(July 16, 2003)

ROBUST SUMMARY FOR FLUOROBENZENE

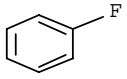
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as additional 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: 462-06-6

Chemical Name: Benzene, fluoro-

Structural Formula:



Other Names: Fluorobenzene
Monofluorobenzene
Phenyl fluoride

Exposure Limits: DuPont Acceptable Exposure Limit (AEL): 25 ppm (8- and 12-hour TWA)

2.0 Physical/Chemical Properties

2.1 Melting Point/Freezing Point

Value:	-40°C
Decomposition:	No Data
Sublimation:	No Data
Pressure:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Budavari, S. et al. (1996). The Merck Index, 12th ed., p. 4212, Merck and Co., Inc., Rahway, NJ.
Reliability:	Not assignable because limited study information was available.

Additional References for Melting Point:

Lewis, R. J. Sr. (1997). Hawley's Condensed Chemical Dictionary, 13th ed., p. 509, John Wiley & Sons, Inc., New York.

Lide, D. R. (2001-2002). CRC Handbook of Chemistry and Physics, 82nd ed.,

p. 3-48, CRC Press, Boca Raton, FL.

DuPont Co. (1993). Material Safety Data Sheet No. DU002805 (March 9).

Weast, R. C. and M. J. Astle (eds.) (1989). CRC Handbook of Data on Organic Compounds, Vol. I, p. 175, CRC Press, Inc., Boca Raton, FL (cited in NTP Chemical Repository (1991). Radian Corporation August 29, http://ntp-db.niehs.nih.gov/NTP_Chem_H&S/NTP_Chem4/Radian462-06-6 accessed on June 25, 2002).

CHRIS (Hazmat data from the US Coast Guard) (CH-00000686).

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 12th ed., Vol. II, p. 1796, John Wiley & Sons, Inc., New York.

2.2 Boiling Point

Value:	84.73°C @ 760 mm Hg 200°C @ 13 atmospheres 275°C @ 38 atmospheres
Decomposition:	No Data
Pressure:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Budavari, S. et al. (1996). The Merck Index, 12th ed., p. 4212, Merck and Co., Inc., Rahway, NJ.
Reliability:	Not assignable because limited study information was available.

Additional References for Boiling Point:

Lewis, R. J. Sr. (1997). Hawley's Condensed Chemical Dictionary, 13th ed., p. 509, John Wiley & Sons, Inc., New York.

Lide, D. R. (2001-2002). CRC Handbook of Chemistry and Physics, 82nd ed., p. 3-48, CRC Press, Boca Raton, FL.

DuPont Co. (1993). Material Safety Data Sheet No. DU002805 (March 9).

Weast, R. C. and M. J. Astle (eds.) (1989). CRC Handbook of Data on Organic Compounds, Vol. I, p. 175, CRC Press, Inc., Boca Raton, FL (cited in NTP Chemical Repository (1991). Radian Corporation August 29 accessed on http://ntp-db.niehs.nih.gov/NTP_Chem_H&S/NTP_Chem4/Radian462-06-6 accessed on June 25, 2002).

CHRIS (Hazmat data from the US Coast Guard) (CH-00000686).

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 12th ed., Vol II, p. 1796, John Wiley & Sons, Inc., New York.

2.3 Density

Value:	1.024 g/mL
Temperature:	No Data
Method:	No Data
GLP:	Unknown
Results:	No additional data.
Reference:	Budavari, S. et al. (1996). The Merck Index, 12th ed., p. 4212, Merck and Co., Inc., Rahway, NJ.
Reliability:	Not assignable because limited study information was available.

Additional References for Density:

Lewis, R. J. Sr. (1997). Hawley's Condensed Chemical Dictionary, 13th ed., p. 509, John Wiley & Sons, Inc., New York.

Lide, D. R. (2001-2002). CRC Handbook of Chemistry and Physics, 82nd ed., p. 3-48, CRC Press, Boca Raton, FL.

DuPont Co. (1993). Material Safety Data Sheet No. DU002805 (March 9).

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 12th ed., Vol. II, p. 1796, John Wiley & Sons, Inc., New York.

Lenga, R. E. (1985). The Sigma-Aldrich Library of Chemical Safety Data, Ed. 1, p. 953, Aldrich Chemical Co., Inc., Milwaukee, WI (cited in NTP Chemical Repository (1991). Radian Corporation August 29, http://ntp-db.niehs.nih.gov/NTP_Chem_H&S/NTP_Chem4/Radian462-06-6 accessed on June 25, 2002).

Aldrich Chemical Co. (1988). Aldrich Catalog/Handbook of Fine Chemicals, p. 750, Aldrich Chemical Co., Inc., Milwaukee, WI (cited in NTP Chemical Repository (1991). Radian Corporation August 29, http://ntp-db.niehs.nih.gov/NTP_Chem_H&S/NTP_Chem4/Radian462-06-6 accessed on June 25, 2002).

CHRIS (Hazmat data from the US Coast Guard) (CH-00000686).

2.4 Vapor Pressure

Value:	60 mm Hg @ 19.6°C

	100 mm Hg @ 30.4°C 1 mm Hg @ -43.4°C 5 mm Hg @ -22.8°C 10 mm Hg @ -12.4°C 20 mm Hg @ -1.2°C 40 mm Hg @ 11.5°C 200 mm Hg @ 47.2°C 400 mm Hg @ 65.7°C 760 mm Hg @ 84.7°C
Temperature:	See above
Decomposition:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Stull, D. R. (1947). Ind. Eng. Chem., 39(4):523 (cited in NTP Chemical Repository (1991). Radian Corporation August 29, http://ntp-db.niehs.nih.gov/NTP_Chem_H&S/NTP_Chem4/Radian462-06-6 accessed on June 25, 2002).
Reliability:	Not assignable because limited study information was available.

Additional References for Vapor Pressure:

Lide, D. R. (2001-2002). CRC Handbook of Chemistry and Physics, 82nd ed., p. 3-48, CRC Press, Boca Raton, FL.

DuPont Co. (1993). Material Safety Data Sheet No. DU002805 (March 9).

Dreisbach, R. R. (1961). Physical Properties of Chemical Compounds, Vol. III, American Chemical Society, Washington, DC (IS-0008277).

Daubert, T. E. and R. P. Danner (1989). Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation, Hemisphere Publ. Corp., New York (EF-0013126).

2.5 Partition Coefficient (log Kow)

Value:	2.27
Temperature:	No Data
Method:	Measured
GLP:	Unknown
Reference:	Fujita, T. and J. Owasa (1964). J. Amer. Chem. Soc., 86:5175 (IS-0008279 and EF-0013125).
Reliability:	Medium because a suboptimal study design was used.

Additional References for Partition Coefficient (log Kow):

Liu, Z. T. et al. (1996). Bull. Environ. Contam. Toxicol., 57:421-425.

Freed, V. H. et al. (1979). Environ. Health Perspect., 30:75-80.

2.6 Water Solubility

Value:	1.54 g/1000 g H_2O
Temperature:	20°C
pH/pKa:	No Data
Method:	No Data
GLP:	Unknown
Reference:	Budavari, S. et al. (1996). The Merck Index, 12th ed., p. 4212, Merck and Co., Inc., Rahway, NJ.
Reliability:	Not assignable because limited study information was available.

Additional References for Water Solubility:

Lewis, R. J. Sr. (1997). Hawley's Condensed Chemical Dictionary, 13th ed., p. 509, John Wiley & Sons, Inc., New York.

DuPont Co. (1993). Material Safety Data Sheet No. DU002805 (March 9).

NTP Chemical Repository (1991). Radian Corporation August 29, http://ntp-db.niehs.nih.gov/NTP_Chem_H&S/NTP_Chem4/Radian462-06-6 accessed on June 25, 2002.

Chiou, C. T. et al. (1977). Environ. Sci. Technol., 11:475-478 (EF-0013124).

Freed, V. H. et al. (1979). Environ. Health Perspect., 30:75-80.

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 12th ed., Vol. II, p. 1796, John Wiley & Sons, Inc., New York.

2.7 Flash Point

Value:	-15ºC
Method:	No Data
GLP:	Unknown
Reference:	National Fire Protection Association (1986). Fire Protection Guide on Hazardous Materials, 9th ed., p. 325M-54, National Fire Protection Association, Quincy, MA (cited in NTP Chemical Repository (1991). Radian Corporation August 29,

	http://ntp-db.niehs.nih.gov/NTP_Chem_H&S/NTP_Chem4/Radian462-06-6 accessed on June 25, 2002)]
Reliability:	Not assignable because limited study information was available.

Additional References for Flash Point:

DuPont Co. (1993). Material Safety Data Sheet No. DU002805 (March 9).

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 12th ed., Vol. II, p. 1796, John Wiley & Sons, Inc., New York.

Bretherick, L. (1985). Handbook of Reactive Chemical Hazards, 3rd ed., p. 577, 1732, Butterworths, London (cited in NTP Chemical Repository (1991). Radian Corporation August 29, http://ntp-db.niehs.nih.gov/NTP_Chem_H&S/NTP_Chem4/Radian462-06-6 accessed on June 25, 2002).

CHRIS (Hazmat data from the US Coast Guard) (CH-00000686).

2.8 Flammability: No Data.

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	25ºC
Direct Photolysis:	No Data
Indirect Photolysis:	Rate constant obtained at 25ºC or at room temperature was 0.69×10^{-12}. Half-life (23.3 days) calculated using an average atmospheric OH concentration of 5×10^5 molecule/cm^3.
Breakdown Products:	No Data
Method:	No Data
GLP:	Not Applicable
Reference:	Atkinson, R. (1989). J. Phy. Chem. Ref. Data, Monograph 1 (EF-0013127).
Reliability:	High based on accepted experimental methodology.

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	No Data
Indirect Photolysis:	Will be subject to radical reactions in surface waters.

Breakdown Products:	No Data
Method:	No Data
GLP:	Not Applicable
Reference:	Mill, T. 2000. "Photoreactions in surface waters", Ch. 15 In: R.S. Boethling and D. Mackay, Handbook of Property Estimation Methods for Chemicals, Lewis Publ., Boca Raton, FL.
Reliability:	High based on behavior of analogs.

Additional References for Photodegradation: None Found.

3.2 Stability in Water

Concentration:	No Data
Half-life:	No Data
% Hydrolyzed:	No Data
Method:	The HYDROWIN v1.67 module of EPIWIN v3.05 (Syracuse Research Corporation) can not estimate a hydrolysis rate constant for this type of chemical structure. The prediction methodology was developed for the U.S. Environmental Protection Agency and is outlined in Mill et al., 1987.
GLP:	Not Applicable
Reference:	Mill, T. et al. (1987). "Environmental Fate and Exposure Studies Development of a PC-SAR for Hydrolysis: Esters, Alkyl Halides and Epoxides," EPA Contract No. 68-02-4254, SRI International, Menlo Park, CA.
Reliability:	Not Applicable.

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 (advection + reaction)
Air	40.9	558
Water	44	900
Soil	14.8	1800
Sediment	0.245	8100

Adsorption Coefficient:	Log Koc = 1.88
Desorption:	No Data
Volatility:	Henry's Law Constant = 0.0063 atm-m^3/mole
Method:	Modeled. EPIWIN 3.11

Henry's Law Constant - HENRYWIN v3.10 module of EPIWIN v3.05 (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 v3.05 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.05 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.

Parameter Values:
Molecular Wt: 96.11
Henry's LC : 0.0063 atm-m^3/mole (HENRYWIN)
Vapor Press : 71.7 mm Hg (MPBPWIN program)
Log Kow : 2.27 (KOWWIN program)
Soil Koc : 76.3 (calc by model)

GLP: Not Applicable

Reference: HENRYWIN –

Hine, J. 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 v3.05 (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:	0.0199 – Does not biodegrade fast
Non-Linear Model Prediction:	0.0008 – Does not biodegrade fast
Ultimate Biodegradation Timeframe:	2.60 – weeks to months; corresponds to an estimated half-life of 37.5 days
Primary Biodegradation Timeframe:	3.73 – days to weeks
MITI Linear Model Prediction:	0.4847 - Does not readily biodegrade
MITI Non-Linear Model Prediction:	0.0257 – Does not readily biodegrade

Breakdown Products: No Data

Method: Modeled. BIOWIN, v4.0 module of EPIWIN v3.05 (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). Predicting Ready Biodegradability in the MITI Test. Environ. Toxicol. Chem., accepted for publication.

Reliability: Estimated value based on accepted model.

Additional Reference for Biodegradation:

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. The study reports no determination of test compound toxicity, which causes the information on test compound biodegradability to be inconclusive.

Urano, K. and Z. Kato (1986). J. Hazard. Mater., 13(2):147-159 (CA105:65719x).

3.5 Bioconcentration

Value:	BCF: 11.17
Method:	Modeled. BCFWIN v2.4 module of EPINWIN v3.05 (Syracuse Research Corporation). BCFWIN estimates the bioconcentration factor (BCF) of an organic compound using the compound's log octanol-water partition coefficient (Kow) with correction factors based on molecular fragments.
GLP:	Not Applicable
Reference:	"Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient", SRC TR-97-006 (2nd Update), July 22, 1997; prepared for Robert S. Boethling, EPA-OPPT, Washington, DC, Contract No. 68-D5-0012; prepared by William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup, and Sybil Gouchie, Syracuse Research Corp.
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:	*Pimephales promelas*, fathead minnows
Value:	210 mg/L (95% confidence limits, 190-230 mg/L).
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The test material, prepared as a 1 mg/mL stock solution in laboratory distilled water, was placed into 5-L glass aquaria and diluted with laboratory well water to yield the desired nominal exposure concentrations in 4-L final volumes. An identical vessel, containing only laboratory well water, was designated as the control.

Ten juvenile, unsexed fathead minnows, 2.0 cm mean standard length and 0.074 g mean wet weight, were randomly placed in each test vessel, 1 test vessel per concentration. Concentrations tested included 100, 133, 178, 237, 316, 422, 562.5, 750, and 1000 mg/L. Fish were not fed for approximately 48 hours prior to or during the exposure. The test solutions were not aerated, and temperature was maintained between 21.8 and 22.1ºC. 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, medium, and high test concentrations (100, 316, and 1000 mg/L, respectively) at the beginning of the test, at 24-hour intervals during the 96-hour exposure period, or if total mortality occurred in a test concentration (72 hours at 316 mg/L, 20 minutes after test initiation at 1000 mg/L). Total alkalinity, hardness (EDTA), and conductivity were measured at the beginning of the test in the water control.

Concentration data were not transformed and the 96-hour LC_{50} and confidence intervals were calculated by probit analysis.

GLP: Yes

Test Substance: Fluorobenzene, purity >99%

Results: Control water alkalinity, hardness, and conductivity at 0 hours were 81mg/L as $CaCO_3$, 93 mg/L as $CaCO_3$, and 171 µmhos/cm, respectively. Dissolved oxygen concentrations and pH throughout the test ranged from 6.9-8.8 mg/L and 7.9-8.1, respectively.

The observed mortality at 96 hours was 0, 0, 0, 10, 90, 100, 90, 100, 100, and 100% for the 0, 100, 133, 178, 237, 316, 422, 562.5, 750, and 1000 mg/L concentrations, respectively.

Clinical signs observed on some fish at 100 mg/L and

	greater included erratic swimming, darkening in color, swimming at the surface, gasping for air, hyperactive, lying on the bottom, lethargy, moribundity, partial loss of equilibrium, rapid respiration, and blood stain at the gill area 5 to 10 minutes after the test was initiated. At 750 and 1000 mg/L, all the fish died 20 minutes after the test was initiated.
Reference:	DuPont Co. (1986). Unpublished Data, Haskell Laboratory Report No. 376-86, "Static Acute 96-Hour LC_{50} of Fluorobenzene to Fathead Minnows" (June 28). Chromey, N. C. et al. (1992). J. Am. Coll. Toxicol., 11(6):673-674.
Reliability:	Medium because a suboptimal study design with nominal concentrations was used for testing.
Type:	**48-hour LC_{50}**
Species:	*Carassias auratus*, goldfish
Value:	$log1/LC_{50}$ value = 4.48 mol/L (430.5 mg/L)
Method:	The procedures used in the test were based on the recommendations of the following guideline: OECD Guideline (1984). Directive 203. *Carassias auratus* were tested for 48-hours using a static-renewal method with test solution renewal at 12-hour intervals. Four fish (approximately 3.5 g weight and 4.0 cm length) were tested in 6-L glass beakers containing 4-L of test solution. Four to six concentrations were tested with 2 replicates of each concentration. Actual concentrations were not reported. Fish were not fed during exposure. The photoperiod consisted of 16-hours of light and 8-hours of darkness. Water temperature, dissolved oxygen, pH, and hardness were recorded. LC_{50} value was calculated using probit analysis.
GLP:	Unknown
Test Substance:	Fluorobenzene, purity ≥ 95%
Results:	Conditions of experimental water were temperature: 20±1ºC, dissolved oxygen: 8.2±0.5 mg/L, pH: 7.5±0.3, hardness (as $CaCO_3$): 110±10 mg/L.
Reference:	Liu, Z. T. et al. (1996). Bull. Environ. Contam. Toxicol., 57:421-425.
Reliability:	Medium because a suboptimal study design with nominal concentrations was used for testing.

Type:	**96-hour LC_{50}**
Species:	Fish
Value:	47.2 mg/L (log_{10} Kow of 2.19)
Method:	Modeled
GLP:	Not Applicable
Test Substance:	Fluorobenzene
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 (submitted for publication).
Reliability:	Estimated value based on accepted model.

Supporting Data

Type:	**96-hour LC_{50}**
Species:	*Salmo gairdneri*, rainbow trout
Value:	10.4 mg/L
Method:	The procedures used in the test were based on the recommendations of the following guideline: OECD Guideline 203.

Rainbow trout with a total length of 5±1 cm were used in the test. Light was provided with a daily photoperiod of 12 hours. Fish were not fed 24 hours prior to initiation of the test.

Glass tanks were filled with 18 L of reconstituted water. Tanks were covered with specially fitted glass plates assuring aeration and free exchange of the atmosphere. Test water was checked to verify that dissolved oxygen concentration, temperature, and pH were within specification limits. Test material was added to separate vessels at 0.03, 1.8, 3.2, 5.8, 10, 18, 32, 58, or 100 mg/L. A control vessel was also used. The contents of the tank were mixed with a mechanical stirrer. Air was continuously bubbled into the test medium through "flow out stones" directly connected to the aerator with PVC tubes. Aeration was necessary because O_2 concentration dropped below 60% of saturation within 6-8 hours. Fish were added to the tanks 2 hours later. Fish were inspected at 0, 24, 48, and 72 hours after study initiation. Dead fish were removed from the tanks and surviving fish were observed for illness.

	LC_{50} values were obtained via probit analysis. Samples of test medium were taken at the beginning, after 48 hours, and at the end of the test and were analyzed via GC-ECD. The first analytical tests were unsatisfactory because of high losses of test material during the storage time of the samples. Therefore, vessels were prepared containing concentrations equal to the LC_0, LC_{50}, and LC_{100} in the test. Samples were analyzed immediately.
GLP:	Yes
Test Substance:	Chlorobenzene, purity not reported
Results:	Analytical measurements of test concentration in the vessels indicated that only 0.26-2.2% of test material was recovered. Results of the second test revealed 10 (erroneous), 53, 3.5, and 2.4% recovery of a 5.8 mg/L nominal concentration at 0, 2, 6, and 20 hours; and 105, 60, 24, and 3.4% recovery of an 18 mg/L nominal concentration at 0, 2, 6, and 20 hours. Based on the % recovery at 20 hours, the average analytical concentrations over a 20-hour period for 5.8 (LC_0), 10.4 (LC_{50}), and 18 mg/L (LC_{100}) were 0.24, 0.3, and 0.61 mg/L. The value for the 10.4 mg/L concentration was calculated from an estimated average recovery of 2.9%. Results of the analytical tests showed that most of the test material was lost during the first 20 hours of the test. The fish that died either succumbed or showed abnormal behavior during the first few hours when the actual concentration was near the nominal concentration. Since it took 20 hours for all the fish to die, the data from this test were considered to be indicative of a 20-hour test. The nominal concentrations were considered to be more relevant for the evaluation of the test because all the fish that died were harmed by the high concentrations they were exposed to in the first hours of the test. No mortality was observed at 5.8 mg/L (nominal). In the 10 mg/L group (nominal), there was 40% mortality and at higher concentrations there was 100% mortality. All deaths occurred within 24 hours. Water was maintained anywhere from 91-100% saturation, a pH of 7.2-7.8, and a temperature of 14.1-15.5°C.
Reference:	Jones, W. (1990). "Investigation of the lethal effects of the test material chlorobenzene to the rainbow trout (static test) according to OECD Guideline 203" NATEC Project NA 89-9434 (April) (cited in Robust Summaries and Repository

	of Knowledge for CAS No. 108-90-7, http://www.epa.gov/chemrtk/viewsrch.htm accessed on March 4, 2003)
Reliability:	Medium because a suboptimal study design was used.

Type:	**96-hour LC_{50}**
Species:	Fish
Value:	20.9 mg/L (log_{10} Kow of 2.64)
Method:	Modeled
GLP:	Not Applicable
Test Substance:	Chlorobenzene
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 (submitted for publication).
Reliability:	Estimated value based on accepted model.

Type:	**96-hour LC_{50}**
Species:	Fish
Value:	15.7 mg/L (log_{10} Kow of 2.84): 1-Chloro-2-fluorobenzene 15.7 mg/L (log_{10} Kow of 2.84): 1-Chloro-3-fluorobenzene 15.7 mg/L (log_{10} Kow of 2.84): 1-Chloro-4-fluorobenzene
Method:	Modeled
GLP:	Not Applicable
Test Substance:	1-Chloro-2-fluorobenzene 1-Chloro-3-fluorobenzene 1-Chloro-4-fluorobenzene
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 (submitted for publication).
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Fish: None Found.

4.2 Acute Toxicity to Invertebrates

Type:	**24-hour EC_{50}**

Species:	*Daphnia*
Value:	7.37 mg/L (confidence limits, 6.42-8.40 mg/L)
Method:	The procedures used in the test were based on the recommendations of the following guidelines: OECD Guideline No. 202 and EEC Commission Directive 84/449, Test No. C-2. Dilution water was prepared by mixing Milli-Q and tap water in a basically 1:1 ratio, which was adjusted to attain a hardness of 150 mg/L ($CaCO_3$); total hardness of 130 mg/L ($CaCO_3$), pH of 8.2±0.5, and conductivity of 400±25 µs/cm. Stock solutions were prepared by adding the test chemical to the dilution water under mechanical stirring. Test solutions were obtained by diluting the stock solutions. The concentration of the test solutions was determined at the beginning and end of the experiment via high performance liquid chromatography. Ten daphnids, < 24 hours old, were subdivided into 2 replicates per concentration. At least 5 concentrations and a control were tested. The tests were performed in closed bottles filled to the top in order to avoid loss of chemical due to volatilization. The temperature was 20±1ºC and the photoperiod was 16 hours light, 8 hours dark. The raw data were analyzed by probit analysis. Estimates were obtained for the 24-hour EC_{50} as well as the slope of the concentration effect curve with their respective confidence intervals.
GLP:	Unknown
Test Substance:	Fluorobenzene, purity 99%
Results:	The slope of the dose response curve was 10.8 (confidence limits, 5.3-16.4).
Reference:	Tosato, M. L. et al. (1993). Sci. Total. Environ., Suppl. (1/2):1479-1490 (CIS/AQ-0161368).
Reliability:	High because a scientifically defensible or guideline method was used.

Type:	**48-hour EC_{50}**
Species:	Daphnid
Value:	51.3 mg/L (log_{10} Kow of 2.19)
Method:	Modeled
GLP:	Not Applicable
Test Substance:	Fluorobenzene
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 (submitted for publication).
Reliability:	Estimated value based on accepted model.

Supporting Data

Type:	**24-hour EC_{50}**
Species:	*Daphnia*
Value:	4.3 mg/L (95% confidence limits, 3.25-5.7 mg/L)
Method:	The procedures used in the test were based on the recommendations of the following guidelines: AFNOR, Norme Experimentale N. F. T. 90-301 (1974). The AFNOR test was used to define the 24-hour IC_{50}, the immobilization concentration for 50% of the animals at 24 hours. The concentration of chlorobenzene in the test waters was determined at the beginning and end of the experiment and analyzed via gas chromatography. The tests were carried out in closed systems. Effective concentrations (EC_{50}) for immobilization data were extrapolated from empirical curves fitted by eye on log-probability paper and not elaborated, being very close to the concentration with 0 and 100% immobilized animals.
GLP:	No Data
Test Substances:	Chlorobenzene, pure compound analytical grade
Results:	Results are reported as nominal concentrations since the differences between the observed and expected concentrations did not exceed 10% of the initial value. Repeated measurements of pH and O_2 in the test solutions did not show fluctuations higher than 10%. No other details on water chemistry parameters were reported.
Reference:	Calamari, D. et al. (1983). Chemosphere, 12(2):253-262.
Reliability:	High because a scientifically defensible or guideline method was used.

Type:	**48-hour EC_{50}**
Species:	Daphnid
Value:	23.4 mg/L (log_{10} Kow of 2.64)
Method:	Modeled
GLP:	Not Applicable
Test Substance:	Chlorobenzene

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 (submitted for publication).
Reliability:	Estimated value based on accepted model.
Type:	**48-hour EC_{50}**
Species:	*Daphnia*
Value:	2.28 mg/L (95% confidence limits, 1.86 – 2.55 mg/L): 1-Chloro-2-fluorobenzene 3.64 mg/L (95% confidence limits, 3.19 – 4.19 mg/L): 1-Chloro-3-fluorobenzene 1.70 mg/L (95% confidence limits, 1.24 – 2.13 mg/L): 1-Chloro-4-fluorobenzene
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Test solutions were obtained from saturated stock solutions prepared by adding excess chemical to dilution water and slowly stirring for at least 20 hours. The dilution water was bottled natural mineral water diluted with distilled water and aerated to reach oxygen saturation. The water had a pH of 8.3±1, conductivity of 311±33 µs/cm, and hardness of 160±20 mg/L as $CaCO_3$. Daphnia were < 24 hours old. Tests were run in a thermostatic room at 21.5ºC with a 16:8 hour light:dark photoperiod. A minimum of 5 concentrations plus the control were tested, spaced by a geometric factor of 1.2 to 1.8. Twenty animals, divided into 4 replicates, were exposed to each concentration in 50 mL glass flasks. The flasks were completed filled and were closed with glass stoppers. At the beginning and end of the test, temperature, pH, dissolved oxygen, and conductivity were measured in the control and a minimum of 2 other concentrations. Hardness was measured in the control and highest concentration. Analyses were performed with gas chromatography. Toxicity data were analyzed using the probit analysis.

GLP:	No Data
Test Substances:	1-Chloro-2-fluorobenzene, purity >98% 1-Chloro-3-fluorobenzene, purity >98% 1-Chloro-4-fluorobenzene, purity >98%
Results:	At the end of the test, immobilization in the control was ≤10% and dissolved oxygen was maintained above 75% saturation. Test concentrations were generally within 20% of nominal concentrations. No other details on water chemistry parameters were reported.
Reference:	Marchini, S. et al. (1999). Environ. Toxicol. Chem., 18(2):2759-2766.
Reliability:	High because a scientifically defensible or guideline method was used.

Type:	**48-hour EC_{50}**
Species:	Daphnid
Value:	17.8 mg/L (log_{10} Kow of 2.84): 1-Chloro-2-fluorobenzene 17.8 mg/L (log_{10} Kow of 2.84): 1-Chloro-3-fluorobenzene 17.8 mg/L (log_{10} Kow of 2.84): 1-Chloro-4-fluorobenzene
Method:	Modeled
GLP:	Not Applicable
Test Substance:	1-Chloro-2-fluorobenzene 1-Chloro-3-fluorobenzene 1-Chloro-4-fluorobenzene
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 (submitted for publication).
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:	32.4 mg/L (log_{10} Kow of 2.19)
Method:	Modeled

GLP:	Not Applicable
Test Substance:	Fluorobenzene
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 (submitted for publication).
Reliability:	Estimated value based on accepted model.

Supporting Data

Type:	**96-hour EC_{50}**
Species:	*Selenastrum capricornutum*, algae
Value:	12.5 mg/L
Method:	The procedures used in the test were based on a modification of the Algal Assay Procedure Bottle Test (AAPBT) (USEPA) batch test. The procedure permits maintenance of a constant concentration of toxicant in the culture and calculation of the concentration in the culture medium at equilibrium, on the basis of physical characteristics of the chemical. Algal cultures were set up in 2-L spherical flasks closed by screw cap with both silicone rubber and teflon gaskets. The caps were pierced by a stainless steel needle dipping in to the culture medium. Sampling for measurement of algal growth and toxicant concentration was made through the needle by means of a syringe. The volume of the culture medium was 100 mL. The measured medium to flask volume ratio (0.047) was low enough to avoid notable carbon dioxide deficiency. Culture medium and test conditions were similar to the AAPBT, with the exception that the temperature was 20±1ºC. Stock solutions were prepared as follows: an amount of the chemical 10 times higher than the saturation solubility was added to distilled water in a closed vessel, stirred for 48 hours, and decanted for 24 hours. The supernatant was filtered through paper-filters, and the concentration was measured. Final solutions were made by adding 10 mL of stock culture medium to different amounts of toxicant stock solution. Solutions were diluted to 100 mL with distilled water and quickly transferred into the culture flask. Capped flasks were shaken for 24 hours at 20ºC to let vapor and

liquid phases equilibrate. The algal inoculum was added, after reaching equilibrium, at a starting cell concentration of $5x10^6$ cells/L.

The concentration of the test substance was measured by gas chromatographic analysis after the 24 hour equilibrium and 48 and 96 hours after the inoculum was added.

Algal growth was measured at 24, 48, and 96 hours by *in vivo* fluorescence. Results were expressed as a percentage of growth in the control culture and graphically elaborated for the evaluation of the EC_{50}.

GLP: No Data

Test Substance: Chlorobenzene, purity not reported

Results: Initial concentrations could not be measured due to the high volatility of the test material. Within a few minutes of adding the test material to the flasks the concentration was very low compared to theoretical values. Therefore, the initial concentrations calculated from the dilution of the titrated stock solutions were assumed to be the initial concentrations. Equilibrium concentrations were calculated as the mean of the analytical concentrations in samples taken after the equilibrium period and 48 and 96 hours. For initial concentrations of 31.6, 63.2, 94.8, 126.4, 158.0, 221.2, and 284.4 mg/L, equilibrium concentrations of 6.5, 14.3, 23.3, 29.6, 37.8, 45.0, and 63.0 were determined, respectively. The mean initial concentration/equilibrium concentration was 4.5±0.3. The calculated Henry's constant (0.16) was fairly close to the reported value of 0.11, confirming the validity of the method for prediction of concentrations at equilibrium.

After a 24-hour equilibrium period, the concentration of the test material in the culture medium remained almost constant. Differences in the values obtained at equilibrium and after 48 and 96 hours were within the range of acceptable analytical variability.

The 96-hour EC_{50} value calculated for chlorobenzene inhibition of algal fluorescence was 12.5 mg/L. The maximum tested concentration that produced no effect was <6.8 mg/L and the minimum concentration that was 100% effective was 46.3 mg/L.

Reference: Galassi, S. and M. Vighi (1981). Chemosphere, 10(10):1123-1126.

Reliability: High because a scientifically defensible or guideline method

was used.

Type:	**96-hour EC_{50}**
Species:	Green algae
Value:	15.2 mg/L (log_{10} Kow of 2.64)
Method:	Modeled
GLP:	Not Applicable
Test Substance:	Chlorobenzene
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 (submitted for publication).
Reliability:	Estimated value based on accepted model.

Type:	**96-hour EC_{50}**
Species:	Green algae
Value:	11.7 mg/L (log_{10} Kow of 2.84): 1-Chloro-2-fluorobenzene 11.7 mg/L (log_{10} Kow of 2.84): 1-Chloro-3-fluorobenzene 11.7 mg/L (log_{10} Kow of 2.84): 1-Chloro-4-fluorobenzene
Method:	Modeled
GLP:	Not Applicable
Test Substance:	1-Chloro-2-fluorobenzene 1-Chloro-3-fluorobenzene 1-Chloro-4-fluorobenzene
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 (submitted for publication).
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:	Male rats/Crl:CD®(SD)BR

Value:	11,000 mg/kg
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. The test substance was suspended in corn oil and administered to 1 rat per dose level by intragastric intubation. Dose levels used in the study included 2300, 3300, 5000, 7500, and 11,000 mg/kg. Male rats were 7 weeks of age when received for the study and 8 weeks of age at test substance administration. Following administration of the test substance, rats were observed for clinical signs of toxicity. Surviving rats were weighed and observed daily until signs of toxicity subsided, and then at least 3 times a week throughout the 14-day observation period. Pathological examinations were not performed.
GLP:	Yes
Test Substance:	Fluorobenzene, purity >99%
Results:	Mortality occurred in the 11,000 mg/kg dose group only. At this dose level, severe body weight loss (i.e., 11% of body weight) was observed 1 day after dosing. Clinical signs of toxicity included limpness, no righting reflex, rapid breathing, and clear discharge from both eyes. Death occurred within 2 days of dosing. At the non-lethal doses, slight to severe weight losses (i.e., 5-13% of body weight) were observed 1 day after dosing. There were no other common clinical signs of toxicity observed.
Reference:	DuPont Co. (1986). Unpublished Data, Haskell Laboratory Report No. 408-86, "Approximate Lethal Dose (ALD) of Fluorobenzene in Rats" (July 23). Chromey, N. C. et al. (1992). J. Am. Coll. Toxicol., 11(6):673-674.
Reliability:	High because a scientifically defensible or guideline method was used.

Type:	**Oral LD_{50}**
Species/Strain:	Rat/strain not specified
Value:	4399 – 9500 mg/kg
Method:	No Data
GLP:	Unknown
Test Substance:	Fluorobenzene, purity not reported

Results:	Eitingon, A. I and I. P. Ulanova, 1975 reported an LD_{50} value of 4399 mg/kg. Hoechst AG, 1969 reported an LD_{50} value of 9500 mg/kg.
Reference:	Eitingon, A. I. and I. P. Ulanova (1975). Gig. Tr. Prof. Zabol., (9):36-39 (CA84:26568a) (RTECS/DA0800000). Hoechst AG (1969). Project No. 124/69 (cited in Anon. (1995). Toxikologische Bewertung, 126:1-13).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Acute Oral 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.

Azouz, W. M. et al. (1952). Biochem. J., 50:702-706 (CA46:5116d).

Type:	**Inhalation ALC**
Species/Strain:	Male rats/Crl:CD®(SD)BR
Exposure Time:	4 hours
Value:	6200 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Vapor atmospheres of fluorobenzene were generated by pumping the liquid test material into a 3-neck glass mixing flask. The flask was heated to 84-93ºC to facilitate evaporation. The flask temperature was controlled with a controller and was monitored with a thermocouple thermometer. Air introduced at the flask swept the fluorobenzene vapors through a glass dispersion funnel and into the exposure chamber. Additional dilution air was added to the vapor mixture prior to its entry into the chamber. The atmospheric concentration of the fluorobenzene was determined at approximately 30-minute intervals during each exposure by gas chromatography. During each exposure, chamber temperature, relative humidity, and chamber oxygen content were measured. Each group of 6 rats was exposed nose-only for 4 continuous hours to 50, 520, 3700, 6200, or 10,000 ppm fluorobenzene. Rats were 8 weeks old and weighed between 229 and 269 grams on the day they were exposed.

	Rats were weighed and observed prior to exposure. Group observation of clinical signs of toxicity were taken during each exposure and when rats were released from the restrainers after exposure. Surviving rats were weighed and observed daily for 14 days post-exposure, weekends and holidays included when warranted by the rats' condition. No pathological examination was conducted.
GLP:	Yes
Test Substance:	Fluorobenzene, purity >99%
Results:	Chamber temperature ranged from 21-24ºC, relative humidity ranged from 7-14%, and chamber oxygen ranged from 20-21%. Mortality of 0/6, 0/6, 0/6, 2/6, and 5/6 was observed in the 50, 520, 3700, 6200, 10,000 ppm groups, respectively. During or immediately after exposure, rats exposed to 50, 520, or 6200 ppm had red nasal or ocular discharges, effects common to rats under restraint. Rats exposed to 10,000 ppm had no response to sound during exposure. When released from restrainers after exposure, rats exposed to 3700 ppm and rats that survived exposure to 6200 and 10,000 ppm had rapid breathing, tremors, spasms, no righting reflex, and clear ocular discharge. During the post-exposure period, no significant weight loss or adverse clinical signs were observed in rats that survived exposure to fluorobenzene.
Reference:	DuPont Co. (1986). Unpublished Data, Haskell Laboratory Report No. 769-86, "Inhalation Approximate Lethal Concentration (ALC) of Fluorobenzene" (December 19). Chromey, N. C. et al. (1992). J. Am. Coll. Toxicol., 11(6):673-674.
Reliability:	High because a scientifically defensible or guideline method was used.
Type:	**Inhalation LC_{50}**
Species/Strain:	Rat/strain not specified
Exposure Time:	4 hours
Value:	6835 ppm (26,908 mg/m^3)
Method:	No Data
GLP:	Unknown
Test Substance:	Fluorobenzene, purity not reported
Results:	No additional data.

Reference: Eitingon, A. I. and I. P. Ulanova (1975). Gig. Tr. Prof. Zabol., (9):36-39 (CA84:26568a) (RTECS/DA0800000).
Reliability: Not assignable because limited study information was available.

Additional Reference for Acute Inhalation 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.

Lapik, A. S. (1965). Izv. Sibirsk. Otd. Akad. Nauk S.S.S.R., Ser. Biol-Med. Nauk., (3):91-94 (CA64:20497f).

Type: **Dermal Toxicity:** No Data

Type: **Dermal Irritation**
Species/Strain: Female rabbits/New Zealand White
Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

On the day prior to exposure, the hair of 6 rabbits was closely clipped to expose the back from the scapular to the lumbar region. The rabbits weighed from 3051 to 3611 g on the day of treatment.

Each rabbit was placed in a stock which had been fitted with rubber sheeting. The rabbits remained in the stock throughout the exposure period and during that time did not have access to food or water. A 0.5 mL aliquot of fluorobenzene was applied directly to the test site beneath a 1-inch gauze square held in place with tape. The rubber sheeting was then wrapped around the animal and secured with clips to retard evaporation and to keep the test material in contact with the skin without undue pressure.

Approximately 24 hours after treatment, the wrappings were removed. Excess test substance was washed from the rabbit's back. The skin was patted dry and the animals were returned to their cages.

Approximately 25 and 48 hours after application of the test material, the test sites were examined for erythema, edema, and other evidence of dermal effects and were scored according to the Draize scale. Adjacent areas of the

	untreated skin were used for comparison. No pathology examinations were conducted.
GLP:	Yes
Test Substance:	Fluorobenzene, purity >99%
Results:	Fluorobenzene produced slight to mild erythema in 3 of 6 rabbits 25 hours after treatment. Mild to severe edema was observed in 2 rabbits. At 48 hours, slight to mild erythema was observed in 4 rabbits and slight to mild edema was noted in 3 rabbits. At 72 hours post-treatment, slight to mild erythema was noted in 4 of 6 rabbits and slight to mild edema was observed in 3 rabbits. No other dermal effects were noted. Fluorobenzene was considered a mild skin irritant.
Reference:	DuPont Co. (1986). Unpublished Data, Haskell Laboratory Report No. 548-86, "Skin Irritation Test in Rabbits of Fluorobenzene" (September 2).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional Reference for Dermal 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.

Bagley, D. M. et al. (1996). Toxicol. *In Vitro*, 10:1-6.

Type:	**Dermal Sensitization**
Species/Strain:	Guinea Pig/strain not reported
Method:	No Data
GLP:	Unknown
Test Substance:	Fluorobenzene, purity not reported
Results:	Fluorobenzene does not induce sensitization in the skin of guinea pigs.
Reference:	BG Chemie (1993). Toxikol. Bewertung, No. 126 (August) (cited in Bayer, E. and G. Fleischhauer (1993). Chemosphere, 26(10):1789-1822).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Dermal Sensitization:

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.

Hoechst AG (1969). Project No. 124/69 (cited in Anon. (1995). Toxikologische Bewertung, 126:1-13).

Type:	**Eye Irritation**
Species/Strain:	Male rabbits/New Zealand White
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. On the day of study initiation, the eyes of 2 rabbits were examined to ensure that no pre-existing corneal or conjunctival injury or irritation was present. The rabbits weighed 2587 and 3875 g on the day of treatment. A 0.01 mL aliquot of fluorobenzene was introduced into the lower conjunctival sac of the left eye of 2 rabbits. The right eyes served as controls. The treated and control eyes of 1 rabbit remained unwashed. Approximately 20 seconds after the test material was administered, both eyes of the remaining rabbit were rinsed for 1 minute with lukewarm water. Approximately 1 and 4 hours and 1, 2, and 3 days after treatment, the rabbits were examined for evidence of eye irritation. The washed eye was also examined 7 days after treatment. At each observation, the treated eyes were examined using illumination and magnification and scored for ocular reactions using the Draize scale. Fluorescein dye was used to evaluate corneal ulceration and irritation starting at the 24-hour observation and at each subsequent observation. Biomicroscopic examinations for corneal injury were conducted at the 24-hour observation period and each subsequent observation.
GLP:	Yes
Test Substance:	Fluorobenzene, purity >99%
Results:	Instillation of the undiluted liquid into the rabbit eye produced no corneal opacity, mild conjunctival redness with slight chemosis, and moderate blood-tinged discharge in the unwashed eye. Washing of the exposed eye produced more severe effects (slight corneal opacity, moderate conjunctival redness with mild chemosis, and copious blood-tinged discharge). The unwashed eye was normal by day 3 post-instillation and the washed eye was normal by day 7. Biomicroscopic and fluorescein staining evaluations were negative at all intervals for corneal injury.

	Fluorobenzene was considered a moderate eye irritant.
Reference:	DuPont Co. (1986). Unpublished Data, Report No. 420-86, "Eye Irritation Test in Rabbits of Fluorobenzene" (August 21).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Eye Irritation:

Data from these additional sources indicate that fluorobenzene is a severe eye irritant. These studies were not chosen for detailed summarization because limited study information was available.

BG Chemie, Toxikol. Bewertung (1993). No. 126 (August) (cited in Bayer, E. and G. Fleischhauer (1993). Chemosphere, 26(10):1789-1822).

Hoechst AG (1969). Project No. 124/69 (cited in Anon. (1995). Toxikologische Bewertung, 126:1-13).

5.2 Repeated Dose Toxicity

Type:	**28-Day Inhalation Study**
Species/Strain:	Rats/Sprague-Dawley CD
Sex/Number:	Male and female/5 per sex per group
Exposure Period:	28 consecutive days
Frequency of Treatment:	6 hours/day
Exposure Levels:	0, 0.4, 1.5, 6.0 mg/L (0, 94, 381, 1585 ppm)
Method:	The procedures used in the test were based on the recommendations of the following guidelines: Method B8, Annex V of the EEC Commission Directive 84/449/EEC and OECD Guideline 412. With the exception of the 6-hour exposure, the rats were housed in groups of 5 by sex. At the start of treatment, male rats weighed 168-212 g and female rats weighed 136-188 g, and were approximately 7-8 weeks old. For atmosphere generation, the test material was contained in glass flasks held in water baths and maintained at 20ºC. Compressed air was supplied by a compressor and was passed through a water trap and respiratory quality filters before it reached the system. The main air supply was fed through a tangential channel at the top of each chamber. A small amount of this air was diverted and bubbled through

the test material before being ducted to the top of the exposure chamber. The control chamber received air only at a similar flow rate to the other chambers. The cylindrical exposure chambers had a volume of ~30 L. The concentration in the chambers was controlled by adjusting the flow rate of the air through the test material.

Each rat was individually restrained in a tapered, polycarbonate tube fitted onto a single tier of the exposure chamber. The animals' positions were rotated daily. Only the noses of the animals were exposed to the test atmosphere.

The temperature and relative humidity inside the exposure chambers were measured daily. Oxygen levels in the chambers were measured weekly. The concentration of the test atmosphere was measured daily by high performance liquid chromatography.

Animals were continuously monitored during the exposure for any changes in appearance, respiratory, and behavioral patterns. Clinical observations were recorded prior to the start of exposure and on removal from the chambers. Body weights, food consumption, and water consumption were measured periodically throughout the study.

Home cage observations, open field, and functional observations were performed on the day prior to the start of dosing and subsequently on days 13 and 14, and 27 and 28 for males and females, respectively.

Hematological and blood chemistry investigations were performed on all animals prior to necropsy on day 29. Animals were not fasted prior to sampling. Urine samples were collected over a period of ~16 hours, by housing the rats in metabolism cages. Animals were maintained under conditions of normal hydration during collection, but did not have access to food. Ten hematology parameters, 15 blood chemistry parameters, and 11 urinalysis parameters were measured or calculated.

At study termination, all rats underwent a gross necropsy. Organ weights relative to brain and body weights were calculated for 9 organs. Representative samples of approximately 35 tissues were taken. All preserved tissue sections from the control and high dose group were

prepared, sectioned, and stained with hematoxylin and eosin for subsequent microscopic examinations. Lungs, any gross lesions, liver, and kidneys from animals in the low and intermediate dose groups were also examined.

Samples of sternum bone and teeth were taken from each animal and pooled per cage group for fluoride analysis.

Data were processed to give group mean values and standard deviations where appropriate. Absolute and relative organ weights, hematological, and blood chemistry data were analyzed by one-way analysis of variance incorporating F- max test for homogeneity of variance. Data showing heterogeneous variances were analyzed using Kruskal Wallis analysis of variance and Mann Whitney U-Test.

GLP: Yes

Test Substance: Fluorobenzene, purity not reported

Results: The mean achieved atmosphere concentrations were 0.37, 1.50, and 6.24 mg/L for the 0.4, 1.5, and 6.0 mg/L groups, respectively.

There were no deaths during the study. Incidents of red/brown staining of the external body surface and wetness of the fur were detected in all groups. The authors note that these were normal findings associated the restraint procedure and they were not indicative of toxicity. Hunched posture and piloerection were observed in the intermediate (1.50 mg/L) and high dose group (6.24 mg/L) animals. The 6.24 mg/L animals began showing these clinical signs on removal from the chamber from day 7 onwards. The incidence increased as the study progressed, and by day 24 all animals in this group were showing the signs both prior to exposure and on removal from the chamber. The 1.50 mg/L animals began showing these signs from day 21 onwards.

There was no evidence of significant neurotoxicity. No adverse effects on body weight gain, food consumption, water consumption, hematology parameters, blood chemistry parameters, or urinalysis were detected. There were no treatment-related macroscopic abnormalities detected at necropsy.

A statistically significant increase in absolute and relative liver weight was detected in the 1.50 and 6.24 mg/L males, and relative liver weight was elevated in the 6.24 mg/L females. Kidney weight, relative to body weight, showed a

statistically significant increase in the 6.24 mg/L males. No treatment-related effects were detected in the 0.37 mg/L groups.

Other effects of treatment were confined to adaptive liver changes (centribolular hepatocyte enlargement) and unique male rat hydrocarbon nephropathy. There was no associated evidence of hepatocellular degeneration and no associated inflammatory response. Although the adaptive liver changes extended into the low dose group (0.37 mg/L), the condition was not considered to be a toxicologically important adverse effect of treatment. In the kidneys, eosinophilic droplets were observed in the proximal tubular epithelium of male rats exposed to 1.50 and 6.24 mg/L. This condition was considered to be related to treatment even though the females were not affected. The authors note that eosinophilic droplet formation in the renal tubular epithelium is a typical consequence of hydrocarbon administration, and is peculiar to the male rat.

The incidence of the above mentioned effects in male rats is presented in the table below:

	Exposure Level (mg/L)			
	0	0.37	1.50	6.24
Kidneys: Eosinophilic droplets proximal tubular epithelium				
Absent	5	5	2	1
Minimal	0	0	3	3
Slight	0	0	0	1
Liver: Centrilobular hepatocyte enlargement				
Absent	5	3	2	1
Minimal	0	2	3	3
Slight	0	0	0	1

A substantial increase in fluoride levels was detected in the pooled teeth and sternum samples from all treatment groups. A clear dose response was apparent.

The NOAEL was considered to be 0.37 mg/L (94 ppm). Furthermore, the slight changes observed in physical

	condition were not indicative of serious damage to the health of the animals. There was, however, evidence of a treatment-related increase in fluoride concentration in bones and teeth of animals from all exposure groups.
Reference:	Safepharm Labs. Ltd. (1993). Project No. 121/194, "28-Day Subacute (nose-only) Inhalation Toxicity Study in the Rat" (January 12) (cited in TSCA Fiche OTS0572061).
Reliability:	High because a scientifically defensible or guideline method 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.

DuPont Co. (1992). Unpublished Data, Haskell Laboratory Report No. 277-92, "Two-Week Inhalation Toxicity Study in Rats with Fluorobenzene" (October 5).

Sellei, C. et al. (1953). Arch. Geschwulstforsch., 5:263-264 (CA49:13451d).

Nemeth, L. et al. (1957). Arch. Geschwulstforsch., 11:101-111 (CA54:3739c).

5.3 Developmental Toxicity

Developmental Study 1

Species/Strain:	Rat/Fischer-344
Sex/Number:	Female/30-33
Route of Administration:	Inhalation
Exposure Period:	Gestation Days 6-15
Frequency of Treatment:	6 hours/day
Exposure Levels:	0, 75, 210, 590 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. After at least a 2-week acclimation period, adult virgin female rats (175-220g) were bred to adult males (1 female to 1 male) of the same strain. Day 0 of gestation was defined as the day sperm was found in a vaginal smear. Rats were housed in wire-bottom cages. Animal rooms were targeted at ~22ºC and relative humidity of ~50%. A 12-hour light/dark photoperiod was employed. Feed and tap water were available *ad libitum* except during inhalation exposures.

Treated and control animals were held in separate rooms.

Exposure concentrations were chosen based on the results of a preliminary study in which test atmospheres of 1000 ppm and greater produced severe toxicosis in pregnant rats.

Inhalation exposures were conducted in 4.3 m^3 Rochester-type stainless steel and glass chambers under dynamic airflow conditions (~800 L air/minute). Temperature and humidity of the chambers was targeted at 21ºC and ~50%, respectively. Temperature and humidity were recorded daily for each chamber. Exposure concentrations were generated by metering the liquid test material at controlled rates into vaporization tubes. Vapors from the tubes were then swept into the chamber inlet ducts with compressed air where they were mixed and diluted with incoming air by turbulence. The compressed air supply to the vaporization tubes was preheated to facilitate complete vaporization of the liquid test material. Chlorobenzene concentrations in the chambers were analyzed throughout the exposure period by infrared spectrophotometry. The control group was exposed to filtered room air.

The animals were observed daily for indications of toxicity, and body weights were recorded on gestation days 6, 9, 12, 16, and 21. Food and water consumption were recorded at 3-day intervals beginning on gestation day 6. Test animals were sacrificed on gestation day 21. The uterine horns were exteriorized and the following data were recorded: number and position of fetuses *in utero*, number of live and dead fetuses, number and position of resorption sites, number of corpora lutea, sex, body weight, and crown-rump length of each fetus, and any gross external alterations. One-half of each litter was examined for evidence of soft tissue alterations. All fetuses were examined for skeletal alterations. Maternal liver weights were obtained during the cesarean section.

Statistical evaluation of the frequency of alterations and of resorptions among litters and the fetal population was conducted by the Wilcoxon test as modified by Haseman, J. K. and D. G. Hoel (1974). J. Statist. Comput. Simul., 3:117-135. Statistical analysis of the percentage of pregnancy and other incidence data were conducted by the Fisher exact probability test. Analyses of other data were made by parametric or nonparametric analysis of variance

followed by either the Dunnett test or the Wilcoxon test, as appropriate.

GLP: No Data

Test Substance: Chlorobenzene, purity 99.982%

Results: Close agreement existed between the mean analytical concentrations and the mean nominal concentrations indicating that test material losses were minimized in the exposure system.

No maternal deaths occurred during the study. No significant effects on general appearance or demeanor were observed during gestation days 6-15. Females in the 590 ppm group gained significantly less weight than controls during gestation days 6-8 and the absolute and relative liver weights on gestation day 21 were significantly increased. No significant effects on body weight gain or liver weights were observed in the 75 or 210 ppm groups.

There was no effect on pregnancy rate. No adverse effects were observed on the mean litter size or incidence of implantations which were undergoing resorption. Actual values for corpora lutea, implantations, number of resorptions, total number of fetuses, total number of live fetuses, mean fetal weight, and sex ratio were not reported.

The incidence of malformations, when considered individually or collectively, was not significantly increased for any concentration group (N=4 in 4 litters in the control, N = 1 in 1 litter at 75 ppm, N = 2 in 2 litters at 210 ppm, N=3 in 3 litters at 590 ppm) With exception of a cleft palate which was observed in a single fetus at 75 ppm, the malformations observed among litters of treated rats were similar to the study control and were at historical incidences for controls. Decreases in the incidence of focal necrosis in the liver were observed in litters from the 210 and 590 ppm groups. This was not considered to be of toxicological importance. See table below for incidence data.

Skeletal examination of the fetuses revealed increased incidences of some minor variants. The incidence of delayed ossification of centra of the cervical vertebrae was significantly increased over controls in the 75 and 590 ppm groups, but not in the 210 ppm group. Other variants noted included a statistically identified increase in the occurrence of bilobed centra of the thoracic vertebrae and a statistical decrease in the incidence of spurs on the fifth cervical

vertebrae in the 590 ppm group. None of the skeletal variants were considered to be indicative of a teratogenic response. See table below for incidence data.

	Concentration (ppm)			
Observation:	0	75	210	590
No. fetuses (No. litters) examined				
External and skeletal exams	241(27)	256(29)	267(27)	258(28)
Soft tissue exams	128(27)	138(29)	141(27)	139(28)
No. fetuses (No. litters) affected				
External alteration:				
Omphalocele*	1(1)	0	0	0
Cleft palate*	0	1(1)	0	0
Soft-tissue alteration:				
Liver, focal necrosis	30(21)	25(18)	22(14)a	19(14)a
Renal agenesis*	1(1)b	0	0	0
Diluted renal pelvis*	0	0	1(1)	2(2)
Right-sided aortic arch*	1(1)b	0	0	0
Microphthalmia *	2(2)b	0	0	1(1)
Anophthalmia*	1(1)	0	1(1)	0
Skeletal alterations:				
Delayed ossification of centra	59(23)	92(27)a	73(23)	103(27)a
Bilobed centra	8(5)	8(7)	3(2)	12(11)a
Cervical spur	25(17)	35(18)	22(14)	13(11)a

* = Considered to be a malformation
a = Statistically different from control
b = One fetus exhibited renal agenesis, right-sided aortic arch, and microphthalmia.

The maternal NOAEL was 210 ppm. Maternal toxicity was evidenced by decreased body weight gain (590 ppm) and increased absolute and relative liver weights (590 ppm).

Significant increases in 2 skeletal variants (delayed ossification of vertebrae centra and bilobed thoracic centra) were indicative of a slight delay in skeletal development

among the fetuses of the dams exposed to 590 ppm (a maternally toxic dose). The fetal NOAEL was 210 ppm. Skeletal variations, indicative of mild fetotoxicity, were observed at doses that also resulted in mild maternal toxicity (590 ppm).

Chlorobenzene was not a unique developmental toxin.

Reference: John, J. A. et al. (1984). Toxicol. Appl. Pharmacol., 76:365-373.

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

Developmental Study 2

Species/Strain: Rabbit/New Zealand White

Sex/Number: Female/30

Route of Administration: Inhalation

Exposure Period: Gestation Days 6-18

Exposure Levels: 0, 75, 210, 590 ppm (first study); 0, 10, 30, 75, 590 ppm (second study)

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

After at least a 2-week acclimation period, female rabbits (3.5-4.5 kg) were artificially inseminated. Day 0 of gestation was defined as the day of artificial insemination. Rabbits were housed in wire-bottom cages. Animal rooms were targeted at ~22ºC and relative humidity of ~50%. A 12-hour light/dark photoperiod was employed. Feed and tap water were available *ad libitum* except during inhalation exposures. Treated and control animals were held in separate rooms.

Exposure concentrations were chosen based on the results of a preliminary study in which test atmospheres of 1000 ppm and greater produced severe toxicosis in pregnant rats.

Inhalation exposures were conducted in 4.3 m^3 Rochester-type stainless steel and glass chambers under dynamic airflow conditions (~800 L air/minute). Temperature and humidity of the chambers was targeted at 21ºC and ~50%, respectively. Temperature and humidity were recorded daily for each chamber. Exposure concentrations were generated by metering the liquid test material at controlled rates into vaporization tubes. Vapors from the tubes were then swept into the chamber inlet ducts

with compressed air where they mixed and diluted with incoming air by turbulence. The compressed air supply to the vaporization tubes was preheated to facilitate complete vaporization of the liquid test material. Chlorobenzene concentrations in the chambers were analyzed throughout the exposure period by infrared spectrophotometry. The control group was exposed to filtered room air.

The animals were observed daily for indications of toxicity and body weights were recorded on gestation days 6, 9, 12, 15, 19, and 29. Test animals were sacrificed on gestation day 29. The uterine horns were exteriorized and the following data were recorded: number and position of fetuses *in utero*, number of live and dead fetuses, number and position of resorption sites, number of corpora lutea, sex, body weight, and crown-rump length of each fetus, and any gross external alterations. One-half of each litter was examined for evidence of soft tissue alterations. All fetuses were examined for skeletal alterations. Maternal liver weights were obtained during the cesarean section.

Statistical evaluation of the frequency of alterations and of resorptions among litters and the fetal population was conducted by the Wilcoxon test as modified by Haseman, J. K. and D. G. Hoel (1974). J. Statist. Comput. Simul., 3:117-135. Statistical analysis of the percentage of pregnancy and other incidence data were conducted by the Fisher exact probability test. Analyses of other data were made by parametric or nonparametric analysis of variance followed by either the Dunnett test or the Wilcoxon test, as appropriate.

Due to the presence of a variety of external and visceral malformations among only the exposed groups, a second study was initiated to further evaluate the test material. The second study was conducted at lower dose levels in the same manner as described above.

GLP: No Data

Test Substance: Chlorobenzene, purity 99.982%

Results: Close agreement existed between the mean analytical concentrations and the mean nominal concentrations indicating that test material losses were minimized in the exposure system.

Study 1: In the first study, there were increased absolute and relative liver weights in rabbits exposed to 210 or 590 ppm. There was no effect of treatment on pregnancy rate, mean

litter size, or the incidence of resorptions. Pregnancy rates for the 0, 75, 210, and 590 ppm groups were 97% (29/30), 93% (28/30), 93% (28/30), and 97% (29/30), respectively. A summary of reproductive outcomes (means/litter unless otherwise noted) is provided in the table below:

	Concentration (ppm)			
Observation	0	75	210	590
Corpora lutea:	NR	NR	NR	NR
Implantation sites/dam:	9±2	9±2	8±2	9±2
% litters with resorptions	41 (11/27)	58 (15/26)	41 (11/27)	41 (12/29)
Fetuses/litter	8±2	8±2	7±2	8±2
Total No. of Live Fetuses:	NR	NR	NR	NR
Mean Fetal Weight (g):	35.67	35.51	38.17	37.58
Sex Ratio:	NR	NR	NR	NR
NR = Not Reported				

Exposure to 75, 210, or 590 ppm resulted in a variety of malformations in all groups at incidences slightly higher than historical controls. The incidence of malformation at these concentrations was 11 (in 6 litters), 8 (in 7 litters), 6 (in 5 litters), and 8 (in 7 litters). Forelimb flexure, the malformation most often observed, occurred more often among controls than among any of the treatment groups, as did malformations of the skeletal system. The latter included hemivertebrae, missing or fused vertebrae, crooked long bones, and a variety of rib malformations. However, there were several cases of external and visceral malformations which were scattered among the exposed groups. A single case of spina bifida and a low incidence of heart anomalies were observed in the 210 and 590 ppm groups, whereas these malformations were not observed among the control group.

The fetus at 210 ppm exhibited a ventricular septal defect, one fetus at 590 ppm also showed a septal defect whereas a second fetus exhibited a persistent truncus arteriosus. In several cases, affected fetuses had more than one malformation. There was no apparent trend for a dose-related increase in the occurrence of any single malformation, with the possible exception of the heart anomalies previously mentioned. The incidence of skeletal alterations were unaffected by exposure, with the exception of an increased incidence of extra ribs in the high dose animals (113 in 26 litters vs. 79 in 24 control litters). This alteration was considered to be a variant in this species. To determine if findings were true effects of treatment, the study was repeated.

Study 2: To ascertain whether the low incidence of head and facial anomalies and heart defects was a true effect of treatment, additional groups were exposed to 0, 10, 30, 75, or 590 ppm. An increase in liver weight of the maternal animals was observed, as was the case in the first study. Pregnancy rates for the 0, 10, 30, 75, and 590 ppm groups were 94% (30/32), 93% (27/29), 97% (29/30), 93% (28/30), and 97% (31/32), respectively. A significant increase in the percentage of implantations undergoing resorption was observed in the 590 ppm group (61% vs 41%). Since the 61% value was within the historical control range for the laboratory (mean 40%, range 19-67%), the apparent increase was not interpreted to be indicative of an embryotoxic effect. The resorption rate was not significantly altered at the lower exposure concentrations and was unaffected in the first study. Fetal body measurements were not adversely affected by treatment. A summary of reproductive outcomes (means/litter unless otherwise noted) is provided in the table below:

	Concentration (ppm)				
Observation	0	10	30	75	590
Corpora lutea:	NR	NR	NR	NR	NR
Implantation sites/dam:	8±3	8±3	9±3	8±2	8±2
% litters with resorptions	41 (11/27)	48 (12/25)	50 (13/26)	50 (14/28)	61 (19/31)
Fetuses/litter	8±3	7±3	7±3	8±3	7±2
Total No. of Live Fetuses:	NR	NR	NR	NR	NR
Mean Fetal Weight (g):	37.44	38.87	37.30	38.49	39.29
Sex Ratio:	NR	NR	NR	NR	NR
NR = Not Reported					

The incidence of malformations from the exposed groups, when considered individually or collectively, was not significantly increased compared to the control group. The incidence of malformations in fetuses from animals treated with 0, 10, 30, 75, or 590 ppm was 14 (in 11 litters), 3 (in 3 litters), 14 (in 8 litters), 7 (in 5 litters), and 14 (in 5 litters). Fetuses with external, soft tissue, and skeletal malformations were observed among all groups including controls. There was no trend for clustering of any anomalies among the exposed groups in the second study. There were 7 fetuses with ablepharia (missing eye lid) in the 590 ppm group; however, this was a single litter effect. This anomaly was not observed in the first study. Heart anomalies were observed in controls as well as some exposed groups and there was no indication of a dose-related effect in the occurrence of heart anomalies (2 in controls and 0-2 in treated). No head or facial abnormalities were observed in any group.

Skeletal examination revealed a significant increase in the

incidence of extra ribs in the 10 ppm group. This alteration is considered a skeletal variant and the increased incidence in the lowest exposure group was not considered to be toxicologically important.

The maternal NOAEL was 75 ppm. Maternal toxicity was evidenced by significant increases in liver weight at 210 and 590 ppm. The fetal NOAEL was > 590 ppm. Therefore, the test material was not teratogenic.

Reference: John, J. A. et al. (1984). Toxicol. Appl. Pharmacol., 76:365-373.

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

Additional References for Developmental Toxicity: None Found.

5.4 Reproductive Toxicity: No Data. Not a required endpoint.

5.5 Genetic Toxicity

Type:	***In vitro* Bacterial Reverse Mutation Assay**
Tester Strain:	*Salmonella typhimurium* strains TA98, TA100, TA1535
Exogenous Metabolic Activation:	With and without Aroclor®-induced rat and hamster liver S9
Exposure Concentrations:	0, 5, 10, 25, 33, 50, 100, 250, 333, 500, 750, 1000, 1666 µg/plate (TA100) 0, 5, 10, 25, 33, 50, 100, 333, 500, 1000, 1666 µg/plate (TA98) 0, 5, 10, 50, 100, 250, 500, 750 µg/plate (TA1535)
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. A preincubation modification of the *Salmonella*/mammalian microsome mutagenicity (Ames test) was conducted. The tests were conducted in 2 laboratories under contract to the NTP. The protocol used and the data evaluation criteria have been previously described (Zeiger, E. et al. (1992). Environ. Mol. Mutagen., 16(Suppl. 18):1-14). Chemicals were tested in a preincubation procedure in strains TA98 and TA100 without metabolic activation and with activation provided by Aroclor-induced rat and hamster liver

	homogenates (S9). If a positive response was seen in 1 of these 2 strains, the strain/metabolic activation combination producing that response was repeated, and no further testing was performed. If no positive responses were seen, the chemical was tested in strain TA1535.
GLP:	Unknown
Test Substance:	Fluorobenzene, purity not reported
Results:	Positive
Remarks:	A positive result with hamster liver activation was observed in strains TA100 and TA1535.
Reference:	Zeiger, E. and B. H. Margolin (2000). Regul. Toxicol. Pharmacol., 32:219-225. NTP (1992). Annual Report for Fiscal Year.
Reliability:	High because a scientifically defensible or guideline method was used.
Type:	***In vitro* Bacterial Reverse Mutation Assay**
Tester Strain:	*Salmonella typhimurium* strains TA98, TA1538, TA1537, TA100, TA1535
Exogenous Metabolic Activation:	With and without rat liver S9
Exposure Concentrations:	0.08, 0.16, 0.32, 0.64, 1.28, 2.56, 5.12, 10.24 µL
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. A pour plate method for quantitative determination following the Ames procedure was conducted. Each concentration of test substance was added to sterile test tubes containing 3-6 x 10^7 bacterial cells and S9 mix or sodium phosphate buffer (pH 7.4). The mixture was preincubated in a shaker water bath at 37ºC for 15 minutes, then added to molten top agar (45ºC). The tubes were mixed well and then the contents were immediately poured onto the surface of a minimal agar plate. Plates were inverted and incubated at 37ºC in the dark for 3 days. Colonies of his+ revertants were counted after incubation. If the chemical induced more than twice the number of revertant colonies compared to the control plate, it was considered mutagenic. All tests were performed in duplicate and repeated at least 3 times separately.

	The test compound was dissolved in dimethyl sulphoxide (DMSO) to obtain appropriate test concentrations. The control plate contained DMSO. The S9 mix contained S9, $MgCl_2$, KCl, glucose 6-posphate, NADH, NADPH, and sodium phosphate. N-Ethyl-N'-nitro-N-nitrosoguanidine, 2-nitrofluorene, 9-aminoacridine, and 2-aminoanthracene were used as positive controls.
GLP:	Unknown
Test Substance:	Fluorobenzene, purity 99%
Results:	Negative
Remarks:	No additional data.
Reference:	Shimizu, M. et al. (1983). Mutat. Res., 116(3-4):217-238.
Reliability:	High because a scientifically defensible or guideline method was used.

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

Type:	***In vivo* Mouse Micronucleus Assay**
Species/Strain:	Mice/NMRI
Sex/Number:	Male and female/42 per sex
Route of Administration:	No Data
Concentrations:	No Data
Method:	The procedure used in the test were based on the recommendations of the following guidelines: OECD Guideline 474. Mice weighed approximately 30 g.
GLP:	Unknown
Test Substance:	Fluorobenzene, purity 99.7%
Results:	Negative
Remarks:	No additional data.
Reference:	Cytotest Cell Research Gmbh & Co. (1991). (cited in Anon. (1995). Toxikologische Bewertung, 126:1-13).
Reliability:	Medium because a guideline method was used; however, limited study information was available.

Additional Reference for *In vivo* Genetic 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.

BG Chemie (1993). Toxikol. Bewertung, No. 126 (August) (cited in Bayer, E. and G. Fleischhauer (1993). Chemosphere, 26(10):1789-1822).