

SCREENING-LEVEL HAZARD CHARACTERIZATION

2,2-Dichloro-1,1,1-trifluoroethane (CASRN 306-83-2)

The High Production Volume (HPV) Challenge Program¹ was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to "SIDS" (Screening Information Data Set^{1,2}) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency's Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance^{2,3} and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor's responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT's focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

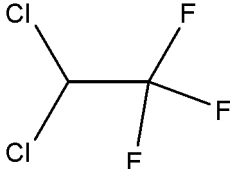
OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

¹ U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

² U.S. EPA. HPV Challenge Program – Information Sources; <http://www.epa.gov/chemrtk/pubs/general/guidocs.htm>.

³ U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public.

<p>Chemical Abstract Service Registry Number (CASRN)</p>	<p>306-83-2</p>
<p>Chemical Abstract Index Name</p>	<p>Ethane, 2,2-dichloro-1,1,1-trifluoro-</p>
<p>Structural Formula</p>	
<p style="text-align: center;">Summary</p> <p>This chemical is a clear colorless, highly volatile liquid with high water solubility and high vapor pressure. It is expected to have high mobility in soil. Volatilization of 2,2-dichloro-1,1,1-trifluoroethane from water and moist soil is considered high based on its Henry's Law constant. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered negligible. It is expected to have high persistence (P3) and low bioaccumulation potential (B1).</p> <p>Acute oral and dermal toxicity of this chemical in rats and rabbits is low and the acute inhalation toxicity in rats is moderate. It is mild to moderately irritating to rabbit eyes and is a cardiac sensitizer in dogs. A two-year repeated-dose toxicity study by the inhalation route in rats showed decreases in body weight, changes in clinical chemistry parameters, histopathology of the liver, and increases in hepatic peroxisomal beta oxidation activity in females, and histological changes in various organs in males and females at a concentration of 1.9 mg/L/day, the lowest concentration; the NOAEL for systemic toxicity was not established. A two-generation reproductive toxicity study by the inhalation route in rats showed decreases in body weight gain in adults at 0.63 mg/L/day; the NOAEL for systemic toxicity was 6.25 mg/L/day. There was no evidence of reproductive toxicity in this study and the NOAEL was 6.25 mg/L/day. In the same study, there was developmental toxicity at 0.19 mg/L/day, the lowest concentration, as demonstrated by decreases in pup body weight gain; the NOAEL for developmental toxicity was not established. A prenatal developmental toxicity study by the inhalation route in rats showed clinical signs of toxicity in the dams at 62.5 mg/L/day, the only concentration tested; the NOAEL for maternal toxicity was not established. In the same study, there was no evidence of developmental toxicity and the NOAEL was 62.5 mg/L/day. A prenatal developmental toxicity study by the inhalation route in rabbits showed decreases in body weight in the dams at 3.1 mg/L/day, the lowest concentration; the NOAEL for maternal toxicity was not established. In the same study, there was no evidence of developmental toxicity and the NOAEL for developmental toxicity was 3.1 mg/L/day. This chemical did not induce gene mutation when tested <i>in vitro</i>. This chemical induced chromosome aberrations in human lymphocytes when tested <i>in vitro</i>, but did not induce chromosome aberrations in rats or increase micronucleus formation in mice when tested <i>in vivo</i>. This chemical showed evidence of carcinogenicity in a two-year inhalation chronic toxicity/carcinogenicity study in rats.</p> <p>The 96-hour LC₅₀ of this chemical to fish is 55.5 mg/L, the 48-hour EC₅₀ to aquatic invertebrates is 17.3 mg/L, and the 96-hour EC₅₀ to aquatic plants is 67.8 mg/L (biomass).</p>	

No data gaps were identified under the HPV Challenge Program.

The sponsor, DuPont Chemical Company, submitted a Test Plan and Robust Summaries to EPA for 2,2-dichloro-1,1,1-trifluoroethane (CASRN 306-83-2) on December 11, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on January 24, 2002 (<http://www.epa.gov/chemrtk/pubs/summaries/dichloro/c13403tc.htm>). EPA comments on the original submission were posted to the website on August 12, 2002. Public comments were also received and posted to the website.

1. Chemical Identity

1.1 Identification and Purity

The HPV submission for this chemical did not include information on identification and purity in the Test Plan (2001).

1.2 Physical-Chemical Properties

The physical-chemical properties of 2,2-dichloro-1,1,1-trifluoroethane are summarized in Table 1. 2,2-Dichloro-1,1,1-trifluoroethane is a clear colorless, highly volatile liquid with high water solubility and high vapor pressure.

Table 1. Physical-Chemical Properties of 2,2-dichloro-1,1,1-trifluoroethane¹	
Property	Value
CASRN	306-83-2
Molecular Weight	152.93
Physical State	Clear colorless liquid
Melting Point	-107°C (measured)
Boiling Point	27.8°C (measured)
Vapor Pressure	718 mm Hg at 25°C (measured)
Water Solubility	2100 mg/L at 25°C (measured) ²
Dissociation Constant (pK _a)	Not applicable
Henry's Law Constant	0.0256 atm·m ³ /mole (measured)
Log K _{ow}	2.307 (estimated); 1.75 (estimated) ³ ; 2.17 (estimated) ⁴

¹DuPont Chemical Company. December 19, 2001. Robust Summary and Test Plan for 2,2-dichloro-1,1,1-trifluoroethane. <http://www.epa.gov/oppt/chemrtk/pubs/summaries/dichloro/c13403tc.htm>.

²HSDB. 2008. Hazardous Substances Data Bank. Accessed August 22, 2008. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>.

³Calculated using Advanced Chemistry Development (ACD/Labs) Software V9.04. The value was cited in STN CAS's EPROP database.

⁴US EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. United States Environmental Protection Agency, Washington, DC, USA. <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

This chemical has an aggregated production and/or import volume in the United States between 10 million and 50 million pounds.

Non-confidential information in the IUR indicates that the industrial processing and uses of this chemical include processing as an intermediate in other basic chemical manufacturing. The HPV submission for this chemical indicates that this chemical is used as a refrigerant and as an intermediate in the production of trifluoroacetylchloride, various agricultural chemicals and HCFC-124 and HCFC-125. The HSDB states that the chemical is used as a refrigerant in commercial chillers and AC units.

This chemical is on the Toxics Release Inventory. TRI information includes releases to air and water.

2.2 Environmental Exposure and Fate

No quantitative information is available on releases of this chemical to the environment.

The environmental fate properties are provided in Table 2. 2,2-Dichloro-1,1,1-trifluoroethane is expected to have high mobility in soil. The rate of biodegradation is considered slow based on the results of a ready biodegradation test. The rate of volatilization of 2,2-dichloro-1,1,1-trifluoroethane from water and moist soil is considered high based on its Henry's Law constant. The rate of hydrolysis is considered negligible under environmental conditions. When released to the environment, 2,2-dichloro-1,1,1-trifluoroethane will partition to the atmosphere where its rate of degradation is negligible. 2,2-dichloro-1,1,1-trifluoroethane is expected to have high persistence (P3) and low bioaccumulation potential (B1).

Property	Value
Photodegradation Half-life	479 days (measured rate constant)
Hydrolysis Half-life	134 years at pH 7 and 25°C (estimated) ² ; 13.4 years at pH 8 and 25°C (estimated) ²
Biodegradation	24% after 28 days (measured, not readily biodegradable)
Bioconcentration	BCF = 33 (estimated)
Log K _{oc}	1.9 (estimated)
Fugacity (Level III Model)	Air = 99.8% Water = 0.121% Soil = 0.0426% Sediment = 6.86×10 ⁻⁴ %
Persistence ³	P3 (high)
Bioaccumulation ³	B1 (low)

¹DuPont Chemical Company. December 19, 2001. Robust Summary and Test Plan for 2,2-dichloro-1,1,1-trifluoroethane. <http://www.epa.gov/oppt/chemrtk/pubs/summaries/dichloro/c13403tc.htm>.

²US EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. United States Environmental Protection Agency, Washington, DC, USA. <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

³Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

3. Human Health Effects

Acute Oral Toxicity

Male Charles River-CD rats (1/dose) were given a single dose of 2250, 3400, 5000, 7500, 9000, 11,000, 13,934 or 15,024 mg/kg-bw of 2,2-dichloro-1,1,1-trifluoroethane in corn oil by oral gavage. Death occurred within one hour at 9000 mg/kg-bw and within three minutes at 11,000 mg/kg-bw and greater.

LD₅₀ = 9,000 mg/kg-bw

Acute Inhalation Toxicity

Male Charles River-CD rats (6/dose) were exposed to vapor concentrations of 20, 700, 32,000, 33,700, 42,100, 52,500 or 55,000 ppm of 2,2-dichloro-1,1,1-trifluoroethane for 4 hours. Mortality ratios for these concentrations were 0/6, 3/6, 3/6, 6/6 and 6/6, respectively.

4-h LC₅₀ < 700 ppm (approximately 4.4 mg/L)

Acute Dermal Toxicity

Male and female Crl:CD BR rats (5/sex) and New Zealand White rabbits (5/sex) were exposed to a single dose of 2,2-dichloro-1,1,1-trifluoroethane for 24 hours at 2000 mg/kg-bw and observed for 14 days. No animals died within the 14-day observation period.

LD₅₀ > 2000 mg/kg-bw

Repeated-Dose Toxicity

In a two-year repeated-dose toxicity study, Crl:CD BR rats (80/sex) were exposed whole-body via vapor inhalation to 2,2-dichloro-1,1,1-trifluoroethane at concentrations of 0, 300, 1000 or 5000 ppm (approximately 0, 1.9, 6.25 or 31.25 mg/L/day) for 6 hours/day, 5 days/week for 104 weeks (Malley, L.A. *et al.* 1995). Clinical pathology was evaluated at 6, 12, 18, and 24 months. At the sixth month interval, non-fasted rats were evaluated for compound related changes in lipid and carbohydrate metabolism. Non-fasted male rats showed a significant dose-related decrease in serum triglycerides at 5000 ppm; decreased serum globulin at 1000 or 5000 ppm; and an increase in serum glucose and serum albumin at 1000 and higher. Non-fasted female rats showed a significant dose-related decrease in serum triglycerides at 300 ppm and higher, and a decrease in serum cholesterol at 300 ppm and higher when compared to the control. An increase in serum cholesterol at 300 ppm and higher was seen when compared to fasted rats. In addition, non-fasted females rats showed a significant increase in serum glucose at 300 ppm and higher; and an increase in serum albumin and a decrease in serum globulin at 1000 ppm and higher. Decreases in body weight and body weight gain were seen in female rats at 300 ppm and 1000 ppm and in male and female rats at 5000 ppm in the absence of any changes in food consumption. Twelve months after study initiation, 10 rats/sex/dose were sacrificed and necropsied, with the first 5/sex/dose also evaluated for cell proliferation. All surviving animals were necropsied at 24 months and tissues were examined macroscopically and microscopically. Non-cancer histopathological lesions were seen in the liver of males at 5000 ppm and females at all doses; the pancreas in all male dose groups; adrenals, testes at all doses; and in the retina in both sexes and all dose groups. Tumors were observed in the liver, pancreas, and testes of all dose groups in male and female rats. Increased hepatic peroxisomal beta oxidation activity was observed in males at 5000 ppm and in females at all doses.

LOAEL = 300 ppm (approximately 1.9 mg/L/day) based on decreases in body weight, changes in clinical chemistry parameters and histopathology of the liver, and increases in hepatic peroxisomal beta oxidation activity in females; and histological changes in various organs in males and females, all beginning at 300.

NOAEL = Not established

Reproductive Toxicity

In a two-generation reproductive toxicity study (Malinverno *et al.*, 1996) Charles River CD rats (32/sex/F₀ generation and 28/sex/F₁ generation) were exposed by vapor inhalation to 2,2-dichloro-1,1,1-trifluoroethane at concentrations of 0, 30, 100, 300 or 1000 ppm (approximately 0, 0.19, 0.625, 1.9 or 6.25 mg/L/day) for 6 hours/day, 7 days/week (treatment of the F₀ began at 6 weeks of age and continued up to weaning for F₁ pups; direct treatment of the F₁ began at 4 weeks of age and continued up to weaning for F₂ pups). At doses of 100 ppm and higher, a statistical significant decrease in body weight gain was seen in F₀ and F₁ adults; males beginning at week 14 and females at week 8; and in the F₁ adults beginning at week 48 of the study. Increased cholesterol levels were seen in both F₀ and F₁ adult males in all treatment groups, but results were somewhat variable. Dose-related decreases in cholesterol were observed in F₀ and F₁ adult females beginning at 100 ppm. Decreased serum triglyceride levels were seen in adult F₀ and F₁ animals in a dose-related manner beginning at 100 ppm. At 300 and 1000 ppm, increases in F₀ and F₁ adult liver weight were reported along with microscopic changes that

included hepatocyte enlargement and vacuolation; at 100 ppm microscopic changes were limited to hepatocyte enlargement. Other differences in biochemical parameters were reported but the study authors considered these differences to be spurious in nature and not treatment-related. Decreased implantation counts were seen in F₁ females exposed to 1000 ppm, this appeared to significantly affect litter size in the F₂ generation at the same dose. No additional mating and fertility parameters were affected by treatment in either generation. No significant differences were reported for reproductive organ weights or histopathology in the adults. Significant decreases in F₀ pup body weight gain was observed at 100, 300 and 1000 ppm dose groups; in the F₁, this effect was also observed beginning at 30 ppm. No effects on pup viability at birth, pup body weight at birth through postnatal day 4, sex ratios, or sexual maturation were observed in either generation of offspring. No other effects were reported.

LOAEL (systemic toxicity) = 100 ppm (approximately 0.63 mg/L/day) based on decreased body weight gain in adults.

NOAEL (reproductive toxicity) = 1000 ppm (approximately 6.25 mg/L/day) based on no adverse treatment-related effects observed.

LOAEL (developmental toxicity) = 30 ppm (approximately 0.19 mg/L/day) based on decreases in pup body weight gain.

NOAEL (developmental toxicity) = not established

Developmental Toxicity

(1) In a prenatal developmental toxicity study, pregnant New Zealand White rabbits (24/dose) were exposed via vapor inhalation (whole-body) to 2,2-dichloro-1,1,1-trifluoroethane at concentrations of 0, 500, 1500 or 5000 ppm (approximately 3.1, 9.3 or 31.2 mg/L/day) for 6 hours/day during gestation days 6-18. Signs of maternal toxicity included decreases in body weight in all treatment groups in a dose related manner. No treatment related effects were seen in the offspring.

LOAEL (maternal toxicity) = 500 ppm (approximately 3.1 mg/L/day) based on decreases in body weight

NOAEL (maternal toxicity) = Not established

NOAEL (developmental toxicity) = 5000 ppm (approximately 31 mg/L/day)

(2) In a prenatal developmental toxicity study, pregnant Charles Rivers-CD Albino rats (25/dose) were exposed via vapor inhalation (whole-body) to 2,2-dichloro-1,1,1-trifluoroethane at 0 or 10,000 ppm (approximately 62.5 mg/L/day) for 6 hours/day during gestation days 6-15.

Maternal body weight gain was similar to controls. Clinical signs of toxicity in the dams during the beginning of the study included lack of coordination, reduced activity and responsiveness to noise. No treatment-related toxicity on reproductive parameters was observed. No signs of developmental toxicity were reported in the offspring.

LOAEL (maternal toxicity) = 10,000 ppm (approximately 62.5 mg/L/day) based on a lack of coordination and reduced responsiveness to noise

NOAEL (maternal toxicity) = Not established

NOAEL (developmental toxicity) = 10,000 ppm (approximately 62.5 mg/L/day, only concentration tested)

Genetic Toxicity -- Gene Mutation

In vitro

In a bacterial reverse mutation assay, *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 were exposed to the test substance at concentrations of 0, 0.01, 0.02, 0.05, 0.1, 0.25 or 0.5 mL/vessel, with and without metabolic activation. Cytotoxicity was seen at the highest concentration. Positive controls responded as expected.

2,2-Dichloro-1,1,1-trifluoroethane was not mutagenic in this assay.

Genetic Toxicity -- Chromosomal Aberrations

In vitro

An *in vitro* chromosomal aberrations test with 2,2-dichloro-1,1,1-trifluoroethane was conducted in human lymphocytes for 3 hours with and without metabolic activation (concentrations of 0, 7.5, 15 and 30% v/v) and for 24 hours without metabolic activation (concentrations of 0, 2.5, 5 and 10%). Exposure for 3 hours in the absence of metabolic activation produced minor increases in the frequency of aberrant metaphases ($p < 0.05$ for 7.5%; $p < 0.01$ for 30%), but only when gaps were included in the analysis. A 3-hour exposure with metabolic activation produced a larger increase in the frequency of aberrant metaphases, both including and excluding gaps ($p < 0.001$ for 30%) and an increase in the number of polyploid cells. Exposure for 24 hours in the absence of activation produced dose-related, biologically and statistically significant increases in the frequency of aberrant metaphases at all concentrations tested, both including and excluding gaps ($p < 0.01$ at 2.5% and $p < 0.001$ at 5 and 10%). No effect on the number of polyploid cells was observed under these conditions. The cytogenetic analyses of the 2.5 and 10% treatment groups were based on two cultures with a total of 200 metaphase cells, respectively.

2,2-Dichloro-1,1,1-trifluoroethane induced chromosomal aberrations in this assay.

In vivo

(1) In an *in vivo* chromosomal aberration assay, male Sprague Dawley rats (10/dose) were treated via inhalation to 2,2-dichloro-1,1,1-trifluoroethane at concentrations of 0, 300, 1000 or 5000 ppm for 6 hours/day, 7 days/week for 14 weeks. Negative findings were reported.

2,2-Dichloro-1,1,1-trifluoroethane did not induce chromosomal aberrations in this assay.

(2) In a mouse micronucleus assay, NMRI mice (15/sex/dose) were treated via inhalation (head and nose) to 2,2-dichloro-1,1,1-trifluoroethane at concentrations of 0, 2000, 6000 or 18,000 ppm for 6 hours. Negative findings were reported.

2,2-Dichloro-1,1,1-trifluoroethane was not mutagenic in this assay.

(3) In an unscheduled DNA synthesis assay, male Alderley Park rats (5/dose) were treated via inhalation (whole body) to 2,2-dichloro-1,1,1-trifluoroethane at concentrations of 0, 8000, 12500, and 20000ppm for 6 hours. Negative findings were reported.

2,2-Dichloro-1,1,1-trifluoroethane was not mutagenic in this assay.

Additional Information

Skin Irritation

(1) New Zealand white rabbits male (4) and female (2) were evaluated for skin irritation after exposure to 2,2-dichloro-1,1,1-trifluoroethane for 4 hours. A 0.5mL aliquot was applied directly to the skin then covered and taped. Sodium lauryl sulfate was used as a positive control. No skin irritation was observed in any treatment. Test sites were evaluated for dermal effects after 4 hours and approximately 24, 48, and 72 hours after patch removal. Control animals were observed daily (excluding weekends) until study termination (day 15). Skin irritation was not observed in any animals treated with 2,2-dichloro-1,1,1-trifluoroethane.

2,2-dichloro-1,1,1-trifluoroethane was not irritating to rabbit skin.

(2) Male albino guinea pigs (10) were given 1 drop (~0.05mL) of a 50% and 10% solution (wt/vol) of 2,2-dichloro-1,1,1-trifluoroethane in propylene glycol on the shaved intact shoulder skin. Skin irritation was not observed in any treatment group.

2,2-dichloro-1,1,1-trifluoroethane was not irritating to guinea pig skin.

Eye Irritation

Albino rabbits (2/dose/sex not determined) were exposed to 2,2-dichloro-1,1,1-trifluoroethane (0.1mL undiluted, 0.2mL/propylene glycol, and 0.1mL of propylene glycol) in the right conjunctival sac. After 20 seconds one eye in each dose was washed with tap water for one minute. The cornea, iris, and conjunctiva were observed at one and four hours, and at 1, 2, 3, 7, and 14 days. The test substance produced mild to moderate conjunctival irritation with no corneal or iritic involvement in unwashed eyes of albino rabbits.

2,2-dichloro-1,1,1-trifluoroethane is mild to moderately irritating to the rabbit eye.

Sensitization

In the skin irritation study mention above male albino guinea pigs (10) were also tested for sensitization. A series of 4 sacral intradermal injections were given at 0.1mL of a 1% solution (vol/vol) of 2,2-dichloro-1,1,1-trifluoroethane in dimethyl phthalate (DMP) once a week for three weeks.

2,2-dichloro-1,1,1-trifluoroethane was not a sensitizer in guinea pigs.

Cardiac Sensitization

Twelve male beagle dogs were exposed to various concentrations of 2,2-dichloro-1,1,1-trifluoroethane for five minutes after an intravenous control injection of adrenalin (0.008 mg/kg) and prior to a challenge injection of the same control dosage. The staircase method was used to estimate an EC50 for cardiac sensitization. A concentration of 40000 ppm was chosen as the estimated X₀ and concentrations were selected below and above this level. Three dogs were exposed to 10000 ppm, six were exposed to 20000 ppm, and three were exposed to 40000 ppm. Six animals exhibited ventricular fibrillation and death.

2,2-dichloro-1,1,1-trifluoroethane was a cardiac sensitizer in dogs.

Chronic Toxicity/Carcinogenicity

In the two-year repeated-dose toxicity study previously mentioned, Crl:CD BR rats (80/sex) were exposed whole-body via vapor inhalation to 2,2-dichloro-1,1,1-trifluoroethane at concentrations of 0, 300, 1000 or 5000 ppm (approximately 0, 1.9, 6.25 or 31.25 mg/L/day) for 6 hours/day, 5 days/week for 104 weeks (Malley, L.A. et al.1995). Clinical pathology was evaluated at 6, 12, 18, and 24 months. Twelve months after study initiation, 10 rats/sex/dose were sacrificed and evaluated for hepatic cell proliferation and beta oxidation activity. All surviving animals were necropsied at 24 months and tissues were examined macroscopically and microscopically. Significantly increased incidences of liver tumors were observed in male and female rats. In addition, significant increased incidences of benign tumors were observed in the testes and pancreas in male rats. Significantly increased hepatic peroxisomal beta oxidation activity was observed in males at 5000 ppm and in females at all doses. Hepatic cell proliferation was not observed at 12 months.

2,2-dichloro-1,1,1-trifluoroethane did increase the incidence of tumors in rats and it appears to be a peroxisomal proliferator.

Conclusion: Acute oral and dermal toxicity of this chemical in rats and rabbits is low and the acute inhalation toxicity in rats is moderate. It is mild to moderately irritating to rabbit eyes and is a cardiac sensitizer in dogs. A two-year repeated-dose toxicity study by the inhalation route in rats showed decreases in body weight, changes in clinical chemistry parameters, histopathology of the liver, and increases in hepatic peroxisomal beta oxidation activity in females; and histological changes in various organs in males and females at a concentration of 1.9 mg/L/day, the lowest concentration; the NOAEL for systemic toxicity was not established. A two-generation reproductive toxicity study by the inhalation route in rats showed decreases in body weight gain in adults at 0.63 mg/L/day; the NOAEL for systemic toxicity was 6.25 mg/L/day. There was no evidence of reproductive toxicity in this study and the NOAEL was 6.25 mg/L/day. In the same study, there was developmental toxicity at 0.19 mg/L/day, the lowest concentration, as demonstrated by decreases in pup body weight gain; the NOAEL for developmental toxicity was not established. A prenatal developmental toxicity study by the inhalation route in rats showed clinical signs of toxicity in the dams at 62.5 mg/L/day, the only concentration tested; the NOAEL for maternal toxicity was not established. In the same study, there was no evidence of developmental toxicity and the NOAEL was 62.5 mg/L/day. A prenatal developmental toxicity study by the inhalation route in rabbits showed decreases in body weight in the dams at 3.1 mg/L/day, the lowest concentration; the NOAEL for maternal toxicity was not established. In the same study, there was no evidence of developmental toxicity and the NOAEL for developmental toxicity was 3.1 mg/L/day. This chemical did not induce gene mutation when tested *in vitro*. This chemical induced chromosome aberrations in human lymphocytes when tested *in vitro*, but did not induce chromosome aberrations in rats or increase micronucleus formation in mice when tested *in vivo*. This chemical showed evidence of carcinogenicity in a two-year inhalation chronic toxicity/carcinogenicity study in rats.

4. Environmental Effects – Aquatic Toxicity

Acute Toxicity to Fish

Rainbow trout (*Oncorhynchus mykiss*, formerly *Salmo gairdneri*) in groups of 10/concentration were exposed to 2,2-dichloro-1,1,1-trifluoroethane at nominal concentrations of 13.3 (15.3 mg/L mean measured concentration), 23.5, 42.5 (33.3 mg/L mean measured concentration), 74.3 or 133 mg/L (90.6 mg/L mean measured concentration) for 96 hours under semi-static exposure conditions in a closed system. At 74.3 and 133 mg/L, all fish exhibited effects within 4 hours, including darkened pigmentation, lethargic behavior and loss of coordination. At 13.3, 23.5 and 42.5 mg/L, 2, 3 and 4 fish were affected by the end of the test, exhibiting either darkened pigmentation or lethargic behavior. The nominal mean lethal concentration was 65.4 mg/L (55.5 mg/L mean measured concentration).

96-h LC₅₀ = 55.5 mg/L

Acute Toxicity to Aquatic Invertebrates

Daphnia magna (20/concentration) were exposed to 2,2-dichloro-1,1,1-trifluoroethane at nominal concentrations of 3.47 (2.24 mg/L mean measured concentration), 6.94, 13.9, 27.7 or 55.2 mg/L (44.0 mg/L mean measured concentration) for 48 hours under static conditions in a closed system. Effect concentrations were based on immobilization. There was 5% immobilization at the lowest concentration (3.47 mg/L) and 100% immobilization at the highest concentration (55.2 mg/L) after 48 hours. The nominal mean lethal concentration was 27.7 mg/L (17.3 mg/L mean measured concentration).

48-h EC₅₀ = 17.3 mg/L

Toxicity to Aquatic Plants

Green algae, *Pseudokirchneriella subcapitata* were exposed to nominal concentrations of 13.3, 42.5, 133, 425 (56.3 mg/L mean measured concentration) or 1,327 mg/L (169 mg/L mean measured concentration) of 2,2-dichloro-1,1,1-trifluoroethane for 96 hours. Measured concentrations were 50 to 93% of nominal values. The two highest concentrations, 425 and 1,326 mg/L, produced a decrease in biomass. .

96-h EC₅₀ (biomass) = 67.8 mg/L

96-h EC₅₀ (growth) = 96.6 mg/L

Conclusion: The 96-hour LC₅₀ of this chemical to fish is 55.5 mg/L, the 48-hour EC₅₀ to aquatic invertebrates is 17.3 mg/L, and the 96-hour EC₅₀ to aquatic plants is 67.8 mg/L (biomass).

5. References

Malinverno, G. et al. Inhalation Teratology and Reproduction Studies with 1,1-Dichloro-2,2,2-Trifluoroethane (HCFC-123). *Fundamental and Applied Toxicology* 34, 276-287 (1996).

Malley, L.A., et al. Two-Year Inhalation Toxicity Study in Rats with Hydrochlorofluorocarbon 123. *Fundamental and Applied Toxicology* 25, 101-114 (1995).

Table 3. Summary Table of the Screening Information Data Set as submitted under the U.S. HPV Challenge Program	
Endpoints	SPONSORED CHEMICAL 2,2-Dichloro-1,1,1-trifluoroethane (306-83-2)
Summary of Human Health Data	
Acute Oral Toxicity LD₅₀ (mg/kg-bw)	9,000
Acute Dermal Toxicity LD₅₀ (mg/kg-bw)	> 2,000
Acute Inhalation Toxicity LC₅₀ (mg/L/4h/day)	4.4
Repeated-Dose (2-Year) Toxicity Vapor/NOAEL/LOAEL (mg/L/day)	LOAEL = 1.9 NOAEL = not established
Reproductive Toxicity NOAEL/LOAEL (mg/L/day)	
Systemic	LOAEL = 0.63
Reproductive	NOAEL = 6.25
Developmental	LOAEL = 0.19 NOAEL = not established
Developmental Toxicity NOAEL/LOAEL (mg/L/day)	
Rabbits Maternal	LOAEL = 3.1 NOAEL = Not established
Developmental	NOAEL = 31.2 (highest concentration tested)
Rats Maternal	LOAEL = 62.5 NOAEL = Not established
Developmental	NOAEL = 62.5 (only concentration tested)
Mutagenicity – Gene Mutation <i>In vitro</i>	Negative

Table 3. Summary Table of the Screening Information Data Set as submitted under the U.S. HPV Challenge Program	
Endpoints	SPONSORED CHEMICAL 2,2-Dichloro-1,1,1-trifluoroethane (306-83-2)
Mutagenicity – Chromosomal Aberrations <i>In vitro</i>	Positive
Mutagenicity – Chromosomal Aberrations <i>In vivo</i>	Negative
<i>Additional Information</i> Skin irritation Eye irritation Sensitization Guinea Pig Dog	Not irritating Mild to moderate Not a dermal sensitizer Cardiac Sensitizer
Chronic Toxicity/Carcinogenicity	Increase in the incidence of tumors (rat).
Summary of Environmental Effects – Aquatic Toxicity Data	
Fish 96-h LC₅₀ (mg/L)	55.5
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	17.3
Aquatic Plants 96-h EC₅₀ (mg/L) (growth)	96.6
(biomass)	67.8