201-15842

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March 18, 2005

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Michael O. Leavitt, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 2216

Attn: Chemical Right-to-Know Program

Dear Administrator Leavitt,

E. I. du Pont de Nemours & Company, Inc. is pleased to submit the proposed test plan along with the robust summary for the Fluoroethane category. The chemicals included in this category are 1,1,2-trichloro-1,2,2-trifluoroethane (FC-113) CAS# 76-13-1, 1,1,1-trichloro-2,2,2-trifluoroethane (FC-113a) CAS# 354-58-5, 1,2-dichloro-1,1,2,2-tetrafluoroethane (FC-114) CAS# 74-14-2, and 1,1-dichloro-1,2,2,2-tetrafluoroethane (FC-114a) CAS# 374-07-2. DuPont understands there will be a 120-day review period for the test plan and that all comments received by the EPA will be forwarded to DuPont for consideration.

This submission includes one electronic copy in .pdf format.

Please contact me by phone at (302) 773-0910 or by e-mail, Edwin.L.Mongan-1@usa.dupont.com, if you have any questions regarding this matter.

Sincerely,

Edwin L. Mongan, III
Manager, Environmental Stewardship
DuPont Safety, Health & Environment

Cc: Charles Auer – U.S. EPA
Office of Pollution Prevention & Toxics
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

18 March 2005

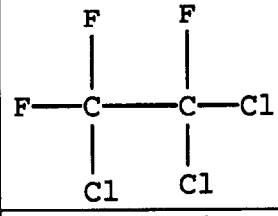
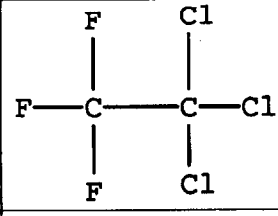
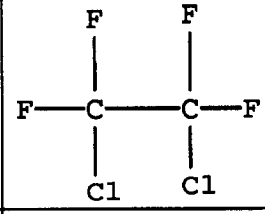
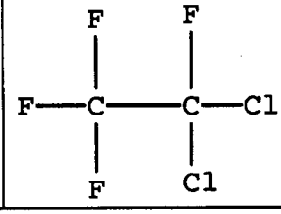
201-15842B

ROBUST SUMMARY FOR FLUOROETHANE CATEGORY

Summary

Identification of a structure based category

The fluoroethane category is comprised of test substances composed 2 carbon chains containing attached fluorine and chlorine atoms. The discrete materials vary by the number and positions of fluorine and chlorine atoms that are attached to the chain. Structures of these fluoroethanes are presented below.

Chemical Name	CAS Registry Number	Structure
Ethane, 1,1,2-trichloro-1,2,2-trifluoro (FC-113)	76-13-1	
Ethane, 1,1,1-trichloro-2,2,2-trifluoro (FC-113a)	354-58-5	
1,2-Dichloro-1,1,2,2-tetrafluoroethane (FC-114)	76-14-2	
Ethane, 1,1-dichloro-1,2,2,2-tetrafluoro (FC-114a)	374-07-2	

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Scientific literature was searched and summarized. Data were identified for materials in the category (Table 1). A majority of the SIDS endpoints were covered for the individual materials, as well as the category. Each study on category materials was evaluated for adequacy. Robust summaries were developed for each study addressing specific SIDS endpoints. Summaries were also developed for studies that were either considered inadequate but that provided information of relevance for hazard identification and evaluation, or covered non-SIDS endpoints

(Appendices A-D). The information presented in these data summaries indicates that these materials share similar physical chemical properties, environmental fate characteristics, ecotoxicity, and mammalian toxicity.

Table 1: Matrix of Available and Adequate Data for Fluoroethane Category

	FC-113	FC-113a	FC-114	FC-114a
PHYSICAL/CHEMICAL CHARACTERISTICS				
Melting Point	√	√	√	√
Boiling Point	√	√	√	√
Vapor Pressure	√	√	√	√
Partition Coefficient	√	√	√	√
Water Solubility	√	√	√	√
ENVIRONMENTAL FATE				
Photodegradation	√	√	√	√
Stability in Water	√	√	√	√
Transport (Fugacity)	√	√	√	√
Biodegradation	√	√	√	√
ECOTOXICITY				
Acute Toxicity to Fish	√	√/–	√/–	√
Acute Toxicity to Invertebrates	√	√/–	√	√
Acute Toxicity to Aquatic Plants	√/–	√/–	√/–	√/–
MAMMALIAN TOXICITY				
Acute Toxicity	√	√	√	√
Repeated Dose Toxicity	√	√/–	√	√/–
Developmental Toxicity	√	–	–	–
Reproductive Toxicity	√	–/*	–/*	–/*
Genetic Toxicity Gene Mutations	√	–	√	–
Genetic Toxicity Chromosomal Aberrations	–	–	–	–
Genetic Toxicity *in vivo* Studies (Dominant lethal in mice)	√	–	–	–

√ = Data are available and considered adequate.
√/– = Data are available, but considered inadequate.
– = No data available.
–/* = No reproductive toxicity studies were available; however, detailed information on the evaluation of reproductive organs is presented in the repeated-dose toxicity studies for these test substances.

Evaluation of Data Matrix Patterns

The available adequate data were broken out by discipline (physical chemical, environmental fate, ecotoxicology, and mammalian toxicology). These comparisons were conducted to determine if a pattern existed among the materials and to determine if additional testing needed to be conducted to complete the data set for the category. In general, the most striking pattern across the group of materials is their low mammalian toxicity.

All four fluoroethanes have roughly equivalent physical chemical properties as a result of structural similarity. FC-113 and FC-113a are clear, colorless liquids with a slight ethereal odor, neutral pH, and molecular weight of 187.4. FC-114 is a colorless gas and FC-114a is colorless to clear liquefied gas, both containing a slight ethereal odor and molecular weight of 170.9. Melting points range from -94°C to 14.2°C at 760 mm Hg. Boiling points of FC-113 and FC-113a are 47.7 and 46.1°C at 760 mm Hg, respectively. Boiling points of FC-114 and FC-114a are 3.8 and 4°C at 760 mm Hg, respectively. Vapor pressures of FC-113 and FC-113a are 362.5 and 360 mm Hg at 25°C respectively. Vapor pressures of FC-114 and FC-114a are 2014 and 1653 mm Hg at 25°C respectively. **No additional testing is recommended for physical and chemical characteristics.**

Table 2: Physical and Chemical Characteristics

	FC-113	**FC-113a**	**FC-114**	**FC-114a**
Physical Appearance	Clear, colorless liquid with a slight ethereal odor	Clear, colorless liquid with a slight ethereal odor	Colorless gas with a slight ethereal odor	Colorless to clear liquefied gas with a slight ethereal odor
Molecular Weight	187.4	187.4	170.9	170.9
Water Solubility	170 mg/L @ 25°C *	20.9 mg/L @ 25°C	130 mg/L @ 25°C	137 mg/L @ 25°C
Melting Point	-35°C @ 760 mm Hg	14.2°C @ 760 mm Hg	-94°C @ 760 mm Hg	-56.6°C (pressure not reported)
Boiling Point	47.7°C @ 760 mm Hg	46.1°C @ 760 mm Hg	3.8°C @ 760 mm Hg	4°C @ 760 mm Hg
Vapor Pressure	362.5 mm Hg @ 25°C	360 mm Hg @ 25°C	2014 mm Hg @ 25°C	1635 mm Hg @ 25°C
Density	1.56 @ 25°/4°C	1.58 @ 20°/4°C	1.46 @ 25°C	1.46 @ 25°/4°C
Partition Coefficient (log Kow)	3.16	3.09*	2.82	2.78*
* Estimated value.				

Environmental fate data are essentially equivalent for the category members (Table 3). The environmental fate data indicate all materials are not readily biodegradable and estimated BCF's indicate that these substances have low potential to bioaccumulate. Fugacity model predictions for the fluoroethanes indicate these materials will act similarly in regard to partitioning in the environment. Modeled data shows that all 4 test materials are essentially the same in terms of partitioning, with the majority of the material partitioning to the air and water, with virtually none going to soil or sediment. If released to air, vapor pressures indicates that FC-113 and FC-113a will exist solely as a vapor, and FC-114 and FC-114a will exist solely in the gas phase in the ambient atmosphere. Chlorofluorocarbons are expected to be persistent. These test substances do not react with photochemically produced hydroxyl radicals, ozone molecules, and/or nitrate radicals in the troposphere. FC-113 and FC-114 will gradually diffuse into the stratosphere above the ozone layer where they will slowly degrade due to direct photolysis from UV-C radiation and contribute to the catalytic removal of stratospheric ozone. In the stratosphere, FC-114a will slowly photolyze, releasing chlorine atoms that in turn are responsible for removing ozone. Calculated stratospheric lifetimes for other completely halogenated fluorochloroethanes are generally hundreds of years. Volatilization from moist soil surfaces is expected to be an important fate process based upon estimated Henry's Law constants. If released into water, these test substances may adsorb to suspended solids and sediment based upon estimated Koc values, however, volatilization from water surfaces is expected to be an important fate process based upon the test substances' estimated Henry's Law constants. Estimated volatilization half-lives for FC-113 and FC-113a using a model river and model lake are 4 hours and 5 days, respectively. Estimated volatilization half-lives for FC-114 and 114a using a model river and model lake are 1-1.3 hours and 5 days, respectively. **No additional testing is recommended for environmental fate endpoints.**

Table 3: Environmental Fate

	FC-113	**FC-113a**	**FC-114**	**FC-114a**
Stability in Water*	Rapidly volatilize	Rapidly volatilize	Rapidly volatilize	Rapidly volatilize
Bioaccumulation	Low BCF = 11-33 @ 0.19 mg/L and 14-86 @ 0.01 mg/L	Low BCF = 48.2*	Low BCF = 16-32 @ 400 mg/L and 15-28 @ 40 mg/L	Low BCF = 30*
Biodegradation	Not readily biodegradable	Not readily biodegradable*	Not readily biodegradable*	Not readily biodegradable*
Fugacity*	Air 49.3% Water 47.3% Soil 1.66% Sediment 1.74%	Air 47.5% Water 48.4% Soil 2.38% Sediment 1.72%	Air 50.4% Water 48.3% Soil 0.5% Sediment 0.8%	Air 50.5% Water 48.3% Soil 0.5% Sediment 0.7%
* Modeled data.				

Actual and estimated data on ecotoxicology support a category approach for these chemicals. A limited number of ecotoxicological studies have been conducted with these fluoroethane chemicals. Modeling of physical-chemical parameters (i.e., Kow) and aquatic toxicity was conducted to help provide insight into the behavior in the environment and the aquatic toxicity of FC-113, FC-113a, FC-114, and FC-114a (Table 4). Syracuse Research Corporation models for estimating physical-chemical properties were used to estimate $\log_{10}$ Kow (Meylan and Howard, 1995) for subsequent use in the ECOSAR program (Table 1). ECOSAR (Meylan and Howard, 1999) was used to estimate the missing aquatic toxicity data for the 4 fluoroethane chemicals to green algae, daphnids (planktonic freshwater crustaceans), and fish, if necessary.

The existing test data, coupled with ECOSAR predictions, indicate that fluoroethanes possess moderate acute toxicity potential to aquatic organisms. Results of the available aquatic test data with fish and daphnid data indicate that the 96-hour fish LC_{50} was 7.4-15 mg/L and the 48-hour daphnid EC_{50} was 38-71 mg/L. The ECOSAR predictions of toxicity to these 2 species are in general agreement with the actual measured values when available. Although no measured data exists for algae, ECOSAR predictions of toxicity are in general agreement with the other species tested. The volatility of these chemicals would necessitate the use of a closed test system for algae testing. This type of testing is difficult with algae. Given the similarity of actual test data and ECOSAR estimated data for other species, and the mode of action of these compounds, no algal testing will be conducted. **Therefore, no additional testing is recommended for ecotoxicity endpoints.**

Table 4: Ecotoxicity

	FC-113	**FC-113a**	**FC-114**	**FC-114a**
Toxicity to Fish (96-hour LC_{50} value)	7.4 mg/L (M) 11.28 mg/L (E)	 13.1 mg/L (E)	ca. 2 mg/L (NOEC; 48-hours)[a] ca. 1.5 mg/L (NOEC; 24-hours)[a] 21.5 mg/L (E)	15 mg/L (M) 23.4 mg/L (E)
Toxicity to Invertebrates (48-hour EC_{50} value)	71 mg/L (M) 13.1 mg/L (E)	 15.2 mg/L (E)	>100% saturation at 25°C (N; Atlantic oyster embryo) 10% saturation at 18°C (N; grass shrimp) 24.4 mg/L (E)	38 mg/L (M) 26.5 mg/L (E)
Toxicity to Algae (96-hour EC_{50} value)	8.75 mg/L (E)	10.1 mg/L (E)	16.0 mg/L (E)	17.3 mg/L (E)

E = estimated value
M = measured value
N = nominal value
[a] It was not defined if this value was nominal or measured.
The log Kow values used in the ECOSAR model are listed in Table 2.

Acute toxicity data indicates that these chemicals exhibit similar acute toxicity (Table 5) and thus support the category approach. In mammalian species, all 4 fluoroethanes had very low acute inhalation toxicity, with ALC or LC_{50} values in rats or mice of >49,500 ppm. FC-113 had very low acute oral toxicity with an LD_{50} in rats of 43,000 mg/kg, and FC-114 was at most slightly toxic via the oral route with an ALD in rats of >2250 mg/kg. FC-113 had very low acute dermal toxicity with a dermal ALD of >11,000 mg/kg. FC-113 and FC-114 produced no to mild skin and eye irritation, and FC-113 was reported to have minimal skin sensitizing potential. Both FC-113 and FC-114 were cardiac sensitizers in dogs. The acute data that exists for these chemicals indicates that the chemicals produce similar toxicity profiles for acute toxicity. **No additional testing is recommended for acute toxicity endpoints.**

Table 5: Acute Mammalian Toxicity

	FC-113	**FC-113a**	**FC-114**	**FC-114a**
Oral LD_{50} (rat)	43,000 mg/kg	No Data	ALD >2250 mg/kg	No Data
Inhalation LC_{50} (rat)	4-hour ALC = 56,000 ppm	4-hour > 49,500 ppm	30-minute = 700,000 ppm (mice)	5.25-hour ALC ≥ 153,000 ppm
Cardiac Sensitization	Sensitizer	No Data	Sensitizer	No Data
Dermal LD_{50} (rabbit)	ALD > 11,000 mg/kg	No Data	No Data	No Data
Dermal Irritation	No to mild irritation	No Data	Mild irritation	No Data
Eye Irritation	Practically non-irritating	No Data	Mild irritation	No Data
Dermal Sensitization	Minimal skin sensitizing potential	No Data	No Data	No Data

Repeated Dose

Repeated exposure studies in rats and/or dogs with FC-113 (90-day and 2-year rat inhalation), FC-113a (2-week rat inhalation; 21-day rat oral), FC-114 (2-week rat inhalation; 2-month rat and mouse inhalation; 90-day rat and dog oral), and FC-114a (2-week rat inhalation) have indicated a low degree of toxicity.

In a 90-day rat inhalation study with FC-113, significant increases in lung weights were observed in males at 17,500/20,000 ppm. These findings were positively correlated with gross and microscopic evidence of multi-focal granulomatous interstitial pneumonia. Although the granulomatous pneumonia was not considered to be induced by the test substance, exposure to FC-113 may have resulted in a stress-related enhancement of the existing pneumonic conditions, which was accompanied by increases in lung weight in these rats. Long-term exposure to rats (2 years) to FC-113 was not associated with remarkable toxicity. With the exception of a decreased rate of body weight gain among female rats at 1 and 2% and male rats at 2%, and a slight, transient decrease in serum glucose level in male rats at 2%, no test substance-related abnormities were observed. In addition, FC-113 was not found to be oncogenic.

In a 2-week rat inhalation study with FC-113a, no test substance related effects were observed at exposures of 2000, 10,000, or 20,000 ppm, except for a minimal change in the nasal epithelium in all test substance-exposed groups. This minimal change was reversible after 2 weeks, and was

not considered biologically significant, and may not have been related to FC-113a exposure. In a 21-day oral gavage study in rats with FC-113a, no differences in final mean body weights, body weight gains, clinical signs of toxicity, organ weights, urinalysis parameters, or microscopic effects in the kidney or liver were observed at doses ≤1.24 mmol/kg (highest dose tested).

In a 2-week inhalation study with FC-114 in mice and rats, no mortality was observed. Transient weight loss was observed in mice at 200,000 ppm, and hematologic effects were noted at 200,000 ppm. Only the rats exposed to 200,000 ppm showed lesions. These were congestive and exudative phenomena. No structural alterations were observed at the levels of the alveolar and bronchial walls. These changes were reversible and disappeared 15 days after stopping the exposure. In a 2-month inhalation study in rats and mice at 10,000 ppm, there was a slight loss of red blood cells and a slight increase in white blood cells during the 1st month of exposure, which were practically non-existent at the end of the 2nd month. No changes in blood composition or lung effects were observed. Oral administration of FC-114 to rats and dogs for 90-days at doses of 0.5 and 3% (rats) or 25% (dogs) resulted in no test substance-related effects.

Rats exposed to FC-114a at measured concentrations of up to 41,300 ppm for 2 weeks via inhalation, showed no test substance-related effects. **No additional testing is recommended for repeated dose toxicity.**

Developmental

Pregnant female rats were exposed to 5000, 12,500, or 25,000 ppm of FC-113 via inhalation during Days 6-15 of gestation. Maternal toxicity evidenced as test substance-related reduced body weight gain and food consumption, and increased signs of hyperactivity were observed at 25,000 ppm. No toxicological significant test substance-related findings were observed in the dams at ≤12,500 ppm. No test substance-related effects on the fetuses were observed. Therefore, the test substance was not teratogenic in rats at exposure concentrations ≤25,000 ppm. Although no developmental toxicity data was available for FC-113a, FC-114, and FC-114a, these test substances, based on acute data, are expected to have similar toxicological properties to that of FC-113. **Therefore, no additional testing is recommended for developmental toxicity.**

Reproductive

Male and female rats were exposed to FC-113 at concentrations of 5000 and 12,500 ppm in a reproductive toxicity study. The test substance had no apparent effects on the reproductive parameters examined, with the exception of possible slight effects on pre-coital interval at 5000 and 12,500 ppm, and ovulation at 12,500 ppm. While no formal reproductive toxicity studies have been conducted on FC-113a, FC-114, and FC-114a, pathological examination of the reproductive organs was performed in repeated dose studies for these test substances. No effects on testis or epididymides was observed in repeated dose rat inhalation studies conducted with FC-113a and FC-114a. No test substance-related effects on testis, epididymides, prostate, ovaries, uterus, and/or mammary glands were observed in rat and dog inhalation studies conducted with FC-114. **No additional testing is recommended for reproductive toxicity.**

Table 6: Repeated Dose, Developmental, and Reproductive Toxicity

	FC-113	**FC-113a**	**FC-114**	**FC-114a**
Repeated Dose Toxicity	90-Day Rat Inhalation: NOAEL = 12,500 ppm 2-Year rat inhalation: NOEL = 0.2% 5-Day human inhalation: No apparent effect at ≤1000 ppm 30-Day human dermal: No adverse effect on the structure and function of skin of scalp and forehead	2-Week Rat Inhalation: NOAEL = 20,000 ppm 21-Day rat gavage: NOAEL ≥1.24 mmol/kg	2-Week Rat Inhalation: NOAEL = 100,000 ppm 2-Week Mouse Inhalation: NOAEL = 100,000 ppm 2-Month Rat Inhalation: NOAEL = 10,000 ppm 2-Month Mouse Inhalation: NOAEL = 10,000 ppm 90-Day Rat Gavage: NOAEL = 3% 90-Day Dog Gavage: NOAEL = 25%	2-Week Rat Inhalation: NOAEL = 41,300 ppm
Developmental Toxicity	Not embryotoxic or teratogenic up to 25,000 ppm in rats	No Data	No Data	No Data
Reproductive Toxicity	Possible slight effect on pre-coital interval at ≥ 5000 ppm and ovulation at 12,500 ppm in rats	No effect on reproductive organs in repeated exposure studies	No effect on reproductive organs in repeated exposure studies	No effect on reproductive organs in a repeated exposure study

Based on structural similarities and chemical properties, genetic toxicity data can be assumed to be similar between the chemicals (Table 7). Neither FC-113 nor FC-114 were mutagenic in the bacterial reverse mutation assay using *Salmonella typhimurium*. No data were available on the mutagenicity of FC-113a or FC-114a. FC-113 was negative in a dominant lethal study in mice. The negative bacterial reverse mutation assay results for 2 of the 4 compounds, in combination with the negative dominant lethal results, are considered sufficient to exclude any concern about genotoxic effects associated with this chemical category. **Therefore, no additional testing is recommended for genetic toxicity endpoints.**

Table 7: Genetic Toxicity

	FC-113	**FC-113a**	**FC-114**	**FC-114a**
Mutagenic	Negative	No Data	Negative	No Data
Clastogenic	No Data	No Data	No Data	No Data
In Vivo	Negative (Dominant Lethal in mice)	No Data	No Data	No Data

Overall, the toxicology database for fluoroethanes is relatively complete, and the information available does not suggest a high level of concern. As a chemical category can be used for these chemicals, where data are missing for a single test substance, a read across approach is appropriate. As such, **no further testing for the fluoroethanes is recommended.**

Human Exposure

Air concentrations of Freons 113, 113a, 114 and 114a in manufacturing operations are very low (NIOSH, 1978), and except in the case of accidental releases, there is little potential for significant worker exposure. DuPont has no Acceptable Exposure Limit for FC-113 or FC-114. The DuPont Acceptable Exposure Limit for FC-113a and FC-114a are 1000 ppm, 8- and 12-hour TWA. The ACGIH Threshold Limit Value for FC-113 and FC-114 is 1000 ppm, 8-hour TWA (with a STEL for FC-113 of 1250 ppm), and the OSHA Permissible Exposure Level is 1000 ppm, 8-hour TWA.

Reports investigating health effects of occupational exposure to FC-113 were available. In the first of these, Imbus and Adkins (1972) documented exposure to FC-113 among clean room workers at the Kennedy Space Center over a period of approximately 4.5 years, and compared clinical findings between groups of 50 exposed and non-exposed workers. FC-113 concentrations ranged from 46-4750 ppm over the study period, with mean and median concentrations of 669 ppm and 435 ppm, respectively. The average daily exposure duration was 6 hours, and the average duration of employment in the clean rooms was 2.77 years. Exposed and non-exposed workers were compared with respect to general medical history, clinical chemistry, chest x-ray and selected respiratory parameters. With the exception of dry skin in one

individual, no differences were observed between exposed and non-exposed groups that could be attributed to FC-113 exposure.

A second study of occupational exposure to FC-113 conducted by NIOSH (1980), documented exposure to FC-113 among workers using a vapor degreaser. At the time of the survey, room air concentrations of FC-113 were less that 15% of the current TLV (7600 mg/m^3). Interviews with employees in this work area did not reveal evidence of health problems associated with FC-113 exposure.

In a third study, a group of 13 workers occupationally exposed to 23-62 ppm FC-113 from a few minutes up to a few hours per day were examined. No adverse effects were observed (Triebig and Burkhardt, 1978).

Several cases of accidental death due to occupational exposure to excessive concentrations of FC-113 have been reported (May and Blotzer, 1984; Yonemitsu et al., 1983; Clark et al., 1985; Lehmann, 1980; Stansbury, 1983; Hoshika et al., 1989; McGee et al., 1990; NIOSH, 1989; Kaufman et al., 1994). In the cases that reported actual concentrations, workers were exposed to concentrations of FC-113 ranging from approximately 5000 ppm to 142,000 ppm, which is approximately 5-142 times the documented TLV value.

Other effects due to occupational exposure to FC-113 have been reported, however, in the majority of the reports the exposure concentration was not reported. Two cases of occupational exposure resulted in cardiac anomalies, including cardiac arrest, arrythmias, and/or atrial hypertension (Kaufman et al., 1994; Voge, 1996). Two studies reported decreased nerve conduction velocity, however in one case there was improvement after occupational exposure ceased (Campbell et al., 1986). In the second incident involving a refrigeration repair worker, a follow-up study with 27 refrigeration workers and control group of 14 pipefitters resulted in no difference in conduction velocity between the two groups, although the refrigeration workers reported an elevated incidence of “lightheadedness” (Raffi and Violante, 1981; O’Donoghue, 1985). Liver effects were noted in 2 cases where exposure was at high concentrations (actual concentrations not reported) (Lun and Schmidt, 1979).

Additional clinical reports of human exposure or epidemiology studies with FC-113 were reported; however, exposure to other chemicals/solvents also occurred at that time (AT&T, 1991; Boeing, 1992; Esswein, 1993; Neghab et al., 1997; Rasmussen et al., 1988; Rasmussen et al., 1993a; 1993b; 1993c).

Air monitoring results from a product packaging area of a fluorochemical manufacturing plant indicated FC-114 air concentrations ranging from 0.0022-0.2033% during product loading (NIOSH, 1978).

No reports of human occupational exposure to FC-113a or FC-114a were found.

18 March 2005

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O'Donoghue, J. L. (ed.) (1985). Neurotoxicity of Industrial and Commercial Chemicals, Volume II, p. 110, CRC Press, Inc., Boca Raton, FL (HSDB/145).

Raffi, G. B. and Violante, F. S. (1981). Int. Arch. Occup. Environ. Health, 49:125-127.

Rasmussen, K. et al. (1988). Eur. Neurol., 28(4):205-207 (BIOSIS/88/29222).

Rasmussen, K. et al. (1993a). Int. Arch. Occup. Environ. Health, 64(6):445-448 (NIOSH/00227803).

Rasmussen, K. et al. (1993b). Am. J. Ind. Med., 24(5):553-565 (NIOSH/00217191).

Rasmussen, K. et al. (1993c). Am. J. Ind. Med., 23(5):779-792 (NIOSH/00214460).

Stansbury, J. (1983). Solidarity, 26(12):11-16 (cited in May and Blotzer, 1984).

Triebig, G. and K. Burkhardt (1978). Int. Arch. Occup. Environ. Health, 42:129-135 (CA90:126793n).

Voge, V. M. (1996). South Med. J., 89(5):516-518 (TOXBIB/96/211036).

Yonemitsu et al (1983). Nippon Hoigaku Zasshi, 37(4):428-433 (CA100:62979t).

Appendix A

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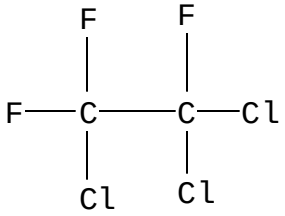
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 76-13-1

Chemical Name: Ethane, 1,1,2-trichloro-1,2,2-trifluoro

Structural Formula:



Other Names:

AI3-62874
Arcton® 63
Arklone P
Ashifron 113
BRN 1740335
Chlorofluorocarbon 113
Daiflon S 3
Daiflon 113
Delifrene 113
Delifrene LS
Dymel® 113
F113
FC 113
FKW 113
Flugene 113
Fluorocarbon 113
Forane 113
Freon® 113
Freon® TF
Freon® TS
Freon® F113
Freon® R 113
Freon® 113TR-T
Fridohna
Frigen 113
Frigen 113a
Frigen 113tr
Frigen 113 TR-H
Frigen 113tr-N
Frigen 113tr-T
Fron 113
Fronsolve 113
Fronsolve AD 9
Genesolv D
Genetron 113
Halocarbon 113
Isceon 113
Kaiser chemicals 11
Kaltron 113MDR
Khladon 113
Ledon 113
P113
Propellant 113
R 113
R 113 (halocarbon)
Racon 113
Refrigerant 113
Refrigerant R 113
Tctfe
Trichlorotrifluoroethane
TTE
Ucon 113
Ucon fluorocarbon 113
Ucon 113/Halocarbon 113

Exposure Limits: OSHA PEL: 1000 ppm (7600 mg/m^3), 8-hour TWA; 1250 ppm (9500 mg/m^3), STEL
ACGIH TLV: 1000 ppm, 8-hour TWA; 1250 ppm, STEL
NIOSH: 1000 ppm (7600 mg/m^3), 10-hour TWA; 1250 ppm (9500 mg/m^3), 15-minute STEL

2.0 Physical/Chemical Properties

2.1 Melting Point

Value:	-35°C
Decomposition:	No Data
Sublimation:	No Data
Pressure:	760 mm Hg
Method:	No Data
GLP:	Not Applicable
Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-157, CRC Press, Inc., Boca Raton, FL (HSDB/145).
Reliability:	Not assignable because limited study information was available.

Additional References for Melting Point:

Aldrich Chemical Co., Inc. (2003). Material Safety Data Sheet.

Desoille, H. L. et al. (1968). Arch. Maladies Profess. Med Trav. Securite Sociale, 29(7-8):381-388.

Grasselli, J. G. and W. M. Ritchey (1975). Chemical Rubber Company Atlas of Spectral Data and Physical Constants for Organic Compounds, 2nd ed., CRC Press, Inc., Cleveland, Ohio (ISHOW-0001509).

Hümpfner, D. H. (1974). Zbl. Arbeitsmed., 4:103-104.

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 10th ed., p. 1835, John Wiley & Sons, Inc., New York, NY.

Mallinckrodt Baker, Inc. (2000). Material Safety Data Sheet T5100 (August 2).

Matheson Tri-Gas, Inc. (1999). Material Safety Data Sheet (March 16).

Riddick, J. A. et al. (1986). Techniques of Chemistry, 4th ed., p. 1325, Wiley-Interscience, New York, NY (ENVIROFATE-0003898).

2.2 Boiling Point

Value:	47.7°C
Decomposition:	No Data
Pressure:	760 mm Hg
Method:	No Data
GLP:	Not Applicable
Reference:	Grasselli, J. G. and W. M. Ritchey (1975). Chemical Rubber Company Atlas of Spectral Data and Physical Constants for Organic Compounds, 2nd ed., CRC Press, Inc., Cleveland, Ohio (ISHOW-0001509).
Reliability:	Not assignable because limited study information was available.

Additional References for Boiling Point:

DuPont Co. (1996). Material Safety Data Sheet DU000126 (October 19).

Eastman Kodak Company (1986). Material Safety Data Sheet Accession Number 911300 (December 9).

Hümpfner, D. H. (1974). Zbl. Arbeitsmed., 4:103-104.

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 10th ed., p. 1835, John Wiley & Sons, Inc., New York, NY.

Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-157, CRC Press, Inc., Boca Raton, FL (HSDB/145).

Mallinckrodt Baker, Inc. (2000). Material Safety Data Sheet T5100 (August 2).

Matheson Tri-Gas, Inc. (1999). Material Safety Data Sheet (March 16).

National Academy of Sciences – National Research Council (1960). Reports prepared under Contract N7onr-291(61), Washington, DC.

Riddick, J. A. et al. (1986). Techniques of Chemistry, 4th ed., p. 1325, Wiley-Interscience, New York, NY (ENVIROFATE-0003899).

2.3 Density

Value:	1.5635
Temperature:	25°C/4°C
Method:	No Data
GLP:	No Data
Results:	No additional data.

Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-157, CRC Press, Inc., Boca Raton, FL (HSDB/145).
Reliability:	Not assignable because limited study information was available.

Additional References for Density:

Aldrich Chemical Co., Inc. (2003). Material Safety Data Sheet.

DuPont Co. (1996). Material Safety Data Sheet DU000126 (October 19).

Eastman Kodak Company (1986). Material Safety Data Sheet Accession Number 911300 (December 9).

Hümpfner, D. H. (1974). Zbl. Arbeitsmed., 4:103-104.

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 10th ed., p. 1835, John Wiley & Sons, Inc., New York, NY.

Mackison F. W. et al. (1981). NIOSH/OSHA – Occupational Health Guidelines for Chemical Hazards, DHHS (NIOSH) Publication No. 81-123, U.S. Government Printing Office, Washington, DC (HSDB/148).

Mallinckrodt Baker, Inc. (2000). Material Safety Data Sheet T5100 (August 2).

Matheson Tri-Gas, Inc. (1999). Material Safety Data Sheet (March 16).

Weast R. C. (1969). Chemical Rubber Company Handbook of Chemistry and Physics, 50th ed., CRC Press, Inc., Cleveland, Ohio (ISHOW-0001511).

2.4 Vapor Pressure

Value:	362.5 mm Hg
Temperature:	25°C
Decomposition:	No Data
Method:	No Data
GLP:	Not Applicable
Reference:	Boublik, T. et al. (1984). The Vapor Pressures of Pure Substances: Selected Values of the Temperature Dependence of the Vapor Pressures of Some Pure Substances in the Normal and Low Pressure Region, Vol. 17, Elsevier Sci. Publ., Amsterdam, Netherlands (ENVIROFATE-0003893).
Reliability:	Not assignable because limited study information was available.

Additional References for Vapor Pressure:

Aldrich Chemical Co., Inc. (2003). Material Safety Data Sheet.

Daubert T. E. and R. P. Danner (1989). Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation, Vol. 4, Design Institute for Physical Property Data, American Institute of Chemical Engineers Hemisphere Pub. Corp. New York, NY (ENVIROFATE-0003901).

DuPont Co. (1996). Material Safety Data Sheet DU000126 (October 19).

Eastman Kodak Company (1986). Material Safety Data Sheet Accession Number 911300 (December 9).

Mackison, F. W. et al. (ed.) (1981). NIOSH/OSHA – Occupational Health Guidelines for Chemical Hazards, DHHS(NIOSH) Publication, p. 2, No. 81-123 (HSDB/145).

Matheson Tri-Gas, Inc. (1999). Material Safety Data Sheet (March 16).

National Academy of Sciences – National Research Council (1960). Reports prepared under Contract N7onr-291(61), Washington, DC.

2.5 Partition Coefficient (log Kow)

Value:	3.16
Temperature:	25°C
Method:	No Data
GLP:	Not Applicable
Reference:	Hansch, C. et al. (1995). Exploring QSAR – Hydrophobic, Electronic, and Steric Constants, American Chemical Society, Washington, DC (HSDB/145).
Reliability:	Not assignable because limited study information was available.

Additional References for Partition Coefficient (log Kow):

Leo, A. J. (1978). Report on the Calculation of Octanol/Water Log P Values for Structures in EPA Files (ISHOW-0001513).

Lynam, W. J. et al. (1982). Handbook of Chemical Property Estimation Methods, pp. 4-9, 5-5, 15-21 to 15-32 (HSDB/145).

McDuffie, B. (1981). Chemosphere, 10:73-83 (ENVIROFATE-0003896).

2.6 Water Solubility

Value:	170 mg/L
Temperature:	25°C
pH/pKa:	Estimated pKa: Not applicable; no exchangeable hydrogens.
Method:	No Data
GLP:	Not Applicable
Reference:	Hovarth, A. L. et al. (1999). J. Phys. Chem. Ref. Data, 28:395-507. pKa - http://ibmlc2.chem.uga.edu/sparc/index.cfm
Reliability:	Estimated values based on accepted models.

Additional References for Water Solubility:

Hümpfner, D. H. (1974). Zbl. Arbeitsmed., 4:103-104.

DuPont Co. (1996). Material Safety Data Sheet DU000126 (October 19).

Eastman Kodak Company (1986). Material Safety Data Sheet Accession Number 911300 (December 9).

Mallinckrodt Baker, Inc. (2000). Material Safety Data Sheet T5100 (August 2).

Matheson Tri-Gas, Inc. (1999). Material Safety Data Sheet (March 16).

Riddick, J. A. et al. (1986). Techniques of Chemistry, 4th ed., p. 1325, Wiley-Interscience, New York, NY (ENVIROFATE-0003892).

Weast R. C. (1969). Chemical Rubber Company Handbook of Chemistry and Physics, 50th ed., CRC Press, Inc., Cleveland, Ohio (ISHOW-0001512).

2.7 Flash Point: No Data.

2.8 Flammability

Results:	Will not burn; Autodecomposition = 300°C
Method:	No Data
GLP:	No Data
Reference:	DuPont Co. (1996). Material Safety Data Sheet DU000126 (October 19).
Reliability:	Not assignable because limited study information was available.

Additional References for Flammability:

Aldrich Chemical Co., Inc. (2003). Material Safety Data Sheet.

Hümpfner, D. H. (1974). Zbl. Arbeitsmed., 4:103-104.

Matheson Tri-Gas, Inc. (1999). Material Safety Data Sheet (March 16).

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	No mechanism for direct photoalteration of this chemical in the lower atmosphere due to irradiation at $\geq$ 290 nm.
Indirect Photolysis:	An estimated half-life of 53,480 days was calculated using an average atmospheric OH concentration of $5x10^5$ molecule/cm^3 at 25°C.
Breakdown Products:	No Data
Method:	No Data
GLP:	Not Applicable
Reference:	Direct Photolysis: Doucet, J. et al. (1973). J. Chem. Phys., 58:3078-3716 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva). Doucet, J. et al. (1974). J. Chem. Phys., 62(2):355-359 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva). Indirect Photolysis: Atkinson R. (1989). J. Phys. Chem. Ref. Data, Monograph No. 1 (ENVIROFATE-0003900).
Reliability:	Estimate based on known qualitative structure-activity relationships.

Additional References for Photodegradation:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

USEPA (1983). Health Assessment Document for 1,1,2-Trichloro-1,2,2-trifluoroethane, p. 2, EPA-600/58-002F (HSDB/145).

Kloepffer, W. and B. Daniel (1990). Reaktionskonstanten zum abiotischen Abbau von organischen Chemikalien in der Atmosphaere, R-67.233-4, Battelle-Institut e.V., Frankfurt/Main 90 (cited in Verschueren, K. (2001). Handbook of Environmental Data on Organic Chemicals, 4th ed., Vol. 1, pp. 2098-2100, John Wiley & Sons, Inc., New York, NY).

3.2 Stability in Water

Concentration:	No Data
Half-life:	The Henry's Law constant for FC-113 is estimated as 5.3×10^{-1} atm m^3/mole (SRC, n.d.) based upon its vapor pressure, 363 mm Hg, and water solubility, 170 mg/L. This Henry's Law constant indicates that FC-113 is expected to volatilize rapidly from water surfaces (Lyman et al., 1990). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) (Lyman et al., 1990) is estimated as 4 hours (SRC, n.d.). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) (Lyman et al., 1990) is estimated as 5 days (SRC, n.d.).
% Hydrolyzed:	No Data
Method:	Estimated
GLP:	Not Applicable
Reference:	Lyman, W. J. et al. (1990). Handbook of Chemical Property Estimation Methods, pp. 15-1 to 15-29, Amer. Chem. Soc., Washington, DC (HSDB/145). SRC (n.d.). Syracuse Research Corporation (HSDB/145).
Reliability:	Estimated value based on accepted model.

Additional References for Stability in Water:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Riddick, J. A. et al. (1986). Organic Solvents: Properties and Methods of Purification, 4th ed., Wiley-Interscience, NY, pp. 567-569 (HSDB/145).

Lynam, W. J. et al. (1982). Handbook of Chemical Property Estimation Methods, pp. 4-9, 5-5, 15-21 to 15-32 (HSDB/145).

Okouchi, S. (1992). Environ. Inter., 18:389-396.

3.3 Transport (Fugacity)

Media: Air, Water, Soil, and Sediments

Distributions:

Compartment	% of total distribution	½ life, hours (advection + reaction)
Air	49.3	1e5
Water	47.3	1.44 e3
Soil	1.66	2.88e3
Sediment	1.74	1.3e4

Adsorption Coefficient: Koc = 593

Desorption: No Data

Volatility: Henry's Law Constant = 0.526 atm-m^3/mole

Method: Modeled.
SMILES: FC(F)(C(F)(CL)CL)CL
Molecular Wt: 187.38
Vapor Pressure: 363 mm Hg
Log Kow: 3.16
Soil Koc: 593 (calc by model)

Henry's Law Constant - HENRYWIN v3.10 module of EPIWIN v3.11 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available.

Koc – Calculated from log Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.11 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.

GLP: Not Applicable

Reference: HENRYWIN –

J. Hine and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-298.

Meylan, W. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293.

Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in:

Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated values based on accepted models.

Additional References for Transport (Fugacity): None Found.

3.4 Biodegradation

Value: Not readily biodegradable. 1,1,2-Trichloro-1,2,2-trifluoroethane, reached 0-5% of its theoretical BOD in 4 weeks.

Breakdown Products: No Data

Method: 1,1,2-Trichloro-1,2,2-trifluoroethane, present at 100 mg/L, reached 0-5% of its theoretical BOD in 4 weeks at 25°C, using an activated sludge inoculum at 30 mg/L and the Japanese MITI test.

GLP: No Data

Reference:	Chemicals Inspection and Testing Institute (1992). Japan Chemical Industry Ecology – Toxicology and Information Center, ISBN 4-89074-101-1, p. 2-22 (HSDB/145).
	Chemicals Evaluation and Research Institute Website. April 21, 2004. http://qsar.cerij.or.jp/cgi-bin/DEGACC/index.cgi?E
Reliability:	Medium based on accepted method and limited study information.

Additional References for Biodegradation:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Blum, S. (1991). Ecotoxicol. Environ. Saf., 22(2):198-224 (cited in Verschueren, K. (2001). Handbook of Enviornmental Data on Organic Chemicals, 4th ed., Vol. 1, pp. 2098-2100, John Wiley & Sons, Inc., New York, NY).

Deipser, A. (1998). Waste Management & Research, 16(45):330-341 (BIOSIS/98/30230).

Deipser, A. and R. Stegmann (1997). Environ. Sci. Pollut. Res. Inter., 4(4):209-216 (BIOSIS/97/33223).

DuPont Co. (1989). "Degradation Studies of Certain Organics by Anaerobic Digestion" (cited in TSCA Fiche OTS0520187).

Jackson, R. E. et al. (1992). Environ. Sci. Pollut. Control Ser. 4(Groundwater Contam. Anal. Haz. Waste Sites), pp. 511-526, Lesage, S. and R. E. Jackson (eds.), M. Dekker, New York, NY (HSDB/145).

3M (Minnesota Mining and Manufacturing) Co. (1982). "Product Environmental Data" (cited in TSCA Fiche OTS0206107, OTS0206116, OTS0206110).

Rutgers (1978). "Degradation Studies of Certain Organics by Anaerobic Digestion," Department of Environmental Science, Cook College, Rutgers, The State University New Brunswick, NJ (August 14) (cited in TSCA Fiche OTSO520187).

Semprini, L. et al. (1992). Environ. Sci. Technol., 26:2454-2461 (HSDB/145).

Hoechst (1986). Unpublished Data der Abt. Umweltschutz (cited in IUCLID (2000). IUCLID Dataset, "1,1,2-Trichlorotrifluoroethane (Feb. 19)).

Hoechst (1986). Unpublished Data, Abt. Umweltschutz (W 86-339) (cited in Verschueren, K. (2001). Handbook of Enviornmental Data on Organic Chemicals, 4th ed., Vol. 1, pp. 2098-2100, John Wiley & Sons, Inc., New York, NY).

Hoechst (1984). Unpublished Data der Abt. Umweltschutz (cited in IUCLID (2000). IUCLID Dataset, "1,1,2-Trichlorotrifluoroethane (Feb. 19)).

Hoechst (1973). Unpublished Data der Abt. Reinhaltung von Wasser und Luft (cited in IUCLID (2000). IUCLID Dataset, "1,1,2-Trichlorotrifluoroethane (Feb. 19)).

3.5 Bioconcentration

Value:	Reported BCF Range of 11-33 and 14-86 at exposure levels of 0.19 and 0.01 mg/L, respectively, based on a 6-week continuous flow assay using carp (*Cyprinus carpio*). According to a classification scheme (Franke, C. et al. (1994). Chemosphere, 29:1501-1504), BCFs of 11-86 suggest the potential for bioconcentration in aquatic organisms is low.
Method:	Chemicals Inspection and Testing Institute (1992). Biodegradation and bioaccumulation data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology – Toxicology and Information Center, ISBN 4-89074-101-1, p. 2-22 (HSDB/145). Chemicals Evaluation and Research Institute Website. April 21, 2004. http://qsar.cerij.or.jp/cgi-bin/DEGACC/index.cgi?E
GLP:	Not Applicable
Reference:	Chemicals Inspection and Testing Institute (1992). Biodegradation and bioaccumulation data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology – Toxicology and Information Center, ISBN 4-89074-101-1, p. 2-22 (HSDB/145).
Reliability:	Not assignable because limited study information was available.

Additional References for Bioconcentration:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Riddick, J. A. et al. (1986). Organic Solvents: Properties and Methods of Purification, 4th ed., Wiley-Interscience, NY, pp. 567-569 (HSDB/145).

McDuffie, B. (1981). Chemosphere, 10:73-82 (HSDB/145).

Lynam, W. J. et al. (1982). Handbook of Chemical Property Estimation Methods, pp. 4-9, 5-5, 15-21 to 15-32 (HSDB/145).

SRC (1988). Syracuse Research Corporation (ENVIROFATE-0003897).

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type:	**96-Hour LC_{50}**
Species:	*Salmo gairdneri*, rainbow trout
Value:	7.4 mg/L (95% confidence interval, 6.4-8.8 mg/L)
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The exposure system consisted of 8 commercial, rectangular, glass aquaria equipped with overflow drains to maintain 12-liter exposure volumes (15 cm liquid depth). These aquaria were fed by a modified Mount and Brungs diluter, calibrated to deliver about 2.5 aquarium volume turnovers per 24 hours with fresh solution added approximately every 48 minutes. During the study, a check of the diluter function was made at least once daily.

The source of the dilution water was a 350-foot well, cased and sealed to bedrock to prevent contamination from surface run-off. The well water was aerated and filtered through a 10 µ filter to remove particulates and then distributed to the test system through aged PVC pipe.

The test material was prepared as 200 mg/L stock solution. Each day a fresh aqueous solution of the test material was made up in well water for the test. Three days before the fish were added to the aquaria, the diluter was started to equilibrate the system to the desired test concentrations.

Nominal test concentrations were 0, 9, 16, 26, 44, 72, 120, and 200 mg/L.

Ten juvenile, unsexed rainbow trout, with a 3.4 cm mean standard length (range 3.0 to 3.8 cm) and 0.72 g mean wet weight (range 0.47 to 1.12 g) were placed in the test vessels, 1 test vessel per concentration. Rainbow trout were identified by labeling the culture and test vessels. The fish were maintained for approximately 102 days in a 115-gallon Fiberglass tank before being used for the test. Holding temperature was within 1°C of testing temperature throughout the holding period. The dissolved oxygen concentration during acclimatization was assumed to be at or near saturation because air was continuously bubbled through the water. No treatment of the fish for diseases was required during the holding period. Fish were not fed for approximately 48 hours prior to nor during the exposure. The test solutions were not aerated, and temperature was maintained between 12.2 and 12.5°C. Photoperiod was maintained at 16 hours light:8 hours dark.

Mortality counts and observations were made approximately every 24 hours during the 96-hour exposure period. Dissolved oxygen and pH were measured in the water control and in the low test concentrations at the beginning of the test and at approximately 24-hour intervals during the 96-hour exposure period. Dissolved oxygen and pH were measured in the medium and high test concentrations at the beginning of the test and at 24 hours, by which time all the fish were dead. Total alkalinity, hardness (EDTA), and conductivity were measured at the beginning of the test in the water control. Concentration data were scale-of-dose transformed to log 10 and the 96-hour LC_{50} and confidence intervals were calculated by probit analysis.

Daily analysis of the test material in each aquarium was done by a head space technique using a Miran infrared spectrophotometer equipped with a pump and closed loop sampling system capable of monitoring the gas space of the glass covered aquaria.

GLP: Yes

Test Substance: FC-113, purity >99.99%

Results: Measured test concentrations were 4.1, 6.2, 5.0, 9.4, 14.3, 28.6, and 48.1 mg/L at nominal concentrations of 9, 16, 26, 44, 72, 120, and 200 mg/L, respectively. At test start dissolved oxygen ranged from 9.2-9.4. At study completion

(96 hours for 0 and 9 mg/L and 24 hours for 72 and 200 mg/L) dissolved oxygen ranged from 8.8-9.0 mg/L. At test start pH ranged from 7.5-7.6. At study completion (96 hours for 0 and 9 mg/L and 24 hours for 72 and 200 mg/L) pH was 7.5 at all concentrations tested. Total alkalinity, EDTA hardness, and conductivity of the water control at 0 hours were 98 mg/L as $CaCO_3$, 82 mg/L as $CaCO_3$, and 154 µmhos/cm, respectively. All chemical and physical parameters measured during the study were within acceptable ranges.

Mortality at 96 hours was 0, 0, 0, 20, 90, 100, 100, and 100% at 0, 9, 16, 26, 44, 72, 120, and 200 mg/L, respectively. Clinical signs observed in some fish included darkening in color, erratic swimming, swimming at the surface, partial loss of equilibrium, lethargy, moribundity, laying on the bottom, gasping for air, and rapid respiration at test concentrations of 9.4 mg/L and greater.

Reference: DuPont Co. (1986). Unpublished Data, Haskell Laboratory Report No. 726-86, "Flow-Through Acute 96-Hour LC_{50} of Freon® 113 to Rainbow Trout" (November 14) (also cited in TSCA Fiche OTS0520358).

Reliability: High because a scientifically defensible or guideline method was used.

Type: **96-hour LC_{50}**
Species: Fish
Value: 11.28 mg/L; log Kow = 3.16
Method: Modeled
GLP: Not Applicable
Test Substance: FC-113
Results: No additional details
Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability: Estimated value based on accepted model.

Additional References for Acute Toxicity to Fish:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Chemicals Evaluation and Research Institute Website. April 21, 2004. http://qsar.cerij.or.jp/cgi-bin/DEGACC/index.cgi?E.

Hoechst Celanese (1989). "Acute Fish Toxicity, Chronic *Daphnia* Toxicity, and Bacteria Toxicity on Frigen 113" (cited in TSCA Fiche OTS0516686, OTS0520414, OTS0520415, OTS0520417, OTS0520418).

Hoechst Celanese (1973). " Fish Toxicity of Frigens" (cited in TSCA Fiche OTS0520416).

Data from these additional sources were not summarized because the study design was not adequate.

DuPont Co. (1971). Unpublished Data, Haskell Laboratory Report No. 398-71, "Acute Toxicity of Freon® 113 to the Atlantic Oyster Embryo (*Crassostrea virginica*), the Grass Shrimp (*Palaemonetes vulgaris*), and the Killifish (*Fundulus heteroclitus*)" (October) (also cited in TSCA Fiche OTS0520348).

DuPont Co. (1977). Unpublished Data, Haskell Laboratory Report No. 751-77, "96-Hour LC_{50} in Fathead Minnows" (September 16) (also cited in TSCA Fiche OTS0520349).

Data from these additional sources were not summarized because the test substance was a mixture or otherwise inappropriate.

3M (Minnesota Mining and Manufacturing) Co. (1982). "Product Environmental Data" (cited in TSCA Fiche OTS0206107, OTS0206116, OTS0206110).

4.2 Acute Toxicity to Invertebrates

Type:	**48-hour EC_{50}**
Species:	*Daphnia magna*
Value:	71 mg/L (95% confidence interval, 63-78 mg/L)
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Hard reconstituted water was prepared for use as dilution water. The test material was prepared as a 200 mg/L stock solution in hard reconstituted water and diluted with hard reconstituted water to yield the desired nominal exposure concentrations of 20, 27, 36, 47, 63, 84, 113, 150, and 200 mg/L. The desired amount of the appropriate stock solution was brought to 100 mL test volumes in 120 mL amber glass serum bottles fitted with Mininert® valves to facilitate the withdrawal of head space samples for analysis. Five identical vessels containing only hard reconstituted water were designated as water controls. Five daphnids, less than 24 hours old, were placed into each of 4 test vessels per concentration. No daphnids were placed into the 5th test vessel per concentration. Food was not provided during the test. Test solutions were not aerated, and the temperature was maintained between 20.0 and 20.3°C. Photoperiod was maintained at 16 hours light:8 hours dark. Immobility counts and observations were made at 48 hours after the exposure was initiated. Dissolved oxygen and pH were measured in the water control and in the low, medium, and high exposure concentrations at the beginning and end of the exposure. The total alkalinity, hardness (EDTA), and conductivity of the water control were measured at the beginning of the exposure. Concentration data were transformed to log 10, and the 48-hour EC_{50} and 95% confidence limits were calculated by probit analysis.
GLP:	Yes
Test Substance:	FC-113, purity >99.99%
Results:	Measured test concentrations were 21, 28, 36, 47, 66, 91, 122, 146, and 191 mg/L at 20, 27, 36, 47, 63, 84, 113, 150, and 200 mg/L, respectively. Dissolved oxygen at study start was 8.4, 8.5, 8.5, and 7.9 at 0, 21, 66, and 191 mg/L. Dissolved oxygen at study completion was 8.6, 8.5, 8.5, and 7.7 at 0, 21, 66, and 191 mg/L. pH at study start was 8.3,

	8.3, 8.3, and 8.4 at 0, 21, 66, and 191 mg/L. pH at study completion was 8.4, 8.4, 8.4, and 8.5 at 0, 21, 66, and 191 mg/L. Total alkalinity, EDTA hardness, and conductivity of the water control at study start were 121 mg/L as $CaCO_3$, 170 mg/L as $CaCO_3$, and 600 µmhos/cm, respectively.
Reference:	DuPont Co. (1986). Unpublished Data, Haskell Laboratory Report No. 699-86, "*Daphnia magna* Static Acute 48-Hour EC_{50} of Freon® 113" (November 14) (also cited in TSCA Fiche OTS0520350).
Reliability:	High because a scientifically defensible or guideline method was used.

Type:	**48-hour LC_{50}**
Species:	Daphnid
Value:	13.1 mg/L; log Kow = 3.16
Method:	Modeled
GLP:	Not Applicable
Test Substance:	FC-113
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates:

Data from this additional source supports the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Hoechst Celanese (1989). Hoechst Celanese Corp. (1989). "Datenblatt Altstoffe Toxciological Profiles for 3 Chemicals" (cited in TSCA Fiche OTS0516686, OTS0520414, OTS0520415, OTS0520417, OTS0520418).

Data from this additional source was not summarized because the study design was not adequate.

DuPont Co. (1971). Unpublished Data, Haskell Laboratory Report No. 398-71, "Acute Toxicity of Freon® 113 to the Atlantic Oyster Embryo (*Crassostrea virginica*), the Grass Shrimp (*Palaemonetes vulgaris*), and the Killifish (*Fundulus heteroclitus*)" (October) (also cited in TSCA Fiche OTS0520348).

4.3 Acute Toxicity to Aquatic Plants: No Data.

Type:	**96-hour EC_{50}**
Species:	Green algae
Value:	8.75 mg/L; log Kow = 3.16
Method:	Modeled
GLP:	Not Applicable
Test Substance:	FC-113
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Aquatic Plants: None Found.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type:	**Oral LD_{50}**
Species/Strain:	Male rats/Sprague-Dawley
Value:	43,000 mg/kg
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Acute oral toxicity was determined in 30 male rats (200-300g) at 5 rats per dose. Twelve hours prior to intubation of the test substance, food only was withheld from the animals to ensure uniformity as to stomach contents. The test substance was administered with no added diluents. It was necessary to administer the test substance in more than 1 dose at the higher dose levels. Such dosages were scheduled at 3-hour intervals, and the total dose administered over a period of 12 hours. Consequently, the volume administered varied from 1.0 to 12.0 mL, depending upon the dosage administered. However, no more than 4.0 mL was administered to any animal at any one time.

	Following administration of the test substance, all animals were fed food and water *ad libitum*, housed individually, and observed for a period of 14 days. During the observation period, all physical and behavioral changes, as well as date and approximate time of death were noted. Autopsies for gross pathological changes in tissues and organs were performed on all animals dying during the 14-day observation period. Surviving animals were weighed and sacrificed at the end of the test period and autopsied for gross pathological changes.
GLP:	No
Test Substance:	FC-113, purity not reported
Results:	Immediately following administration, all animals became lethargic, their coats were ruffled, and facial edema occurred. The abdominal area was greatly distended regardless of the dosage administered. All the animals were observed to have a liquid fecal discharge. These conditions persisted for 24 hours. At the end of 48 hours, all symptoms disappeared, with the exception of the ruffled appearance, which lasted at all levels for the duration of the study. All of the animals dying during the experiment showed consistent gross pathological changes. Of particular significance was hemorrhage in the lungs, possibly resulting from contact of the lung tissue with the test substance (due to its high volatility). The livers also exhibited a mottled surface with normal color. The stomach and gastrointestinal tract were distended with gas and fluid. All other tissues appeared normal. Weight loss was noted in animals dying during the study, but all survivors gained weight. Animals at lower levels died sooner than those at higher levels. The surviving animals showed no gross pathological changes, except for a slight lung hemorrhage at the higher levels.
Reference:	Michaelson, J. B. and D. J. Huntsman (1964). J. Med. Chem., 7:378-379.
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Oral Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Dow Chemical (1949). Unpublished Data, "Results of Range Finding Toxicological Test of Some Fixed Chlorofluorohydrocarbons" (April 12) (cited in TSCA Fiche OTS0520705).

DuPont Co. (1967). Unpublished Data, "Oral ALD Test with Rabbits" (May 26).

Hümpfner, D. H. (1974). Zbl. Arbeitsmed., 4:118-119.

Data from this additional source were not summarized because the study design was not adequate.

DuPont (1970). Unpublished Data, Haskell Laboratory Report No. 91-70, "Aspiration in Rats" (February 26) (also cited in TSCA Fiche OTS0520332).

Data from this additional source were not summarized because the test substance was a mixture or otherwise inappropriate.

DuPont Co. (1982). Unpublished Data, Haskell Laboratory Report HL-606-82, "Oral LD_{50} Test in Rats" (September 27).

Type:	**Inhalation ALC**
Species/Strain:	Male rats/ChR-CD
Value:	56,000 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. The test substance was metered into a heated (55-65°C) stainless steel tube with a syringe infusion pump. Houseline air carried the vapor into a 20-liter exposure chamber containing 6 male rats of 248-290 g initial body weight. Average analytical concentrations tested were 27,500, 43,000, 56,000, and 59,000 ppm. The concentration of the chamber atmosphere was determined by gas chromatography analysis (thermal conductivity detector). Samples were taken every 15-20 minutes.

	The exposure lasted 4 hours. All surviving animals were weighed and observed daily for 14 days post-exposure. No histopathological examinations were performed.
GLP:	No
Test Substance:	FC-113, purity >99.9%
Results:	Mortality was 0/6, 0/6, 1/6, and 1/6 at 27,500, 43,000, 56,000, and 59,000 ppm, respectively. At all levels, excitation and front leg tremors ("piano player syndrome") occurred during the first few minutes of exposure, followed by prostration and whole-body tremors during the remainder of the exposure.
Reference:	DuPont Co. (1975). Unpublished Data, Haskell Laboratory Report No. 447-75, "Acute Inhalation Toxicities" (July 31) (also cited in TSCA Fiche OTS0571755).
Reliability:	High because a scientifically defensible or guideline method was used.

Type:	**Human Inhalation Exposure**
Species/Strain:	Human volunteers
Exposure Levels:	0, 1500, 2500, 3500, 4500 ppm
Method:	A small exposure booth was constructed having a plywood floor and ceiling and covered on 3 sides by 7 mil Mylar® film. The 4th side was closed by a metal clad plywood door sealed to the chamber by a plastic magnetic gasket. This closure arrangement meant that the exposure chamber door could be opened and closed from both inside and outside without catches and locks which might have been potential sources of gas leakage. "Mylar" film was also used to cover the inside surfaces of the plywood ceiling and floor to prevent vapors being taken up by the wood. All edges of the "Mylar" were sealed with "Mylar" adhesive tape to provide a gas-tight joint and a 3-inch fabric adhesive tape for abrasion resistance. Below the door, a series of copper tubes passed through the plywood wall and acted as bulkhead connectors for gas sampling lines and electrical wiring. The tubes and wires were sealed within the copper tubes. The air or air-vapor mixture for the exposure was led in through the roof of the chamber and was distributed within the chamber by a sheet of perforated "Mylar" film forming a shallow plenum above the subject. The exhaust gases from the chamber were led out through a flexible hose to an exhaust fan, and thence to the outside of the building. The desired test substance vapor concentration in air was created by taking air suitable for supplying human respiration and feeding it into 2 pipes. The larger of the

2 pipes fed the air to a flowmeter fitted with a feedback differential pressure regulator so that the flow downstream from the regulator remained constant despite changes in upstream pressure. The smaller pipe fed the air through a similar flowmeter and feedback regulator combination and thence into a glass gas-washing bottle containing a weighed amount of the test substance. The air bubbled through the test substance and the vapor from the gas-washing bottle was then injected into the large gas stream and the mixture was led to the exposure chamber. To change the concentration of the vapor in the chamber, the small air flow was increased or decreased but, except for major changes in concentration, the large or diluting flow was kept constant.

Checks on the concentration of test substance being produced were made in 3 ways. First, the weight loss of the compound during the time of the exposure was measured and related to the total amount of air drawn through the chamber, enabling the nominal concentration of test substance in air to be calculated. Second, a continuous sample of the vapor in the chamber was drawn through a flame ionization analyzer and a continuous record was drawn out on a strip chart recorder. Because the flame ionization analyzer was not calibrated for use with the test substance, it was not possible to read the concentration of test substance directly from the strip chart recording, but it did enable any change in the concentration to be detected. Thus the flame ionization analyzer was used to monitor the chamber concentration continuously, and if the test substance levels showed little or no fluctuation, the nominal concentration obtained from the evaporative weight loss of the test substance was assumed to hold throughout the exposure. The 3rd method consisted of periodic sampling of the chamber atmosphere by the subject in the chamber using evacuated bottles, which were opened to the chamber atmosphere, then sealed, and subsequently analyzed by gas chromatography. This last method positively identified the test substance and also measured the concentration of the test substance present in the air.

Preliminary calibration established the correct flowmeter settings to be used to obtain the desired test substance concentrations and demonstrated that these could be held constant within $\pm$100 ppm during a 3-hour period. Experiments were then conducted to check whether carbon dioxide rose to unacceptable levels when a person occupied

the chamber for a period of 2 hours. These experiments showed that no problem was expected due to a buildup in carbon dioxide levels with time.

To monitor the performance of the subject in the chamber, a battery of tests was given at intervals during each exposure to the test substance, and the results of these tests were compared with control runs on the day preceding and the day following the exposure to the test substance. During the control runs, the test situation remained the same as during the test substance exposure, except that no vapor was injected into the air flowing into the chamber. The battery of tests consisted of:

The Crawford Small Parts Dexterity Test – Part A of this test consisted of taking small set screws, and with the aid of a screwdriver, screwing them through tapped holes in a metal plate. The score represented the number of screws completely inserted in a period of 3 minutes. Part B consisted of inserting metal pins into a series of holes in a plate with the aid of tweezers. Small metal collars were then dropped over the pins as they projected from the plate. The score represented the number of pins and collars assembled in 3 minutes.

The Short Employment Test-Clerical (S.E.T) – This test was one of vigilance and consisted of coding a series of names according to the financial balance shown against these names on a facing page of the test. The number correctly coded in 3 minutes was taken as the score.

Card Sorting – A pack of playing cards was sorted into suits as rapidly and accurately as possible. The time taken to complete the task was taken as the score.

Card Sorting with an Auxiliary Task – In this test, the same subject sorted the cards as above, but at the same time was asked to add groups of 3 single digit numbers presented to him at fixed intervals by means of a tape recorder. The time taken to complete the card sorting was taken as the score, but a record of the errors in addition and in card sorting was also kept.

Two male subjects were used. Prior to exposure, both subjects were judged to be in good health on the basis of their medical history, physical examination, hematology,

liver function tests, and urinalysis. A series of preliminary studies were conducted as training experiments to reduce the learning factor in the tests during the series of test substance exposures.

No tests were run on Mondays, since previous experience indicated that subjects returning from weekends with the associated change in their activities often showed less reproducible experimental results than those from experiments conducted later in the week. One subject was used during morning exposures and the other during afternoon exposures. No alcohol was taken during the week and only an occasional beer was taken on the weekends. No drugs were taken during the entire series of experiments, and the subjects attempted to maintain constant eating and sleeping habits during the series, but were not placed on a fixed diet or restricted in their activities outside of laboratory hours.

Air control exposures alternated with test substance vapor exposures so that every test exposure was bracketed by 2 air control experiments. The scores from the tests conducted during the air exposures were then averaged and treated as the "zero" line to which the results of the tests during the test substance exposure were related in terms of percent decrement or increment in the scores. Four concentrations of test substance vapor were selected: 1500, 2500, 3500, and 4500 ppm.

The concentration within the chamber took approximately 0.75 hour to build up to the desired concentration after the subject entered, while a further arbitrary period of 0.5 hour was allowed for equilibration to take place between the chamber atmosphere and the subject's tissues. At the end of this 0.5-hour period, the subject had completed 1.25 hours in the chamber and this represented the beginning of the 1.5 hour exposure to the constant level of the test substance. The end of the equilibration period was also the signal to proceed with the 1st battery of tests. The battery was completed in 17 minutes and the same battery was then repeated beginning 2 hours and 10 minutes after entering the chamber. Between each series of tests the time in the chamber was spent in taking air samples for analysis, recording the chamber temperature, preparing the test materials and in reading.

When the series of tests was completed, liver function tests, urinalysis, and hematological studies were repeated on each subject.

GLP: No

Test Substance: FC-113, purity approximately 100%

Results: The results of the 1st and 2nd series of tests showed no consistent trend that might indicate that during this relatively short experiment the longer the exposure, the greater the deterioration in test scores. Therefore, the results from the 2 sets of tests were averaged and compared with the average of the test scores on the air exposures before and after this particular test substance exposure. When the test substance exposure results were then plotted as a percent change from the air control value, there was some evidence of an effect of the test substance at 2500 ppm in the Manual Dexterity A, S.E.T Clerical, and Card Sorting with the Auxiliary Task. With the exception of one subject in the S.E.T Clerical test, a further deterioration took place at 3500 ppm, and the 2nd subject showed deterioration in card sorting. At 4500 ppm, both subjects showed a similar degree of impairment, and in the Card Sorting with the Auxiliary Task the impairment was highly significant.

The subjective impressions bore out the test results. After a few minutes exposure at any of the 4 concentrations employed, the subjects were no longer aware of the smell of the test substance, but after a period of about 0.5 to 1 hour at the 3 highest concentrations definite subjective sensations appeared. These were loss of concentration on the task at hand (e.g., reading, a slight tendency to somnolence, a feeling of “heaviness” in the head but no actual headache, and a slight loss of correspondence between the visual and labyrinthine sensations of rotation on turning the head rapidly to the left or right. These effects were experienced by both subjects with apparently equal intensity, quickly diminished on leaving the chamber, and were completely gone in 15 minutes.

Within the limits of these experiments (small number of subjects and exposures) there would appear to be no significant effect of test substance on psychomotor performance at 1500 ppm. A 2500 ppm, there was definite, but slight deterioration as shown by the scores on the more complicated tasks, and for the higher concentrations there was evidence of a further decrement in performance for each rise in test substance concentration. When the series of tests

was completed, the liver function tests, urinalysis, and hematological studies were repeated on each subject, and showed no significant change form the pre-test series.

Reference: DuPont Co. (1970). Unpublished Data, Haskell Laboratory Report No. 141-64, "Human Exposures to Freon®-113 Precision Cleaning Agent" (November 12) (also cited in TSCA Fiche OTS0520328).

Stoops, G. J. and M. McLaughlin (1967). Am. Ind. Hyg. Assoc. J., 28:43-50.

Reliability: Medium because a suboptimal study design was used. A small number of subjects were used for the study.

Additional References for Acute Inhalation Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database**.**

DuPont Co. (1945). Unpublished Data, Haskell Laboratory Report No. 23-45, "Kitchen Tests on Freon® Refrigerants" (November 5) (also cited in TSCA Fiche OTS0520347, OTS0520870, and OTS0520988).

DuPont Co. (1954). Unpublished Data, Haskell Laboratory Report No. 3-54, "Inhalation Toxicity of Freon®-113 (1,1,2-Trichloro-1,2,2-trifluoroethane)" (March 16).

DuPont Co. (1961). Unpublished Data, Haskell Laboratory Report No. 72-61, "Acute Inhalation Test" (December 13) (also cited in TSCA Fiche OTS0555701 and OTS0520336).

DuPont Co. (1967). Unpublished Data, Haskell Laboratory Report No. 241-67, "Acute Inhalation Exposures, LC_{50} Determination – Rabbits" (June 23) (also cited in TSCA Fiche OTS0520343 and OTS0555498).

DuPont Co. (1968). Unpublished Data, "Memo Regarding Freon® 113 Exposure in Rats."

DuPont Co. (1969). Unpublished Data, Haskell Laboratory Report 141-69, "Acute Inhalation Toxicity (LC_{50})" (June 5).

DuPont Co. (1969). Unpublished Data, "Acute Inhalation Toxicity of Freon® 113 in Rats – Summary Report" (October 8).

DuPont Co. (1969). Unpublished Data, Haskell Laboratory Pathology Report 10-69, "Freon® 113" (January 21).

DuPont Co. (1970). Unpublished Data, Haskell Laboratory Report No. 217-70, "Acute Inhalation Toxicity" (May 19) (also cited in TSCA Fiche OTS0555587 and OTS0520340).

DuPont Co. (1971). Unpublished Data, Haskell Laboratory Report No. 46-71, "Acute Inhalation Toxicity" (February 17) (also cited in TSCA Fiche OTS0571387 and OTS0520333).

DuPont Co. (1971). Unpublished Data, Haskell Laboratory Report No. 104-71, "Four-Hour Inhalation Toxicity" (April 7).

DuPont Co. (1973). Unpublished Data, Haskell Laboratory Report No. 179-73, "Acute Inhalation Toxicity" (March 23) (also cited in TSCA Fiche OTS0571326 and OTS0520335).

DuPont Co. (1973). Unpublished Data, Haskell Laboratory Report No. 125-73, "Acute Inhalation Toxicity Study in the Rat" (March 26) (also cited in TSCA Fiche OTS0571420).

DuPont Co. (1975). Unpublished Data, Haskell Laboratory Report No. 173-75, "Acute Inhalation Toxicity"(April 23) (also cited in TSCA Fiche OTS0520344 and OTS0555820).

DuPont Co. (1976). Unpublished Data, Haskell Laboratory Report No. 318-76, "Acute Inhalation Toxicity" (April 27) (also cited in TSCA Fiche OTS0571401 and OTS0520346).

DuPont Co. (1968). Unpublished Data, Haskell Laboratory Report No. 249-68, "One-Hour Inhalation Toxicity Test" (November 8).

Clark, D. G. and D. J. Tinston (1982). Hum. Toxicol., 1(3):239-247.

Clayton, J. W., Jr. (1962). J. Occup. Med., 4:262-273.

Clayton, G. D. and F. E. Clayton (eds.) (1981-1982). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology, 3rd ed., p. 3100, John Wiley & Sons, New York (HSDB/145).

Department of the Army (1969). "Inhalation Toxicity of 1,1,2-Trichloro-1,2,2-trifluoroethane (TCTFE) Study No. 33-18-68/96," NTIS AD854705.

Desoille, H. L. et al. (1968). Arch. Maladies Profess. Med. Trav. Securite Sociale, 29(7-8):381-388.

Eastman Kodak Co. (1954). Data, "Toxicity Report" (November 18) (cited in TSCA Fiche OTS0516748).

Gage, J. C. (1981). ICI Ltd., Unpublished Data, Report No. TR/107, "1,1,2-Trichloro-1,2,2-trifluoroethane (Arcton 113): Reproductive Toxicity Study in Rats" (January).

Hümpfner, D. H. (1974). Zbl. Arbeitsmed., 4:118-119.

Inagaki, M. et al. (1966). Tohoku J. Exp. Med., 89:143-150.

Mellon Institute of Industrial Research (1972). Data "Additional Safety Evaluation Studies on UCON Fluorocarbon 113" (June 29) (cited in TSCA Fiche OTS0516797).

National Academy of Sciences – National Research Council (1960). Reports prepared under Contract N7onr-291(61), Washington, DC.

Pharmacopathics Research Lab (1976). "Acute Inhalation Toxicity Study in the Rat Using Freon 113" (cited in TSCA Fiche OTS0520341).

Philadelphia Naval Shipyard (1952). Industrial Test Laboratory, Progress Report NS-041-001.

Raventos, J. and P. G. Lemon (1965). Br. J. Anaesth., 37:716-737.

Reinhardt, C. F. et al. (1971). Am. Ind. Hyg. Assoc. J., 32(3):143-152.

Scholz, J. (1962). Ber. Aerosol-Kongr., 4:420-429.

Underwriters Laboratories Inc. (1941). Miscellaneous Hazard No. 3072.

Data from these additional sources were not summarized because insufficient study information was available.

Anon. (1961). Anesthesia, 16:3 (cited in Lewis, R. L. (1996). Sax's Dangerous Properties of Industrial Materials, 10th ed., John Wiley & Sons, Inc., New York, NY).

Anon. (1963). Tr. Leningr. Sanit. Gig. Med., 75:241 (RTECS/34765).

Burn, J. H. et al. (1959). Br. J. Anaesth., 31:518-529 (CA54:10125g).

DuPont Co. (1967). Unpublished Data, "Rat Inhalation" (August) (cited in ACGIH (2001). Documentation of TLV's, American Conference of Governmental Industrial Hygienists, Cincinnati, Ohio).

Union Carbide (1989). "Health and Safety Studies for 19 Chemicals" (cited in TSCA Fiche OTS0516797).

Data from these additional sources were not summarized because the test substance was a mixture or otherwise inappropriate.

Anon. (1993-1994). "Initial Submission: Letter from [ ] to USEPA Regarding Acute Inhalation Toxicity of Perfluorinated Organic Peroxide in Rats (sanitized) (cited in TSCA Fiche OTS0570797).

DuPont Co. (1962). Unpublished Data, Haskell Laboratory Report No. 70-62, "Acute Inhalation Toxicity" (August 17) (also cited in TSCA Fiche OTS0520338).

DuPont Co. (1962). Unpublished Data, Haskell Laboratory Report No. 83-62, "Acute Inhalation Toxicity" (October 30) (also cited in TSCA Fiche OTS0520337).

DuPont Co. (1964). Unpublished Data, Haskell Laboratory Report No. 63-64, "Inhalation Toxicity" (June 5) (also cited in TSCA fiche OTS0520322).

DuPont Co. (1964). Unpublished Data, Haskell Laboratory Report No. 135-64, "Inhalation Toxicity" (November 19).

DuPont Co. (1964). Unpublished Data, Haskell Laboratory Report No. 134-64, "Inhalation Toxicity" (December 14) (also cited in TSCA Fiche OTS0555724).

DuPont Co. (1964). Unpublished Data, Haskell Laboratory Report No. 151-64, "Preliminary Studies on the Inhalation Toxicity of Technical 1,1-Dichloro-2,2,2-trifluoroethane" (December 4) (also cited in TSCA Fiche OTS0520325).

DuPont Co. (1968). Unpublished Data, Haskell Laboratory Report No. 35-68, "One-Hour Inhalation Toxicity Test" (February 19) (also cited in TSCA Fiche OTS0555862).

DuPont Co. (1983). Unpublished Data, Haskell Laboratory Report No. 239-83, "Inhalation Approximate Lethal Concentration (ALC)" (July 20).

DuPont Co. (1986). Unpublished Data, Haskell Laboratory Report No. 161-86, "Inhalation Approximate Lethal Concentration (ALC)" (April 10).

DuPont Co. (1986). Unpublished Data, Haskell Laboratory Report No. 149-86, "Inhalation Approximate Lethal Concentration (ALC)" (March 14).

DuPont Co. (1987). Unpublished Data, Haskell Laboratory Report No. 546-87, "Inhalation Median Lethal Concentration (LC_{50})" (October 23) (also cited in TSCA Fiche OTS0570959).

Data from these additional sources were not summarized because the study design was not adequate.

Pyrolysis

Downing, R. C. et al. (1960). Aerosol Age, 5(9):3-8.

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Aspiration

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DuPont Co. (1970). Unpublished Data, Haskell Laboratory Report No. 91-70, "Aspiration in Rats" (February 26) (also cited in TSCA Fiche OTS0520332).

Type:	**Cardiac Sensitization**
Species/Strain:	Male dogs/Beagle
Exposure Time:	5 minutes
Value:	0.5-1.0%
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Healthy, male, beagle dogs, 13-26 months old, weighing 7-14 kg were used in the study. The dogs were kept in a laboratory kennel environment for several weeks prior to their use. They were trained to maintain a standing position while lightly supported by a cloth sling with a hole for each leg, to wear a mask over their snout, and to accept a venipuncture. The test substance was generated by passing air through the compound, which was contained in a gas-washing bottle. The bottle was partially immersed in a water bath maintained at the optimum temperature for generation of the desired concentration. The water bath was heated by an electric Automerse Heater, agitated by an electric stirrer, and the temperature was maintained by a Thermistemp temperature controller. Once the optimum bath temperature was established, the concentration of vapor being generated was controlled by varying the air flow through the test substance.

A heating tape was wrapped around the tubing (copper or stainless steel) just beyond the vaporizer to overcome evaporative cooling, and thus prevent condensation of the vapor.

A short distance beyond the vaporizer, a tube fitted with a toggle valve led to the exhaust reservoir. This enabled the air stream from the vaporizer to by-pass the dog, and thus permitted only fresh air to pass through the dog mask at those times when it was necessary for the mask to remain in place without the animal being exposed to the vapor. This arrangement also provided a means of uninterrupted vaporization, and thus ensured that the desired vapor concentration could be immediately supplied to the animal by moving the toggle valves.

The diluting air flow was fed through a flowmeter fitted with a feedback differential pressure regulator so that the flow downstream from the regulator remained constant despite changes in the upstream pressure. This flow was maintained at a constant level of 21.4 L/min throughout all of the exposures.

The final vapor-air mixture then passed into a copper tube about 3 feet in length, and was carried to the dog mask. Since the vaporizing and diluting flows entered this tubing within a few centimeters of each other, mixing of the 2 flows occurred rapidly. The vapor-air mixture was exhausted to the outside atmosphere by means of an exhaust fan. A 20.5-gallon drum with an opening to the laboratory atmosphere was placed in the exhaust line to absorb changes in flow rates due to the dog's respiration. The relatively high rate of vapor-air flow, coupled with a slight negative pressure applied to the exhaust tube from the mask, assured an adequate air supply to the dog and rapid removal of the expired air.

Later in the experiment, an infusion pump was used to deliver the solvent into a heated air stream for the generation of the desired vapor concentration. In this case, the total air supply to the dog was carried through the vaporizing tube rather than as in the previously described delivery system, where the major portion of the diluting air entered beyond the point of vaporization. When fresh air only was required, it was supplied in essentially the same manner as that described above.

A small portion of the vapor-air mixture was withdrawn continuously for analysis at a point just before the mixture entered the mask. Initially, a thermal conductivity gas analyzer, previously calibrated by gas chromatography, was used for the analysis. Later a gas chromatograph, incorporating a hydrogen flame ionization detector with nitrogen serving as the carrier gas, was used to measure the vapor concentration.

The dog mask was constructed from a standard 8-ounce paper cup, fitted with intake and exhaust ports without valves, and a rubber sleeve for a tight fit over the dog's snout. The rubber sleeve was the cuff of a standard size 7 surgeon's glove. All parts of the mask were coated with a heavy coat of epoxy resin and the mask, although held in place by an external cloth cover, was supported by hand.

The epinephrine was administered intravenously into the cephalic vein of the foreleg of the dog. The injection was made by an automatic infusion technique, using a continuous automatic infusion/withdrawl pump. The pump was set to deliver the total epinephrine dosage of either 0.008 mg/kg or 0.004 mg/kg in a volume of 1 mL or normal saline in 9 seconds.

An electrocardiogram was recorded continuously during each experimental run. The electrodes were held in place on the dog by a rubber strap extending around the body and were positioned over shaved areas as follows: 1) 2 active electrodes – 1 on each side of the chest just behind the foreleg, and 2) 1 indifferent electrode over the sternum.

Two types of exposures were given. The first was a so-called standard exposure that was similar to those done in the past by other investigators in this field. The second was an exposure of 30 seconds or less to determine whether a short-term exposure would be capable of producing cardiac sensitization.

Since the experimental procedure required relatively quiet and cooperative animals, the maximum concentration of the test substance was that which the animals would tolerate for about 10 minutes without undue struggling or incoordination. For the test substance, this concentration was determined by exposing 1 or 2 dogs, in a 200-L chamber

for 10-20 minutes, to an increasing concentration of the agent, and observing their reaction. A level slightly below that at which they began to lose coordination was chosen as the upper test level. The lower test levels studied were chosen to determine a concentration at which no significant cardiac arrhythmias developed.

The general protocol for the standard exposure was as follows:

At 0 minutes, exposure to air only began. At 2 minutes, epinephrine was administered intravenously. At 7 minutes, the test substance was administered. At 12 minutes, a challenge injection of epinephrine was administered. At 17 minutes, test substance administration was stopped (end of the experiment).

The general protocol for the short-term exposure was as follows:

At 0 minutes, exposure to air only began. At 2 minutes, epinephrine was administered intravenously. At 12 minutes, the test substance was administered, along with a challenge injection of epinephrine. At 12.5 minutes, test substance administration was stopped (dogs were exposed to air only). At 15 minutes the experiment ended.

GLP: No

Test Substance: FC-113, purity not reported

Results: The test substance was capable of sensitizing the dog heart to epinephrine. It produced cardiac sensitization at concentrations of 0.5-1.0%. Results are provided in the table below.

Standard Exposure						
Epinephrine Dosage	0.004 mg/kg		0.008 mg/kg			
Concentration (% by volume in air)	0.25 (0.22-0.28)	0.50 (0.41-0.58)	0.25 (0.25-0.27)	0.50 (0.40-0.57)	1.00 (0.90-0.95)	2.00 (2.30-2.50)
Number of Dog Exposures	12	24	12	29	4	2[a]
Total Number of Responses	3	18	6	20	3	2
% Total Responses	25	75	50	69	75	100
Multiple Ventricular Beats	0	6	0	9	2	2
Ventricular Fibrillation with Cardiac Arrest	0	3	0	1	1	0
% Marked Responses	0	37.5	0	34.5	75	100
a = These 2 dogs struggled after breathing the test substance for 2 minutes, and exhibited multiple ventricular beats without the challenge injection of epinephrine.						

Short-Term Exposure			
Epinephrine Dosage	0.008 mg/kg		
Concentration (% by volume in air)	0.5 (0.34-0.51)	1.00 (0.96-1.08)	2.00 (2.03-2.22)
Number of Dog Exposures	19	18	8
Total Number of Responses	13	15	7
% Total Responses	68.4	83.3	87.5
Multiple Ventricular Beats	2	4	5
Ventricular Fibrillation with Cardiac Arrest	0	0	1
% Marked Responses	10.5	22.2	75

Reference: DuPont Co. (1969). Unpublished Data, Haskell Laboratory Report No. 14-69, "Cardiac Arrhythmias Induced by Epinephrine During Inhalation of Certain Halogenated Hydrocarbons" (January 14) (also cited in TSCA Fiche OTS0520367).

Reliability: Medium because a suboptimal study design was used where animals were not individually titrated with epinephrine.

Additional References for Cardiac Sensitization:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Clark, D. G. (1973). Br. J. Pharmacol., 49(2):355-357.

Clark, D. G. and D. J. Tinston (1982). Human Toxicol., 1(3):239-247.

DuPont Co. (1966). Unpublished Data, Haskell Laboratory Report No. 19-66, "Study of Cardiac Sensitization Properties of Freon® 113" (February 15) (cited in TSCA Fiche OTS0520363).

DuPont Co. (1967). Unpublished Data, Haskell Laboratory, "Cardiac Sensitization".

DuPont Co. (1969). Unpublished Data, Haskell Laboratory Report No. 325-69, "Cardiac Sensitization" (October 15) (also cited in TSCA Fiche OTS0520365).

DuPont Co. (1969). Unpublished Data, Haskell Laboratory Report No. 364-69, "Cardiac Sensitization" (November 26) (also cited in TSCA Fiche OTS0520364 and OTS0571669).

DuPont Co. (1966). Unpublished Data, Haskell Laboratory Report No. 19-66, "Study of Cardiac Sensitization Properties of Freon® 113" (February 15) (cited in TSCA Fiche OTS0520363 and OTS0571673).

DuPont Co. (1971). Unpublished Data, Haskell Laboratory Report No. 279-71, "Halogenated Hydrocarbon Induced Cardiac Arrhythmias Associated with Release of Endogenous Epinephrine" (August 31).

DuPont Co. (1972). Unpublished Data, Haskell Laboratory, "Cardiopulmonary Effects of FC-113 in Dogs".

DuPont Co. (1973). Unpublished Data, Haskell Laboratory Report No. 471-73, "Blood Levels of Fluorocarbon Related to Cardiac Sensitization" (September 28) (also cited in TSCA Fiche OTS0520366).

DuPont Co. (1977). Unpublished Data, Haskell Laboratory Report No. 1014-76, "Mechanism of Fluorocarbon Action on the Heart Relative to the Production of Cardiac Sensitization" (January 4) (also cited in TSCA Fiche OTS0520369).

Kobayashi, H. et al. (1989). Sangyo Igaku, 31(3):136-141 (PMID: 2795984).

Philadelphia Naval Shipyard (1952). Report to file, Code 372a, L5(2335) (February 2).

Reinhardt, C. F. (1972). Ind. Hyg. News Report, 15(4):3-4.

Reinhardt, C. F. et al. (1973). J. Occup. Med., 15(2):953-955.

Trochimowicz, H. J. et al. (1974). Am. Ind. Hyg. Assoc. J., 35:632-639.

Data from this additional source were not summarized because the test substance was a mixture or otherwise inappropriate.

DuPont Co. (1968). Unpublished Data, Haskell Laboratory Report No. 93-68, "Cardiac Sensitization Screening Study" (May 8) (also cited in TSCA Fiche OTS0520324 and OTS0571837).

Type:	**Dermal ALD**
Species/Strain:	Rabbit/Albino
Exposure Time:	10 or 15 minutes
Value:	>11,000 mg/kg
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Undiluted test substance was applied to the clipped skin of rabbits and spread to cover an area equivalent to approximately 10% of the total surface area of the animal at doses of 7500 or 11,000 mg/kg. Evaporation of the test substance was slowed by an occlusive wrapping. The rabbits were observed for a 14-day post-observation period.
GLP:	No
Test Substance:	FC-113, purity >99.9%
Results:	Although the compound caused mild local irritation that persisted for 10 or 14 days, there were no signs indicating systemic toxicity.
Reference:	DuPont Co. (1964). Unpublished Data, "Acute Skin Absorption Toxicity Test" (August 20).
Reliability:	Medium because a suboptimal study design was used.

Type:	**Skin Absorption in Humans**
Species/Strain:	Male and female human volunteers
Exposure Time:	30 minutes (hand and forearm) 15 minutes (scalp)
Exposure Level:	2-10 ppm (hand and forearm) 7-13 ppm (scalp)

Method: Two male and 1 female human ranging in age from 21 to 33 years served as subjects. They were in good health, and the skin to be exposed was examined by a physician and in each case was judged to be normal.

Hand and Forearm Exposure:

A long, narrow pan 3-4 inches deep was placed inside a hood where it was filled with the test substance in order to prevent escape of the vapor into the room air. The subject put on an airline respirator prior to entering the room to ensure that no vapor was inhaled during the exposure. The subject then entered the room, sat beside the hood face, and immersed his hand and forearm in the pan of test substance for a period of 30 minutes. At the termination of the exposure, the subject removed his arm from the pan, but kept it inside the hood for an additional 15 seconds to allow for complete vaporization of any residual test substance that might have been present. He then took a deep breath, removed the respirator, put on a nose clip, and preceded immediately to another room for breath analysis as described below.

Scalp Exposure:

A similar procedure was followed for the scalp exposure as for the hand and forearm. The male subject had short hair of medium thickness and the female had thick hair of medium length. The subject entered the room in the same manner as described above, putting on the airline respirator before entering the room. The test substance was already in a bowl in the hood. The subject lay on his back on a table the length of which was placed at a right angle to the hood face. S/he permitted her/his head to extend beyond the end of the table and into the bowl of test substance until the hair and scalp were submerged. The exposure period lasted 15 minutes. At the termination of the exposure, the head was blotted with a towel and residual test substance was allowed to vaporize for about 15 seconds. The hair was then covered with a shower cap to prevent escape of any remaining vapor into the room air. The subject then removed the respirator and proceeded to a nearby room as previously described.

The subject, holding his/her breath all the while, arrived in the other room within about 30 seconds after the end of the exposure, was quickly seated before a Rahn sampler,

inserted a mouthpiece of the sampler into his mouth, and began breathing. The Rahn sampler was used to sample the end-tidal (alveolar) air, which is the final portion of air expelled from the lungs during a normal expiration.

A small portion of the end-tidal air was continuously pumped through a gas sampling valve that was attached to a gas chromatograph. The chromatograph incorporated a hydrogen flame ionization detector with nitrogen serving as the carrier gas. There was some variation in the sampling times following each exposure, but in most cases samples were collected at approximately 30, 45, 60, 90, 120, and 180 minutes after the exposure.

Prior to each exposure, the subject's alveolar air was analyzed for the test substance, and in all cases none was detected.

GLP: No

Test Substance: FC-113, purity 99.98%

Results: *Hand and Forearm Exposure:*

The maximum concentration of test substance in the end-tidal air of 1 subject was 9.6 ppm, and was reached 11.5 minutes after the end of the exposure, while for the 2nd subject the maximum concentration was 1.7 ppm and was reached 23 minutes after termination of the exposure. The concentration of test substance in the end-tidal air of the first subject dropped below 0.5 ppm within 90 minutes after the exposure, while for the 2nd subject, the concentration was below this level within only 30 minutes after the exposure. A trace amount of test substance (approximately 0.1 ppm, which was the lower limit of sensitivity) was detected in the alveolar air of the 1st subject about 18 hours after the exposure.

Scalp Exposure:

The maximum concentration of test substance in the end-tidal air of the 1st subject was 12.7 ppm, and was reached 20.5 minutes after the exposure had ended. The 2nd subject had a maximum concentration of 7.4 ppm, reached 18.5 minutes after the end of exposure. The concentration of test substance in the end-tidal air of both subjects had fallen below 0.5 ppm within about 90 minutes after the end of the exposure.

The subjects noticed almost immediately a tingling sensation upon immersion of the exposed part. As the exposure progressed, there was a feeling of numbness and coldness, which was uncomfortable, but not extremely painful. After the exposed area was removed from the solvent, there was a fine chalky-white scale over the skin with a mild erythema. Large bits of detritus flaked off the scalp. These changes resolved within 1-2 hours after exposure.

It was concluded that the test substance is able to penetrate human skin, but that a toxicologically significant amount of this solvent would not be absorbed during brief, intermittent exposures involving a relatively small skin area.

Reference: DuPont Co. (1968). Unpublished Data, Haskell Laboratory Report No. 84-68, "Human Skin Absorption Studies with Trichlorotrifluoroethane, F-113" (April 15) (also cited in TSCA Fiche OTS0520330).

Reliability: Medium because a suboptimal study design was used. A small sample size was used for the study.

Additional References for Acute Dermal Toxicity:

Data from these additional sources support the human study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1971). Unpublished Data, Haskell Laboratory Report No. 113-71, "Cutaneous Absorption of Fluorocarbon 113 Following Swabbing of the Abdominal Skin of Human Subjects, and the Concentration of the Vapor in the Vicinity of the Subject and Observer" (April 26) (also cited in TSCA Fiche OTS0520327).

Egeland, G. et al. (1991). Am. J. Epidemiol., 134(7):742-743.

Data from this additional source were not summarized because the test substance was a mixture or otherwise inappropriate.

DuPont Co. (1977). Unpublished Data, Haskell Laboratory Report No. 1024-77, "Skin Absorption ALD - Rabbits" (December 22) (also cited in TSCA Fiche OTS0520354).

Type: **Dermal Irritation**

Species/Strain: Rabbit/Albino

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

	Undiluted test substance was applied to the clipped skin of rabbits and spread to cover an area equivalent to approximately 10% of the total surface area of the animal at doses of 7500 or 11,000 mg/kg. Evaporation of the test substance was slowed by an occlusive wrapping. The rabbits were observed for a 14-day post-observation period.
GLP:	No
Test Substance:	FC-113, purity >99.9%
Results:	The compound caused mild local irritation that persisted for 10 or 14 days.
Reference:	DuPont Co. (1964). Unpublished Data, "Acute Skin Absorption Toxicity Test" (August 20).
Reliability:	Medium because a suboptimal study design was used. The study was not specifically designed to test for dermal irritation.

Type:	**Dermal Irritation**
Species/Strain:	Rabbit/Albino
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Six rabbits weighing between 2-3 kg were clipped free of hair on the trunk and lateral areas and placed in FDA-type stocks. The test material was placed under a gauze pad and the trunk of each rabbit was then loosely wrapped with rubber sheeting. After 4 hours, the rabbits were removed from the stocks, washed, and their reactions read according to the system of the Federal Hazardous Substances Act. Readings were also made at 24 and 48 hours.
GLP:	No
Test Substance:	FC-113, purity 99.9%
Results:	No irritation was observed throughout the study.
Reference:	DuPont Co. (1976). Unpublished Data, Haskell Laboratory Report No. 723-76, "Department of Transportation Skin Corrosion Test on Rabbit Skin" (October 1) (also cited in TSCA Fiche OTS0520356).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Dermal Irritation:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Clayton, J. W., Jr. (1966). Handb. Exp. Pharmakol., 20:459-500 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva).

Dow Chemical (1949). Unpublished Data, "Results of Range Finding Toxicological Test of Some Fixed Chlorofluorohydrocarbons" (April 12) (cited in TSCA Fiche OTS0520705).

DuPrat, P. et al. (1976). Eur. J. Toxicol. Environ. Hyg., 9(3):171-177 (CA85:138167w).

Marhold, J. (1988). Prehled Prumyslove Toxikologie; Organicke Latky, p. 137, Avicenum, Prague, Czechoslovakia (RTECS/KJ4000000).

Union Carbide (1970). Data Sheet, 7/10 (cited in Lewis, R. L. (1996). Sax's Dangerous Properties of Industrial Materials, 10th ed., John Wiley & Sons, Inc., New York, NY).

Waritz, R. S. (1971). NTIS AD Report No. 751429 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva).

Matheson Tri-Gas, Inc. (1999). Material Safety Data Sheet (March 16).

Data from these additional sources were not summarized because the test substance was a mixture or otherwise inappropriate.

DuPont Co. (1988). Unpublished Data, Haskell Laboratory Report No. 614-88, "Skin Irritation Test in Rabbits" (September 9).

DuPont Co. (1977). Unpublished Data, Haskell Laboratory Report No. 1024-77, "Skin Absorption ALD - Rabbits" (December 22) (also cited in TSCA Fiche OTS0520354).

DuPont Co. (1976). Unpublished Data, Haskell Laboratory Report No. 724-76, "Department of Transportation Skin Corrosion Test on Rabbit Skin" (October 1) (also cited in TSCA Fiche OTS0520357).

Type:	**Dermal Sensitization**
Species/Strain:	Guinea pigs/Hartley
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. One mL of Freon® 113 was applied under an occlusive patch to the clipped and depilated backs of Hartley albino guinea pigs 4 times in 10 days. At the time of the 3rd application, 0.2 mL of Freund's complete adjuvant was injected intradermally adjacent to the insult test site. After a 10-day rest period, the animals were challenged at sites remote from the insult site with test material. Any guinea pig showing a reaction of 2 or greater for hyperemia and/or edema in the challenge phase was considered sensitized. To demonstrate sensitization, test reaction tissue responses observed in the challenge phase should have been greater than the test reaction tissue responses observed in the induction phase.
GLP:	Yes
Test Substance:	FC-113, purity 100 wt%
Results:	In the challenge phase, none of the test substance-treated guinea pigs showed a skin reaction of 2 or greater for hyperemia or edema. There was no significant difference between the weight gain of the treated animals and that of either control. Under the conditions of this test, the test substance had minimal skin sensitizing potential.
Reference:	Dow Corning (1989). "Skin Sensitization Study of Dow Corning® 355" (June 15) (cited in TSCA Fiche OTS0520470 and OTS0520471).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Dermal Sensitization:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Horiguchi, Y. et al. (1985). Kanagawa-ken Eisei Kenkyusho Kenkyu Hokpku, 15:39-41 (CA105:129070p).

Miyahara, C. et al. (1986). Toxicol. Lett., 31(Suppl.):221 (Abstract P15-1).

Dow Corning (1989). "Skin Sensitization Study of Dow Corning® 355 Adhesive/Scotchpak® X1022 Laminate" (June 15) (cited in TSCA Fiche OTS0520470).

Data from this additional source were not summarized because the test substance was a mixture or otherwise inappropriate.

Dow Corning Corp. (1965). Unpublished Data, "Human Repeated Insult Test on Medical Adhesive Type B Lot H0010 TX95" (July 30) (cited in TSCA Fiche OTS0520469).

Type:	**Eye Irritation**
Species/Strain:	Rabbit/Albino
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Three male albino rabbits were tested. The test substance (0.1 mL) was placed in both eyes of each animal. One eye from each animal was washed with water 20 seconds after exposure. The other eye from each animal was not washed. Observations were made for up to 72 hours.
GLP:	No
Test Substance:	FC-113, purity not reported
Results:	In the eyes that were washed, 1 of 3 exhibited mild conjunctivitis at 24 hours, and all eyes were normal at 48 and 72 hours. In the eyes that were not washed, 1 of 3 rabbits exhibited minimal corneal dullness at 24 hours, and all eyes were normal at 48 and 72 hours. The test substance was considered practically non-irritating to rabbit eyes.
Reference:	DuPont Co. (1962). Unpublished Data, Haskell Laboratory Report No. 39-62, "Eye Irritation in Rabbits" (June 12) (cited in TSCA Fiche OTS0520352).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Eye Irritation:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Dow Chemical (1949). Unpublished Data, "Results of Range Finding Toxicological Test of Some Fixed Chlorofluorohydrocarbons" (April 12) (cited in TSCA Fiche OTS0520705).

Duprat, P. et al. (1976). Eur. J. Toxicol. Environ. Hyg., 9(3):171-177 (CA85:138167w).

Scholz, J. (1962). Ber. Aerosol-Kongr., 4:420-429.

Data from these additional sources were not summarized because the test substance was a mixture or otherwise inappropriate.

DuPont Co. (1970). Unpublished Data, Haskell Laboratory Report No. 9-70, "Eye Irritation Test" (January 13) (also cited in TSCA Fiche OTS0520353).

DuPont Co. (1988). Unpublished Data, Haskell Laboratory Report No. 587-88, "Eye Irritation Test in Rabbits" (August 30).

DuPont Co. (1990). Unpublished Data, Haskell Laboratory Report No. 651-90, "Primary Eye Irritation Study" (November 16).

5.2 Repeated Dose Toxicity

Type:	**90-Day Rat Inhalation Study**
Species/Strain:	Rats/CD®
Sex/Number:	Male and female/15 per sex per concentration
Exposure Period:	13 weeks
Frequency of Treatment:	6 hours/day, 5 days/week
Exposure Levels:	0, 7500, 12,500, 17,500/20,000 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Male and female rats were exposed to nominal concentrations of 0, 7500, 12,500, and 17,500 ppm. On the 19th exposure, the high concentration was increased from 17,500 to 20,000 ppm in order to enhance the likelihood of producing clinical abnormalities.

Throughout the pretest and non-exposure periods, all test rats were housed in conventional animal rooms. All rats received food and water *ad libitum*, except during exposures.

Four 3.5 m^3 Rochester-type stainless steel and glass chambers were dedicated to the study. The chambers were operated in a one-pass, flow-through mode with an air flow rate of approximately 1000 L/minute. During the exposures, temperature was maintained between 18-24.5°C.

Test atmospheres were generated by passing filtered and compressed ambient air through 0.21 m^3 drums filled with the test substance. The drums were heated with heating tapes to 23-28°C in order to achieve saturation of the carrier gas (air) passing through the drums. The test substance-saturated air was passed from the heated drums into the exposure chambers. The control chamber received dilution air only.

Chamber concentrations were analyzed quantitatively for test substance by a gas chromatograph equipped with a thermal conductivity detector and a gas sampling valve. Chamber atmospheres were monitored at least once an hour with daily time-weighted average concentrations for each exposure chamber calculated from these data.

All rats were observed at least once daily for gross signs of toxicity and changes in appearance and behavior. Rats were weighed once a week during the test period, and were individually examined at these times for clinical signs of toxicity.

Male and female rats (5 per sex), randomly selected from each group and sacrificed after 43 days on test, and all rats that survived approximately 94 days on test were sacrificed and necropsied. One rat that was sacrificed *in extremis* was also necropsied. The brain, heart, lungs, liver, spleen, kidneys, testes, thymus, adrenals, and pituitary were weighed, and mean organ to final body weight ratios (relative organ weights) were calculated for each group. At the interim and final sacrifices, tissues from the control and high level exposure groups only were examined microscopically; tissues from the low and intermediate level exposure groups were held in block stage. Representative sections were prepared for microscopic examination from approximately 39 organs or tissues.

Body weight data were subjected to one-way analysis of variance. Organ weight and final body weight data were subjected to one-way analysis of variance and Dunnett's test.

GLP: Yes

Test Substance: FC-113, purity 100%

Results: Over the 14-week exposure period, the overall means of the weekly time-weighted average concentrations for the low and intermediate exposures were 99.6 and 99.3% of the design concentrations, respectively. For the first 4 weeks of

the study, the highest design concentration was 17,500 ppm. For this period, the overall mean of the weekly time-weighted average concentrations was 98.8% of the high design concentration. From weeks 5-14 of the study, the high design concentration was increased to 20,000 ppm; the overall mean of the weekly time-weighted average concentrations for this period was 99.7% of the design concentration. Over the 14-week exposure, the overall mean of the time-weighted average concentrations conducted at design concentrations of 17,500 and 20,000 ppm was 19,186 ppm.

Exposure to the test substance did not alter body growth in male or female rats over the 14-week exposure period. All rats, except a control female that was sacrificed *in extremis* on test day 72, survived the exposure period. No test substance-related gross or histologic alterations were observed.

In male rats exposed to 17,500/20,000 ppm, significant increases in both the mean absolute and relative lung weights were observed. These findings were positively correlated with gross and microscopic evidence of multi-focal granulomatous interstitial pneumonia. Granulomatous pneumonia is a common finding in young adult, laboratory-reared rats and occurred in both male and female control rats in this study. However, the lesions seen in the male 17,500/20,000 ppm group tended to be of greater severity than those seen in the male controls. Although the granulomatous pneumonia observed in the male 17,500/20,000 ppm group was not considered to be induced by the test substance, exposure to the test substance may have resulted in a stress-related enhancement of the existing pneumonic condition, which was accompanied by increases in both mean absolute and relative lung weights in these rats.

Reference: DuPont Co. (1981). Unpublished Data, Haskell Laboratory Report No. 724-81, "Ninety-Day Inhalation Study with Freon® 113 in Rats" (December) (also cited in TSCA Fiche OTS0555243 and OTS0520331).

Reliability: High because a scientifically defensible or guideline method was used.

Type: **2-Year Rat Inhalation Study**

Species/Strain: Rats/Crl:CD®(SD)BR

Sex/Number: Male and female/100 per sex per group

Exposure Period: 2 years

Frequency of Treatment: 6 hours/day, 5 days/week

Exposure Levels: 0, 0.2, 1, 2% (v/v)

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

During the pretest and test periods, rats were housed 3 per cage, sexes separate, in stainless steel, wire-mesh cages. During the test period, test substance-exposed rats and control rats were housed in separate rooms. Throughout the pretest and test periods, all rats received food and water *ad libitum*, except during exposures.

Four, 4.6 m^3 stainless steel and glass exposure chambers were dedicated for use in the study. Each chamber was the same in design, being quadrangular with pyramidal tops and bottoms. All chambers were cleaned after each exposure and air-dried prior to the subsequent exposure.

To generate test-exposure atmospheres, houseline air was passed through a heated (25°C) compressed gas cylinder containing liquid test substance. The vaporized test substance was then metered through rotameters into streams of houseline air to achieve the concentrations of 0.2, 1, or 2% (v/v). The vapors so diluted were then directed to the appropriate exposure chambers. Control exposure atmospheres consisted of houseline air alone, metered by a rotometer. All chambers were operated in a single-pass, flow-through mode at a rate of 700-1400 L/minute, adjusted as needed to maintain chamber temperature at 24±3°C and relative humidity of 50±10%, to ensure normal respiration of the rats and minimal exposure of the rats to volatile materials arising from their excreta.

Each exposure lasted approximately 6 hours. All exposures were conducted Monday through Friday (excluding holidays) during approximately the same 8-hour period of the day to minimize potential influences of variation of this parameter on the diurnal physiological cycle of the rats.

During each exposure, chamber atmosphere was sampled approximately every 0.5 hour for analysis of test substance concentration. Samples of atmosphere were drawn by vacuum pump from the center of each exposure chamber through tubing connected directly to a gas chromatograph

equipped with a thermal conductivity detector.

Individual body weights of rats in the study were collected once weekly during the first 11 weeks of the study and once every 2 weeks for the remainder of the study. Each rat was also weighed just prior to being sacrificed.

During the workweek, cage-site examinations were conducted twice daily to detect abnormal appearance or behavior among rats in the study and to detect dead or moribund rats. During the collection of body weight data, each rat was carefully examined for abnormalities in appearance or behavior and for palpable tissue masses. On weekends and holidays, cage-site examinations were conducted once daily to detect dead or moribund rats.

Approximately 3, 6, 12, 18, and 24 months after initiation of the study, 10 male and 10 female rats were subjected to a 24-hour fast; urine was collected during the last 16 hours of this period. At the termination of the fasting period, a blood sample was collected from each of the rats.

The blood samples collected were evaluated for approximately 25 endpoints. The urine samples collected were evaluated for approximately 13 endpoints.

At the time of the 6-month clinical laboratory evaluation, the 10 male rats from the control group used for the evaluation were placed in the room housing rats that were in the 0.2% test substance group, and the 10 male rats from the 0.2% test substance group used for the evaluation were placed in the room housing control group rats. Consequently, for 11 exposures, these control rats were exposed to 0.2% of the test substance, and the 0.2% test substance group rats were exposed to air. Upon discovery of the error, the rats were returned to their correct housing and were continued on test.

The original design of the study specified that the rats sampled for the 3-month clinical laboratory measurements would subsequently be re-sampled at 6 and 12 months. However, after the discovery of the misplaced rats in the control and 0.2% groups following the 6-month clinical laboratory sampling, 10 different rats from the control group were selected, and with the originally designated 0.2% group rats, the 6 month clinical laboratory measurements were repeated. At 12 months, clinical laboratory evaluations were

made on all rats originally designated for this purpose. The decision to include the incorrectly exposed rats in the 12-month clinical laboratory determinations and interim sacrifice was based on data obtained from these rats before and after discovery of the mistake. These data indicated that the small number of incorrect exposures was not associated with any adverse effects on the rats as evidenced by body weight parameters, physical appearance, and behavior.

Twelve months after initiation of the study, the 10 male and 10 female rats from each treatment group that were subjected to the 3- and 12-month clinical laboratory measurements were sacrificed and necropsied. The adrenal glands, brain, heart, kidneys, liver, lungs, pituitary, spleen, testes, and thymus from these rats were collected and weighed. Approximately 43 tissues or organs were saved for possible histopathological evaluation.

All tissues collected from the control and high exposure groups, from rats found dead or sacrificed *in extremis* during the first 12 months of the study, and tissues with gross lesions and/or tissue masses collected from rats in the low- and intermediate-exposure groups were further processed to slides and examined microscopically. The remaining tissues collected from rats in the low- and intermediate-exposure groups were not examined microscopically because evaluation of tissues from rats in the high-exposure group failed to reveal test substance-related abnormalities.

Approximately 24 months after initiation of the study, all surviving rats were sacrificed and necropsied. All rats found dead or sacrificed *in extremis* during the last 12 months of the study were also necropsied. The same tissues for the interim sacrifice were collected from all rats and saved for possible histopathological evaluation. The tissues from the control and high-exposure groups and the tissues from rats that were found dead or sacrificed *in extremis* during the last 12 months of the study were further processed and examined microscopically. Tissues with gross lesions and/or tissue masses and, based upon the presence of nasal tumors in 2 male rats in the intermediate-exposure group that had been sacrificed *in extremis* during the 2nd year of the study, nasal turbinates from rats in the low- and intermediate-exposure groups were also processed and examined.

Exposure concentrations were estimated from daily time-weighted averages of analytical values for chamber atmospheres.

Body weights, body weight gains, organ weights (relative and absolute) and clinical laboratory measurements were analyzed using a one-way analysis of variance. For the 18- and 24-month clinical laboratory measurements, values from rats that were found infected by *Corynebacterium kutscheri* were excluded from analysis. When the test for differences among exposure group means (F-test) was significant, pairwise comparisons were made between test and control groups. For body weights and body weight gains, these comparisons were made utilizing the Least Significant Difference (LSD) test. For organ weights, the comparisons were made using both LSD and Dunnett's test. Bartlett's test for homogeneity of variances was performed on the organ weight and clinical laboratory data.

Survival probabilities were estimated using the Kaplan-Meier procedure. Survival among groups was compared using the Mantel-Haenszel test and Fisher's Exact test.

Tumor incidence was examined for all rats in the study, as well as for the subgroups; that is, for all rats with pathological symptoms characteristic of *C. kutscheri* infection and for all rats without these symptoms. Fisher's Exact tests were conducted for comparison of tumor incidence between control and exposure groups.

GLP: Yes

Test Substance: FC-113, purity >99.8%

Results: The average, daily chamber concentrations for all exposures during the study were 0.20±0.01%, 0.99±0.05%, and 1.99±0.10% for the 0.2, 1.0, and 2.0% groups, respectively. Average daily chamber concentrations ranged between 0.12-0.26, 0.71-1.24, and 1.42-2.31% test substance for the 0.2, 1.0, and 2.0%, respectively.

Approximately 14 months after initiation of the study, an intercurrent respiratory infection by *C. kutscheri* was identified in rats in the study. While not generally considered highly virulent or fulminant, by the end of the study, approximately 18-35% of the male rats and 5-8% of the female rats in the exposure groups had died as a consequence of the tuberculosis-like *C. kutscheri* infection. Efforts to control the onset and spread of the infection

among rats in the study through quarantine measures and short-term discontinuance of test substance exposures (23 days; 14 exposures) to reduce stress, were ineffective. Similarly, tetracycline therapy failed to eradicate or prevent the spread of the infection. The observation of a higher incidence of the infection among male than among female rats in the study was consistent with observations made in other studies that contained rats infected by *C. kutscheri*. The reason for this difference is unknown.

Rats in each of the test groups that survived the study period received the following approximate number of exposures:

Targeted Chamber Concentration (%)	No. of Exposures	
	Male	Female
0.2	506	507
1.0	490*	505
2.0	489*	503
* Exposure of the male rats in these exposure groups had been discontinued during test weeks 61-64, while the rats were quarantined due to *C. kutscheri* infection.		

Survival of rats in the test substance exposure groups was generally comparable or superior to the survival of controls. Test substance exposure did not apparently predispose rats to *C. kutscheri*-induced mortality.

Overall mortality of rats and mortality adjusted for deaths due to *C. kutscheri* during the study were:

Targeted Chamber Concentration (%)	Overall Mortality (No. Rats Dead/No. Rats in Group)		Mortality Adjusted for *C. kutscheri* Deaths (No. Rats Dead/No. Rats in Group)	
	Male	Female	Male	Female
0	74/100	53/100	39/100	45/100
0.2	72/100	42/100	46/100	34/100
1.0	65/100	40/100	47/100	35/100
2.0	59/100	33/100	34/100	30/100

Long-term exposure of male and female rats to 2%, and of female rats to 1% was associated with a decreased rate of weight gain. However, as food intake by the rats in the

study was not measured, it is unclear whether these decreases were due directly to a test substance-induced reduction in the efficiency of food utilization for body weight gain or whether the decreases were due secondarily to decreased food consumption. The decreases in rate of body weight gain did not appear to be related to the presence of *C. kutscheri* in the study, since both in male and female rats the incidence of infected animals in the test substance exposure groups were either similar to or less than that of the controls. Additionally, the onset of the decreased rates of body weight gain did not correspond well to the first observations of *C. kutscheri* infection.

Clinical observations of abnormalities in appearance or behavior among rats in the study were unremarkable. The observations were neither associated with test substance exposure, nor was there a clear relationship between the observations and infection of the rats by *C. kutscheri*.

Of the differences between the control and the test substance exposed rats in hematological and clinical chemistry measurements, the only difference that was considered related to test substance exposure was slightly decreased serum glucose levels observed in males at 2% at 3 and 6 months after study initiation.

During the study, urinary excretion of fluoride by rats at 1 and 2% was occasionally higher than that of controls. These findings may suggest that the test substance is metabolized slightly by the rat.

Among rats sacrificed 1 year after study initiation, absolute and relative liver weights were increased in male rats in all test substance-exposed groups and in female rats at 1 and 2%. Male rats in all exposed groups also exhibited increased relative kidney weights. Male rats at 2% exhibited decreased absolute, but not relative, mean pituitary weight. After 1 year of exposure, female rats exhibited increased relative lung and spleen weights. None of the organ weight differences between the control and test substance-exposed groups were associated with abnormalities in clinical laboratory parameters or pathological changes that would indicate toxicological significance. Furthermore, with the exception of an increase in liver weights of male rats at 0.2%, none of the organ weight differences were evident in rats sacrificed at the end of the study. Thus, the differences

in organ weights between control and exposed rats are considered unrelated to test substance exposure, and of no biological significance.

Noteworthy pathological findings observed in the study consisted of the presence of primary nasal tumors in 1 and 3 male rats at 0.2 and 1%, respectively, and in 1 female at 1%. Also observed was a statistically significant increase in pancreatic islet-cell adenomas in females at 2%.

While notable in that primary nasal tumors are only infrequently observed in control rats, the nasal tumors from each rat were morphologically distinct and were not all located in the same region of the nasal turbinates. Furthermore, the incidence of the nasal tumors among the exposure groups did not exhibit a dose-response relationship. Thus, the occurrence of nasal tumors among rats in the exposure groups, while unusual, was not considered related to exposure to the test substance.

The incidence of pancreatic islet-cell adenomas observed in female rats at 2% sacrificed at the termination of the study, though statistically significant, lies within the anticipated incidence of this finding among untreated rats of this strain. Thus, though statistically significant, this finding was not considered related to exposure to the test substance.

The *C. kutscheri* infection during the 2nd year of the study was not considered to have interfered with evaluation of the potential adverse pathological effects of exposure to the test substance. When rats that exhibited evidence of *C. kutscheri* infection were excluded from consideration, none of the histological abnormalities observed in the non-infected rats appeared related to test substance exposure. Similarly, no apparent test substance-related histological abnormalities were evident among those rats that exhibited *C. kutscheri* infection.

In conclusion, long-term exposure of rats to the test substance was not associated with remarkable toxicity. With the exception of a decreased rate of body weight gain among female rats at 1 and 2% and male rats at 2%, and a slight, transient decrease in serum glucose levels in male rats at 2%, no test substance-related abnormalities were observed. Under the conditions of this study, the test substance was not found to be oncogenic. Based on the effects cited above, the

	NOEL for this study was considered to be 0.2%.
Reference:	DuPont Co. (1985). Unpublished Data, Haskell Laboratory Report No. 488-84, "Two-Year Inhalation Toxicity Study With 1,1,2-Trichloro-1,2,2-trifluoroethane in Rats" (March 5) (also cited in TSCA Fiche OTS0520796 and OTS0520995). Trochimowicz, H. J. et al. (1988). Fundam. Appl. Toxicol., 11(1):68-75.
Reliability:	High because a scientifically defensible or guideline method was used.
Type:	**5-Day Dermal in Rabbits**
Species/Strain:	Rabbits/Albino
Sex/Number:	Male/4
Exposure Period:	5 days
Frequency of Treatment:	2 hour/day
Exposure Levels:	5000 mg/kg
Method:	The test material was applied in original form to the abdomen and/or back of rabbits under occlusion for 2 hours/day for 5 days. Two rabbits were killed 3 days after the last dose and 2 rabbits were killed after a 14-day recovery period. Body weight and clinical signs were recorded, and gross and histopathology examinations were performed.
GLP:	No
Test Substance:	FC-113, purity >99.9%
Results:	No mortality occurred during the test or recovery periods. Fluctuating weight loss was the only sign of systemic toxicity, which could have been caused by restraining for at least 2 hours each day. Locally there was mild skin irritation after the 1st treatment, which gradually became severe by the 5th treatment. During the recovery period, the skin was leathery and cracked, with minor bleeding, which gradually healed and was almost normal when the rabbits were killed. Significant gross findings attributable to the exposure were cracked, thickened, and dry abdominal skin, and slight thickening of the back skin. The severity of the lesions was considerably less 14 days following the exposure than 3 days following the exposure. Histologic changes attributable to the exposure were most pronounced in abdominal skin from rabbits with a 3-day recovery. These changes were necrosis and sloughing of the

horny and granular layer of the epidermis with hyperplasia of the stratum malpighii. The dermis just ventral to the basal layer of the epidermis was hyperemic and infiltrated with many inflammatory cells of both lymphocytic and poymorphonuclear morphology. Focal necrosis of hair follicles occurred. In those sections of abdominal skin from animals with a 14-day recovery, hyperplasia of the stratum malpighii, increased keratinization and thickening of the connective tissue adjacent to the epidermis were remarkable. Sections of back skin (in all animals) had less severe changes consisting of infiltration of the dermis with inflammatory cells and increased keratinization. Liver changes were enlargement of the hepatocytes with movement of the larger cytoplasmic particles to the periphery of the cell. These changes were present in the same degree in rabbits with both a 3-day and 14-day recovery period. No other test-substance related lesions were noted.

Reference: DuPont Co. (1964). Unpublished Data, "Subacute Skin Absorption Toxicity Test" (October 22).

Reliability: Medium because a suboptimal study design was used.

Type: **5-Day Inhalation in Humans**

Species/Strain: Human volunteers

Sex/Number: Male/4

Exposure Period: 5 days

Frequency of Treatment: 6 hours/day

Exposure Levels: 500 and 1000 ppm

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Four healthy, male humans (ranging in age from 22 to 30 years) were exposed to the test substance at concentrations of 500 and 1000 ppm by volume for 6 hours/day for 5 days. A control period was also conducted, in which the subjects were exposed to air alone the week preceding the start of the vapor exposures.

Each subject underwent a pre- and post-exposure physical examination including hematologic studies, urinalysis, and liver function tests. Pulmonary function measurements were obtained daily during the control week and twice weekly during the test substance exposures. Breath samples were collected before and after each day's exposure for

measurement of test sample concentration. Temperature, pulse, and equilibrium were also checked daily.

Subjective impressions were recorded and psychomotor tests were performed twice each day during both the air-control and vapor-exposure periods. These tests included 1) Short Employment Test – Clerical (S.E.T.), 2) manual dexterity (Crawford Small Parts Dexterity test), 3) card sorting, 4) card sorting with auxiliary task (mental arithmetic), and 5) time discrimination test.

One subject received a prophylactic dose of human gamma globulin from his personal physician during the 1st week of the experiment, and 1 subject took 2 aspirin tablets with the onset of a cold; otherwise, no drugs were taken during the experiment. One other subject had a mild upper respiratory infection during the course of the study. The subjects attempted to maintain constant eating and sleeping habits during this experiment, but were not placed on a fixed diet or restricted in their activities outside of laboratory hours.

The exposures were carried out in a chamber constructed of a steel framework enclosed with DuPont polyester film. Air suitable for human breathing was supplied at a rate of about 11 ft^3/minute, which was sufficient to keep carbon dioxide levels in the chamber below 0.33% by volume. This level was judged to have an insignificant physiological effect, and the same level of carbon dioxide would be present for both the test substance and the air-control exposures. An exhaust fan and damper in the exhaust system permitted maintenance of a slight negative pressure in the chamber so that any air leakage would be inward.

The exposure chamber was in a controlled environment with a temperature of 68°F dry bulb. This environment allowed maintenance of a temperature below 79°F in the exposure chamber in spite of the metabolic heat produced by the subjects. The temperature, relative humidity, and carbon dioxide level within the exposure chamber were measured.

The desired test substance concentration was achieved by injecting the test substance by an infusion pump into a stream of air that was heated by a controlled temperature heating tape to ensure complete vaporization of the test material. This concentrated vapor-air mixture was further diluted with a larger volume air stream and then delivered

through a hose into the chamber, where it was discharged under a hassock-type fan for complete mixing throughout the chamber. Flow in both air streams was controlled by rotameters. A 2nd infusion pump and set of syringes was mounted in parallel so that a continuous flow of test substance was maintained throughout the exposure. Before each exposure, the chamber was "primed" by injecting the test substance directly into the combined air streams, by hand, from a syringe, to bring the chamber concentration to the desired level within 10 minutes.

Chamber atmosphere was analyzed by gas chromatography. Samples were generally taken in the breathing zone of the subjects; however, during the exposures some samples were taken at numerous points in the chamber.

Each tidal breath sample was collected from each of the 4 subjects every morning prior to exposure and 1 minute after the subjects left the chamber every afternoon. Samples were collected in sampling bags having an open tube attached to one corner. Each subject breathed the final portion of 6 consecutive exhalations into his bag, covering the opening of the tube with his thumb between breaths. The tube was then stoppered with a serum cap. For analysis, 4 samples of breath were taken from each bag with a gas-tight syringe and injected into a gas chromatograph, which had been previously calibrated to analyze low concentrations of the test substance. The average of these 4 measurements was used as the test substance concentration for that particular sample bag. The analysis of the morning samples was done approximately 3 hours after collection of the sample, while the afternoon samples were analyzed within 15-30 minutes after collection.

A resting steady-state carbon monoxide diffusing capacity and fractional uptake of carbon monoxide were measured.

The following psychomotor tests were performed:

1) The Short Employment Test – Clerical (S.E.T.) (The Psychological Corporation) – A test of vigilance, consisted of coding a series of names according to the financial balance shown against these names on a facing page of the test. The number correctly coded in 3 minutes was taken as the score. Five variations of this test were used to minimize the effect of learning.

2) Manual Dexterity (Crawford Small Parts Dexterity Test) (The Psychological Corporation) – Part A of this test consisted of taking small set screws and, with the aid of a screwdriver, screwing them through threaded holes in a metal plate. The score was the number of screws completely inserted in a period of 3 minutes. Part B consisted of inserting metal pins into a series of holes in a plate with the aid of tweezers. Small metal collars were then dropped over the pins as they projected from the plate. The score was the number of pins and collars assembled in 2 minutes.

3) Card Sorting – Playing cards were sorted into suits as rapidly and accurately as possible. The number sorted correctly in 1 minute was taken as the score.

4) Card Sorting with an Auxiliary Task (Mental Arithmetic) – The subjects sorted the cards as above, but at the same time were asked to respond to a series of arithmetic problems. The test consisted of 30 additional problems of 3 single-digit numbers. The numbers were selected from a table of random numbers, but adjusted so that there were no duplicate numbers in any 1 problem. The problems were recorded on magnetic tape with 1 second for each number, an answer given on the 4th second, and then a 1-second pause before the start of the next problem. Half of the answers given were correct, the other half in error by plus or minus 1 or 2 units appearing in approximately equal numbers distributed randomly throughout the test. The subject was informed that not all answers were correct and instructed to respond to correct answers by pressing a right foot pedal and pressing a left foot pedal for incorrect answers. These responses were recorded. Five tapes were made with variations of the arithmetic problems in order to minimize the effect of learning the number sequences. These test tapes were checked for degree of difficulty with a separate group of subjects, and an analysis of variance indicated no significant difference in difficulty between test variations. The test was scored by subtracting 3 times the number of math errors from the number of cards sorted correctly in the 2.5 minute duration of the test.

5) Time Discrimination Test – The subjects were presented with a series of 2 tones and then asked to judge whether the 2nd tone was shorter, longer, or the same duration as the 1st. The number judged correct out of 25 pairs was taken as the

score.

In order to keep the time sequence and form of directions consistent throughout the experimental program, the test commands were recorded on cassette cartridge-type magnetic tapes using an identical script for each tape and played on a tape recorder. Some time variation was found to exist between test tapes, probably due to power variation in the battery operated recorder; however, it was considered to be too small to warrant applying a time correction to the test scores. The 5 tapes used in the experiment were alternated so that every tape was presented twice at each exposure level, once in the morning and once in the afternoon. The same test was never presented twice in the same day.

Immediately before each exposure day, including air-control period, the oral temperature and pulse rate of each subject was checked and they were questioned about possible symptoms of intercurrent disease and whether they had taken any medication. Except during the control week, when only 1 sample was checked, a breath sample (alveolar air) was taken each morning prior to the exposure.

During each control and exposure day psychophysiologic (psychomotor) testing was performed twice during each day (a.m. and p.m.). The time required for these tests was about 30 minutes. The subjects were free to do such things as reading, writing, and playing games while they were not undergoing psychomotor testing. The subjects were asked to volunteer any subjective impressions related to the experiment. A simple neurological test, standing on 1 leg with eyes opened and closed, to evaluate equilibrium was performed just before termination of the exposure.

After each control and exposure day, except during the control week when only 1 sample was checked, a breath sample (alveolar air) was taken about 1 minute after termination of exposure. The pulmonary function measurements were obtained at the end of each day during the control week, but only twice each week during the vapor exposure period.

Breath samples (alveolar air) were collected approximately 72 and 96 hours after the final exposure. Pulmonary function measurements were obtained 4 days after the final exposure.

GLP:	No
Test Substance:	FC-113, purity >99.8%
Results:	The relative humidity did not exceed 44% and the carbon dioxide concentration never went above 0.33%. Samples taken at numerous points in the chamber indicated a uniform vapor concentration. The complete lack of any adverse subjective impressions or abnormal findings revealed by the physical examination, laboratory tests, or clinical observations made during the study indicate that exposure to 500 or 1000 ppm had no detrimental effect. While the effects of continued learning makes interpretation of the results of the psychomotor tests difficult, there appeared to be no decrement in performance attributable to exposure to the test substance. The data do not demonstrate a significant body buildup of test substance with repeated exposure.
Reference:	DuPont Co. (1970). Unpublished Data, Haskell Laboratory Report No. 403-70, "Human Exposures to Fluorocarbon 113" (September 18) (also cited in TSCA Fiche OTS0520329). Reinhardt, C. F. et al. (1971). Am. Ind. Hyg. Assoc. J., 32(3):143-152.
Reliability:	Medium because of the complications in data interpretation due to the continued learning effect.
Type:	**Repeated Dermal Administration to Humans**
Species/Strain:	Humans
Sex/Number:	Male and female/10 per sex
Exposure Period:	Days 1-5: 3 times/day for 30 seconds Day 6: Single 30 second application Days 7-30: 1 time/day for 1.5 minutes
Exposure Levels:	No Data
Method:	The test substance was applied to the entire scalp and most of the forehead by a special apparatus. Complete data was collected on 15 subjects. The following special tests were done: *Biopsies* The scalps of 5 subjects and the foreheads of another 5 were biopsied before and after the study. The stains used were hematoxylin and eosin for general cytology and architecture; hale-orecin for acid mucopolysaccharides of the ground substance and elastic fibers; Mallory's aniline blue for

collagen; toluidine blue for mast cells; Fontana's modification of Masson's ammoniacal silver nitrate for permelanin and melanin.

Anagen-telogen Ratios

Hair roots were plucked by grasping bundles of hair between the jaws of a smooth-bladed hemostat. At least 50 hairs from the crown of the scalp were examined using Van Scott's method of floating the hairs in a petri dish. Anagen-telogen ratios were determined before and after the study. Hair samples were submitted for stress strain measurements on days 6, 21, 31, and 48. In addition, the cuticular pattern was examined by fastening the hairs to a glass slide and examining the preparation by reflected light.

Quantitative Determination of Bacterial Flora

The scalp and foreheads of 10 subjects were sampled before and after the study by the method of Williamson and Kligman. In addition, the test substance, which had been used for several days, was examined for the survival of resident and transient organisms.

Sebum Production

The method of Kligman and Shelley was used to estimate sebum secretion on the forehead. After defatting with ether, cigarette papers were applied to the mid forehead for 6 hours under a gauze bandage held firmly in place by an elastic band encircling the head. The quantity of sebum absorbed by the papers for the 6-hour period was gravimetrically determined after ether extraction and evaporation. Sebum output was determined on 2 successive days before and after treatment.

Eccrine Sweat Secretion

Sweat patterns of the forehead were obtained before and after the treatment by the method of Christophers and Kligman. The forehead was painted with iodine solution over which a starch castor oil emulsion was applied. To stimulate sweating, the subjects were placed in a chamber at 115°F, after which a sweat "print" was obtained by gently pressing a sheet of paper toweling over the sweating area. This procedure permitted a semi-quantitative estimate of the

number and activity of the eccrine glands.

Permeability Studies

The prevention of water loss is one of the skin's most important functions. The horny layer serves as the water proofing seal that keeps diffusional water loses at a low level. Even minor damage insufficient to be detected microscopically, will be reflected in an increased water diffusion rate. This determination is an extraordinarily sensitive way of establishing the normalcy of the outermost coherent membrane of the skin. Highly accurate values may be secured using the principle of electrical hygrometry described by Baker and Kligman. Bone-dry air was conducted through a skin chamber and the relative humidity of the effluent stream was hygrometrically assessed. Given the rate of air flow, the temperature, and the relative humidity, the rate of diffusion of water in terms of mg/cm^2/hour were calculated. The skin is prevented from sweating by pre-treatment with the benzoyl ester of scopolamine.

In addition, the permeability characteristics of the horny layer was determined directly be establishing the permeation time of the fluorescent dye tetrachlorosalicylanilide (TCSA) after the method of Baker and Kligman. A 1.5% solution of the dye in ethylene glycol monomethyl ether was applied in cups fastened to the forehead skin for varying periods of time. Complete permeation was verified by stripping the treated sites with scotch tape. This procedure was carried out under the Woods Lamp (peak emission 3600 A); the horny cells on each strip should fluoresce brightly through the entire depth of the stratum corneum until the glistening layer is reached. The TCSA permeation decreases when the horny layer is damaged.

Finally, the time required for a topically applied vasodilator to reach the dermal blood vessels provided a simple measure of percutaneous absorption. A volume of 0.02 mL of a 0.01% aqueous solution of the nicotinate ester, Trafuril, was applied within a circle 2 cm in diameter and was immediately covered with plastic wrap. The area was observed until the 1st reddening occurred.

Ultra-Violet Response

Prior injury of the skin, even below the level of microscopic detection, markedly enhances the susceptibility to ultra-violet. Lowering the threshold dose indicated a pre-existing abnormality. The lamp service was a fluorescent sun lamp that emitted a continuous spectrum between 2900 and 3200 Å with a peak of about 3000 Å, which corresponds to the sunburn spectrum. The minimal erythema dose (M.E.D.) was determined on the forehead by an incremental series in which each dose was 30% greater than the previous one. The irradiated site was 1 cm^2. The M.E.D. was the least exposure that uniformly reddened the exposure site.

Response to Chemical Irritants

Two agents were used to test a change in susceptibility to chemical irritants: croton oil, which produces follicular pustules, and mercuric chloride, which elicits erythema.

Croton oil was dissolved in mineral oil in concentrations ranging from 3 to 90%. A circle of non-woven cloth was wetted with the fresh solution and applied to the forehead for 6 hours under an occlusive dressing of plastic wrap and impermeable plastic tape. The least concentration evoking a minimum of 3 pustules was taken as the threshold.

Aqueous solutions of mercuric chloride were prepared in concentrations ranging from 0.1 to 4%. These were applied for 6 hours in the same fashion as the croton oil. The least concentration eliciting redness was regarded as the threshold dose.

Urine Samples

Twenty-four-hour urine samples were collected on days 14, 21, 35, and 48. Urine was also collected from 20 control subjects. NaOH was added to the collection bottle as a preservative. Aliquots were submitted for analysis.

GLP: No

Test Substance: FC-113, purity >99.9%

Results: *Clinical Observations*

The test substance exposures were well tolerated. In no instance was there any indication of cutaneous irritation or sensitization. Neither subjectively nor objectively was any subject adversely affected. Subjects with dandruff believed they experienced improvement, and this was the impression of the observers. Frequent mention was made of the "cleansing" effect of the treatment. Several women stated that their hair was more manageable. The evidence is strong that the test substance was clinically quite innocuous. The only adverse comment was related to the test substance odor, which was usually traceable to the looseness of the headband.

Histology

The pre- and post-treatment biopsies were read "blind." The post-treatment histological and histochemical findings were indistinguishable from the controls. There was no evidence of inflammation, irritation, or stimulation. The epidermis was of normal thickness with typical cytology. The mucopolysaccharides of the ground substance were unaltered. There were no changes in the collagen or elastic fibers. The mast cell population was neither increased nor decreased. The melanin stains did not suggest an increase in the density or activity of the melanocytes. The melanin content of the keratinocytes was not altered. With the methods used it was not possible to detect structural or chemical microscopic changes in the skin for the forehead and scalp after treatment.

Anagen-telogen ratios

No important deviation from the control values was found. Previous experience indicates that certain toxic substances may prematurely terminate the growing (Anagen) phase, with a resulting increased proportion of resting hairs. The test substance had no effect on this parameter.

Sebum Production

The values were not highly reproducible from day to day since the collection method was fairly crude. Mean differences of <30% were not considered significant.

The test substance did not appear to exert an appreciable effect on the activity of the sebaceous glands. Sebum output was dependent on the size of the glands. The histologic findings were consistent with the gravimetric data, in that gland volume was not altered.

Eccrine Sweat Secretion

Side by side examination of the pre- and post-treatment sweat prints failed to disclose a difference. The number and activity of the eccrine glands was apparently not influenced by treatment.

Permeability Studies

The water diffusion rates determined hygrometrically were not affected by exposure. This was a sensitive measurement, which strongly indicated a lack of alteration of the epidermis and horny layer.

The TCSA permeation times were not influenced by exposure. This was congruent with the water diffusion measurements.

Similarly, the percutaneous absorption of Trafuril was not affected by exposure. The penetration times remained the same.

These findings indicated that the permeability characteristics of the skin were not significantly influenced by exposure to the test substance. The "barrier" to water and chemicals remained intact, indicating lack of toxicity on the superficial cutaneous tissues.

Ultra-Violet Reaction

The post-treatment M.E.D's were not significantly different. The unaltered reactivity to sunburn ultra-violet radiation was consistent with the above findings of lack of toxicity. Values were not obtained on 5 subjects.

Response to Chemical Irritants

The threshold concentrations of mercuric chloride and croton oil that produced erythema and pustules, respectively, were

not on the average influenced by the test substance. The instances in which the threshold values were increased were offset by decreases in other subjects.

Conclusion

By the above parameters, the exaggerated use of the test substance did not adversely affect the structure and function of the skin of the scalp and forehead. It is highly probable that under conventional circumstances of use, the test substance will not have significant cutaneous toxicity.

Reference: DuPont Co. (1967). Unpublished Data, Haskell Laboratory Report No. 260-67, "Toxicology of Freon" (January 30).

Reliability: Medium because a suboptimal study design was used.

Additional References for Repeated Dose Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

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Desoille, H. L. et al. (1968). Arch. Maladies Profess. Med. Trav. Securite Sociale, 29(7-8):381-388.

DuPont Co. (1967). Unpublished Data, “Skin Irritation Test with Rabbits” (May 26).

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Schloz, J. (1962). Fortschr. Biol. Aerosol-Forsch., 4:420-429 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva).

Data from these additional sources were not summarized because the test substance was a mixture or otherwise inappropriate.

DuPont Co. (1964). Unpublished Data, Haskell Laboratory Report No. 135-64, "Inhalation Toxicity" (November 19).

Desoille, H. L. (1975). Arch. Maladies Profess. Med. Trav. Securite Sociale, 56:5-18 (cited in ACGIH (1991-1992). ACGIH TLV® Booklet).

5.3 Developmental Toxicity

Species/Strain:	Rats/Alderley Park
Sex/Number:	Female/24 per concentration
Route of Administration:	Inhalation
Exposure Period:	6 hours/day on Days 6-15 of gestation
Exposure Levels:	0, 5000, 12,500, 25,000 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Nulliparous specific pathogen free female rats were used. The rats had a weight range of 188-292 g, and were approximately 11-13 weeks old on arrival. Four batches of rats were allocated for mating. The rats in each batch were mated overnight and the following morning vaginal smears were taken for confirmation of mating. Sufficient rats were mated to provide 24 in each batch. The day on which spermatozoa were detected in the smear was considered to be day 0 of pregnancy, and on that day the rats were delivered to the laboratory.

The rats were housed singly in wire-mesh cages. The rats were offered PC diet and tap water *ad libitum*, except during each exposure period. The cages were supported in holding chambers, 1 chamber per group.

On days 6-15 (inclusive) of gestation, the rats were exposed to the test substance for 6 hours/day.

The chambers had an internal volume of approximately 3.4 m^3. They were constructed of stainless steel and access

was gained to each chamber through a door fitted with a safety glass window.

Air entered at the front of each chamber and was extracted at the back. Within each chamber were 6 cage levels and excreta collection trays that rotated concurrently (0.5 times per minute) with the direction of flow of the input air. The air flow rate through each chamber was set to approximately 300 L/minute using a flowmeter (rotameter). The chamber air supply was conditioned nominally to 22°C and 50% relative humidity, and the temperature and relative humidity in each chamber were recorded daily. A 12-hour warm white fluorescent light (starting at 0600 hours) and 12-hour dark cycle were maintained within each chamber.

Dynamic atmospheres of the test substance vapor were generated by metering appropriate amounts of vaporized test substance into the input air of each chamber. The test substance was metered from the reservoir onto a condenser coil by means of a peristaltic pump fitted with solvent resistant tubing. Hot water (approximately 70°C) from a thermocirculator was circulated through the condenser coil to aid in the volatilization of the test substance. A carrier airflow (approximately 5 L/min) was passed down the condenser jacket and through the flask. The carrier air plus the test substance vapor was then passed into the input air of the chamber.

The concentrations of test substance in each chamber were analyzed 3 or 4 times per hour for each period of exposure. Each of the chambers had an atmosphere sampling point in the back wall connected by copper tubing to an automatic sampling system and gas chromatograph. The gas chromatograph was equipped with a flame ionization detector and a stainless steel column.

The body weight of each rat was recorded on Days 0, 5, 6-15 (after exposure on each day), 16, 18, and 21 of gestation. Food consumption was measured for pairs of females sharing the same food hopper on Days 1, 6-16 (inclusive), 19, and 21 of gestation. The food in each hopper was weighed on the afternoon before these specified days and re-weighed the following morning. The amount of food left was recorded, and the amount of food consumed per rat was calculated. Each rat was observed daily for changes in clinical condition and during each exposure period for any

abnormalities.

On day 21 of pregnancy, each rat was killed. The uterus was immediately dissected out, and the gravid uterus was weighed. The number of corpora lutea in each ovary was counted. The number of implantations and the number of early and late intra-uterine deaths were counted. Intra-uterine deaths were identified as being late when fetal tissues were distinguishable. Each live fetus was removed from the uterus and was weighed and examined externally for gross abnormalities, including cleft palate.

Approximately 2/3 of the fetuses in each litter were fixed in methanol. These fetuses were subsequently eviscerated and stained with Alizarin Red S. The remaining fetuses in each litter were fixed in Bouin's fluid.

During evisceration of the methanol-fixed fetuses, the abdominal and thoracic contents were examined and any abnormalities were recorded. At this time, the sex of each fetus was determined externally and confirmed by internal examination. Those fetuses fixed in Bouin's fluid were stored until decalcification was complete. They were then transferred to methanol. Each fetus was then sectioned at approximately 1.5-2 mm intervals, then the sections examined under a stereo-microscope. The sex of each fetus was determined and all abnormalities were recorded.

The osseous skeletons of all fetuses fixed in methanol and stained with Alizarin Red S were examined under a stereo-microscope to assess morphological development and the degree of ossification.

Data relating to rats that were not pregnant were not included in statistical analysis. Initial maternal body weight and maternal body weight gain and food consumption were considered by analysis of variance. In addition, food utilization and litter parameters were considered by analysis of variance. Litter parameters included the number of corpora lutea per dam, the number of implantations per dam, the number of live fetuses, percentage of pre-implantation and percentage of post-implantation loss (after transformation using the double arcsine transformation), gravid uterus weight, total litter weight (live fetuses) and mean live fetal weight (all calculated on an individual litter basis). Individual treatment group means were compared

with the control group mean using Student's t-test based on the error mean square in the analysis of variance.

Where, for a particular animal, the observed number of corpora lutea was recorded as less than the number of implantations, the number of corpora lutea was assumed to be equal to the number of implantations, and the pre-implantation loss assumed to be zero in these analyses.

In addition to the above analyses, a comparison between each treated group and the control group using Fisher's exact test was also carried out for each of the following parameters: the proportion of females with any pre-implantation loss, post-implantation loss, early intrauterine death, late intra-uterine death, and the proportion of fetuses that were male.

All statistical tests of significance used were one-sided, except for body weight gain, food consumption, food utilization, the number of corpora lutea, and the proportion of male fetuses, which were two-sided.

The majority of individual skeletal findings were considered in the following way. The proportion of fetuses, in which individual skeletal findings were observed, was considered by comparing each exposed group with the control group using Fisher's exact test, one-sided. In addition, the findings were analyzed in a similar manner, but on a litter basis, to the proportion of litters in which, for each individual skeletal finding, any fetus was affected. For most findings, data were only tabulated on a fetus basis, and not on a litter basis, although all statistically significant effects that existed when data were analyzed on a litter basis were referred to, where appropriate. In the case of the finding of vestigial 14th ribs, the data were tabulated on both a fetus and a litter basis.

The mean manus and pes score per fetus, the number of ossified vertebra per fetus, the number of partially ossified sternebra per fetus, and the percentage of fetuses with any partially ossified sternebra and with any 14th rib (after transformation using the double arcsine transformation) were all considered by analysis of variance, which allowed for the 4 batches of rats. Individual treatment group means were compared with the control group mean using Student's t-test, one-sided, based on the error mean square in the analysis.

GLP: Yes

Test Substance: FC-113, purity >99.9%

Results: Mean measured concentrations were 4985, 12,532, and 25,265 ppm for the 5000, 12,500, and 25,000 ppm concentrations. Each daily mean concentration was within ±5% of the target concentration, with the exception of the 5000 ppm level on 1 day, which was 8% below the target concentration.

Pregnant rats exposed to all concentrations of the test substance had reduced body weight gains and poorer food utilization during exposure. Food consumption was only reduced at 25,000 ppm during exposure. In addition to the reduced body weight gain and the food consumption at 25,000 ppm, signs of hyperactivity were observed during each exposure period. There were no clinical abnormalities that could be attributed to the test substance at 5000 and 12,500 ppm.

Previous studies on pregnant and non-pregnant rats showed that 25,000 ppm of the test substance caused reduced body weight gain and food consumption, but 12,500, 7500, or 5000 ppm did not produce these effects. It is possible that the higher weight gain of the 12,500 and 5000 ppm groups during the pre-exposure period in the present study reduced the potential for comparable weight gain during the exposure. Moreover, there was no dose-response relationship at ≤12,500 ppm during the exposure period, and the overall body weight gains were similar to controls. Thus, the body weight gain, food consumption, and clinical effects indicate maternal toxicity at 25,000 ppm, but the body weight gain and food utilization effects at ≤12,500 ppm were not of toxicological significance.

There was no evidence of fetal toxicity in any of the exposed groups. The slight reduction in the mean number of implantations, the mean number of live fetuses, the mean gravid uterus weight, and the mean total litter weight at 12,500 ppm was not observed at 25,000 ppm, and the apparent effects are, therefore, not related to exposure to the test substance.

The only fetal variant that appeared to be related to exposure to the test substance was the incidence of extra ribs. The background range for this variant over recent studies was 7.9-36.0%. The control group value of 9.9% was at the lower extreme of the range, and the treated groups at the

upper end. Hence, though the values in the treated groups were statistically significantly different from controls, no biological significance was attributed to the finding.

Therefore, the test substance is not teratogenic in rats at the exposure concentrations used in this study.

Reference: ICI Ltd. (1982). Unpublished Data, Report No. CTL/P/731, "1,2-Trichloro-1,2,2-tetrafluoroethane ("Arcton" 113): Teratogenicity Study in Rats) (also cited in TSCA Fiche OTS0520488).

Reliability: High because a scientifically defensible or guideline method was used.

Species/Strain: Rabbits/New Zealand White

Sex/Number: Female/12 per concentration

Route of Administration: Inhalation

Exposure Period: Days 8-16G

Frequency of Treatment: 2 hours/day

Exposure Levels: 0, 2000, 20,000 ppm

Method: No specific test guideline was reported.

Female rabbits were mated 1 buck to 1 doe once per day for 2 consecutive days. Hand breeding was used to check for conception. The 2nd day of breeding was deemed Day 0 of gestation.

Female rabbits were exposed to the test substance for 2 hours per day on gestation Days 8-16 at concentrations of 0, 2000, or 20,000 ppm. All exposures were conducted in 1000-liter stainless steel chambers. During the exposures, the rabbits were housed in compartmented cages centered in the chamber with 6 rabbits per layer. Following each exposure, all rabbits were returned to individual housing quarters.

The higher concentration of test substance vapor was produced by bubbling compressed air at 4.9 liters per minute through approximately 300 mL of the test substance liquid contained in a 1-liter 3-neck distilling flask. To produce the lower concentration, compressed air was bubbled at 685 mL per minute through approximately 150 mL of the test substance liquid contained in a 500 mL 3-neck distilling flask. A fairly constant test substance volume was maintained in each flask by continuously replenishing the

liquid at intervals. The liquid was drawn from the metal reservoir through tubing and a 3-way stopcock into a 50 mL graduated syringe that was secured in a rubber stopper located in the center neck of the distilling flask. A measured volume of the test substance was then delivered into the flask. Two identical vapor-generating systems were prepared for the exposure at 20,000 ppm; 1 assembly was used for the 2000 ppm concentration.

The vapor-laden air was delivered into the inlet port of the chamber via a rotameter that served as an indicator of the consistency of the test substance vaporization. A steady rate of vaporization was maintained by immersing the flasks in a water bath maintained at 23°C.

The airflow through the chamber was maintained by a positive pressure rotary pump located at the exhaust side of the chamber and was monitored by a rotameter. The nominal chamber concentration was determined from the ratio of the total weight of the test substance evaporated to the total chamber airflow (volume of air bubbled through the evaporation flasks plus the volume of make-up air) per unit time. A gas chromatograph was used to monitor the actual chamber concentration. Readings were taken every 5 minutes by analyzing a 10-mL gas sample drawn from the chamber by a constant volume sampling arrangement.

Daily and throughout the study and during the 2-hour exposure periods, mortality, appearance, and behavior were observed. Body weights were recorded weekly during gestation and at terminal sacrifice.

Five or 6 of the does in each group were sacrificed on Day 29 or 30 of gestation. Cesarean sections were performed and the following observations recorded: number and placement of uterine implantation sites; number and placement of live, dead, and resorbed fetuses; individual fetal weight and length (crown-rump); external fetal anatomy and gross visceral features. Gross necropsies with examination of uterine and visceral structures were performed on all does sacrificed for cesarean delivery.

The remaining does in each group were allowed to hutch normally, and the following observations were recorded: number of live and dead pups; individual pup weight and length (crown-rump); and external pup anatomy. After

completion of delivery, each female and all pups were sacrificed. Visceral features of each pup and uterine and visceral structures of each doe were grossly examined. Sacrifice of those does designated for natural delivery that did not produce litters began on Day 35. Gross necropsies were performed on each of these females and on 1 female that died during the study.

The fetuses and pups were skinned and eviscerated with a gross examination of the structure and placement of viscera in the thoracic, abdominal, and pelvic areas. The fetuses and pups were then macerated, stained with 0.5% alizarin red, and cleared with gylcerine. Each skeleton was evaluated for relative differences in size, location, normal or abnormal structure or formation, degree of ossification, and the presence or absence of bone structure.

The lung, liver, kidney, ovary, and uterus of each doe, with the exception of 1 female at 20,000 ppm that died and was autolyzed, were preserved in buffered formalin. Following cesarean sections or natural deliveries, all fetuses and sacrificed pups were preserved in buffered formalin. All stained and cleared fetuses and pups were preserved in glycerin, and viscera preserved in buffered formalin.

GLP: No

Test Substance: FC-113, purity 100%

Results: Mean daily chamber concentrations were 2027 and 19,747 ppm at nominal concentrations of 2000 and 20,000 ppm, respectively.

One pregnant female exposed to 20,000 ppm was found dead on Day 20. Due to advanced autolysis, no tissues were taken from this female. On Day 29, 1 female exposed to 20,000 ppm aborted. Neither the death, nor the abortion was attributed to administration of the test substance. A total of 15 of the 36 does used for the study became pregnant (4 control, 4 low concentration, and 7 high concentration). The low fertility was due to seasonal variation and was not attributed to administration of the test substance.

During exposure only, slight eye irritation indicated by partial or total eye closure was observed at 20,000 ppm. Otherwise, the appearance and behavior of the test rabbits was comparable to the controls. There was no evidence of a test substance effect in maternal survival or body weight gain. Gross necropsy findings were similar in control and

both test groups, apart from lungs gray in color with gray areas noted among does exposed to 2000 and 20,000 ppm.

Evaluation of the following criteria revealed no evidence of test substance effect: number and placement of implantation sites, resorption sites, or live or dead fetuses from cesarean deliveries; weight and length of fetuses; fetal external appearance, and gross visceral anatomy; the number of live and dead pups from full-term litters; pup weight and length; external appearance; and gross visceral anatomy. The development and structure of test fetal and pup skeletons were comparable with the control animals and with accumulated control data. No effect on fetal development was discernible with administration of the test substance to female albino rabbits from Day 8 through Day 16 of gestation.

A summary of other reproductive outcomes (represented as means/litter, except for resorptions and live litters) are provided in the table below:

Concentration (ppm):	0	2000	20,000
Number Pregnant:	4/12	4/12	7/12
Deaths:	0	0	1
Number of litters (Cesarean):	2	1	3
Number of litters (Normal Delivery):	2	3	2
Aborted:	0	0	1
Number of Implantation Sites (Cesarean):	9.5	14	8.7
Number of Implantation Sites (Normal Delivery):	10	7	8
Number of live fetuses (Cesarean):	9.5	8	8
Number of live fetuses (Normal Delivery):	9.5	6	8
Number of dead fetuses (Cesarean):	0	1	0.7
Number of dead fetuses (Normal Delivery):	0.5	0.33	0
Number of resorptions (Cesarean):	0	5	0
Number of resorptions (Normal Delivery):	0	0	0
Fetal weight (Cesarean) (g):	45.0	45.0	41.7
Fetal weight (Normal Delivery) (g):	56	61	54

Reference:	DuPont (1967). Unpublished Data, Haskell Laboratory Report No. 242-67, "Teratology Study – Rabbits" (December 21) (also cited in TSCA Fiche OTS0520359).
Reliability:	Low because an inappropriate method or study design was used.

Additional Reference for Developmental Toxicity:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1967). Unpublished Data, Haskell Laboratory Report No. 258-67, "Modified Somer's Reproduction Study in Rabbits" (February 22) (also cited in TSCA Fiche OTS0571230).

5.4 Reproductive Toxicity

Species/Strain:	Rats/Alderley Park
Sex/Number:	Male and Female/12 males and 24 females per concentration
Route of Administration:	Inhalation
Exposure Period:	Pre-mating: 10 weeks for males and 3 weeks for females Mating: Maximum of 2 weeks Post-mating: Until Day 20 of gestation for ½ of the females and no additional exposures for ½ of the females
Frequency of Treatment:	Pre-mating: 6 hours/day, 5 days/week Mating: 6 hours/day Post-mating: 6 hour/day, 7 days/week
Exposure Levels:	0, 5000, 12,500 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Rats were housed in cages within exposure chambers, males 1 per cage and females 2 per cage. They remained in the exposure chambers continuously throughout those phases of the study where exposure to the test substance was scheduled. The exposure chambers had an internal volume of approximately 3.4 m^3. They were constructed of stainless steel and access was gained to each chamber through a door fitted with a safety glass window.

Air entered at the front of each chamber and was extracted at the back. Within each chamber were 6 cage levels, and excreta collection trays that rotated concurrently (0.5 times per minute) with the direction of flow of the input air. The air flow rate through each chamber was set to approximately 300 L/minute using a flowmeter (rotameter). The air supply to the chambers was nominally conditioned to 22°C and 50% relative humidity. The temperature and relative humidity in each chamber were measured using wet and dry bulb thermometers during those phases of the study where exposure was scheduled.

A 12-hour warm white fluorescent light (starting at 0600 hours) and 12-hour dark cycle was maintained in the chambers.

The cages were made of wire mesh, and each was divided into 2 halves by a wire mesh partition. Each half had a water bottle, and a central food hopper served both halves of the cage. The rats were allowed tap water and food *ad libitum* throughout the study, except during exposure to the test substance.

Atmospheres of the test substance were generated by metering appropriate amounts of vaporized test substance into the input air of each chamber. The generation system for each exposure level consisted of a reservoir of test substance, a peristaltic pump, a glass condenser, and a round-bottom flask. The test substance was metered from the reservoir onto the condenser coil by means of the peristaltic pump fitted with solvent resistant tubing. Hot water (70°C) from a thermocirculator was circulated through the condenser coil to aid in the volatilization of the test substance. The bottom of the condenser fitted into a round-bottom flask that contained a sufficient number of glass beads to cover approximately a quarter of the internal surface area. The flask was warmed by means of a heating mantle. Any test substance that had not volatilized on the condenser coil, was volatilized in the round-bottom flask. The maximum temperature inside the flask was approximately 80°C. A carrier air flow (5 L/min) was passed down the condenser jacket and through the flask. The carrier air plus the test substance vapor was then passed into the input air of the chamber.

The concentration of the test substance in each chamber was analyzed at least once per hour. Each of the chambers had an atmosphere sampling point in the back wall connected by copper tubing to a multipoint sampling system. The sampling valve delivered a sample to a gas chromatograph. An infra-red analyzer was used for atmosphere analysis when there were malfunctions of the gas chromatograph.

Pre-mating:

The rats were exposed to the test substance for 6 hours/day, 5 days/week. The males were exposed for 10 weeks, and the females for 3 weeks immediately prior to the start of the mating period.

The body weight of each rat and the food intake for each cage of rats was recorded the day before exposure commenced and at weekly intervals thereafter.

Since food was withheld during exposure periods, food intake was measured by weighing the amount of food offered to the rats and the amount of food remaining the following morning. The amount of food consumed per cage for rats was then calculated. This procedure was adopted throughout the study.

Clinical condition and behavioral characteristics were recorded on the day before exposure commenced, then daily both during and after each of the exposure periods.

Mating:

After the last exposure of the pre-mating period, the male rats were paired with the females such that 1 male and 2 females were housed together. During the mating period, the rats were exposed daily for 6 hours/day for a maximum duration of 2 weeks.

The day following the last exposure of the pre-mating period was termed Day 1 of the mating period, and on that day each female rat was examined for evidence of mating. This was done daily until successful mating occurred or until 2 weeks had elapsed. Positive evidence of a successful mating (termed Day 0 of gestation) was either a sperm-positive vaginal smear or the presence of a vaginal plug. Success or failure of coitus and pre-coital interval (in days) was

determined for each female rat.

The 1st female rat, of each pair in a cage, that showed evidence of successful mating was allocated to sub-group A, separated from the trio, and housed singly in another cage on the same level of the chamber in which it was paired. This rat along with other rats of the same sub-group continued to be exposed to the test material.

The 2nd female rat, of each pair in a cage, was allocated to sub-group B, and was housed with the same male until evidence of successful mating was found or until the end of the pairing period. This female rat was then removed from the exposure chamber and housed with other rats of the same sub-group.

Each male was killed within 1 week of successful mating of both females with which it was paired, or within 1 week of the end of the mating period. Each male rat was subjected to a gross post-mortem examination, and the following tissues were preserved in formal saline and stored: abnormal tissue, testes and epididymides, prostate, and pituitary.

Post-mating (sub-group A):

The rats were exposed daily for 6 hours/day until Day 20 of gestation. The body weight and food intake of each rat was measured once every 3 or 4 days. Clinical condition was recorded during and after each daily exposure to the test substance.

After the last exposure period on Day 20 of gestation, the rats were transferred from the exposure chambers and housed singly, in wire-mesh cages fitted with aluminum false bottoms, on a mobile rack. The rats were provided with paper as bedding material. Temperature and relative humidity were recorded daily. The laboratory was illuminated by warm white fluorescent light between 0600 or 0830 and 1600 hours.

Any rats not producing litters by Day 24 were subjected to post-mortem examination within 8 days, in order to determine whether these rats had been pregnant.

The day that parturition occurred was termed Day 1 post-partum. The following parameters/observations were

recorded for the dams and their offspring: date of parturition and duration of pregnancy; number of male and female pups born alive and dead in each litter; number of live and dead pups in each litter, daily, until they were 4 weeks old; detailed observations of each pup at birth; weight of each pup in each litter at birth and then every 3 or 4 days until they were 4 weeks old; body weight and food consumption of each dam every 3 or 4 days until the offspring were 4 weeks old; clinical observations, every 3 or 4 days, on each dam; individual pup development in each litter according to the following criteria: the age of the pup (days) when unfolding of pinna, hair growth, eye opening, and weaning occurred.

For any litter not surviving to 4 weeks post-partum, the mother was subjected to a post-mortem examination, and the following tissues were preserved in formal saline and stored: abnormal tissue, ovaries, uterus, pituitary gland, and mammary tissue. Any dams not surviving to 4 weeks post-partum were also subjected to a post-mortem examination, but mammary tissue was not preserved. At 4 weeks post-partum, all surviving mothers and pups were killed without necropsy and were discarded.

Post-mating (sub-group B):

After removal from the exposure chambers on day 0 of gestation, these rats were housed singly in wire-mesh cages supported on a mobile rack. Allocation to rack position and environmental conditions were as for sub-group A.

The body weight and food intake of each rat were measured once every 3 or 4 days. Clinical observations were carried out daily. Between Days 17 and 20 of gestation, the rats were subjected to a gross post-mortem examination. The uterine contents were examined and the numbers of live and dead fetuses and any resorptions were recorded.

The rats that showed no signs of mating were kept for up to 24 days after the end of the mating period. Since none of the rats produced litters, they were subjected to post-mortem examination and had the following tissues preserved in formol saline and stored: abnormal tissue, ovaries, uterus, and pituitary gland.

GLP: Yes

Test Substance: FC-113, purity not reported

Results: The daily mean concentrations of the test substance were all within ±15% of the target concentrations.

There were isolated statistically significant differences in body weight gain and food consumption between the test substance-exposed groups and the controls during the pre-mating and post-mating phases of the study. There were no statistically significant differences in group mean body weight gains or food consumption of the adult rats during the post-partum phase of the study.

While there were no statistically significant differences between the mean pre-coital intervals of the 2 exposed groups and the controls, there was some suggestion that the rats exposed to the test substance mated successfully in a shorter time period than the controls. The biological significance of this observation was unclear.

The pups in the litters of the 5000 ppm group were statistically significantly heavier than the pups in the control group on most occasions that weights were recorded during the 4 weeks after birth. Eye opening, pinna detachment, and hair growth also tended to occur earlier in this group. There were no differences from the controls in these pup development parameters in the 12,500 ppm group, and, therefore, the effects observed at 5000 ppm were not considered to be of toxicological significance.

There was a treatment-related reduction in the mean number of corpora lutea in the sub-group B females (i.e., those submitted for post-mortem examination between Days 17 and 20 of gestation). This reduction was statistically significant in the 12,500 ppm group. A corresponding statistically significant reduction in the mean number of implantations and fetuses was apparent in the 12,500 ppm group, although there were no increases in the numbers of pre-and post-implantation losses.

The mean corpora lutea count of 12.40 in the 12,500 ppm group was lower than the range observed in the testing laboratory. Since February 1979, the range of group mean values in young mature female rats, not subjected to experimental procedures prior to mating was 13.0-14.2. In 1978, the range was 12.1-13.5. However, the corresponding values for studies conducted since the beginning of 1979, was 11.67-14.26, with a mean of 12.96. Hence, the values

obtained in this study could be considered to be within the overall range for this strain of rat. It should also be noted that the control values were at the top end of the range. Although there was no reduction in the mean litter size of treated rats in sub-group A compared with control, the fact that corpora lutea could not be counted, and the treatment regime was different for sub-group B rats, does not allow this finding to be used to support or refute the above interpretations.

The reproductive toxicity study was designed to provide only an indication of potential effects within the parameters recorded, rather than a definitive evaluation. Thus, the reduction in the number of corpora lutea in the 12,500 ppm group could be considered as a possible effect. On the other hand, 5000 ppm could be considered as a "no-effect" level.

In conclusion, at exposure concentrations of 5000 and 12,500 ppm, the test substance had no apparent effects on the reproductive parameters investigated in this study, with the exception of possible slight effects on pre-coital interval in the 2 exposed groups and ovulation in the 12,500 ppm group.

Reference: Tinston, D. J. et al. (1982). ICI Ltd., Unpublished Data, Report No. CTL/T/1472, "1,1,2-Trichloro-1,2,2-trifluoroethane (Arcton 113): Reproductive Toxicity Study in Rats" (January) (also cited in TSCA Fiche OTS0520487, OTS0520489, and OTS0555705).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Reproductive Toxicity: None Found.

5.5 Genetic Toxicity

Type: ***In vitro* Bacterial Reverse Mutation Assay**

Tester Strain: *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100

Exogenous Metabolic Activation: Rat-liver homogenate activation system (S9 mix)

Exposure Concentrations: Trial 1: 0, 4.8, 12.0%
Trial 2: 0, 4.6, 13.4%

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The tests were performed in the presence and absence of a rat-liver homogenate activation system (S9 mix). In the absence of metabolic activation, approximately 10^8 bacteria were added to top agar. The solution was mixed and poured on the surface of a Davis minimal agar plate prior to exposure to the test gas. The metabolically activated system involved the addition of the S9 mixture to the bacteria-top agar mixture. The S9 mix contained supernatant of homogenized rat liver, $MgCl_2$, KCl, glucose-6-phosphate, NADP, and sodium phosphate (pH 7.4). This mixture was added directly to the top agar immediately before it was poured over the minimal agar plate.

The minimal plates with the bacteria overlay were exposed to the test gas in 9-liter glass chambers. The chambers, with Teflon® stopcocks and o-ring gaskets, were specially designed for this purpose. The open petri plates were held in the chambers by stainless steel racks, 10 plates per chamber. Volumes of 3 mL and 6 mL of the test substance, a liquid at room temperature, were placed in the exposure chambers in glass dishes. The chambers were then placed in a 37°C incubator for 6 hours. The test substance was completely volatilized at 37°C, and the calculation of the concentration of vapor in the chamber was based on ideal gas laws. At the end of the exposure period, the chambers were flushed with air for several minutes, the plates removed and returned to the 37°C incubator to complete the 48-hour incubation period.

The concentration of test gas in the exposure chamber was measured using a gas chromatograph.

GLP: No

Test Substance: FC-113, purity >99.9%

Results: Negative

Remarks: The test substance was not mutagenic in the microbial assay either in the presence or absence of a liver microsomal system.

Reference: DuPont Co. (1976). Unpublished Data, Haskell Laboratory Report No. 641-76, "*In Vitro* Microbial Mutagenicity Study of 1,1,2-Trifluoro,1,2,2-Trichloroethane" (August 24) (also cited in TSCA Fiche OTS0520360).

Reliability: High because a scientifically defensible or guideline method was used.

Type:	***In vitro* Bacterial Reverse Mutation Assay**
Tester Strain:	*Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100
Exogenous Metabolic Activation:	Rat-liver homogenate activation system (S9 mix)
Exposure Concentrations:	Trial I (with activation): 0, 2, 6, 10, 19% Trial I (without activation): 0, 2, 6, 10% Trial II (with and without activation): 0, 2, 6, 10%
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The tests were performed in the presence and absence of a rat-liver homogenate activation system (S9 mix). In the absence of metabolic activation, approximately 10^8 bacteria were added to top agar. Prior to the exposure to the test gas, these components were mixed and poured on the surface of a plate containing Davis minimal agar. To treat in the presence of an activation system, S9 mix was added to the bacteria-top agar mixture. The S9 mix contained supernatant of homogenized rat liver, $MgCl_2$, KCl, glucose-6-phosphate, NADP, and sodium phosphate (pH 7.4). This mixture was added directly to the top agar immediately before it was poured over the minimal agar plate.

The minimal plates with the bacteria overlay (with or without an activation system) were exposed to the test gas in 9-liter glass chambers. The chambers, with Teflon® stopcocks and o-ring gaskets, were specially designed for this purpose. Ten petri plates, without lids were held in the chamber on stainless steel racks. Measured volumes of the liquid test sample were placed in uncovered glass dishes in the chambers. The chambers were closed and placed in a 37°C incubator where the test sample was volatilized. Exposure was for 48 hours. Calculations of the concentration of the test sample in the chambers were based on ideal gas laws. At the end of the exposure period, the chambers were flushed with air for 5 volume changes, the plates removed, and the mutant frequencies determined.

The concentrations of the test gas in the chambers were determined between 2 to 3 hours after treatment was begun, and just before the end of treatment. Samples were measured with a gas chromatograph. Positive (known mutagens) and negative (solvent) controls were included in

each assay. The positive control gas was introduced into the test chambers via a flow-meter system.

The cytotoxicity of the test sample in the presence and absence of an activation system, as measured in strain TA1535, was the basis for selecting concentrations to be used in the mutagenesis experiment. The protocol used to determine the cytotoxicity was identical to the mutagenesis protocol except that 10^3 rather than 10^8 bacteria were used per plate and a non-limiting concentration of histidine was present. Concentrations of test sample that were nontoxic and slightly toxic were selected for the mutagenesis assay.

Data from replicate plates within a single experiment were averaged. The average of these values from different experiments was determined. The highest average number of revertants that was obtained was expressed as a multiple of the control value for the sensitive strain(s).

GLP:	No
Test Substance:	FC-113, purity > 99.9%
Results:	Negative
Remarks:	The compound was not mutagenic either in the presence or absence of a liver microsomal system.
Reference:	DuPont Co. (1977). Unpublished Data, Haskell Laboratory Report No. 915-77, "Mutagenic Activity of Ethane, 1,1,2-trichloro-1,2,2-trifluoro- in the *Salmonella*/Microsome Assay" (November 11) (also cited in TSCA Fiche OTS0520361).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for *In vitro* Bacterial Reverse Mutation Assay:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Douglas, G. R. et al. (1985). Environ. Mutagen., 7(Suppl. 3):31.

Hoechst Celanese Corp. (1977). Bericht Nr. 321/77A (cited in TSCA Fiche OTS0520796).

Hoechst AG (1977). Unpublished Data, 77.0321 (cited in TSCA Fiche OTS0516686).

Longstaff, E. (1988). Ann. N.Y. Accad. Sci., 534:283-298.

Mahurin, R. G. and R. L. Bernstein (1988). Environ. Res., 45(1):101-107 (CA108:126407e).

Simmon, V. F. et al. (1977). Dev. Toxicol. Environ. Sci., 2:249-258.

Gradiski, D. and J. L. Magadur (1974). J. Europ. Toxicol., 7(4):247-254.

Data from these additional sources were not summarized because the test substance was a mixture or otherwise inappropriate.

3M (Minnesota Mining and Manufacturing) Co. (1989). "*In vitro* Microbiological Mutagenicity Assays of 3M Company Compounds T-2962COC and T-2963COC" (cited in TSCA Fiche OTS0516774).

3M (Minnesota Mining and Manufacturing) Co. (1982). "Product Environmental Data" (cited in TSCA Fiche OTS0206107, OTS0206116, OTS0206110).

Anon. (1993-1994). "Initial Submission: Letter from [ ] to USEPA Regarding Acute Inhalation Toxicity of Perfluorinated Organic Peroxide in Rats (sanitized) (cited in TSCA Fiche OTS0570797).

Type: ***In vitro* Clastogenicity Studies:** None Found.

Type: **Dominant Lethal Assay**
Species/Strain: Mice/ ICR/Ha Swiss
Sex/Number: Male and female/7-10 males, 24 per dose level
Route of Administration: i.p. injection
Concentrations: 0, 200, 1000 mg/kg
Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

A single i.p. injection of the test substance was given to 10, 7, and 9 male mice at 0, 200, and 1000 mg/kg, respectively. The males were subsequently caged with 3 untreated virgin female mice, which were replaced weekly for 8 consecutive weeks. All females were sacrificed 13 days after the midweek of their caging and presumptive mating, without being checked for vaginal plugs. At autopsy, each female was scored for pregnancy, and for numbers of total implants, as comprised by live implants, early fetal deaths and late fetal deaths; as late fetal deaths were exceedingly rare, total implants and early fetal deaths were the only implant parameters analyzed. Early fetal deaths were brown or black

	containing necrotic and hemorrhagic material, but no embryo; contrastingly, late fetal deaths were seen as implantation sites containing a subnormal fetus and placenta that may have been white or pale. In the test groups, reduction in mean total implants was determined by contrasting values with concurrent controls. Corpora lutea counts were omitted.
GLP:	No
Test Substance:	FC-113, purity not reported
Results:	Negative
Remarks:	No mortality occurred during the study. No difference from control was observed in early fetal death or preimplantation loss. FC-113 was inactive in this dominant lethal test.
Reference:	Epstein, S. S. et al. (1972). Toxicol. Appl. Pharmacol., 23:288-325.
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for *In vivo* Genetic Toxicity: None Found.

18 March 2005

Appendix B

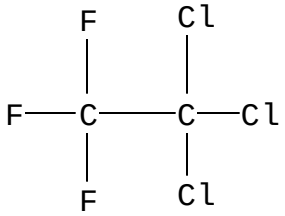
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 354-58-5

Chemical Name: Ethane, 1,1,1-trichloro-2,2,2-trifluoro

Structural Formula:



Other Names:
CFC-113a
CFC 113a
F 113a
FC-113a
FC 133A
Fluorocarbon 113
Freon® 113a
Freon® FT
Precision cleaning agent
R 113a
T-WD602
Trichlorotrifluoroethane
1,1,1-Trichlorotrifluoroethane
1,1,1-Trifluoro-2,2,2-trichloroethane
1,1,1-Trifluorotrichloroethane

Exposure Limits: DuPont Acceptable Exposure Limit (AEL): 1000 ppm, 8- and 12-hour TWA

2.0 Physical/Chemical Properties

2.1 Melting Point

Value:	14.2°C
Decomposition:	No Data
Sublimation:	No Data
Pressure:	760 mm Hg
Method:	No Data

GLP:	Not Applicable
Reference:	Grasselli, J. G. and W. M. Ritchey (1975). Chemical Rubber Company Atlas of Spectral Data and Physical Constants for Organic Compounds, 2nd ed., CRC Press, Inc., Cleveland, Ohio (ISHOW-0008018).
Reliability:	Not assignable because limited study information was available.

Additional References for Melting Point:

Henne, A. L. and E. G. Wiest (1940). J. Am. Chem. Soc., 62:2051-2052 (CA34:6568[3]).

Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-157, CRC Press Inc., Boca Raton, FL.

2.2 Boiling Point

Value:	46.1°C
Decomposition:	No Data
Pressure:	760 mm Hg
Method:	No Data
GLP:	No Data
Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-157, CRC Press Inc., Boca Raton, FL.
Reliability:	Not assignable because limited study information was available.

Additional References for Boiling Point:

DuPont Co. (1995). Material Safety Data Sheet 04212198 (May 12).

Grasselli, J. G. and W. M. Ritchey (1975). Chemical Rubber Company Atlas of Spectral Data and Physical Constants for Organic Compounds, 2nd ed., CRC Press, Inc., Cleveland, Ohio (ISHOW-0008019).

Henne, A. L. and E. G. Wiest (1940). J. Am. Chem. Soc., 62:2051-2052 (CA34:6568[3]).

2.3 Density

Value:	1.5790
Temperature:	20/4°C
Method:	No Data
GLP:	No Data

Results:	No additional data.
Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-157, CRC Press Inc., Boca Raton, FL.
Reliability:	Not assignable because limited study information was available.

Additional References for Density:

DuPont Co. (1995). Material Safety Data Sheet 04212198 (May 12).

Henne, A. L. and E. G. Wiest (1940). J. Am. Chem. Soc., 62:2051-2052 (CA34:6568[3]).

2.4 Vapor Pressure

Value:	360 mm Hg
Temperature:	25°C
Decomposition:	No Data
Method:	No Data
GLP:	No Data
Reference:	Boublik, T. et al. (1984). The Vapor Pressures of Pure Substances, 2nd ed., Elsevier, Amsterdam (HSDB/6501).
Reliability:	Not assignable because limited study information was available.

Additional References for Vapor Pressure:

DuPont Co. (1995). Material Safety Data Sheet 04212198 (May 12).

DuPont Co. (2001). Unpublished Data, "Acceptable Exposure Limit Documentation" (January 25).

2.5 Partition Coefficient (log Kow)

Value:	3.09
Temperature:	25°C
Method:	Modeled. KOWWIN, v1.67, module of EPIWIN v3.11 (Syracuse Research Corporation). KOWWIN uses "fragment constant" methodologies to predict log P. In a "fragment constant" method, a structure is divided into fragments (atom or larger functional groups) and coefficient values of each fragment or group are summed together to yield the log P estimate.
GLP:	Not Applicable
Reference:	Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci.,

	84:83-92.
Reliability:	Estimated value based on accepted model.

Additional References for Partition Coefficient (log Kow):

Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92 (HSDB/6501).

Leo, A. J. (1978). Report on the Calculation of Octanol/Water Log P Values for Structures in EPA Files (ISHOW-0008021).

2.6 Water Solubility

Value:	20.9 mg/L
Temperature:	25°C
pH/pKa:	Estimated pKa: Not applicable. No exchangeable hydrogen.
Method:	Modeled.
	Solubility - WSKOWWIN v1.41, module of EPIWIN v3.11 (Syracuse Research Corporation). Water solubility is estimated from log Kow using molecular weight and molecular fragment correction factors.
	pKa – SPARC on-line calculator, University of Georgia.
GLP:	Not Applicable
Reference:	Solubility - Meylan, W. M. et al. (1996). Environ. Toxicol. Chem., 15:100-106.
	pKa - http://ibmlc2.chem.uga.edu/sparc/index.cfm
Reliability:	Estimated values based on accepted models.

Additional References for Water Solubility:

DuPont Co. (1995). Material Safety Data Sheet 04212198 (May 12).

Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-157, CRC Press Inc., Boca Raton, FL.

Weast, R. C. (1969). Chemical Rubber Company Handbook of Chemistry and Physics, 50th ed., CRC Press, Inc., Cleveland, Ohio (ISHOW-0008020).

2.7 Flash Point: No Data.

2.8 Flammability

Results:	1256°F
Method:	No Data
GLP:	No Data
Reference:	Sax, N. I. (1975). Dangerous Properties of Industrial Materials, 4th ed., p. 1199, Van Nostrand Reinhold, New York.
Reliability:	Not assignable because limited information was available.

Additional References for Flammability: None Found.

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	FC-113a is not expected to undergo direct photochemical degradation in the troposphere (Silverstein and Bassler, 1963).
Indirect Photolysis:	According to a model of gas/particle partitioning of semi-volatile organic compounds in the atmosphere (Bidleman, 1988), FC-113a, which has a vapor pressure of 360 mm Hg at 25°C, is expected to exist solely as a vapor in the ambient atmosphere. Chlorofluorocarbons, such as FC-113a, are expected to be persistent due to their high volatility and chemical stability (Howard and Durkin, 1973). FC-113a is not expected to undergo atmospheric removal by hydroxyl radicals and ozone (Atkinson, 1989).
Breakdown Products:	No Data
Method:	Modeled
GLP:	Not Applicable
Reference:	Bidleman, T. F. (1988). Environ Sci. Technol., 22:361-367. Howard, P. H. and P. R. Durkin (1973). USEPA-560/2-74-001, Washington, DC (HSDB/6501). Atkinson, R. (1989). J. Chem. Phys. Ref. Data Monographs, 1 (HSDB/6501). Silverstein, R. M. and G. C. Bassler (1963). Spectrometric Identification of Organic Compounds, pp. 148-169, Wiley, New York, NY (HSDB/6501).
Reliability:	Estimated value based on accepted model.

Additional References for Photodegradation:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Doucet, J. et al. (1973). J. Chem. Phys., 58:3078-3716 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva).

Doucet, J. et al. (1974). J. Chem. Phys., 62(2):355-359 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva).

3.2 Stability in Water

Concentration:	No Data
Half-life:	The Henry's Law constant for FC-113a is estimated as 0.27 atm-m^3/mole using a fragment constant estimation method (Meylan and Howard, 1991). This Henry's Law constant indicates that FC-113a is expected to volatilize rapidly from water surfaces (Lyman et al., 1990). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) (Lyman et al., 1990) is estimated as 4 hours (SRC, n.d.). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) (Lyman et al., 1990) is estimated as 5 days (SRC, n.d.).
% Hydrolyzed:	No Data
Method:	Estimated
GLP:	Not Applicable
Reference:	Meylan, W. M. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293 (HSDB/6501). Lyman, W. J. et al. (1990). Handbook of Chemical Property Estimation Methods, pp. 15-1 to 15-29, Amer. Chem. Soc., Washington, DC (HSDB/6501). SRC (n.d.). Syracuse Research Corporation (HSDB/6501).
Reliability:	Estimated value based on accepted model.

Additional References for Stability in Water: None Found.

3.3 Transport (Fugacity)

Media: Air, Water, Soil, and Sediments

Distributions:

Compartment	% of total distribution	½ life, hours (advection + reaction)
Air	47.5	1e5
Water	48.4	4.3e3
Soil	2.38	8.6e3
Sediment	1.72	3.9 e4

Adsorption Coefficient: Koc = 504

Desorption: Not Applicable

Volatility: Henry's Law Constant = 0.267 atm-m^3/mole (HENRYWIN program)

Method: Modeled.

SMILES: FC(F)(F)C(CL)(CL)CL
Molecular Wt: 187.38
Vapor Pressure: 360 mm Hg
Log Kow: 3.09 (KOWWIN program)
Soil Koc: 504 (calc by model)

Henry's Law Constant - HENRYWIN v3.10 module of EPIWIN v3.11 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available.

Koc – Calculated from log Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.11 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.

GLP: Not Applicable

Reference: HENRYWIN –

J. Hine and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-298.

Meylan, W. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293.

Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in:

Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated values based on accepted models.

Additional References for Transport (Fugacity): None Found.

3.4 Biodegradation

Value:		
Linear Model Prediction:	-0.38	Does not biodegrade fast
Non-Linear Model Prediction:	0.00	Does not biodegrade fast
Ultimate Biodegradation Timeframe:	1.5	Recalcitrant
Primary Biodegradation Timeframe:	2.8	Weeks
MITI Linear Model Prediction:	0.27	Not readily degradable
MITI Non-Linear Model Prediction:	0.00	Not readily degradable
Breakdown Products:	No Data	

Method: Modeled. BIOWIN, v4.01 module of EPIWIN v3.11 (Syracuse Research Corporation). BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental microorganisms. Estimates are based upon fragment constants that were developed using multiple linear and non-linear regression analyses.

GLP: Not Applicable

Reference: Boethling, R. S. et al. (1994). Environ. Sci. Technol., 28:459-65.

Howard, P. H. et al. (1992). Environ. Toxicol. Chem., 11:593-603.

Howard, P. H. et al. (1987). Environ. Toxicol. Chem., 6:1-10.

Tunkel, J. et al. (2000). Environ. Toxicol. Chem., 19(10):2478-2485.

Reliability: Estimated value based on accepted model.

Additional References for Biodegradation: None Found.

3.5 Bioconcentration

Value: BCF = 48.2
Method: An estimated BCF was calculated using an estimated log Kow of 3.09 and a regression-derived equation.
GLP: Not Applicable
Reference: SRC (n.d.). Syracuse Research Corporation (HSDB/6501).
Reliability: Estimated value based on accepted model.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type: **96-hour LC_{50}**
Species: Fish
Value: 13.1 mg/L; log Kow = 3.09
Method: Modeled
GLP: Not Applicable
Test Substance: FC-113a
Results: No additional data.
Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability: Estimated value based on accepted model.

Additional References for Acute Toxicity to Fish: None Found.

4.2 Acute Toxicity to Invertebrates

Type:	**48-hour LC_{50}**
Species:	Daphnid
Value:	15.2 mg/L; log Kow = 3.09
Method:	Modeled
GLP:	Not Applicable
Test Substance:	FC-113a
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates: None Found.

4.3 Acute Toxicity to Aquatic Plants

Type:	**96-hour EC_{50}**
Species:	Green algae
Value:	10.1 mg/L; log Kow = 3.09
Method:	Modeled
GLP:	Not Applicable
Test Substance:	FC-113a
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Aquatic Plants: None Found.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type: **Oral Toxicity:** No Data.

Type: **Inhalation LC_{50}**
Species/Strain: Male rats/ChR-CD
Exposure Time: 4 hours
Value: > 49,500 ppm
Method: Six male ChR-CD rats, weighing 251-280 g, were exposed to the test substance in a 16-liter bell jar for 4 hours. The test substance was metered at a uniform rate into a heated (65°C) stainless steel T-tube by a syringe drive. Houseline air was used as a diluent to give the desired atmospheric concentration. For analysis, gas samples were taken periodically from the chamber exit and analyzed by a gas chromatographic method. Survivors were sacrificed 14 days later. No histopathologic examinations were performed.
GLP: No
Test Substance: FC-113a, purity not reported
Results: The analytical concentration of the test substance was 49,500 ppm (379 mg/L). The mortality ratio was 0/6. Clinical signs observed during exposure included hyperactivity, irregular respiration, pallor, uncoordinated movements, and "piano-players" syndrome. Normal weight gain and no clinical signs of exposure were observed during the post-exposure period.
Reference: DuPont Co. (1970). Unpublished Data, Haskell Laboratory Report No. 217-70, "Acute Inhalation Toxicity" (May 19) (also cited in TSCA Fiche OTS0555587 and OTS0520340).
Reliability: High because a scientifically defensible or guideline method was used.

Additional Reference for Acute Inhalation Toxicity:

Data from this additional source supports the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1969). Unpublished Data, Haskell Laboratory Report No. 422-69, "Acute Inhalation Toxicity" (December 31) (also cited in TSCA Fiche OTS0571637).

Type: **Cardiac Sensitization:** No Data.

Type: **Dermal Toxicity:** No Data.

Type: **Dermal Irritation:** No Data.

Type: **Dermal Sensitization:** No Data.

Type: **Eye Irritation:** No Data.

5.2 Repeated Dose Toxicity

Type: **2-Week Inhalation**
Species/Strain: Rats/ Crl:CD®BR
Sex/Number: Male/10 per group
Exposure Period: 2 weeks
Frequency of Treatment: 6 hours/day, 5 days/week
Exposure Levels: 0, 2000, 10,000, 20,000 ppm
Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Three groups of 10 male rats were exposed 6 hours/day, 5 days/week for 2 weeks to design concentrations of 2000, 10,000, or 20,000 ppm of the test substance in air. A control group of 10 male rats was exposed simultaneously to air only.

The rats were exposed in stainless steel cage modules that were positioned in 150-liter stainless steel and glass Rochester-style inhalation chambers, which were located in fume hoods. Combined chamber air/test substance flow rates were approximately 30 L/min. A control group of rats was similarly exposed to houseline air at 30 to 40 L/min in chambers, which were located in a walk-in hood. The exposures were followed by a 2-week recovery period.

The test substance was metered from a cylinder that was about 30% immersed in a water bath, which was maintained at 75-80°C. Stainless steel lines carried the vapor to the inhalation chamber air supply. Chamber atmospheres were exhausted through a cold trap and an MSA cartridge filter prior to discharge into a fume hood.

Chamber samples of atmospheric test substance were taken from the animal breathing zone at approximately 30-minute intervals through Teflon® lines leading to an automated gas chromatograph. Chamber temperatures were measured at

least once during each exposure. Chamber relative humidity and oxygen concentrations were measured once daily.

During the exposure, rats were weighed daily, and clinical signs were recorded as group clinical signs, unless a rat showed symptoms that were not typical of the group. During the recovery period, all rats were weighed and observed daily for clinical signs of toxicity, except during weekends.

Urine samples were collected overnight from all rats per group after the 9th exposure, and from the remaining rats per group on the 13th day of recovery, and approximately 13 urine parameters were examined.

Blood samples were collected on all rats per group after the 10th exposure, and from the remaining rats per group on the 14th day of the recovery period, and approximately 23 blood parameters were measured or calculated.

Each group was divided into subgroups of 5 rats. The first 5 rats per group were killed for pathologic examination after the 10th exposure, and the remaining 5 rats per group were killed for pathologic examination on the 14th day of recovery. The lungs, liver, kidneys, spleen, and testes were weighed, and representative samples of 26 tissues or organs were prepared for microscopic examination.

Mean body weights and body weight gains were statistically analyzed by one-way analysis of variance. Exposure group values were compared to controls by the least significant difference test when the ratio of variance (F) indicated a significant among-to-within group variation. For clinical pathology parameters, a one-way analysis of variance (ANOVA) and Bartlett's test were calculated for each sampling time. When the F-test from ANOVA was significant, the Dunnett's test was used to compare means from the control and exposure groups. When the results of the Bartlett test were significant, the Kruskal-Wallis test was employed and the Mann-Whitney U test was used to compare means from the control and exposure groups. Mean body weight (at pathology) and mean absolute and relative organ weights were analyzed using ANOVA. When the F-test from the ANOVA was significant, the Least Significant Difference (LSD) test and Dunnett's test were used to compare means from the control with the test groups.

GLP:	Yes
Test Substance:	CFC-113a, purity 99.9685%
Results:	Mean chamber concentrations were 2020, 10,000, and 20,000 ppm for the 2000, 10,000, and 20,000 concentration groups, respectively. Mean relative humidity was 56, 49, 48, and 53% for the 0, 2000, 10,000, and 20,000 concentration groups, respectively. Mean temperature was 24, 25, 25, and 25°C for the 0, 2000, 10,000, and 20,000 concentration groups, respectively. During the exposures, chamber oxygen concentration was 21%. There were no biologically significant effects observed in test substance-exposed rats at any tested concentration in gross observations at necropsy, hematological or urinalysis measurements, or clinical signs and body weights. There were no exposure-related effects observed histopathologically in rats exposed to the test substance other than a minimal change observed in the nasal epithelium in all test substance-exposed test groups. This minimal change was reversible after 2 weeks and was not considered biologically significant, and may not have been related to CFC-113a exposure.
Reference:	DuPont Co. (1989). Unpublished Data, Haskell Laboratory Report No. 214-89, "Two-Week Inhalation Toxicity Study in Rats" (October 27).
Reliability:	High because a scientifically defensible or guideline method was used.

Type:	**21-Day Oral Gavage**
Species/Strain:	Rats/F344/N
Sex/Number:	Male/5 per group Female/5 for negative control
Exposure Period:	3 weeks
Frequency of Treatment:	Once/day, 7 days/week
Exposure Levels:	0, 0.62, 1.24 mmol/kg
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Dose formulations were prepared by mixing the test substance with corn oil and magnetically stirring the mixtures. Stability studies of the dose formulations under storage conditions and under use conditions (under a nitrogen head space; simulated dosing procedure was performed after a storage interval) were performed with gas chromatography with flame ionization detection (FID).

Male and female rats were 15 weeks old at study start. Rats were housed 5/cage by sex. The animal room was maintained at 69-75°F and 35-65% relative humidity, with 12 hours of fluorescent light per day, and at least 10 room air changes per hour. Feed and drinking water were available *ad libitum*.

Animals were observed twice daily. Rats were weighed and clinical observations were recorded at the beginning of the study, weekly thereafter, and at necropsy. Urine was collected over a 16-hour period that began 4 days before the end of the study, and 8 urine parameters were recorded. Necropsy and histopathologic evaluations were performed on all rats surviving to the end of the study. The right kidney, liver, and right testis were weighed, and the right kidney, left liver lobe, and gross lesions were histopathologically examined.

Organ and body weight data, which were approximately normally distributed, were analyzed with the parametric multiple comparisons procedures of Dunnett. Urinalysis data, which typically had skewed distributions, were analyzed with the nonparametric multiple comparisons methods of Dunn. Jonckheere's test was used to assess the significance of dose-response trends.

The outlier test of Dixon and Massey was employed to detect extreme values. No value selected by the outlier test was eliminated unless it was at least twice the next largest value or at most half of the next smallest value.

GLP: Yes

Test Substance: FC-113a, purity 98-100%

Results: Stability results indicated that the chemical/corn oil solutions were stable for 28 days when stored at 5°C. The test substance showed losses in concentration when stored at room temperature. The test substance also showed losses in concentration under use conditions after storage at room temperature or at 5°C. These results were attributed to the volatility of the chemical. Therefore, 1 set of dose formulations was prepared 1 week before the 3-week study began, and a 2nd set of formulation was prepared for the last week of dosing.

All rats survived until the end of the study. There were no differences in final mean body weights, mean body weight gains, or clinical signs of toxicity. There were no significant

	differences in organ weights or urinalysis parameters. No microscopic effects attributable to the test substance were present in either the kidney or the liver at either dose level.
Reference:	Bucher, J. R. (1996). NTP, Toxicity Report Series No. 45, NIH Publication No. 96-3935 (February).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Repeated Dose Toxicity: None Found.

5.3 Developmental Toxicity: No Data.

5.4 Reproductive Toxicity:

Species/Strain:	Rats/ Crl:CD®BR
Sex/Number:	Male/10 per group
Route of Administration:	Inhalation
Exposure Period:	2 weeks
Frequency of Treatment:	6 hours/day, 5 days/week
Exposure Levels:	0, 2000, 10,000, 20,000 ppm
Method:	A 2-week inhalation study was conducted in male rats (see Section 5.2 for details on the study design). Complete necropsies were performed at study termination. Testes were weighed, and testes and epididymides were examined microscopically.
GLP:	Yes
Test Substance:	CFC-113a, purity 99.9685%
Results:	No test substance-related effects on the testes or epididymides were observed.
Reference:	DuPont Co. (1989). Unpublished Data, Haskell Laboratory Report No. 214-89, "Two-Week Inhalation Toxicity Study in Rats" (October 27).
Reliability:	Medium because a suboptimal study design was used.

Species/Strain:	Rats/F344/N
Sex/Number:	Male/5 per group Female/5 for negative control
Route of Administration:	Oral gavage
Exposure Period:	3 weeks
Frequency of Treatment:	Once/day, 7 days/week
Exposure Levels:	0, 0.62, 1.24 mmol/kg

Method:	A 21-day oral gavage study was conducted in male and female rats (see Section 5.2 for details on the study design). Necropsies were performed at study termination, and the right testis from each male rat was weighed.
GLP:	Yes
Test Substance:	FC-113a, purity 98-100%
Results:	No effect on testis weight was observed.
Reference:	Bucher, J. R. (1996). NTP, Toxicity Report Series No. 45, NIH Publication No. 96-3935 (February).
Reliability:	Medium because a suboptimal study design was used.

Additional References for Reproductive Toxicity: None Found.

5.5 Genetic Toxicity

Type: ***In vitro* Mutagenicity:** No Data.

Type: ***In vitro* Clastogenicity:** No Data.

Type: ***In vivo* Genetic Toxicity:** No Data.

Appendix C

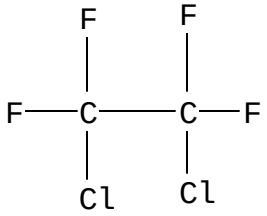
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 76-14-2

Chemical Name: 1,2-Dichloro-1,1,2,2-tetrafluoroethane

Structural Formula:



Other Names:

CFC-114	Freon® 114
Cryofluorane	Frigen 114
Dichlorotetrafluoroethane	Frigiderm
FC 114	Genetron 114
Freon® 114	Genetron 316
1,2-Dichlorotetrafluoroethane	Halocarbon 114
Refrigerant 114	Ledon 114
Arcton 114	Propellant 114
Arcton 33	R 114
Cryofluorane	R 114 (halocarbon)
Cryofluoranum	Refrigerant 114
F 114	Ucon 114
F 114 (halocarbon)	sym-Dichlorotetrafluoroethane
FKW 114	Caswell No 326A
Fluorane 114	Cryofluoran
Fluorocarbon 114	Tetrafluorodichloroethane

Exposure Limits:

OSHA PEL: 1000 ppm (7000 mg/m^3), 8-hour TWA
ACGIH TLV: 1000 ppm (6990 mg/m^3), 8-hour TWA
NIOSH: 1000 ppm (7000 mg/m^3), 10-hour TWA
NIOSH IDLH (Immediately Dangerous to Life or Health): 15,000 ppm

2.0 Physical/Chemical Properties

2.1 Melting Point

Value:	-94°C
Decomposition:	No Data
Sublimation:	No Data
Pressure:	760 mm Hg
Method:	No Data
GLP:	Unknown
Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-154, CRC Press Inc., Boca Raton, FL (HSDB/146).
Reliability:	Not assignable because limited study information was available.

Additional References for Melting Point:

Aldrich Chemical Co., Inc. (5/2002-7/2002). Material Safety Data Sheet.

Verschueren, K. (2001). Handbook of Environmental Data on Organic Chemicals, 4th ed., Vol. 1, pp. 813-814, John Wiley & Sons, Inc., New York, NY.

Windholz, M. (ed.) (1983). The Merck Index. An Encyclopedia of Chemicals and Drugs, 10th ed., Merck & Company, Inc., Rahway, NJ (ENVIROFATE-0003902).

2.2 Boiling Point

Value:	3.8°C
Decomposition:	No Data
Pressure:	760 mm Hg
Method:	No Data
GLP:	Unknown
Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-154, CRC Press Inc., Boca Raton, FL (HSDB/146).
Reliability:	Not assignable because limited study information was available.

Additional References for Boiling Point:

Aldrich Chemical Co., Inc. (5/2002-7/2002). Material Safety Data Sheet.

Chuvatkin, N. N. (1982). Zhurnal Organicheskoi Khimii, 18(5):946-963 (Registry File on STN).

DuPont Co. (1997). Material Safety Data Sheet DU001061 (January 7).

Fokin, A. V. (1985). Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, (10):2298-2302 (Registry File on STN).

Il'in, G. F. (1982). Zhurnal Vsesoyuznogo Khimicheskogo Obshchestva im. D. I. Mendeleeva, 27(3):347-348 (Registry File on STN).

Verschueren, K. (2001). Handbook of Environmental Data on Organic Chemicals, 4th ed., Vol. 1, pp. 813-814, John Wiley & Sons, Inc., New York, NY.

Windholz, M. (ed.) (1983). The Merck Index. An Encyclopedia of Chemicals and Drugs, 10th ed., Merck & Company, Inc., Rahway, NJ (ENVIROFATE-0003903).

2.3 Density

Value:	1.455
Temperature:	25°C
Method:	No Data
GLP:	Unknown
Results:	No additional data.
Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-154, CRC Press Inc., Boca Raton, FL (HSDB/146).
Reliability:	Not assignable because limited study information was available.

Additional References for Density:

DuPont Co. (1997). Material Safety Data Sheet DU001061 (January 7).

Verschueren, K. (2001). Handbook of Environmental Data on Organic Chemicals, 4th ed., Vol. 1, pp. 813-814, John Wiley & Sons, Inc., New York, NY.

2.4 Vapor Pressure

Value:	2014 mm Hg
Temperature:	25°C
Decomposition:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Riddick, J. A. et al. (1986). Techniques of Chemistry, 4th ed., p. 1325, Wiley-Interscience, New York, NY (ENVIROFATE-0003905).
Reliability:	Not assignable because limited study information was available.

Additional References for Vapor Pressure:

Aldrich Chemical Co., Inc. (5/2002-7/2002). Material Safety Data Sheet.

DuPont Co. (1997). Material Safety Data Sheet DU001061 (January 7).

Jordan, E. T. (1954). Vapor Pressure of Organic Compounds, Inter-Science Publishers, Inc., New York, NY (ISHOW-0001516).

Lide, D. R. (ed.) (1991-1992). CRC Handbook of Chemistry and Physics, 72nd ed., p. 6-69, CRC Press, Boca Raton, FL (HSDB/146).

2.5 Partition Coefficient (log Kow)

Value:	2.82
Temperature:	No Data
Method:	No Data
GLP:	Not Applicable
Reference:	Hansch, C. and A. J. Leo (1985). Pomona College MEDCHEM Project Issue #26, Claremont, CA (ENVIROFATE-0003907). Hansch, C. et al. (1995). Exploring QSAR – Hydrophobic, Electronic, and Steric Constants, American Chemical Society, Washington, DC (HSDB/146).
Reliability:	Not assignable because limited study information was available.

Additional References for Partition Coefficient (log Kow):

Jow, P. and C. Hansch (n.d.). Unpublished Results (ISHOW-0001518).

Leo, A. J. (1978). Report on the Calculation of Octanol/Water Log P Values for Structures in EPA Files (ISHOW-0001519).

Verschueren, K. (2001). Handbook of Environmental Data on Organic Chemicals, 4th ed., Vol. 1, pp. 813-814, John Wiley & Sons, Inc., New York, NY.

2.6 Water Solubility

Value:	130 mg/L
Temperature:	25°C
pH/pKa:	No Data
Method:	No Data
GLP:	Not Applicable

Reference:	Riddick, J. A. et al. (1986). Techniques of Chemistry, 4th ed., p. 1325, Wiley-Interscience, New York, NY (ENVIROFATE-0003904).
Reliability:	Not assignable because limited study information was available.

Additional References for Water Solubility:

DuPont Co. (1997). Material Safety Data Sheet DU001061 (January 7).

DuPont Co. (1981). Freon® Technical Bulletin (March 4).

Osol, A. (ed.) (1980). Remington's Pharmaceutical Sciences, 16th ed., p. 1616, Mack Publishing Co., Easton, PA (HSDB/146).

Windholz, M. (1982). The Merck Index, 9th ed., Merck & Company, Inc., Rahway, NJ (ISHOW-0001517).

Verschueren, K. (2001). Handbook of Environmental Data on Organic Chemicals, 4th ed., Vol. 1, pp. 813-814, John Wiley & Sons, Inc., New York, NY.

2.7 Flash Point: No Data.

2.8 Flammability

Results:	Will not burn. Autodecomposition = 593°C
Method:	No Data
GLP:	Unknown
Reference:	DuPont Co. (1997). Material Safety Data Sheet DU001061 (January 7).
Reliability:	Not assignable because limited study information was available.

Additional References for Flammability: None Found.

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	No mechanism for direct photoalteration of this chemical in the lower atmosphere due to irradiation at $\geq$ 290 nm.
Indirect Photolysis:	An estimated half-life of 53,480 days was calculated using an average atmospheric OH concentration of $5x10^5$ molecule/cm^3 at 25°C.

Breakdown Products:	No Data
Method:	Inspection of chemical structure. Modeled
GLP:	Not Applicable
Reference:	Direct Photolysis: Doucet, J. et al. (1973). J. Chem. Phys., 58:3078-3716 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva). Doucet, J. et al. (1974). J. Chem. Phys., 62(2):355-359 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva). Indirect Photolysis: Atkinson R. (1989). J. Phys. Chem. Ref. Data, Monograph No. 1 (ENVIROFATE-0003900).
Reliability:	Estimate based on known qualitative structure-activity relationships.

Additional References for Photodegradation:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Krueger, B. C. and P. Fabian (1986). Ber. Bunsen-Ges. Phys. Chem., 90(11):1062-1066 (BIOSIS/87/10496).

SRC (n.d.). Syracuse Research Corporation (HSDB/146).

3.2 Stability in Water

Concentration:	No Data
Half-life:	The Henry's Law constant for 1,2-dichloro-1,1,2,2-tetrafluoroethane is estimated as 2.8 atm-m^3/mole (SRC, n.d.), from its vapor pressure of 2014 mm Hg (Riddick et al., 1986) and water solubility of 130 mg/L at 25°C (Riddick et al., 1986). This estimated Henry's Law constant indicates that 1,2-dichloro-1,1,2,2-tetrafluoroethane will volatilize rapidly from water surfaces (Lyman et al., 1990). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) (Lyman et al., 1990) is estimated as approximately 1 hour (SRC, n.d.). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) (Lyman et al., 1990) is estimated as

	approximately 5 days (SRC, n.d.).
% Hydrolyzed:	No Data
Method:	Modeled
GLP:	Not Applicable
Reference:	Riddick, J. A. et al. (1986). Organic Solvents: Physical Properties and Methods of Purification, 4th ed., Wiley Interscience, New York, NY (HSDB/146). Lyman, W. J. et al. (1990). Handbook of Chemical Property Estimation Methods, pp. 15-1 to 15-29, American Chemical Society, Washington, DC (HSDB/146). SRC (n.d.). Syracuse Research Corporation (HSDB/146).
Reliability:	Estimated value based on accepted model.

Additional Reference for Stability in Water:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

SRC (n.d.). Syracuse Research Corporation (HSDB/146).

3.3 Transport (Fugacity)

Media: Air, Water, Soil, and Sediments

Distributions:

Compartment	% of total distribution	½ life, hours (advection + reaction)
Air	50.4	1e5
Water	48.3	1.4e3
Soil	0.5	2.8e3
Sediment	0.8	1.3e4

Adsorption Coefficient:	Koc = 271 (calc by model)
Desorption:	Not Applicable
Volatility:	Henry's Law Constant = 2.8 atm-m^3/mole
Method:	Modeled. SMILES: FC(F)(C(F)(F)CL)CL Molecular Wt: 170.92 Vapor Pressure: 2.01e+003 mm Hg Log Kow: 2.82 Henry's Law Constant - HENRYWIN v3.10 module of EPIWIN v3.11 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods

that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available.

Log Koc – Calculated from log Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.11 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.

GLP: Not Applicable

Reference: HENRYWIN –

J. Hine and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-298.

Meylan, W. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293.

Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in:

Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated values based on accepted models.

Additional References for Transport (Fugacity): None Found.

3.4 Biodegradation

Value:		
Linear Model Prediction:	0.076	Does not biodegrade fast
Non-Linear Model	0.0014	Does not biodegrade fast

Prediction: Ultimate Biodegradation Timeframe:	2.05	Months
Primary Biodegradation Timeframe:	3.09	Weeks
MITI Linear Model Prediction:	0.41	Not readily degradable
MITI Non-Linear Model Prediction:	0.00	Not readily degradable
Breakdown Products:	No Data	
Method:	Modeled. BIOWIN, v4.01 module of EPIWIN v3.11 (Syracuse Research Corporation). BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental microorganisms. Estimates are based upon fragment constants that were developed using multiple linear and non-linear regression analyses.	
GLP:	Not Applicable	
Reference:	Boethling, R. S. et al. (1994). Environ. Sci. Technol., 28:459-65. Howard, P. H. et al. (1992). Environ. Toxicol. Chem., 11:593-603. Howard, P. H. et al. (1987). Environ. Toxicol. Chem., 6:1-10. Tunkel, J. et al. (2000). Environ. Toxicol. Chem., 19(10):2478-2485.	
Reliability:	Estimated value based on accepted model.	

Additional References for Biodegradation:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Sylvestre, M. et al. (1997). Crit. Rev. Environ. Sci. Technol., 27:87-111 (HSDB/146).

Chemicals Evaluation and Research Institute Website. April 21, 2004. http://qsar.cerij.or.jp/cgi-bin/DEGACC/index.cgi?E.

3.5 Bioconcentration

Value:	Reported BCF Range of 16-32 and 15-28 at exposure levels of 400 and 40 mg/L, respectively. Based on a six week continuous flow assay using carp (*Cyprinus carpio*). According to a classification scheme (Franke et al., 1994), BCFs of 11-28 suggest the potential for bioconcentration in aquatic organisms is low.
Method:	No Data
GLP:	Not Applicable
Reference:	Chemicals Evaluation and Research Institute Website. April 21, 2004. http://qsar.cerij.or.jp/cgi-bin/DEGACC/index.cgi?E. Franke, C. et al. (1994). Chemosphere, 29:1501-1504.
Reliability:	Not assignable because limited study information was available.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type:	**48-hour NOEC**
Species:	*Leuciscus idus*
Value:	ca. 2 mg/L
Method:	Verification test of unpublished investigation in *Poecilia reticulata.*
GLP:	No
Test Substance:	FC-114, purity not reported
Results:	No additional data.
Reference:	Hoechst AG (1974). Unpublished Data, Abt. Reinhaltung von Wasser und Luft (20.06.1974) (cited in Verschueren, K. (2001). Handbook of Environmental Data on Organic Chemicals, 4th ed., Vol. 1, pp. 813-814, John Wiley & Sons, Inc., New York, NY).
Reliability:	Not assignable because limited study information was available.

Type:	24-hour NOEC
Species:	*Poecilia reticulata*
Value:	ca. 1.5 mg/L
Method:	Comparable to DIN38412, part 15 “The determination of the effect of substances in water on fish.”
GLP:	No

Test Substance:	FC-114, purity not reported
Results:	Lethality was observed starting at 1.8 mg/L. Indication of concentration was inaccurate because of high volatility.
Reference:	Hoechst AG (1973). Unpublished Investigation of the Department of Clean Water and Air.
Reliability:	Medium because a suboptimal study design was used.

Type:	**96-hour LC_{50}**
Species:	Fish
Value:	21.5 mg/L; log Kow = 2.82
Method:	Modeled
GLP:	No Applicable
Test Substance:	FC-114
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Fish:

Data from this additional source were not summarized because insufficient study information was available.

Chemicals Evaluation and Research Institute Website. April 21, 2004. http://qsar.cerij.or.jp/cgi-bin/DEGACC/index.cgi?E.

Data from this additional source were not summarized because the study design was not adequate.

DuPont Co. (1971). Unpublished Data, Haskell Laboratory Report No. 398-71, "Acute Toxicity to the Atlantic Oyster Embryo (*Crassostrea virginica*), the Grass Shrimp (*Palaemonetes vulgaris*), and the killifish (*Fundulus heteroclitus*)" (October) (also cited in TSCA Fiche OTS0520348).

4.2 Acute Toxicity to Invertebrates

Type:	**48-hour or 96-hour TL_{50}**
Species:	Atlantic oyster embryo, *Crassostrea virginica* Grass shrimp, *Palaemonetes vulgaris*
Value:	48-hour TL_{50} (Atlantic oyster embryo, *Crassostrea virginica*) >100% saturation at 25°C

96-hour TL_{50} (Grass shrimp, *Palaemonetes vulgaris*) = 10% saturation at 18°C (95% confidence interval, 4.2-23.7% saturation at 18°C).

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Because of the nature of the Freon® 114 sample (i.e., gas), this material was assayed under static bioassay conditions in a closed system by bubbling the Freon® 114 gas through the diluent water for 3 hours and assuming that the water was saturated. Both the saturated water and dilutions of saturated water were then assayed for toxicity to the test species.

The test procedures used for the oyster embryo assay were those described by Wolke (Wolke, C. E. (1967). Water Quality Criteria, ASTM Spec. Tech. Publ. 416, pp. 112-120, Am. Soc. Testing Mats.) for the measurement of water quality with the Pacific oyster embryo bioassay. Sexually mature Atlantic oysters were collected from Milford harbor and held at the BCF Shellfish Laboratory in filtered seawater for 7 days at a temperature of 22°C. Prior to spawning, the specimens were acclimated to 32°C for 24 hours. Spawn was obtained from both males and females, and eggs were fertilized. Bioassays were conducted in 500 mL beakers containing filtered seawater having a salinity of 26-28 ‰; each unit was inoculated with a sufficient amount of egg suspension to give 75,000-100,000 fertilized eggs per liter. The cultures were covered, incubated for 48 hours at 25°C. Nominal test concentrations were 0, 60, 80, and 100% saturation at 25°C. At the end of this period, samples containing about 200 larvae were taken from each culture and preserved in 4% formalin for microscopic examination. The number of normal and abnormal larvae were counted in each sample.

The shrimp were collected from marsh habitats and acclimated in the laboratory to synthetic seawater for 7 days. The shrimp had a mean length of 18 mm. The shrimp were assayed at 18±0.5°C in synthetic sea water for 96 hours. Nominal concentrations were 0, 5, 10, 25, and 50% saturation at 18°C. Ten specimens were tested at each concentration. The assays were conducted in accordance with the general procedures for dynamic bioassays described in the Fish Bioassay Procedure, Standard Methods (APHA, 13th edition), utilizing a continuous-flow proportional

dilution apparatus. This system provided for the automatic intermittent introduction of the test material and diluent into the test container. Flow rate to each 15-L test chamber was 2.5 L/hour.

The susceptibility of the specimens to the chemical tested was measured in terms of the median tolerance limit (TL_{50}), the concentration of the chemical in water that caused 50% response under the test conditions during the period. The response measured was death, except for the test with oyster larvae, in which normal development to the characteristic "hinged larval form" was utilized as a positive test criteria. The prediction of the TL_{50} value, where possible, was based on conversion of the concentration tested and the corresponding observed percent response to logs and probits, respectively, and the subsequent mathematical calculation of a linear regression equation.

GLP: No

Test Substance: FC-114, purity not reported

Results: Normal development for the Atlantic oyster embryo after 48 hours was 98, 99, 99, and 99% at 0, 60, 80, and 100% saturation at 25°C, respectively. Mortality of grass shrimp was 0, 0, 60, 100, and 100% at 0, 5, 10, 25, and 50% saturation at 18°C, respectively.

Reference: DuPont Co. (1971). Unpublished Data, Haskell Laboratory Report No. 398-71, "Acute Toxicity to the Atlantic Oyster Embryo (*Crassostrea virginica*), the Grass Shrimp (*Palaemonetes vulgaris*), and the killifish (*Fundulus heteroclitus*)" (October) (also cited in TSCA Fiche OTS0520348).

Reliability: Medium because a suboptimal study design was used (nominal test concentrations).

Type: **48-hour LC_{50}**

Species: Daphnid

Value: 24.4 mg/L; log Kow = 2.82

Method: Modeled

GLP: Not Applicable

Test Substance: FC-114

Results: No additional data.

Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center,

	Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates: None Found.

4.3 Acute Toxicity to Aquatic Plants

Type:	**96-hour EC_{50}**
Species:	Green algae
Value:	16.0 mg/L; log Kow = 2.82
Method:	Modeled
GLP:	Not Applicable
Test Substance:	FC-114
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Aquatic Plants: None Found.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type:	**Oral ALD**
Species/Strain:	Rat/Strain not reported
Value:	>2250 mg/kg
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Rats were gavaged with 1000, 1500, or 2250 mg/kg in peanut oil (1 rat/dose group, except for 2250 mg/kg which had 2 rats). Body weights and clinical signs were recorded. Gross autopsy was performed on the 8th or 9th day after dosing.
GLP:	No
Test Substance:	FC-114, purity 6.4% in solution
Results:	No deaths occurred in rats administered 1000, 1500, or 2250 mg/kg of the test substance (largest feasible dose) in peanut oil. The only signs of toxicity were transient diarrhea and slight loss of weight, which were attributed to the use of

	peanut oil as a vehicle. All rats were normal by 24 hours.
Reference:	DuPont Co. (1955). Unpublished Data, Haskell Laboratory, "Acute Oral Toxicity Test" (May 16).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Oral Toxicity: None Found.

Type:	**Inhalation LC_{50}**
Species/Strain:	Mice/Strain not reported
Exposure Time:	30 minutes
Value:	700,000 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. An open circuit device was used. Mice were enclosed in a 36 L rectangular Plexiglas chamber, having a length of 1 m, and were exposed to the test substance at a flow rate of 2-5 L/minute. The gas mixture was produced in a 100 L spirometer, and temporarily placed in storage in 50 L rubber bags to avoid any discontinuity in the gas feed to the chamber. When the percent test substance in the gas mixture exceeded 15%, the oxygen content was brought to 20%. Ten mice per group were exposed to the test substance at 50, 70, or 80% (500,000, 700,000, or 800,000 ppm, respectively) for 30 minutes. A control group was placed in an identical cage and exposed to pure air at the same flow rate.
GLP:	No
Test Substance:	FC-114, purity not reported
Results:	Mortality was 0/10, 5/10, and 8/10 at 500,000, 700,000, and 800,000 ppm, respectively. Mortality occurred within 24 hours.
Reference:	Paulet, G. and S. Desbrousses (1969). Arch. Mal. Prof. Med. Trav. Secur. Soc., 30(9):477-492.
Reliability:	Medium because a suboptimal study design was used and limited study information was available.

Type:	**Human Inhalation Exposures**
Species/Strain:	Humans
Exposure Time:	15, 45, or 60 seconds
Method:	Ten male subjects, aged 20-24 years, were exposed to the test substances or mixtures of propellants, which were

applied from commercial packs, but under somewhat higher pressure than the usual partial pressures of gases in these packs. The gas was applied from a distance of 50 cm and the subjects were asked to breathe normally during the exposure. Each subject was exposed to only 1 propellant or mixture of propellants a day. None of the subjects had a history of any cardiovascular or respiratory disease, or was a regular spray user.

The propellants and their mixtures were sampled with glass syringes at the breathing level of the subject, and the samples were immediately injected into the column of a gas chromatograph.

Maximum expiratory flow-volume (MEFV) curves were recorded and the MEF 50% and MEF 75% were read. The curves were recorded by the flow-volume spirometer. The curve was recorded immediately before the exposure to the propellant (time 0); the subject was then exposed to the propellant for 15 or 45 seconds, and the flow-volume curve was recorded 1, 2, 3, 4, 5, 13, 21, 30, 40, 50, and 60 minutes after the start of the exposure. In the series of 15-second exposures, electrocardiograms were taken before the exposure and after 7, 15, and 55 minutes, with the subject in the supine position. A 3-channel electrocardiograph was used, and recordings were made with 12 standard leads (I, II, III, aVR, aVL, aVF, and V_{1-6}).

In a separate series of experiments, the supine subjects were exposed to the propellant for 60 seconds. Before the exposure period, recordings were taken from all 12 leads in order to exclude any subject with even the slightest electrocardiographic changes. During and after the exposure period continuous 10-minute recordings were taken from the standard leads (I, II, III).

GLP: No

Test Substance: FC-114, purity not reported

Results: The concentration of FC-114 in the air that the subjects inhaled for 15 and 60 seconds was 15.0 $mg/m^3 \times 10^{-4}$. As the concentrations did not change significantly whether exposure was for 15 or 60 seconds, the amounts of propellants inhaled in the 3 series of experiments were considered to be related approximately to the duration of exposure, that is, to be in the ratio 15:45:60.

Each propellant brought about a marked fall in MEF 50% and this was much more pronounced after the exposure to the mixture than to individual freons. All the curves were biphasic with 2 peaks, the 2nd one being more pronounced. Exposure to the mixture of FC-12 and FC-114 caused a maximum fall of 11.1%. The reduction I flow rate induced by exposure to FC-12 or FC-114 was much less pronounced (3.4 and 6.0%, respectively).

The reductions in MEF 50% and MEF 75% following exposure to propellants for 15 seconds were not significantly less than those following 45-second exposure to practically equal concentrations of propellants. With 15-second exposure, as with 45-second exposure, the mixtures had more marked effects than the individual freons. The relative maximum reductions in MEF 75% were slightly greater than those in MEF 50%.

In the electrocardiograms of all the subjects, recorded 7, 15, and 55 minutes respectively after the start of 15-second exposures to propellants, showed a lower heart rate (in some subjects much lower) than those recorded before exposure. Most subjects developed respiratory sinus arrhythmias. In 1 subject, the ECG recorded 15 and 55 minutes after the start of the 15-second exposure to FC-114 showed atrioventricular block (PR interval prolonged to 0.4 s). Only 1 ventricular extra systole was recorded during the whole period of observation of all 10 subjects.

In experiments with 60-second exposure and continuous ECG recording, there were variations in heart rate similar to those observed after 15-second exposure. The subject with AV block 15 and 55 minutes after 15 seconds exposure to FC-114, also suffered intermittent first-degree atrioventricular block within the 1st minute of a 60-second exposure to the same propellant, and this block persisted throughout the recording period.

Reference:

Valic, F. et al. (1977). Br. J. Ind. Med., 34:130-136.

NIOSH (1978). U.S. National Institute for Occupational Safety and Health/Occupational Safety and Health Administration: Occupational Health Guideline for Dichlorotetrafluoroethane (Refrigerant 114). In: Mackison, F. W. et al. (1978). Occupational Health Guidelines for Chemical Hazards, DHHS (NIOSH) Pub. No. 81-123; NTIS Pub. No. PB-83-154-609, U.S. National Technical

Information Service, Springfield, VA (cited in ACGIH (2001). Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents, American Conference of Governmental Industrial Hygienists, Cincinnati, Ohio).

Reliability: Medium because a suboptimal study design was used.

Additional References for Acute Inhalation Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Anon. (1977). Aerosol Report, 10:22-30.

Aviado, D. M. (1971). AD-751426, Cardiopulmonary Effects of Fluorocarbon Compounds, AMRL-TR-71-120-PAPER-4, AD-751426, 10 pp. (cited in Zakhari, S. and D. M. Aviado (1982). Target Organ Toxicology Series Cardiovascular Toxicology, pp. 281-236).

Burn, J. H. (1959). Proc. R. Soc. Med., 52(5):95-98.

Burn, J. H. et al. (1959). Br. J. Anaesth., 31:518-529.

Clark, D. G. (n.d.). Unpublished Data, ICI Ltd., "Inhalation Toxicity."

Clayton, J. W., Jr. (1962). J. Occup. Med., 4(5):262-273.

DuPont Co. (1964). Unpublished Data, Haskell Laboratory Report No. 151-64, "Preliminary Studies on the Inhalation Toxicity of Technical (70.9%) 1,1-Dichloro-2,2,2-trifluoroethane" (December 4) (also cited in TSCA Fiche OTS0520325).

Kuebler, H. (1964). Aerosol Age, 9:44 (cited in Eriksson, L. et al. (1991). Acta Chem. Scand., 45(9):935-944).

Nuckolls, A. H. (1933). Underwriters Lab Report, Misc. Hazards 2375.

Paulet, G. (1969). Aerosol Rep., 8(12):612-622.

Paulet, G. (1969). Labo-Pharma. Probl. Tech., 180:74-78 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlororfluorocarbons, World Health Organization, Geneva).

Paulet, G. (1976). Eur. J. Toxicol., 9(7):385-407.

Quevauviller, A. et al. (1963). Ann. Pharm. Fr., 21(11):727-734.

Scholz, J. (1961). Progress in Biological Aerosol Research, Stuttgart, F.K. Schattaver Verlag (in German) (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlororfluorocarbons, World Health Organization, Geneva).

Scholz, J. (1962). Ber. Aerosol.-Kongr., 4:420-439.

Trochimowicz, H. J. and C. F. Reinhardt (1975). DuPont Innovation, 6(3):12-16.

Yant, W. P. et al. (1932). U. S. Bureau of Mines Report 3185.

Data from these additional sources were not summarized because the test substance was a mixture or otherwise inappropriate.

Gelis, L. G. et al. (1975). Zdravookrhanenie Belorussii, 8:33-34 (NIOSH/00099589).

Shargel, L. and R. Koss (1972). J. Pharm. Sci., 61(9):1445-1449 (CA78:23815u).

Taylor, G. J. et al. (1971). J. Clin. Invest., 50:1546-1550 (HEEP/72/02238).

Type:	**Cardiac Sensitization**
Species/Strain:	Dogs/Beagle
Exposure Time:	5 minutes
Value:	2.5 and 5%
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Twelve beagle dogs per concentration were exposed to the test substance for 5 minutes at 2.5 and 5%. The dogs received a control injection of epinephrine (0.008 mg/kg) intravenously prior to the exposure, and a challenge injection (0.008 mg/kg) after breathing the test material for 5 minutes. The test substance was in the vapor or gaseous phase at normal ambient temperature and pressure and, therefore, was stored in a pressure cylinder. The desired concentration (calculated) was achieved by delivering a metered volume of the vapor from the cylinder and diluting it with a known volume of air. The flowmeter used for monitoring the volume of test material had been previously calibrated by a dry gas test meter.

	A marked response indicated the development, after the challenge injection of epinephrine, of a cardiac arrhythmia that was considered to pose a serious threat to life. Freon® 114 was capable of sensitizing the mammalian heart to epinephrine.
GLP:	No
Test Substance:	FC-114, purity 99.79%
Results:	At 2.5%, 1/12 (8.3%) dogs showed a marked response. At 5%, 7/12 (58.3%) dogs showed a marked response.
Reference:	DuPont Co. (1969). Unpublished Data, Haskell Laboratory Report No. 52-69, "Cardiac Sensitization" (March 20) (also cited in TSCA Fiche OTS0520994, OTS0546572, OTS0555876, and OTS0570941).
Reliability:	Medium because a suboptimal study design was used where animals were not individually titrated with adrenalin.

Additional References for Cardiac Sensitization:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Aviado, D. M. (1971-1972). Unpublished Data, "Cardiopulmonary Toxicity of Propellants for Aerosols. Progress Report No. 1."

Aviado, D. M. (1972). Unpublished Data, "Cardiopulmonary toxicity of Propellants for Aerosols. Progress Report No. 5."

Aviado, D. M. (1975). Toxicology, 3(2):321-332.

Aviado, D. M. and M. A. Belej (1974). Toxicology, 2(1):31-42.

Aviado, D. M. and J. Drimal (1975). J. Clin. Pharmacol., 15 (1 Pt. 2):116-128.

Aviado, D. M. and D. G. Smith (1975). Toxicology, 3(2):241-252.

Belej, M. A. and D. M. Aviado (1975). J. Clin. Pharmacol., 15 (1 Pt. 2):105-115.

Belej, M. A. et al. (1974). Toxicology, 2(4):381-395.

Clark, D. G. and D. J. Tinston (1971). Br. Med. J., III:113-114

Clark, D. G. and D. J. Tinston (1972). Proc. Eur. Soc. Study Drug Toxic., 13:212-217.

Clark, D. G. and D. J. Tinston (1973). Br. J. Pharmacol., 49(2):355-357.

DuPont (1970). Unpublished Data, Haskell Laboratory Report No. 81-70, "Cardiac Sensitization – Fright Exposures" (February 20) (also cited in TSCA Fiche OTS0520983 and OTS0555882).

DuPont Co. (1971). Unpublished Data, Haskell Laboratory Report No. 279-71, "Halogenated Hydrocarbon Induced Cardiac Arrhythmias Associated with Release of Endogenous Epinephrine" (August 31) (also cited in TSCA Fiche OTS0520368 and OTS0546548).

Mullin, L. S. et al. (1972). Am. Ind. Hyg. Assoc. J., 33(6):389-396.

Durakovic, Z. et al. (1976). Jpn. Heart J., 17(6):753-759 (CA86:115732h).

Friedman, S. A. et al. (1973). Toxicology, 1(4):345-355.

Reinhardt, C. F. et al. (1971). Arch. Environ. Health, 22:265-279.

Simaan, J. A. and D. M. Aviado (1975). Toxicology, 5(2):127-138.

Simaan, J. A. and D. M. Aviado (1975). Toxicology, 5(2):139-146.

Taylor, G. J., IV and W. S. Harris (1970). J. Am. Med. Assoc., 214(1):81-85.

Trochimowicz, H. J. et al. (1974). Am. Ind. Hyg. Assoc. J., 35(10):632-639.

Data from this additional source were not summarized because the study design was not adequate.

Nuckolls, A. H. (1933). Underwriters Laboratory Report, Misc. Hazards 2375.

Data from this additional source were not summarized because the test substance was a mixture or otherwise inappropriate.

DuPont Co. (1972). Unpublished Data, Haskell Laboratory Report No. 526-72, "Cardiac Sensitization Potential of Propellant Mixtures" (December 19) (also cited in TSCA Fiche OTS0590003 and OTS0514889).

Type: **Dermal Toxicity:** No Data.

Type: **Dermal Irritation**
Species/Strain: Guinea pig/Hartley
Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

	Sixteen guinea pigs, weighing 300-500 grams, were used in the study. The hair on the back was first clipped and then epilated with pine-tar adhesive tape. Forty-eight hours after epilation, the test substance was spray applied to the test site for 10, 20, and 45 seconds. All guinea pigs were evaluated daily for 4 weeks. At intervals following application, 4.0 mm skin biopsies were removed from the test sites under local anesthesia. Biopsy specimens were frozen in liquid nitrogen, and were sectioned. The slides were stained with hematoxylin and eosin, and were examined to determine the degree and location of the inflammation resulting from the timed freezes.
GLP:	No
Test Substance:	FC-114, purity not reported
Results:	The test sites showed mild induration and erythema 24 and 48 hours after freezing for 10 seconds. Slightly more intense erythema was observed at 48 hours following freezing for 20 seconds. Sites with 45-second freezes with the test substance produced no crusting. The erythema and induration gradually diminished, and the skin was clinically normal in all cases by 14 days post-treatment. Biopsies of sites taken 48 hours following 10-, 20-, and 45-second freezes showed no abnormality.
Reference:	Hanke, C. W. and J. J. O'Brian (1987). J. Dermatol. Surg. Oncol., 13(6):664-669.
Reliability:	High because a scientifically defensible or guideline method was used.
Type:	Dermal Irritation
Species/Strain:	Human volunteers
Method:	The test substance, as a skin refrigerant to quickly obtain temporary anesthesia by freezing, for minor surgery or surgical planning was tested. Four human volunteers were sprayed, from a spray tip 3 inches from the dorsum of the hand, on their hands for less than 5 seconds.
GLP:	No
Test Substance:	FC-114, purity not reported
Results:	All 4 experienced a burning sensation followed by temporary anesthesia of the skin. Once the frost effect disappeared, the sprayed areas became progressively erythematous and painful. Twenty-four to 48 hours later these areas showed signs typical of superficial frostbite. Over the next 7 days, they underwent brawny discoloration and finally desquamation, leaving hypopigmented patches.
Reference:	Collure, D. W. D. et al. (1976). J. Am. Coll. Emergency Phys. (USA), 5(10):814.

Reliability:	Medium because a suboptimal study design was used and limited study information was available.

Additional References for Dermal Irritation:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Clayton, J. W., Jr. (1966). Handb. Exp. Pharmakol., 20:459-500 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva).

DuPont Co. (n.d.). Unpublished Data, Haskell Laboratory, "Skin Sensitization."

DuPont Co. (1967). Unpublished Data, Haskell Laboratory Report No. 110-67, "Skin Tests With Facial Cleanser Containing Freon® 114" (June 30).

Type:	**Dermal Sensitization:** No Data.

Type:	**Eye Irritation**
Species/Strain:	Rabbit/Strain not reported
Method:	No specific test guideline was reported. A 50% (wt/wt) solution of Freon® 114 in mineral oil was sprayed at 1 rabbit's eye from a distance of 6 inches.
GLP:	No
Test Substance:	Freon® 114, purity not reported
Results:	Mild conjunctival irritation was noted during the initial 4 hours. No corneal or iritic effects were seen. There was no permanent corneal damage (grossly or microscopically).
Reference:	DuPont Co. (1955). Unpublished Data, "Eye Irritation Test" (June 20).
Reliability:	Low because an inappropriate method or study design was used. Only a single animal was used and there was no indication of how much test material actually made it into the eye.

Additional Reference for Eye Irritation:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Quevauviller, A. et al. (1964). Therapie, 19:247-263.

5.2 Repeated Dose Toxicity

Type:	**2-Week Inhalation Study**
Species/Strain:	Mice/Strain not reported Rats/Strain not reported
Sex/Number:	Sex not reported/10 per concentration
Exposure Period:	2 weeks
Frequency of Treatment:	2.5 hours/day, 5 days/week
Exposure Levels:	0, 100,000 or 200,000 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. An open circuit device was used. The animals were enclosed in a 36 L rectangular Plexiglas chamber, having a length of 1 m, and were exposed to the test substance at a flow rate of 2-5 L/minute. The gas mixture was produced in a 100 L spirometer, and temporarily placed in storage in 50 L rubber bags to avoid any discontinuity in the gas feed to the chamber. When the percent test substance in the gas mixture exceeded 15%, the oxygen content was brought to 20%. Ten mice and rats per group were exposed to the test substance at 10 or 20% (100,000 or 200,000 ppm, respectively) for 2.5 hours. Observation of the animals involved their weight and blood analysis (cell counts and types of white cells). Half of the animals were sacrificed after the last exposure, and their lungs were removed, fixed, and stained with hematoxylin, hemaluncosin, and Masson trichromium for histopathological analysis. In addition, the collagen and reticulin were revealed by silver impregnation and the mucus, as well as the polysaccharides were objectified by the Mayer Muci-Carmin and reaction to the Mac-Manus P.A.S.
GLP:	No
Test Substance:	FC-114, purity not reported
Results:	No mortality was observed in the study. Mice lost a small amount of weight at 200,000 ppm, but only in a transitory manner. No other body weight changes were noted in mice or rats. No test substance related effects in cell counts and types of cells were observed at 100,000 ppm. At

200,000 ppm, the number of red cells was increased slightly, and the types of cells varied slightly, showing a slight decrease in neutrophils with a corresponding increase in lymphocytes. Some leukocytes appeared as if they were degenerating.

Except for some damage due to the artifacts of preparation, the alveolar walls showed neither alterations in the collagen framework, nor anomalies in the alveolar cells. In some cases, cells were seen in the alveolar aperture, but these were also seen in the control animals. It was possible to observe a more marked congestion in animals treated with 200,000 ppm than in control rats or those treated with 10,000 and 100,000 ppm, but the erythrocyte influx was limited to the walls. No intra-alveolar hemorrhagic suffusions were observed.

In the alveoli, the P.A.S. and muci-carmin colorations, in the case of the cross-sections for animals at 200,000 ppm, showed exudate areas that were more abundant than those of the controls. However, this was an amorphous material, which is slightly colorable and which comprises no leukocyte clusters.

No exudates were observed in the bronchial apertures. The bronchial epithelium cells retained their muco-secreting character.

In the stroma, it was possible to note congestion of the blood vessels and some lymphocytic infiltrates in the fibrillar framework of the alveoli and the bronchial walls. These were also found in the control animals.

Only the rats exposed to 200,000 ppm showed lesions. These were congestive and exudative phenomena. No structural alterations were observed at the levels of the alveolar and bronchial walls. These changes were reversible and disappeared 15 days after stopping the exposure.

Reference: Paulet, G. and S. Desbrousses (1969). Arch. Mal. Prof. Med. Trav. Secur. Soc., 30(9):477-492.

Reliability: Medium because a suboptimal study design was used and limited study information was available.

Type: **2-Month Inhalation Study**

Species/Strain: Rats/Strain not reported
Mice/Strain not reported

Sex/Number:	Sex not reported/20 adult and 10 young rats and 20 adult mice
Exposure Period:	2 months
Frequency of Treatment:	2.5 hours/day, 5 days/week
Exposure Levels:	0, 10,000 ppm
Method:	Twenty adult rats, 10 young rats, and 20 adult mice were exposed for 2.5 hours/day, 5 days/week in a dynamic chamber at 1% (10,000 ppm) in air. The weight change of all the animals was followed. Blood tests were performed on the adult rats. The young rats were sacrificed to examine the pulmonary parenchyma (half after the 1st month and half at the end of the 2nd month). Lungs were removed, fixed, and stained with hematoxylin, hemaluncosin, and Masson trichromium for histopathological analysis.
GLP:	No
Test Substance:	FC-114, purity not reported
Results:	No mortality occurred during the study. Body weight change was normal in all rats and mice. During the 1st month of exposure, there was a slight loss of red blood cells, and a slight increase in white blood cells. These changes became smaller as the exposure continued, and were practically non-existent at the end of the 2nd month, leading the authors to speculate that this was an adaptation phenomenon. No significant change was observed in blood composition. The appearance of a few very polylobal polynuclear neutrophils had no particular pathological significance. The lung examination did not reveal any lesions of the lungs or bronchi.
Reference:	Paulet, G. and S. Desbrousses (1969). Arch. Mal. Prof. Med. Trav. Secur. Soc., 30(9):477-492.
Reliability:	Medium because a suboptimal study design was used and limited study information was available.

Type:	**90-Day Gavage Study**
Species/Strain:	Rats/ChR-CD Dogs/Strain not reported
Sex/Number:	Male and female rats/20 per sex per dose level Male and female dogs/12 per sex per dose level

Exposure Period:	90 days
Frequency of Treatment:	Rats: 7 times/week for the first 4 weeks; 5 times/week for the remainder of the study Dogs: 1 time/day, 7 days/week
Exposure Levels:	Rats: 0, 0.5, 3.0% Dogs: 0, 25%
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The test material was supplied at 0.5, 3.0, and 25% solutions in stoppered glass containers of refrigerated corn oil. At the beginning of each week, the amount of each solution required for the week was received and kept under refrigeration; each solution's weekly supply was divided into 5 or 7 separate containers, 1 container of each solution per day. The percentage of test sample in each solution was that percentage present at refrigerated temperature (6°C).

The 0.5 and 3.0% solutions were used in the study with the rats, and were kept in an iced-water bath during the intubation procedure. The 25% solution was used in the study with dogs; the required amount of refrigerated corn oil solution was measured into gelatin capsules, capped, and then stored at freezer temperature (-13°C) until required.

Control corn oil was kept at the same temperature as the test solutions in each study, and was administered in the same way.

Rats:

Male and female rats were housed in pairs, sexes separate, in suspended stainless steel wire cages. They were given water and fed ground rodent chow containing 1% added corn oil *ad libitum* during a pretest period of 10 days. At the end of the pretest period, they were divided into 3 groups of 20 male and 20 female rats each. Six male and 6 female rats were selected at random from each of the groups for a hematological evaluation that included total red and white blood cell counts, hemoglobin concentration, and hematocrit.

The rats were intubated, with corn oil or the test substance solutions in corn oil, once daily, 7 time per week for the first 4 weeks, and then 5 times per week for the remainder of the study.

Both control and test rats received food plus 1% corn oil on an *ad libitum* basis. Diets were prepared fresh each week and stored in the refrigerator until used.

Because of the potential hazard inherent in the procedure of repeated intubations, an extra 15 male and 15 female rats remaining from the initial supply were maintained on control diet, and served as replacements for animals that succumbed to accidental dosing into the lungs during the first 3 weeks; rats that died after this period as a result of misdosing were not replaced.

All rats were weighed once a week during the entire study. Food consumption data were obtained on a group and sex basis at each weighing period. From body weight and food consumption data, food efficiency was calculated. The average daily dose of the test substance received each week was calculated from average body weight data and the average amount of test substance received by the test animals as a result of the intubation procedure.

During the test, the rats were examined regularly for any abnormal behavior or any other clinical manifestations of toxicity.

Hematological, urine, and biochemical (blood) analyses were conducted on 10 male and 10 female rats from the 0 and 3.0% groups after approximately 30, 60, and 90 days on test. Hematological evaluations included a differential leukocyte count in addition to those measurements mentioned above. Urine analysis consisted of a measure of the 24-hour urine volume concentration in milliosmols/L, fluoride, creatinine, and pH, a test for sugar, blood, protein, and urobilinogen; and an observation of the color and appearance. Specimens with a negative test for blood were combined to form 2 pools of urine for each group, and the sediment from these pools examined microscopically. All specimens with a positive test for blood were examined separately. Except for the creatinine and fluoride analyses, the urine analyses were conducted on specimens collected from each rat subjected to the hematological examination. Separate 24-hour urine collections were used to measure creatinine and fluoride excretion after 1, 4, 8, 9, 10, 11, 12, and 13 weeks. Alkaline phosphatase and glutamic-pyruvic transaminase activities and bilirubin concentrations were

measured in the blood taken from the tails of 10 rats in the 0 and 3% groups at monthly intervals. At the end of the study, when 10 rats were sacrificed, the right tibia was removed from each of the male and female control rats and from the rats administered 0.5 and 3.0%, for fluoride analysis.

After 91-94 days on test, 10 male and 10 female rats from each group were sacrificed and necropsied. The following organs from the rats in all groups were weighed: adrenal, brain, heart, kidney, liver, lungs, pituitary, spleen, stomach, testis, and thymus. Approximately 34 tissues or organs were preserved in Bouin's solution and stained with hemotoxylin-eosin, and were subjected to a histopathologic evaluation.

Dogs:

During a pretest period of 1 month, 12 male and 12 female dogs, approximately 1 year old, were given food and water *ad libitum* between 3:00 pm and 7:00 am. Dogs were examined daily for any abnormal behavior and any clinical manifestations of toxicity. During this period, specimens of blood and urine were collected from each dog at least twice for clinical laboratory measurements. Hematology tests included erythrocyte count, hemoglobin concentration, hematocrit, total and differential leukocyte count. Biochemistry parameters included glucose, urea nitrogen, cholesterol, alkaline phosphatase, glutamic-pyruvic transaminase, total protein, albumin-globulin ratio, creatinine, and bilirubin. Urinalysis parameters included observance of color, appearance, and pH; a measure of the 24-hour urine volume, creatinine, fluoride, and osmolality; a test for sugar, blood, protein, urobilinogen, acetone, and bilirubin; and a microscopic examination of the sediment.

Four male and 4 female dogs were allocated to each of 3 groups, receiving 4.5 mL of corn oil, 2.0 mL of 25% test substance in corn oil (500 mg), or 9.0 mL of 25% test substance in corn oil (2500 mg). The corn oil and corn oil solutions of the test substance were administered to the dogs in the form of gelatin capsules once a day, 7 days a week, for the entire study; the lower test group and control group received 1 capsule, whereas the higher test group received 2 capsules. These control and test capsules, after being filled, had been kept at freezer temperature (-13°C) until they were administered to the dogs. They were kept at this low temperature to minimize the loss of the test substance.

Food consumption and body weight data were obtained each week; from these, calculations were made to determine the approximate daily dose each week of test substance in mg/kg of body weight. Dogs were examined daily for any clinical manifestations of toxicity.

After 1, 2, and 3 months on test, clinical laboratory tests, such as were done during the 1-month pretest period, were conducted on all dogs.

After 90-94 days of feeding, all dogs were sacrificed and submitted to gross and histopathologic evaluation. Organ weights were recorded for the brain, heart, lungs, liver, spleen, pancreas, kidney, testis, prostate, bladder, stomach, thymus, adrenal, pituitary, and thyroid. Approximately 35 organs or tissues were preserved in Bouin's solution and stained with hematoxylin-eosin for future histopathologic evaluation.

GLP: No

Test Substance: FC-114, purity 99.79%

Results: *Rats:*

Two control rats were found dead after 4 and 9 doses, respectively, and were replaced. Gross pathologic evaluation at necropsy indicated that death was probably due to accidental introduction of corn oil into the lungs. Thus, no deaths occurred that could be attributed to the administration of the test substance.

No test substance-related effects in body weight gain, food consumption, food efficiency, clinical signs of toxicity, hematology, urinalysis, biochemistry, or pathology parameters were observed.

The average fluoride excreted by male and female administered the test substance was somewhat higher then controls during the first 11 week of the test, but not at the end of the test. The variation within both treated and control groups was very large; consequently, the small differences in average values are probably not significant. This conclusion was similarly reached when an extensive statistical analysis was conducted on the data.

No increase in bone fluoride was found in the male rats administered the test substance. The slight increase in the

	average bone fluoride with increasing doses of test substance found in the female rats was not considered significant.
	Dogs:
	No test substance-related effects in mortality, body weight, food consumption, clinical signs of toxicity, hematology, urinalysis, biochemistry, or pathology parameters were observed.
Reference:	DuPont Co. (1972). Unpublished Data, Haskell Laboratory Report No. 5-72, "Ninety-Day Feeding Study in Rats and Dogs with Freon® 114" (January 5).
Reliability:	Medium because a suboptimal study design was used.

Additional References for Repeated Dose Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Oral

Clayton, J. W., Jr. (1967). Fluorine Chem. Rev., 1(2):197-252 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva).

DuPont Co. (1955). Unpublished Data, "Subacute Oral Toxicity Test" (August).

DuPont Co. (1969). Unpublished Data, Haskell Laboratory Report No. 381-69, "The Effect of Freon® 114 on Growth Rate, Urinary Fluoride, and Bone Fluoride in Rats" (December 9).

Quevauviller, A. (1965). Prod. Probl. Pharm., 20(1):14-29.

Inhalation

Anon. (1977). Aerosol Report, 10:22-30.

Desoille, H. et al. (1973). Arch. Mal. Prof. Med. Trav. Secur. Soc., 34(3):117-125.

Gage, J. C. (1956). Unpublished Data, ICI Ltd. Report No. TR/61, "Toxicology Report" (December 10).

Leuschner, F. et al. (1983). Arzneim.-Forsch., 33(10):1475-1476 (CA99:207595n).

Paulet, G. (1976). Eur. J. Toxicol., Suppl., 9(7):385-407.

Vieillefosse, R. et al. (1962). Ann. Pharm. Fr., 20(6):545-555 (CA58:2769c).

Watanabe, T. and D. M. Aviado (1975). Pharmacologist, 17(2):192.

Yant, W. P. (1933). Am. J. Public Health, 23:930-934.

Data from these additional sources were not summarized because the study design was not adequate.

DuPont Co. (n.d.). Unpublished Data, "Skin Sensitization."

Quevauviller, A. et al. (1963). Ann. Pharm. Fr., 21(11):727-734.

Quevauviller, A. et al. (1964). Therapie, 19:247-263.

Scholz, J. (1962). Ber. Aerosol.-Kongr., 4:420-429.

Data from these additional sources were not summarized because the test substance was a mixture or otherwise inappropriate.

Desoille, H. et al. (1975). Arch. Mal. Prof. Med. Trav. Secur. Soc., 36(12):697-706.

Smith, J. K. and M. T. Case (1973). Toxicol. Appl. Pharmacol., 26:438-443.

5.3 Developmental Toxicity: No Data.

5.4 Reproductive Toxicity

Species/Strain:	Rats/ChR-CD Dogs/Strain not reported
Sex/Number:	Male and female rats/20 per sex per dose level Male and female dogs/12 per sex per dose level
Route of Administration:	Oral gavage
Exposure Period:	90 days
Frequency of Treatment:	Rats: 7 times/week for the first 4 weeks; 5 times/week for the remainder of the study Dogs: 1 time/day, 7 days/week
Exposure Levels:	Rats: 0, 0.5, 3.0% Dogs: 0, 25%
Method:	A 90-day oral gavage study was conducted in male and female rats and dogs (see Section 5.2 for details on the study

	design). Complete necropsies were performed at study termination. In rats, testes were weighed, and ovary, uterus, fallopian tube, testes, and prostate were examined microscopically. In dogs, testis and prostate were weighed, and testis, prostate, epididymis, ovary, uterus, and mammary gland were examined microscopically.
GLP:	No
Test Substance:	FC-114, purity 99.79%
Results:	No test substance-related effects on reproductive organs were observed in rats or dogs.
Reference:	DuPont Co. (1972). Unpublished Data, Haskell Laboratory Report No. 5-72, "Ninety-Day Feeding Study in Rats and Dogs with Freon® 114" (January 5).
Reliability:	Medium because a suboptimal study design was used.

Additional References for Reproductive Toxicity: None Found.

5.5 Genetic Toxicity

Type:	***In vitro* Bacterial Reverse Mutation Assay**
Tester Strain:	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537
Exogenous Metabolic Activation:	With and without Aroclor 1254-induced rat liver S9
Exposure Concentrations:	Trial I: 0, 10, 10, 32, and 48% Trial II: 0, 6, 12, 21, and 32%
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. In the absence of an activation system, approximately 10^8 bacteria were added to top agar, which was comprised of agar, NaCl, L-histidine, and biotin. Prior to the exposure to the test gas, the components were mixed and poured onto the surface of a plate containing Davis minimal agar. To treat in the presence of an activation system, S9 mix was added to the bacteria-top agar mixture. The S9 mix contained S9, $MgCl_2$, KCl, glucose-6-phosphate, NADP, and sodium phosphate (pH 7.4). The components were mixed and immediately poured over the minimal agar plate. The minimal plates with the bacteria overlay (with or without an activation system) were exposed to the test gas in 9-L glass chambers. These specially designed chambers were fitted with Teflon® stopcocks and Viton® o-rings gaskets. Ten petri plates, without lids, were held in the

chamber on stainless steel racks. The test gas was mixed with filtered air from a compressed air line and introduced into the chambers through a flow-meter system. After the gas-air mixture flowed through the exposure chamber for 5 volume changes, the chambers were closed and placed in a 37°C incubator for 48 hours. At the end of the exposure period, the chambers were flushed with air for 5 volume changes, the plates removed, and revertent frequencies were determined.

The concentrations of the test gas in the chamber were determined between 2-3 hours after the treatment was begun, and just before the end of treatment. Samples were drawn from the chambers through a septum. The concentrations in the chambers, as measured with a gas chromatograph, were compared to similar measurements taken from "standard" chambers of an exact volume and containing no plates. The gas was introduced into the "standard" chambers by the same method employed with the test chambers.

Positive and negative controls were included in each assay.

The cytotoxicity of the test sample in the presence and absence of an activation system, as measured in strain TA1535, was the basis for selecting concentrations to be used in the mutagenesis experiment. The protocol used to determine the cytotoxicity was identical to the mutagenesis protocol, except that 10^3 rather than 10^8 bacteria were used per plate, and a non-limiting concentration of histidine was present. Concentrations of the test sample that were nontoxic and, if possible, slightly toxic were selected for the mutagenesis assay.

The procedure as outlined above was also followed for the positive control gas (10% ethylene chloride).

Data from replicate plates within a single experiment were averaged. The average of these values from different experiments was determined. The highest average number of revertants that were obtained was expressed as a multiple of the control value for the sensitive strain(s).

The chemical was classified as nonmutagenic if the reversion frequency was less than 2 times the spontaneous frequency, and if less than 0.02 revertants/?mole were observed.

GLP:	No
Test Substance:	FC-114, purity 99.89%
Results:	Negative
Remarks:	The test substance was not mutagenic in the presence or absence of an activation system. A thinning of the background lawn, indicating toxicity, was observed without activation at 48% in strain TA1537 in Trial I. Smaller colonies, some pin points, indicating growth inhibition were observed with activation at 32% in strains TA1537 and TA98 in Trial II.
Reference:	DuPont Co. (1978). Unpublished Data, Haskell Laboratory Report No. 19-78, "Mutagenic Activity of Ethane, 1,2-Dichloro-tetrafluoro- in the *Salmonella*/Microsome Assay" (January 20).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for *In vitro* Bacterial Reverse Mutation Assay:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Araki, A. et al. (1994). Mutat. Res., 307(1):335-344.

Longstaff, E. et al. (1984). Toxicol. Appl. Pharmacol., 72(1):15-31.

Type: ***In vitro* Clastogenicity:** No Data.

Type: ***In vivo* Genetic Toxicity:** No Data.

18 March 2005

Appendix D

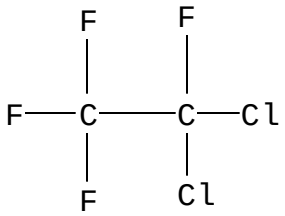
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 374-07-2

Chemical Name: Ethane, 1,1-dichloro-1,2,2,2-tetrafluoro

Structural Formula:



Other Names:
1,1,1,2-Tetrafluoro-2,2-dichloroethane
1,1,1,2-Tetrafluorodichloroethane
1,1-Dichlorotetrafluoroethane
2,2,-Dichloro-1,1,1,2-tetrafluoroethane
CFC 114a
Dichlorotetrafluoroethane
Ethane, 1,1,-dichlorotetrafluoro-
F 114a
Freon® 114a
Frigen 114A
R 114a

Exposure Limits: DuPont Acceptable Exposure Limit (AEL): 1000 ppm, 8- and 12-hour TWA

2.0 Physical/Chemical Properties

2.1 Melting Point

Value:	-56.6°C
Decomposition:	No Data
Sublimation:	No Data
Pressure:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-154, CRC Press, Inc., Boca Raton, FL.

Reliability: Not assignable because limited study information was available.

Additional References for Melting Point:

Grasselli, J. G. and W. M. Ritchey (1975). Chemical Rubber Company Atlas of Spectral Data and Physical Constants for Organic Compounds, 2nd ed., CRC Press, Inc. Cleveland, Ohio (ISHOW-0008104).

Henne, A. L. and R. P. Ruh (1948). J. Am. Chem. Soc., 70:1025.

2.2 Boiling Point

Value:	4°C
Decomposition:	No Data
Pressure:	760 mm Hg
Method:	No Data
GLP:	Unknown
Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-154, CRC Press, Inc., Boca Raton, FL.
Reliability:	Not assignable because limited study information was available.

Additional References for Boiling Point:

Grasselli, J. G. and W. M. Ritchey (1975). Chemical Rubber Company Atlas of Spectral Data and Physical Constants for Organic Compounds, 2nd ed., CRC Press, Inc. Cleveland, Ohio (ISHOW-0008105).

DuPont Co. (1999). Material Safety Data Sheet DU001752 (February 10).

Henne, A. L. and R. P. Ruh (1948). J. Am. Chem. Soc., 70:1025.

Schirmer, G. (1967). Aerosol Rep., 6(5):171-177.

2.3 Density

Value:	1.455
Temperature:	25°C/4°C
Method:	No Data
GLP:	Unknown
Results:	No additional data.
Reference:	Lide, D. R. (ed.) (1998-1999). CRC Handbook of Chemistry and Physics, 79th ed., p. 3-154, CRC Press, Inc., Boca Raton, FL.

Reliability: Not assignable because limited study information was available.

Additional References for Density:

Beacher, J. H. (1955). Chem. Specialities Mfrs. Assoc. Proc., (12):50-56.

DuPont Co. (1999). Material Safety Data Sheet DU001752 (February 10).

Kirk-Othmer Encyclopedia of Chemical Technology (1991-present). 4th ed., Vol. 1, John Wiley and Sons, New York, NY (HSDB/5564).

2.4 Vapor Pressure

Value:	1635 mm Hg
Temperature:	25°C
Decomposition:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Daubert, T. E. and R. P. Danner (1989). Physical and Thermodynamic Properties of Pure Chemicals Data Compilation, Taylor and Francis, Washington, DC.
Reliability:	Not assignable because limited study information was available.

Additional References for Vapor Pressure:

Beacher, J. H. (1955). Chem. Specialities Mfrs. Assoc. Proc., (12):50-56.

DuPont Co. (1999). Material Safety Data Sheet DU001752 (February 10).

Schirmer, G. (1967). Aerosol Rep., 6(5):171-177.

2.5 Partition Coefficient (log Kow)

Value:	2.78
Temperature:	No Data
Method:	Modeled. KOWWIN, v1.67, module of EPIWIN v3.11 (Syracuse Research Corporation). KOWWIN uses "fragment constant" methodologies to predict log P. In a "fragment constant" method, a structure is divided into fragments (atom or larger functional groups) and coefficient values of each fragment or group are summed together to yield the log P estimate.
GLP:	Not Applicable

Reference:	Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92.
Reliability:	Estimated value based on accepted model.

Additional References for Partition Coefficient (log Kow):

Leo, A. J. (1982). Pomona College Medicinal Chemistry Project, Seaver Chemistry Laboratory, Claremont, CA (ISHOW-0008107).

Advanced Chemistry Development (ACD) Software Solaris V4.67 (©1994-2004 ACD)

2.6 Water Solubility

Value:	137 mg/L
Temperature:	25°C
pH/pKa:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Hine, J. and P. K. Mookerjee (1975). J. Org. Chem., 40:292-298 (HSDB/5564).
Reliability:	Not assignable because limited study information was available.

Additional References for Water Solubility:

Grasselli, J. G. and W. M. Ritchey (1975). Chemical Rubber Company Atlas of Spectral Data and Physical Constants for Organic Compounds, 2nd ed., CRC Press, Inc. Cleveland, Ohio (ISHOW-0008106).

DuPont Co. (1999). Material Safety Data Sheet DU001752 (February 10).

2.7 Flash Point: No Data.

2.8 Flammability

Results:	Non-flammable
Method:	No Data
GLP:	Unknown
Reference:	Schirmer, G. (1967). Aerosol Rep., 6(5):171-177.
Reliability:	Not assignable because limited study information was available.

Additional References for Flammability:

DuPont Co. (1999). Material Safety Data Sheet DU001752 (February 10).

Association of American Railroads (1994). Emergency Handling of Hazardous Materials in Surface Transportation, p. 359, Association of American Railroads, Bureau of Explosives, Washington, DC (HSDB/5564).

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	No mechanism for direct photoalteration of this chemical in the lower atmosphere due to irradiation at ≥ 290 nm.
Indirect Photolysis:	According to a model of gas/particle partitioning of semi-volatile organic compounds in the atmosphere (Bidleman, 1988), FC-114a, which has a vapor pressure of 1635 mm Hg at 25°C (Daubert and Danner, 1995), is expected to exist solely as a gas if released to the ambient atmosphere. FC-114a is not expected to degrade in the troposphere and it will disperse and slowly diffuse to the stratosphere, a process that may take decades (Dilling, 1982). In the stratosphere, FC-114a will slowly photolyze, releasing chlorine atoms, which in turn are responsible for removing ozone (Chou et al., 1978). While some FC-114a may be lost from the atmosphere by being scavenged by rain, any loss will be returned to the atmosphere by volatilization (SRC, n.d.).
Breakdown Products:	No Data
Method:	Inspection of chemical structure.
GLP:	Not Applicable
Reference:	*Direct Photolysis:* Doucet, J. et al. (1973). J. Chem. Phys., 58:3078-3716 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva). Doucet, J. et al. (1974). J. Chem. Phys., 62(2):355-359 (cited in WHO (1990). Environmental Health Criteria 113. Fully Halogenated Chlorofluorocarbons, World Health Organization, Geneva). *Indirect Photolysis:* Bidleman, T. F. (1988). Environ. Sci. Technol., 22:361-367 (HSDB/5564).

	Chou, C. C. et al. (1978). J. Phys. Chem., 82:1-7 (HSDB/5564).
	Daubert, T. E. and R. P. Danner (1995). Physical and Thermodynamic Properties of Pure Chemicals Data Compilation, Taylor and Francis, Washington, DC (HSDB/5564).
	Dilling, W. L. (1982). In: Environmental Risk Analysis for Chemicals, pp. 154-197, Conway, R. A. (ed.), Van Nostrand Reinhold, NY, NY (HSDB/5564).
	SRC (n.d.). Syracuse Research Corporation (HSDB/5564).
Reliability:	Estimate based on known qualitative structure-activity relationships.

Additional References for Photodegradation: None Found.

3.2 Stability in Water

Concentration:	No Data
Half-life:	The Henry's Law constant for FC-114a is estimated as 2.68 atm-m^3/mole, derived from its vapor pressure of 1635 mm Hg and water solubility of 137 mg/L. This Henry's Law constant indicates that FC-114a is expected to volatilize rapidly from water surfaces (Lyman et al., 1990). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) (Lyman et al., 1990) is estimated as 1.3 hours (SRC, n.d.). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) (Lyman et al., 1990) is estimated as 5 days (SRC, n.d.).
% Hydrolyzed:	No Data
Method:	Estimated
GLP:	Not Applicable
Reference:	Lyman, W. J. et al. (1990). Handbook of Chemical Property Estimation Methods, pp. 15-1 to 15-29, American Chemical Society, Washington, DC (HSDB/5564).
	SRC (n.d.). Syracuse Research Corporation (HSDB/5564).
Reliability:	Estimated value based on accepted model.

Additional References for Stability in Water: None Found.

3.3 Transport (Fugacity)

Media: Air, Water, Soil, and Sediments

Distributions:

Compartment	% of total distribution	½ life, hours (advection + reaction)
Air	50.5	1e5
Water	48.3	1.44e3
Soil	0.5	2.88e3
Sediment	0.7	1.3e4

Adsorption Coefficient: Koc = 247

Desorption: Not Applicable

Volatility: Henry's Law Constant = 2.65 atm-m^3/mole (calculated from experimental vapor pressure of 1635 mm Hg and experimental water solubility of 137 mg/L)

Method: Modeled.

SMILES: FC(F)(F)C(F)(CL)CL
Molecular Wt: 170.92
Vapor Pressure: 1.64e+003 mm Hg
Log Kow: 2.78 (KOWWIN program)

Henry's Law Constant - HENRYWIN v3.10 module of EPIWIN v3.11 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available.

Koc – Calculated from log Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.11 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.

GLP: Not Applicable

Reference: HENRYWIN –

J. Hine and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-298.

Meylan, W. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293.

Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in:

Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated values based on accepted models.

Additional References for Transport (Fugacity): None Found.

3.4 Biodegradation

Value:		
Linear Model Prediction:	-0.261	Does not biodegrade fast
Non-Linear Model Prediction:	0.00	Does not biodegrade fast
Ultimate Biodegradation Timeframe:	1.75	Months
Primary Biodegradation Timeframe:	2.97	Weeks
MITI Linear Model Prediction:	0.34	Not readily biodegradable
MITI Non-Linear Model Prediction:	0.00	Not readily biodegradable
Breakdown Products:	No Data	

Method: Modeled. BIOWIN, v4.01 module of EPIWIN v3.11 (Syracuse Research Corporation). BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental microorganisms. Estimates are based upon fragment constants that were developed using multiple linear and non-linear regression analyses.

GLP: Not Applicable

Reference: Boethling, R. S. et al. (1994). Environ. Sci. Technol., 28:459-65.

Howard, P. H. et al. (1992). Environ. Toxicol. Chem., 11:593-603.

Howard, P. H. et al. (1987). Environ. Toxicol. Chem., 6:1-10.

Tunkel, J. et al. (2000). Environ. Toxicol. Chem., 19(10):2478-2485.

Reliability: Estimated value based on accepted model.

Additional References for Biodegradation: None Fond.

3.5 Bioconcentration

Value: BCF = 30; The potential for bioconcentration is low (Franke et al., 1994).

Method: Estimated, using an estimated log Kow of 2.78 (Howard and Meylan, 1997) and a regression-derived equation (Meylan et al., 1999).

GLP: Not Applicable

Reference: Howard, P. H. and W. M. Meylan (1997). Handbook of Physical Properties of Organic Chemicals, p. 321, Lewis, Boca Raton, FL (HSDB/5564).

Meylan, W. M. et al. (1999). Environ. Toxicol. Chem., 18:664-672 (HSDB/5564).

Franke, C. et al. (1994). Chemosphere, 29:1501-1514 (HSDB/5564).

Reliability: Estimated value based on accepted model.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type: **96-hour LC_{50}**

Species: *Oncorhynchus mykiss*, fingerling rainbow trout

Value: 15 mg/L (95% confidence limits, 14-17 mg/L)

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

A dilution water control and 6 test concentrations were prepared and maintained using dilution water and a Mount and Brungs Proportional Diluter constructed of glass and Tygon® tubing. Nominal test concentrations were 2.5, 5.0, 10, 20, 40, and 80 mg/L. Test concentrations were delivered intermittently (about every 15 minutes) to replicate 7-L glass exposure chambers; the volume of each replicate was exchanged 7 times daily. Exposure chambers were held in a large, circulating, water bath at approximately 12°C, and whenever possible, were assigned to test concentrations using random numbers.

Rainbow trout fingerlings of age 197 days, mean length 3.9 cm and mean weight 1.0 g were used. Ten fish were added to 1 replicate and 5 fish to the other replicate (2 replicates per concentration; total of 15 fish per test concentration) using random numbers. Trout were not fed for approximately 48 hours prior to the test, nor during the test. Loading was 0.20 g/L passing through the replicate in 24 hours. Test solutions were held between 11.7 and 12.9°C (mean 12.3°C) and were unaerated. A photoperiod of 16 hours light (100 Lux) versus 8 hours darkness was employed with 25 minutes of transitional light (10 Lux) preceding and following the beginning of the 16-hour light interval. Observations were made every 24 hours.

Dissolved oxygen, pH, and temperature were measured in water control and in all test concentrations before fish were added at the beginning of the test, every 24 hours thereafter, and at the end of the test. Total alkalinity, EDTA hardness, and conductivity of both water control replicates were measured before fish were added at the beginning of the test and at the end of the test. Quantitative analysis of control and test solutions were measured by gas chromatography. The LC_{50} was calculated using the moving, average-angle method.

GLP: Yes

Test Substance: FC-114a, purity >99.7%

Results: Mean measured concentrations were 0.6, 1.4, 2.7, 5.7, 13, and 25 mg/L for the 2.5, 5.0, 10, 20, 40, and 80 mg/L nominal concentrations, respectively. The discrepancy between nominal and measured concentrations was related to the apparent solubility limit of the test substance in water, and apparent degassing of solutions within the proportional diluter.

All chemical and physical parameters were within expected ranges. Total alkalinity was 82-83 and 83-85 mg/L as $CaCO_3$ on days 0 and 4, respectively. EDTA hardness was 77-78 and 76-78 mg/L as $CaCO_3$ on days 0 and 4, respectively. Conductivity was 140 µmhos/cm on days 0 and 4. At study start dissolved oxygen was 10.3-10.4, 10.2, 10.3-10.4, 10.5, 10.4-10.5, 10.4, and 10.3 mg/L at 0, 0.6, 1.4, 2.7, 5.7, 13, and 25 mg/L, respectively. At 96 hours dissolved oxygen was 8.0-8.7, 8.2-8.3, 8.5-8.6, 8.1-8.4, 8.0-8.5, and 7.6-8.1 mg/L at 0, 0.6, 1.4, 2.7, 5.7, and 13 mg/L, respectively. The dissolved oxygen was 9.8 mg/L for the 25 mg/L concentration at 48 hours (all fish were dead by 72 hours). The pH was 7.2 for all concentrations at study start and 96 hours. At study start temperature was 12.0, 12.2, 12.0, 11.7-11.8, 11.9, 11.9-12.0, and 12.1°C at 0, 0.6, 1.4, 2.7, 5.7, 13, and 25 mg/L, respectively. At 96 hours temperature was 12.6-12.7, 12.8-12.9, 12.7, 12.5-12.6, 12.7, and 12.5°C at 0, 0.6, 1.4, 2.7, 5.7, and 13 mg/L, respectively. The temperature was 11.8-12.0°C for the 25 mg/L concentration at 48 hours (all fish were dead by 72 hours).

At 96 hours, mortality was 0, 0, 0, 0, 0, 0, and 100% at 0, 0.6, 1.4, 2.7, 5.7, 13, and 25 mg/L, respectively. Fish at 25 mg/L were discolored (dark) and excitable prior to death. At 13 mg/L fish were discolored and excitable throughout the study.

Reference: DuPont Co. (1990). Unpublished Data, Haskell Laboratory Report No. 538-90, "Flow-Through, 96-Hour Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*)" (November 5).

Reliability: High because a scientifically defensible or guideline method was used.

Type: **96-hour LC_{50}**
Species: Fish
Value: 23.4 mg/L; log Kow = 2.78
Method: Modeled
GLP: Not Applicable
Test Substance: FC-114a
Results: No additional data.
Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.

Reliability: Estimated value based on accepted model.

Additional References for Acute Toxicity to Fish: None Found.

4.2 Acute Toxicity to Invertebrates

Type: **48-hour EC_{50}**
Species: *Daphnia magna*
Value: 38 mg/L (95% confidence interval, 33-47 mg/L)
Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Neonates less than 24 hours old were collected from 24-day old parent daphnids for use in the test. Six test concentrations and a water control were prepared using filtered dilution water. Nominal test concentrations were 2.5, 5.0, 10, 20, 40, and 80 mg/L.

Screw-top, Erlenmeyer flasks closed with a Mininert® valve assembly containing about 270 mL of test solution (filled to the top with minimal headspace) were used. Four replicates per concentration were used. Replicates A and B each contained 10 daphnids (<0.1 g daphnid/L). Replicates C and D contained no daphnids, and were used for dissolved oxygen and pH measurements at test start and end. Daphnids were added to the water control and to test containers beginning with the lowest concentration. Random assignment was not used to avoid contamination of test solutions of low concentration from the transfer pipette when daphnids were released under the water surface. Daphnids were not fed during the test. Test solutions were held between 19.8 and 20.1°C (mean 20.0°C) and were unaerated. A photoperiod of 16 hours light (323 to 506 Lux) versus 8 hours darkness was employed.

Dissolved oxygen and pH were measured in the C and D replicates of all test concentrations and water controls at the beginning (C replicate) and end of the test (D replicate). Total alkalinity, EDTA hardness, and conductivity of the dilution water were measured at the beginning of the test. Temperature was measured in the C and D replicates used for dissolved oxygen and pH measurements.

Solutions for quantitative analysis, taken from controls and test solutions, were measured by gas chromatography to

	determine the concentration of the test substance. Probit analysis was used to estimate the 48-hour EC_{50}. A normal probit model was fit to the actual measured concentrations.
GLP:	Yes
Test Substance:	FC-114a, purity >99.7%
Results:	Mean measured concentrations were 0, 1.6, 2.1, 6.2, 14, 32, and 64 mg/L for the 0, 2.5, 5.0, 10, 20, 40, and 80 mg/L nominal concentrations, respectively. The discrepancies between the mean measured and nominal concentrations were caused either by degassing during the process of stock solution dilution and preparation of the individual solutions, by incomplete dissolution of the test substance in the stock solution, or both. All chemical and physical parameters were within expected ranges. Total alkalinity, EDTA hardness, and conductivity at test start were 71 mg/L as $CaCO_3$, 75 mg/L as $CaCO_3$, and 154 µmhos/cm, respectively. At study start dissolved oxygen was 9.0, 9.0, 8.9, 8.8, 8.6, 8.0, and 6.6 mg/L at 0, 1.6, 2.1, 6.2, 14, 32, and 64 mg/L, respectively. At study end dissolved oxygen was 8.8, 8.6, 8.6, 8.4, 8.1, 7.7, and 6.6 mg/L at 0, 1.6, 2.1, 6.2, 14, 32, and 64 mg/L, respectively. At study start the pH was 8.5 at all dose levels. At study end, the pH was 8.1, 8.1, 8.1, 8.2, 8.2, 8.4, and 8.4 at 0, 1.6, 2.1, 6.2, 14, 32, and 64 mg/L, respectively. Temperature was 20.1°C at all dose levels when measured at study start and study end. At 48 hours, mortality was 0, 0, 0, 0, 10, 20, and 100% at 0, 1.6, 2.1, 6.2, 14, 32, and 64 mg/L, respectively.
Reference:	DuPont Co. (1990). Unpublished Data, Haskell Laboratory Report No. 528-90, "Static Acute, 48-Hour EC_{50} to *Daphnia magna*" (October 9).
Reliability:	High because a scientifically defensible or guideline method was used.
Type:	**48-hour LC_{50}**
Species:	Daphnid
Value:	26.5 mg/L; log Kow = 2.78
Method:	Modeled
GLP:	Not Applicable
Test Substance:	FC-114a
Results:	No additional data.

Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates: None Found.

4.3 Acute Toxicity to Aquatic Plants

Type:	**96-hour EC_{50}**
Species:	Green algae
Value:	17.3 mg/L; log Kow = 2.78
Method:	Modeled
GLP:	Not Applicable
Test Substance:	FC-114a
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates: None Found.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type: **Oral Toxicity:** No Data.

Type:	**Inhalation ALC**
Species/Strain:	Male rats/Crl:CD®Br
Exposure Time:	5 hours, 15 minutes
Value:	>153,000 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Four male rats, weighing between 239 and 271 g, were exposed to an average concentration of 153,000 ppm for

	5 hours and 15 minutes. Body weights and clinical signs were recorded.
GLP:	No
Test Substance:	FC-114a, purity 99.7%
Results:	No deaths were observed. The rats showed slight to moderate weight loss on the day following the exposure, followed by a 5-day period of essentially normal weight gain. No other adverse effects were observed.
Reference:	DuPont Co. (1989). Unpublished Data, Haskell Laboratory Report 269-89, "Two-Week Inhalation Toxicity Study in Rats" (August 9).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional Reference for Acute Inhalation Toxicity:

Data from this additional source were not summarized because the test substance was a mixture or otherwise inappropriate.

Paulet, G. and S. Desbrousses (1969). Arch. Mal. Prof. Med. Trav. Secur. Soc., 30(9):477-492.

Type: **Cardiac Sensitization:** No Data.

Type: **Dermal Toxicity:** No Data.

Type: **Dermal Irritation:** No Data.

Type: **Dermal Sensitization:** No Data.

Type: **Eye Irritation:** No Data.

5.2 Repeated Dose Toxicity

Type:	**2-Week Inhalation**
Species/Strain:	Rat/Crl:CD®BR
Sex/Number:	Male/10 per group
Exposure Period:	2 weeks
Frequency of Treatment:	6 hours/day, 5 days/week
Exposure Levels:	Design Concentrations: 0, 2000, 10,000, 40,000 ppm Measured Concentrations: 0, 1900, 11,100, 41,300 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Three groups of 10 male rats were exposed to design concentrations of 2000, 10,000, or 40,000 ppm of the test substance in air. A control group of 10 male rats was exposed simultaneously to air only. Male rats were individually restrained in perforated, stainless steel cylinders with conical nose pieces. Each restrainer was inserted into the face plate of a 29-liter glass exposure chamber such that only the nose of each rat extended into the chamber. The exposures were conducted 6 hours/day (except for the 3rd exposure), 5 days/week for 2 weeks, and were followed by a 14-day recovery period.

The test substance was metered from a cylinder, which was about 30% immersed in a water bath that was maintained at 75-80°F. Stainless steel lines carried the vapor to the inhalation chamber air supply. The chamber exhaust air was passed through a mineral-oil scrubbing tower and an MSA cartridge filter before the air was discharged into a fume hood.

Chamber samples of atmospheric test substance were taken from the animal breathing zone at approximately 30-minute intervals. The samples were analyzed using a gas chromatograph. During each exposure, chamber temperatures were measured once or twice. Relative humidity and oxygen concentration were measured once during each exposure except for the 3rd exposure. No humidity or oxygen measurements were taken during the 3rd exposure because the exposure was terminated early due to unforeseen test sample depletion.

During the exposure period, all rats were weighed daily, and clinical signs were recorded as group clinical signs, unless a rat showed symptoms that were not typical of the group. During the recovery period, all rats were weighed and observed daily for clinical signs of toxicity, except during weekends.

Urine samples were collected overnight from all rats after the 9th exposure, and from the remaining rats on the 13th day of recovery, and approximately 14 urine parameters were examined.

Blood samples were collected on all rats per group after the 10th exposure, and from the remaining rats per group on the 14th day of the recovery period, and approximately 22 blood

parameters were measured or calculated.

Each group was divided into subgroups of 5 rats. The first 5 rats per group were killed for pathologic examination after the 10th exposure, and the remaining 5 rats per group were killed for pathologic examination on the 14th day of recovery. The lungs, liver, kidneys, spleen, and testes were weighed at necropsy, and representative samples of 26 tissues or organs were prepared for microscopic examination.

Mean body weights and body weight gains were statistically analyzed by one-way analysis of variance. Exposure group values were compared to controls by the least-significant-difference test when the ratio of variance (F) indicated a significant among-to-within group variation. For clinical pathology parameters, a one-way analysis of variance (ANOVA) and Bartlett's test were calculated for each sampling time. When the F-test from ANOVA was significant, the Dunnett's test was used to compare means from the control and exposure groups. When the results of the Bartlett test were significant, the Kruskal-Wallis test was employed and the Mann-Whitney U test was used to compare means from the control and exposure groups. Mean body weight (at pathology) and mean absolute and relative organ weights were analyzed using ANOVA. When the F-test from the ANOVA was significant, the Least Significant Difference (LSD) test and Dunnett's test were used to compare means from the control with the test groups.

GLP: Yes

Test Substance: FC-114a, purity 99.7%

Results: The test substance exposure chambers were operated at combined test substance/air flow rates of 10 to 11 L/min. The control chamber was operated at an airflow rate of 25 L/min. The higher air-flow rate apparently was the cause of a lower mean relative humidity measured in the control chamber. Mean chamber concentrations were 0, 1900, 11,100, and 41,300 at 0, 2000, 10,000, and 40,000 ppm, respectively. Relative humidity was 40-60%, temperature was 21-23°C, and oxygen concentration was 20-21%.

There were no biologically significant effects observed in CFC-114a-exposed rats at any tested concentration in gross observations at necropsy, histopathologic observations, hematological or urinalysis measurements, or clinical signs and body weights. The no-observed-effect concentration

	(NOAEL) under the conditions of this study was 41,300 ppm.
Reference:	DuPont Co. (1989). Unpublished Data, Haskell Laboratory Report No. 269-89, "Two-Week Inhalation Toxicity Study in Rats" (August 9).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Repeated Dose Toxicity: None Found.

5.3 Developmental Toxicity: No Data.

5.4 Reproductive Toxicity

Species/Strain:	Rat/Crl:CD®BR
Sex/Number:	Male/10 per group
Route of Administration:	Inhalation
Exposure Period:	2 weeks
Frequency of Treatment:	6 hours/day, 5 days/week
Exposure Levels:	Design Concentrations: 0, 2000, 10,000, 40,000 ppm Measured Concentrations: 0, 1900, 11,100, 41,300 ppm
Method:	A 2-week inhalation study was conducted in male rats (see Section 5.2 for details on the study design). Complete necropsies were performed at study termination. Testes were weighed, and testes and epididymides were examined microscopically.
GLP:	Yes
Test Substance:	FC-114a, purity 99.7%
Results:	No test substance-related effects on the testes or epididymides were observed.
Reference:	DuPont Co. (1989). Unpublished Data, Haskell Laboratory Report No. 269-89, "Two-Week Inhalation Toxicity Study in Rats" (August 9).
Reliability:	Medium because a suboptimal study design was used.

Additional References for Reproductive Toxicity: None Found.

5.5 Genetic Toxicity

Type: ***In vitro* Bacterial Reverse Mutation Assay:** No Data.

Type: ***In vitro* Clastogenicity Studies:** No Data.

Type: ***In vivo* Genetic Toxicity Studies:** No Data.