative organ weights including ovaries and testes.*
- Histopathology incidence and severity : *Non-neoplastic microscopic pathology findings at the interim and final sacrifices including reproduction-related tissues were similar in treated and control groups and were confined to degenerative lesions typical of rats of this strain and age. Neoplastic findings in animals that died during the study or in survivors to termination were similar in all groups and comprised predominantly tumours of the mammary and subcutaneous tissues in females, and pituitary and adrenal adenomas in both sexes. No treatment related increases in tumours of the respiratory tract were noted.*

CONCLUSIONS

Rats receiving exposures to atmosphere of 1-chloro 1,1-difluoroethane at concentrations up to 20000 ppm for 6h/d, 5d/w during 104 weeks, showed no treatment related effects upon mortality, body weight, hematology, clinical chemistry, urinalysis and ophthalmological examinations. Histopathological evaluation did not reveal excess of neoplasm incidences.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') : *Reliability code = 2e*
Remarks field for Data Reliability:

REFERENCES (Free Text)

J. Terril and G.K. Hogan « A two year inhalation toxicity study of fluorocarbon 142b in the rat. Final report » Submitted to : E.I. du Pont de Nemours Company, Wilmington, Delaware, and Penwalt Corporation, King of Prussia, Pennsylvania.. Submitted by Bio/dynamics Inc., East Millstone, New Jersey 08873. Project N° 79-7287, May 31, 1983

J.A. Seckar, H.J. Trochimowicz and GK Hogan. (1986) «Toxicological evaluation of hydrochlorofluorocarbon 142b. » *Fd Chem. Toxic.*, 24, 237-240

4.10 MECHANISM OF ACTION AND TOXICOKINETICS

Studies in rats exposed by inhalation show that 1-chloro-1,1-difluoroethane is rapidly absorbed by the lungs. Analysis of selected tissues from rats and dogs exposed by inhalation for 13 weeks did not revealed the presence of 1-chloro-1,1-difluoroethane and no significant increase in inorganic

fluoride in the urine was observed (Kelly and Trochimowicz, 1976). This is consistent with a low metabolisation of the molecule as indicated by physiologically based pharmacokinetics of uptake by inhalation in rats (Loizou et al, 1996). However Van Dyke (1977) observed a slight dechlorination in vitro after incubation of 1-chloro-1,1-difluoroethane with rat hepatic microsomes.

References:

Kelly DP and Trochimowicz HJ (1976)

« Ninety-day inhalation exposure of rats and dogs to vapors of 1-chloro 1,1-difluoroethane (FC -142b) ». Du Pont de Nemours, Haskell Laboratory for Toxicology and Industrial Medicine. Report N° 469-76, Medical research Project N° 2222. June 28, 1976.

Loizou GD, Eldirdiri NI and King LJ (1996)

“Physiologically based pharmacokinetics of uptake by inhalation of a series of 1,1,1-trihaloethanes: correlation with various physicochemical parameters”
Inhalation Toxicology, 8, 1-19.

Van Dyke RA (1977)

« Dechlorination mechanism of chlorinated olefins »
Environ. Health. Perspec., 21, 121-124.