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HEALTH AND ENVIRONMENTAL EFFECTS DOCUMENT FOR 1,1,2-TRICHLORO-1,2,2-TRIFLUOROETHANE

Prepared for

OFFICE OF SOLID WASTE AND
EMERGENCY RESPONSE

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Health and Environmental Effects Documents (HEEDs) are prepared for the Office of Solid Waste and Emergency Response (OSWER). This document series is intended to support listings under the Resource Conservation and Recovery Act (RCRA) as well as to provide health-related limits and goals for emergency and remedial actions under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained for Agency Program Office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched for in this document and the dates searched are included in "Appendix: Literature Searched." Literature search material is current up to 8 months previous to the final draft date listed on the front cover. Final draft document dates (front cover) reflect the date the document is sent to the Program Officer (OSWER).

Several quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Reference doses (RfDs) for chronic and subchronic exposures for both the inhalation and oral exposures. The subchronic or partial lifetime RfD is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval i.e., for an interval that does not constitute a significant portion of the lifespan. This type of exposure estimate has not been extensively used, or rigorously defined as previous risk assessment efforts have focused primarily on lifetime exposure scenarios. Animal data used for subchronic estimates generally reflect exposure durations of 30-90 days. The general methodology for estimating subchronic RfDs is the same as traditionally employed for chronic estimates, except that subchronic data are utilized when available.

In the case of suspected carcinogens, a carcinogenic potency factor, or q_1^* (U.S. EPA, 1980), is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively. An RfD may also be derived for the noncarcinogenic health effects of compounds that are also carcinogenic.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity, and acute mammalian toxicity). Chemical-specific RQs reflect the lowest of these six primary criteria. The methodology for chronic toxicity and cancer based RQs are defined in U.S. EPA, 1984 and 1986a, respectively.

1,1,2-Trichloro-1,2,2-trifluoroethane is a colorless, volatile liquid with a sweet odor (Hawley, 1981; Verschueren, 1983). 1,1,2-Trichloro-1,2,2-trifluoroethane is manufactured by reacting hexachloroethane with hydrogen fluoride in the presence of a catalyst (Smart, 1980). The extent of chlorine atom replacement is controlled by varying the concentration of hydrogen fluoride and the reaction time and temperature. No production data are available. It is used primarily as a solvent (Borchers et al., 1987).

The key factors affecting the fate of 1,1,2-trichloro-1,2,2-trifluoroethane in the environment are its very high vapor pressure, combined with its low solubility in water and chemical inertness. The Henry's Law constant for 1,1,2-trichloro-1,2,2-trifluoroethane calculated from its vapor pressure, 330 mm Hg at 25°C (Parrish, 1983), and water solubility, 170 mg/ℓ (Smart, 1980), is 0.48 atm-m³/mol. Therefore, its volatilization from water will be very rapid, with the volatilization rate limited by its diffusion through water. The half-life of 1,1,2-trichloro-1,2,2-trifluoroethane in a model river 1 m deep, flowing at 1 m/sec, with a wind of 3 m/sec is estimated to be 4.0 hours (Thomas, 1982). Experimental data regarding the adsorption of 1,1,2-trichloro-1,2,2-trifluoroethane to soil, sediment and suspended solids in the water column were not located in the available literature, and a K_{oc} of 426 was estimated from its water solubility (see Section 2.1.). This moderate K_{oc} indicates that adsorption to sediment and particulate matter in the water column would not compete effectively with volatilization from water. Because of 1,1,2-trichloro-1,2,2-trifluoroethane's high vapor pressure, high Henry's Law constant and moderate adsorption to soil, 1,1,2-trichloro-1,2,2-trifluoroethane would also be expected

to volatilize rapidly from both dry and moist soil. Its K_{oc} of 426 would indicate a moderate potential for leaching into groundwater (Swann et al., 1983).

Pertinent data regarding the fate of 1,1,2-trichloro-1,2,2-trifluoroethane in water or soil as a result of microbial or chemical reactions or interaction with sunlight were not located in the available literature cited in Appendix A. Under environmental conditions, alkyl fluorides are likely to hydrolyze too slowly for this pathway to be significant (Mabey and Mill, 1978). Fluorocarbons are highly resistant to attack by oxidizing agents under environmental conditions (Howard et al., 1975). Lacking any UV absorption >290 nm (Hubrich and Stahl, 1980), direct photolysis should not be significant. While no information was found concerning the biodegradation of 1,1,2-trichloro-1,2,2-trifluoroethane, its rapid volatilization would limit, if not preclude, biodegradation (Howard et al., 1975); therefore, it is unlikely that photooxidation, hydrolysis or biodegradation will be significant in water or soil.

Pertinent data regarding the bioconcentration of 1,1,2-trichloro-1,2,2-trifluoroethane in fish and aquatic organisms were not located in the available literature. The estimated BCF, 148 (see Section 2.1.), indicates that 1,1,2-trichloro-1,2,2-trifluoroethane should have a low potential for bioconcentrating in aquatic organisms.

As a result of its high volatility, 1,1,2-trichloro-1,2,2-trifluoroethane will partition into air. 1,1,2-Trichloro-1,2,2-trifluoroethane is extremely stable in the troposphere (Borchers et al., 1987); it will not directly photolyze or react with photochemically produced hydroxyl radicals. It will disperse over the globe and diffuse slowly into the stratosphere, where it will be destroyed by photolysis, by short wave-length UV radiation

and, to a lesser degree, by $O(^1D)$ attack (Borchers et al., 1987). An intensive 7-year study monitored 1,1,2-trichloro-1,2,2-trifluoroethane weekly at seven locations ranging from the arctic to the antarctic regions. The data applied to a global mass balance equation resulted in a half-life of 48.5 years (Khalil and Rasmussen, 1988). Therefore, the 1,1,2-trichloro-1,2,2-trifluoroethane released to air would be expected to accumulate there. Its concentration in the atmosphere, removed from local sources, would be fairly uniform over the world. 1,1,2-Trichloro-1,2,2-trifluoroethane will be removed from the atmosphere by dry and wet deposition and will return to the atmosphere by volatilization.

1,1,2-Trichloro-1,2,2-trifluoroethane is ubiquitous in the atmosphere. It is entirely derived from anthropogenic sources. Its atmospheric lifetime is extremely long and almost all the pollutant released has accumulated in the atmosphere. As with all inert chemicals that are used as a solvent, refrigerant or blowing agent, essentially all of the chemical produced will eventually be released into the atmosphere. A 7-year monitoring study conducted at seven remote sites around the world reported that concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane in the atmosphere doubled in the last 5 years. As of September 1988, the background concentration of 1,1,2-trichloro-1,2,2-trifluoroethane ranged from 40-50 ppt (Khalil and Rasmussen, 1988). This level appears to increase 14% each year (Borchers et al., 1987). The atmospheric concentration of 1,1,2-trichloro-1,2,2-trifluoroethane in urban and industrial areas may be much higher as 1,1,2-trichloro-1,2,2-trifluoroethane is used in consumer products and as an industrial solvent. The median and maximum concentration of 1,1,2-trichloro-1,2,2-trifluoroethane at 15 selected urban and suburban sites in the United States was 170 and 4100 ppt, respectively (Brodzinsky and Singh, 1982).

Of 79 air samples taken from three urban/industrial areas of the United States, 19 were >19 ppb (Pleil et al., 1988).

Many consumer products contain 1,1,2-trichloro-1,2,2-trifluoroethane as a solvent. The use of these products will expose the user and bystanders to 1,1,2-trichloro-1,2,2-trifluoroethane. Exposure will be by inhalation and dermal contact with the vapor; it may also be from skin contact with the liquid solvent. In a 1987 EPA survey of solvents found in household products, 13% of product categories had one or more brands containing 1,1,2-trichloro-1,2,2-trifluoroethane (Weststat and Midwest Research Institute, 1987). The products most likely to contain 1,1,2-trichloro-1,2,2-trifluoroethane were VCR cleaners (71%), video disk cleaners (67%), electric shaver cleaners (25%) and specialized aerosol cleaners (25%). Many of these products were entirely or almost entirely composed of 1,1,2-trichloro-1,2,2-trifluoroethane and were not labeled as to their contents.

Since 1,1,2-trichloro-1,2,2-trifluoroethane is used primarily as a solvent and is highly volatile, there is a potential for exposure in the workplace. Exposure will be both by inhalation and dermal contact with the vapor and liquid solvents. NIOSH (1988) estimated that 134,476 workers, including 50,482 women, are exposed to 1,1,2-trichlorol,2,2-trifluoroethane in the workplace. In other NIOSH surveys, an air sample at one company contained 0.70 ppm of 1,1,2-trichloro-1,2,2-trifluoroethane (Chrostek, 1980) and personal air samples for workers in another plant contained 1,1,2-trichloro-1,2,2-trifluoroethane ranging from 0.2-6.7 ppm (Lee and Parkinson, 1982). A worker died and others were overcome while cleaning out a large vapor degreaser; the concentration of 1,1,2-trichloro-1,2,2-trifluoroethane may have been as high as 374,000 ppm (Anonymous, 1987). A comprehensive

survey of 1,1,2-trichloro-1,2,2-trifluoroethane levels in occupational atmospheres in France reported that 1.5% of the workplaces had 1,1,2-trichloro-1,2,2-trifluoroethane of which 10% were between 500 and the TLV value (1000 ppm), and 3% had levels >1000 ppm (Ensminger, 1988).

Results of surveys indicate that the general population may be exposed to 1,1,2-trichloro-1,2,2-trifluoroethane in drinking water derived from surface and underground sources. 1,1,2-Trichloro-1,2,2-trifluoroethane has been found in drinking water in the Great Lakes basin. In a survey in which nine raw and treated Canadian water supplies were sampled once during each of three seasons, and a tenth plant was sampled on 5 consecutive days in each sampling period (Otson, 1987), 1-3 samples contained $\geq$0.1 µg/ℓ of 1,1,2-trichloro-1,2,2-trifluoroethane in raw and treated water and an additional 1-11 samples contained trace levels of the pollutant. It has also been found in groundwater (1.3 µg/ℓ) near a municipal solid waste landfill (Sabel and Clark, 1984).

1,1,2-Trichloro-1,2,2-trifluoroethane would tend to partition in air, rather than in soil and water, because of its high volatility; therefore, if 1,1,2-trichloro-1,2,2-trifluoroethane is found in food, it would most likely result from air intake by a plant or animal. 1,1,2-Trichloro-1,2,2-trifluoroethane was found in all eight samples of mothers' milk in a pilot study; the levels were not quantified (Pellizzari et al., 1982). The infants of these mothers would therefore be exposed to 1,1,2-trichloro-1,2,2-trifluoroethane in their food.

Pertinent data regarding the environmental toxicity of 1,2,2-trichloro-1,1,2-trifluoroethane were not located in the available literature cited in Appendix A.

Inhalation experiments in humans with ^{36}Cl-labeled 1,1,2-trichloro-1,2,2-trifluoroethane (Morgan et al., 1972) indicate that, although pulmonary absorption of 1,1,2-trichloro-1,2,2-trifluoroethane occurs, the rate of absorption is lower than that of other chlorinated hydrocarbons such as trichloroethane. Dermal absorption has also been shown to occur in humans (Haskell Laboratory, 1968), but data regarding gastric absorption of 1,1,2-trichloro-1,2,2-trifluoroethane are not available.

Inhalation studies with dogs (Trochimowicz et al., 1974) and rats (Carter et al., 1970; Salvolainen and Pfaffli, 1980) indicate that absorbed 1,1,2-trichloro-1,2,2-trifluoroethane is rapidly distributed by the blood to various organs and tissues (including the brain, liver, adrenal, heart and thyroid) and is preferentially deposited into fat.

Upon cessation of exposure, 1,1,2-trichloro-1,2,2-trifluoroethane is rapidly cleared from the body. 1,1,2-Trichloro-1,2,2-trifluoroethane could not be detected in the brain, liver, heart, adrenal or thyroid of rats 24 and 48 hours after termination of a 14-day exposure regime, and 1,1,2-trichloro-1,2,2-trifluoroethane-levels in fat were decreased by ~80 and 99% during the same respective periods (Carter et al., 1970).

Human data indicate that pulmonary exhalation is a significant excretory route for 1,1,2-trichloro-1,2,2-trifluoroethane. 1,1,2-trichloro-1,2,2-trifluoroethane was detected in the exhaled air of humans following dermal administrations of 1,1,2-trichloro-1,2,2-trifluoroethane (Haskell Laboratory, 1968).

Identifications have not been made of *in vivo* metabolites of 1,1,2-trichloro-1,2,2-trifluoroethane in animals or humans. Based upon the demonstration of *in vitro* binding of 1,1,2-trichloro-1,2,2-trifluoroethane to rat

hepatic cytochrome P-450, a suggestion has been made that 1,1,2-trichloro-1,2,2-trifluoroethane may be oxidized by enzymes associated with P-450 (Vainio et al., 1980), but reaction products have not been identified.

Adverse systemic effects in animals caused by long-term exposure (subchronic or chronic) to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane at concentrations $\leq$2000 ppm have not been identified, but the data base is limited to two rat studies (Blohm et al., 1985; Trochimowicz et al., 1988). At concentrations $\geq$10,000 ppm, adverse body weight changes were observed in rats (Trochimowicz et al., 1988). No adverse changes in body, liver or kidney weights, liver biochemistry or urinary catecholamine metabolites were observed in rats exposed to 1,1,2-trichloro-1,2,2-trifluoroethane vapors at concentrations of 200 ppm for 84 days (Blohm et al., 1985). Chronic exposure (24 months) of rats to 1,1,2-trichloro-1,2,2-trifluoroethane vapors at 2000 ppm caused no adverse changes in blood and urine chemical indices, body and organ weights or in the histology of major organs and tissues (Trochimowicz et al., 1988). The same endpoints were unaffected by higher chronic exposure levels, except for body weight gain, which was decreased in both sexes of rats exposed to 20,000 ppm and in female rats exposed to 10,000 ppm.

No adverse effects were identified in shorter-term studies of dogs, guinea pigs and rats exposed to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane at concentrations of 5100 ppm for ~4 weeks (Steinberg et al., 1969). Carter et al. (1970) also reported no adverse effects in inhalation studies of monkeys, dogs, mice and rats continuously exposed to 2000 ppm for 14 days.

The only report of 1,1,2-trichloro-1,2,2-trifluoroethane-induced systemic effects other than body weight changes in animals exposed to low to moderate concentrations comes from a 2-week inhalation study of rats (Vainio

et al., 1980). Light microscopy revealed lipid accumulation and electron microscopy revealed changes in the smooth endoplasmic reticulum in liver cells from rats exposed to concentrations of 1000 or 2000 ppm. Changes were also noted in enzymic activities and reduced glutathione levels in the liver of rats exposed to 2000 ppm (Vainio et al., 1980).

Adverse systemic effects of long-term exposure of humans to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane have not been clearly identified. In a comparison of chronically exposed human workers with unexposed workers (Imbus and Adkins, 1972), no adverse effects were noted in physical examinations of workers who worked an average 2.8 years in rooms in which average concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane were estimated to be 699 ppm. Epidemiological and case-report studies suggest, however, that long-term occupational exposure to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane may cause neuropsychological effects (Rasmussen and Sabroe, 1986; Rasmussen et al., 1988) or neuropathy (Raffi and Violante, 1981). Further information is needed to substantiate the suggestions of the epidemiological and case-report studies.

Acute exposures (<2 hours) to moderate concentrations ($\geq$2500 ppm) of 1,1,2-trichloro-1,2,2-trifluoroethane vapors altered the performance of volunteers in psychophysiological tests (Stopps and McLaughlin, 1967). Exposure of human volunteers to lower concentrations ($\leq$1000 ppm) for a longer duration (6 hours/day, 5 days/week for 2 weeks) did not cause treatment-related changes in performance in psychophysiological tests or in physical examinations (Reinhardt et al., 1971b).

The acute lethality of 1,1,2-trichloro-1,2,2-trifluoroethane is low when administered to animals by either oral or inhalation routes. An oral LD_{50} of 43 g/kg was determined for rats (Michaelson and Huntsman, 1964), but

rabbits appeared more susceptible. Half of a group of eight rabbits died after receiving one to four doses of 5 g/kg/day (Busey et al., 1967). Two-hour LC_{50} values of 95,000, 120,000 and 110,000 ppm were determined for inhalation exposures of mice, guinea pigs and rats, respectively (Desoille et al.,1968).

Acute exposures to moderate to high concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane caused CNS effects in two animal species. Reversible CNS effects were seen in dogs and rats given 6-hour exposures to 11,000-13,000 ppm (Steinberg et al., 1969), and an EC_{50} value of 28,000 ppm was determined for CNS effects in rats given 10-minute exposures (Clark and Tinston, 1982). The mechanistic connection between these CNS effects and the observation of minor biochemical effects in brain preparations from rats exposed to concentrations $\leq$2000 ppm for 2 weeks (Savolainen and Pfaffli, 1980) currently is unclear.

Accidental and voluntary human exposures to high concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane vapors caused sudden death generally thought to be due to cardiac arrest (May and Blotzer, 1984; Reinhardt et al., 1971a, 1973; Zakhari and Aviado, 1982). This hypothesis has received support from animal studies in which acute exposures (5-10 minutes) to moderate to high concentrations caused adverse cardiac effects. Cardiac sensitization to epinephrine-induced arrhythmias was observed in dogs at concentrations $\geq$5000 ppm (Reinhardt et al. 1973) and in anesthetized mice at concentrations $\geq$50,000 ppm (Aviado and Belej, 1974). An EC_{50} for cardiac sensitization of 10,000 ppm was determined for 5-minute exposures of dogs (Clark and Tinston, 1973). In anesthetized rhesus monkeys, 5-minute exposures to concentrations $\geq$25,000 ppm caused arrhythmias, myocardial depressions and tachycardia, without administration of exogenous epinephrine (Belej et al., 1974).

Acute 5-minute exposures to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane at concentrations ≥25,000 ppm altered pulmonary function in rhesus monkeys (Aviado and Smith, 1975). In vitro experiments with excised rat lungs (Alarie et al., 1975) indicated that this effect may involve interaction of 1,1,2-trichloro-1,2,2-trifluoroethane with surfactant on the inner alveolar surface.

Peritinent data regarding the systemic toxicity of chronic or subchronic exposure to orally administered 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

Data regarding the carcinogenicity of 1,1,2-trichloro-1,2,2-trifluoroethane are limited to a 2-year inhalation study in which rats were exposed to concentrations of 0, 2000, 10,000 or 20,000 ppm (Trochimowicz et al., 1988). No treatment-related increases in tumor incidences were reported. 1,1,2-trichloro-1,2,2-trifluoroethane was not mutagenic in assays for dominant lethal mutations in mice (Epstein et al., 1972) nor in assays for reverse mutations in Salmonella typhimurium (Simmon et al., 1977; Longstaff, 1988; Mahurin and Bernstein, 1988).

The U.S. EPA (1983) summarized three unpublished studies (Ward, 1983; Hazelton Laboratories, 1967a,b), which contain the only available data regarding the teratogenicity and other reproductive effects of 1,1,2-trichloro-1,2,2-trifluoroethane. The summarized data indicate that 1,1,2-trichloro-1,2,2-trifluoroethane was not teratogenic in rats exposed to air containing ≤25,000 ppm on days 6-15 of gestation (Ward, 1983), but conclusions were precluded in rabbit studies (Hazelton Laboratories, 1967a,b) because of marked maternal toxicity and inadequate numbers of animals.

1,1,2-Trichloro-1,2,2-trifluoroethane is assigned to EPA Group D (not classifiable as to carcinogenicity to humans) because no human data are

available and negative data are available for only one animal species -- rats (Trochimowicz et al., 1988). Therefore, neither quantitative estimates of cancer risks (q_1^*s) nor a cancer-based RQ were derived.

An RfD of 27 mg/m³ for chronic inhalation exposure was derived from a LOAEL of 2000 ppm, 6 hours/day, 5 days/week for decreased body weight in female rats relative to controls in the 24-month study by Trochimowicz et al. (1988). Confidence in the inhalation RfD is medium reflecting the high quality of the key study but the inadequacy of supporting information regarding the reproductive and teratogenic effects of inhaled 1,1,2-trichloro-1,2,2-trifluoroethane. Because of a limited data base for subchronic inhalation exposure, the chronic inhalation RfD was also adopted as the RfD for subchronic exposure.

An oral RfD of 3 mg/kg/day for either subchronic or chronic oral exposure was derived from the chronic inhalation RfD, because of a lack of data regarding oral exposures to 1,1,2-trichloro-1,2,2-trifluoroethane. Confidence in the oral RfD is low because of the uncertainty of route-to-route extrapolation. An RQ of 5000 based on chronic inhalation toxicity was also derived for decreased body weights in female rats (Trochimowicz et al., 1988).

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LIST OF ABBREVIATIONS

AEL	Adverse effects level
BCF	Bioconcentration factor
BUN	Blood urea nitrogen
CAS	Chemical Abstract Service
CNS	Central nervous system
CS	Composite score
CT	Computerized tomography
EC_{50}	Concentration effective to 50% of recipients (and all other subscripted concentration levels)
FEL	Frank effect level
HEC	Human equivalent concentration
K_{oc}	Soil sorption coefficient standardized with respect to organic carbons
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients (and all other subscripted dose levels)
LD_{50}	Dose lethal to 50% of recipients
LOAEL	Lowest-observed-adverse-effect level
NADPH	Nicotinamide adenine dinucleotide phosphate (reduced form)
NOEL	No-observed-effect level
ppb	Parts per billion
ppm	Parts per million
ppt	Parts per trillion
RfD	Reference dose
RNA	Ribonucleic acid
RV_d	Dose-rating value
RV_e	Effect-rating value
STEL	Short-term exposure level
TLV	Threshold limit value
TWA	Time-weighted average
UDP	Uridine diphosphate
UV	Ultraviolet

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

1,1,2-Trichloro-1,2,2-trifluoroethane is the chemical name of the compound commonly known as Freon 113. Other synonyms and trade names for this chemical are 1,1,2-trichlorotrifluoroethane, Freon TF, Genetron 113, R113, Uncon Fluorocarbon 113, Arklone P, Frigen A, TR-T and trichlorotrifluoroethane (Chemline, 1989). The molecular structure, molecular weight, empirical formula and CAS Registry number for 1,1,2-trichloro-1,2,2-trifluoroethane are as follows:

Molecular structure: $CCl_2F\text{-}CClF_2$

Molecular weight: 187.38

Empirical formula: $C_2Cl_3F_3$

CAS Registry number: 76-13-1

1.2. PHYSICAL AND CHEMICAL PROPERTIES

1,1,2-Trichloro-1,2,2-trifluoroethane is a colorless, volatile liquid (Hawley, 1981). It has a sweet odor and is noncombustible (Hawley, 1981; Verschueren, 1983). Selected physical properties are listed below:

Boiling point:	47.57°C	Smart, 1980
	46°C	Parrish, 1983
Melting point:	-35°C	Smart, 1980
	-36°C	Parrish, 1983
Density (g/mℓ) (25°C):	1.565	Smart, 1980
	1.56354	Parrish, 1983
Vapor pressure		
at 20°C:	270 mm Hg	Verschueren, 1983
at 25°C:	330 mm Hg	Parrish, 1983
at 30°C:	400 mm Hg	Verschueren, 1983
Vapor density:	6.47	Verschueren, 1983
Flash point:	not available	

Water solubility (25°C):	0.017 wt % 0.01664 wt %	Smart, 1980 Horvath, 1982
Log K_{OW}:	3.16 3.29 (estimated)	McDuffie, 1981 U.S. EPA, 1987
Air odor threshold:	45 ppm	Amoore and Hautala, 1983
Air conversion factor:	1 mg/m³ = 0.13 ppm 1 ppm = 7.69 mg/m³	

1.3. PRODUCTION DATA

1,1,2-Trichloro-1,2,2-trifluoroethane is manufactured by reacting hexachloroethane with hydrogen fluoride in the presence of a chromium oxide or halide, ferric chloride or thorium tetrafluoride catalyst (Smart, 1980). In this process, the chlorine atoms are successively replaced by fluorine atoms; the extent of replacement is controlled by varying the concentration of hydrogen fluoride, the reaction time and temperature. The companies currently producing 1,1,2-trichloro-1,2,2-trifluoroethane in the United States are shown in Table 1-1. No production data are available. The amount of 1,1,2-trichloro-1,2,2-trifluoroethane emitted into the atmosphere annually has increased sharply since it was first used commercially around 1960; the annual emission leveled off in 1980 and was estimated as 97 kiloton/year (88 million kg/year) during 1980-1983 (Borchers et al., 1987). This results in an annual increase of ~15% per year. By applying the results of 7 years of monitoring data of 1,1,2-trichloro-1,2,2-trifluoroethane to a mass balance model, another investigator estimated that emissions over the time period September 1982-September 1988 were 100 million kg/year and were increasing exponentially at 5% per year (Khalil and Rasmussen, 1988).

TABLE 1-1

Manufacturers of 1,1,2-Trichloro-1,2,2-trifluoroethane in the United States as of January, 1987*

Manufacturer	Location
Allied Signal, Inc.	Baton Rouge, LA
E.I. du Pont de Nemours & Co., Inc.	Corpus Christi, TX Montague, MI
Penwalt Corporation	NA

*Source: SRI, 1988; USITC, 1988

NA = Not available

1.4. USE DATA

Since 1960, 1,1,2-trichloro-1,2,2-trifluoroethane has been used primarily as a solvent, although it can also be used as a blowing agent and refrigerant (Borchers et al., 1987). Its use as a dry cleaning agent is limited because of its expense (Parrish, 1983).

1.5. SUMMARY

1,1,2-Trichloro-1,2,2-trifluoroethane is a colorless, volatile liquid with a sweet odor (Hawley, 1981; Verschueren, 1983). 1,1,2-Trichloro-1,2,2-trifluoroethane is manufactured by reacting hexachloroethane with hydrogen fluoride in the presence of a catalyst (Smart, 1980). The extent of chlorine atom replacement is controlled by varying the concentration of hydrogen fluoride and the reaction time and temperature. No production data are available. It is used primarily as a solvent (Borchers et al., 1987).

2. ENVIRONMENTAL FATE AND TRANSPORT

2.1. AIR

1,1,2-Trichloro-1,2,2-trifluoroethane is extremely stable in the troposphere (Borchers et al., 1987). It does not adsorb UV radiation >290 nm (Hubrich and Stahl, 1980) and it will not directly photolyze (Makide et al., 1979). It does not react with photochemically produced hydroxyl radicals (Atkinson, 1985). It will therefore disperse over the globe and diffuse slowly into the stratosphere where it will be photolyzed by the short wave length UV radiation and $O(^1D)$ attack (Borchers et al., 1987). Over 80% of the 1,1,2-trichloro-1,2,2-trifluoroethane in the stratosphere is estimated to be removed by photolysis (Chou et al., 1978). Chlorine radicals generated in the photolysis are responsible for the destruction of the stratospheric ozone layer. An intensive 7-year study monitored 1,1,2-trichloro-1,2,2-trifluoroethane weekly at seven locations ranging from the arctic to the antarctic regions. The data applied to a global mass balance equation resulted in a half-life of 48.5 years (Khalil and Rasmussen, 1988). Previous estimated half-lives for 1,1,2-trichloro-1,2,2-trifluoroethane in the atmosphere range from 44-85 years (Chou et al., 1978); therefore, the 1,1,2-trichloro-1,2,2-trifluoroethane released to the atmosphere would be expected to accumulate and its concentration in air would be fairly uniform over the globe. Its concentration will decrease sharply with altitude as it reaches the stratosphere (Borchers et al., 1987; Fabian, 1986).

1,1,2-Trichloro-1,2,2-trifluoroethane will also be removed from the atmosphere by dry and wet deposition; however, the 1,1,2-trichloro-1,2,2-trifluoroethane removed in this manner will volatilize back into the atmosphere.

2.2. WATER

The fate of 1,1,2-trichloro-1,2,2-trifluoroethane in water depends on its transport, not its degradation. 1,1,2-Trichloro-1,2,2-trifluoroethane has a very high vapor pressure, 330 mm Hg at 25°C (Parrish, 1983), and low solubility in water, 170 mg/ℓ (Smart, 1980). The Henry's Law constant for 1,1,2-trichloro-1,2,2-trifluoroethane calculated from its vapor pressure and water solubility is 0.48 atm-m³/mol; therefore, its volatilization from water will be rapid. The volatilization rate will be controlled by its diffusion through water. The half-life of 1,1,2-trichloro-1,2,2-trifluoroethane in a model river 1 m deep, flowing at 1 m/sec, with a wind of 3 m/sec is estimated to be 4.0 hours (Thomas, 1982). Experimental data regarding the adsorption of 1,1,2-trichloro-1,2,2-trifluoroethane to sediment and suspended solids in the water column were not found in the available literature. Based on its water solubility, 170 mg/ℓ at 25°C (Smart, 1980), a K_{oc} of 426 was estimated using a regression equation based on chlorinated hydrocarbons, log K_{oc} = -0.557 log S + 4.277 (S in μmol/ℓ) (Chiou et al., 1979; Lyman, 1982). Therefore, 1,1,2-trichloro-1,2,2-trifluoroethane would probably adsorb moderately to sediment and suspended solids in the water column.

Fluorocarbons are chemically inert under environmental conditions (Council on Environmental Quality, 1975). Under environmental conditions, alkyl fluorides are likely to hydrolyze too slowly for this pathway to be significant (Mabey and Mill, 1978). The reactivity of fluorinated alkanes decreases as the fluorine content of the molecule increases (Smart, 1980). The rate of hydrolysis of 1,1,2-trichloro-1,2,2-trifluoroethane is very low, (<0.005 g/ℓ-yr) at 30°C. (Du Pont de Nemours Co., 1980). Fluorocarbons are highly resistant to attack by oxidizing agents under environmental

conditions (Howard et al., 1975). Lacking any UV absorption >290 nm (Hubrich and Stahl, 1980), direct photolysis should not be significant. Its inertness to photooxidation is illustrated by its use as a solvent for determining the photooxidation of organic compounds by hydroxyl radicals (Dilling et al., 1988). While no information was found concerning the biodegradation of 1,1,2-trichloro-1,2,2-trifluoroethane, its rapid volatilization would limit, if not preclude, biodegradation (Howard et al., 1975). No experimental data were found regarding the bioconcentration of 1,1,2-trichloro-1,2,2-trifluoroethane in fish and aquatic organics. No reports concerning its detection in fish were located. Based on its log K_{ow} determined by high pressure liquid chromatography to be 3.16 (McDuffie, 1981), a BCF of 148 may be estimated from the equation log BCF = 0.76 log K_{ow} 0.23 (Bysshe, 1982). This indicates that 1,1,2-trichloro-1,2,2-trifluoroethane should have a fairly low potential for bioconcentrating in aquatic organisms.

2.3. SOIL

Pertinent data regarding the adsorption of 1,1,2-trichloro-1,2,2-trifluoroethane to soil were not located in the literature cited in Appendix A. Its estimated K_{oc} of 426 (see Section 2.1.) would indicate a medium potential for leaching into groundwater (Swann et al., 1983). To ascertain its leaching potential from landfills, columns of domestic waste contaminated with 1,1,2-trichloro-1,2,2-trifluoroethane and other halogenated organic solvents were eluted with water (Jones et al., 1978). The concentration of the 1,1,2-trichloro-1,2,2-trifluoroethane was at least 2 orders of magnitude lower than in the solid waste, suggesting that evaporation and possibly adsorption effectively reduces the solvent leached from landfills.

It has been reported in contaminated groundwater near a municipal solid waste landfill (Sabel and Clark, 1984). Because of its very high vapor pressure, very high Henry's Law constant and moderate adsorption to soil, 1,1,2-trichloro-1,2,2-trifluoroethane would be expected to volatilize rapidly from both dry and moist soil.

Pertinent data regarding the fate of 1,1,2-trichloro-1,2,2-trifluoroethane in soil as a result of microbial or chemical reactions or interaction with sunlight were not located in the available literature cited in Appendix A. Based on its very high volatility and general unreactivity, it is unlikely that photooxidation, hydrolysis or biodegradation will be significant in soil.

2.4. SUMMARY

The key factors affecting the fate of 1,1,2-trichloro-1,2,2-trifluoroethane in the environment are its very high vapor pressure, combined with its low solubility in water and chemical inertness. The Henry's Law constant for 1,1,2-trichloro-1,2,2-trifluoroethane calculated from its vapor pressure, 330 mm Hg at 25°C (Parrish, 1983), and water solubility, 170 mg/ℓ (Smart, 1980), is 0.48 atm-m³/mol. Therefore, its volatilization from water will be very rapid, with the volatilization rate limited by its diffusion through water. The half-life of 1,1,2-trichloro-1,2,2-trifluoroethane in a model river 1 m deep, flowing at 1 m/sec, with a wind of 3 m/sec is estimated to be 4.0 hours (Thomas, 1982). Experimental data regarding the adsorption of 1,1,2-trichloro-1,2,2-trifluoroethane to soil, sediment and suspended solids in the water column were not located in the available literature, and a K_{oc} of 426 was estimated from its water solubility (see Section 2.1.). This moderate K_{oc} indicates that adsorption to sediment and particulate matter in the water column would not compete effectively

with volatilization from water. Because of 1,1,2-trichloro-1,2,2-trifluoroethane's high vapor pressure, high Henry's Law constant and moderate adsorption to soil, 1,1,2-trichloro-1,2,2-trifluoroethane would also be expected to volatilize rapidly from both dry and moist soil. Its K_{oc} of 426 would indicate a moderate potential for leaching into groundwater (Swann et al., 1983).

Pertinent data regarding the fate of 1,1,2-trichloro-1,2,2-trifluoroethane in water or soil as a result of microbial or chemical reactions or interaction with sunlight were not located in the available literature cited in Appendix A. Under environmental conditions, alkyl fluorides are likely to hydrolyze too slowly for this pathway to be significant (Mabey and Mill, 1978). Fluorocarbons are highly resistant to attack by oxidizing agents under environmental conditions (Howard et al., 1975). Lacking any UV absorption >290 nm (Hubrich and Stahl, 1980), direct photolysis should not be significant. While no information was found concerning the biodegradation of 1,1,2-trichloro-1,2,2-trifluoroethane, its rapid volatilization would limit, if not preclude, biodegradation (Howard et al., 1975); therefore, it is unlikely that photooxidation, hydrolysis or biodegradation will be significant in water or soil.

Pertinent data regarding the bioconcentration of 1,1,2-trichloro-1,2,2-trifluoroethane in fish and aquatic organisms were not located in the available literature. The estimated BCF, 148 (see Section 2.1.), indicates that 1,1,2-trichloro-1,2,2-trifluoroethane should have a low potential for bioconcentrating in aquatic organisms.

As a result of its high volatility, 1,1,2-trichloro-1,2,2-trifluoroethane will partition into air. 1,1,2-Trichloro-1,2,2-trifluoroethane is extremely stable in the troposphere (Borchers et al., 1987); it will not directly photolyze or react with photochemically produced hydroxyl radicals.

It will disperse over the globe and diffuse slowly into the stratosphere, where it will be destroyed by photolysis by short wave length UV radiation and, to a lesser degree, by $O(^1D)$ attack (Borchers et al., 1987). An intensive 7-year study monitored 1,1,2-trichloro-1,2,2-trifluoroethane weekly at seven locations ranging from the arctic to the antarctic regions. The data applied to a global mass balance equation resulted in a half-life of 48.5 years (Khalil and Rasmussen, 1988). Therefore, the 1,1,2-trichloro-1,2,2-trifluoroethane released to air would be expected to accumulate there. Its concentration in the atmosphere, removed from local sources, would be fairly uniform over the world. 1,1,2-Trichloro-1,2,2-trifluoroethane will be removed from the atmosphere by dry and wet deposition and will return to the atmosphere by volatilization.

3. EXPOSURE

3.1. WATER

A study was conducted to determine the levels of selected volatile pollutants in raw and treated drinking water along a portion of the Great Lakes basin. Nine raw and treated Canadian water supplies were sampled once during summer, 1982; winter, 1983; and spring, 1983. A tenth plant was sampled on 5 consecutive days in each period (Otson, 1987). In all time periods, 1-3 of the 14 samples contained $\geq$0.1 µg/ℓ of 1,1,2-trichloro-1,2,2-trifluoroethane in raw and treated water. An additional 1-11 samples contained trace levels of the pollutant. In all cases, the mean value of 1,1,2-trichloro-1,2,2-trifluoroethane was <0.1 µg/ℓ. Another study of the Great Lakes basin found 1,1,2-trichloro-1,2,2-trifluoroethane in water samples taken from the Niagara River (Lake Ontario basin) and Cayuhoga River (Lake Erie Basin), but not the western section of Lake Ontario (Great Lakes Water Quality Board, 1983). No concentration levels were reported. In a survey of leaching from municipal solid waste landfills in Minnesota, 1,1,2-trichloro-1,2,2-trifluoroethane was found in 1 of 13 groundwater samples at a concentration of 1.3 µg/ℓ (Sabel and Clark, 1984). 1,1,2-Trichloro-1,2,2-trifluoroethane has been found at 8 of 1177 hazardous waste sites listed on the National Priorities List (MITRE, 1988). It could leach from these landfills into groundwater. These studies indicate that the general population may be exposed to 1,1,2-trichloro-1,2,2-trifluoroethane in water.

3.2. FOOD

1,1,2-Trichloro-1,2,2-trifluoroethane would tend to partition in air, rather than soil and water, because of its high volatility; therefore, if 1,1,2-trichloro-1,2,2-trifluoroethane occurs in food, it would most likely

result from air intake by a plant or animal. A pilot study of volatile organic chemicals in mothers' milk found that all eight samples of milk obtained from women in four urban areas in the United States contained 1,1,2-trichloro-1,2,2-trifluoroethane; the levels were not quantified (Pellizzari, 1982). The infants of these mothers would therefore be exposed to 1,1,2-trichloro-1,2,2-trifluoroethane in their food. No other data were located in the available literature in which 1,1,2-trichloro-1,2,2-trifluoroethane was found in food.

3.3. INHALATION

1,1,2-Trichloro-1,2,2-trifluoroethane found in the atmosphere originates entirely from anthropogenic sources. Since its atmospheric lifetime is extremely long, almost all the pollutant released has accumulated in the atmosphere. A 7-year monitoring study conducted at seven remote sites around the world reported that the concentration of 1,1,2-trichloro-1,2,2-trifluoroethane in the atmosphere has doubled in the last 5 years. As of September 1988, the concentration ranged from 40-50 ppt (Khalil and Rasmussen, 1988). An analysis of data collected in 2 years of monitoring at Barrows, AK, indicates that the level of 1,1,2-trichloro-1,2,2-trifluoroethane in the atmosphere is increasing 14% each year (Borchers et al., 1987); therefore, we are exposed to 1,1,2-trichloro-1,2,2-trifluoroethane in air all over the world.

The median concentration of 1,1,2-trichloro-1,2,2-trifluoroethane at six selected rural and remote sites and 15 selected urban and suburban sites in the United States was 31 and 170 ppt, respectively (Brodzinsky and Singh, 1982). The maximum concentration reported in urban/suburban sites was 4100 ppt. The data summarized in this survey came from a number of studies and spanned many years. Assuming an air concentration of 31 and 170 ppt in

rural and urban areas and an air intake of 20 m^3, a person would breathe in 4.8 and 26 µg of 1,1,2-trichloro-1,2,2-trifluoroethane daily. Of 79 air samples taken from the Kanawana Valley, WV (March, 1986), Los Angeles, CA (August, 1986) and Houston, TX (August, 1986 to March, 1987), 60 were <1 ppb (mean value of 0.27 ppb) and 19 were >1 ppb (mean 6.69 ppb) (Pleil et al., 1988).

In 1987, the results of an EPA survey of solvents found in household products was published (Weststat, Inc. and Midwest Research Institute, 1987). In the survey, various brands of products in 82 product categories were analyzed. Of these, 67 contained solvents and 11 of these product categories had one or more brands containing 1,1,2-trichloro-1,2,2-trifluoroethane. The products most likely to contain 1,1,2-trichloro-1,2,2-trifluoroethane were VCR cleaners (71%), video disk cleaners (67%), electric shaver cleaners (25%) and specialized aerosol cleaners (25%). Many of these products were entirely or almost entirely composed of 1,1,2-trichloro-1,2,2-trifluoroethane and were not labeled as to their contents. Any volatile solvent will expose people in the vicinity to the compound unless extreme precautions are taken. No concentration levels of 1,1,2-trichloro-1,2,2-trifluoroethane in homes where products containing 1,1,2-trichloro-1,2,2-trifluoroethane were found in the available literature.

Since 1,1,2-trichloro-1,2,2-trifluoroethane is used primarily as a solvent and is highly volatile, there is a great potential for exposure in the workplace. According to statistical estimates, 134,476 workers, including 50,482 women, are exposed to 1,1,2-trichloro-1,2,2-trifluoroethane in the workplace (NIOSH, 1988). The National Occupational Exposure Survey (NOES) was based on field surveys of 4490 facilities and designed as a nationwide survey based on a statistical sample of virtually all workplace

environments in the United States where eight or more persons are employed in all standard industrial codes except mining and agriculture. A German survey conducted from 1978-1982 of organic solvents present in 275 products commonly found in the workplace reported that 1.5% of these products contained 1,1,2-trichloro-1,2,2-trifluoroethane (Lehmann et al., 1986).

1,1,2-Trichloro-1,2,2-trifluoroethane was monitored in several health hazard evaluations conducted by NIOSH. An air sample at the Fischer and Porter Company in Warminster, PA, contained 5.4 mg/m³ (0.70 ppm) of 1,1,2-trichloro-1,2,2-trifluoroethane (Chrostek, 1980). 1,1,2-trichloro-1,2,2-trifluoroethane was used as a degreaser in the plant. Personal air samples for workers in a plant in Pennsylvania that manufactured automobile speakers ranged from 0.2-6.7 ppm (Lee and Parkinson, 1982). A worker died and others were overcome while cleaning out a large vapor degreaser at a chemical fuel plant (Anonymous, 1987). The degreasing tank had been drained of all the solvent except for 1 gallon. The concentration of 1,1,2-trichloro-1,2,2-trifluoroethane may have been as high as 374,000 ppm.

Ensminger (1988) sampled organic solvents in 543 workplaces in France from 1981-1985. Of the 2013 samples, 30 contained 1,1,2-trichloro-1,2,2-trifluoroethane as follows: 43.5% were <10% of the TLV, 43.5% were >10% and <50% of the TLV, 10% were >50% and <100% of the TLV and 3% were >100% of the TLV. The ACGIH TLV is 1000 ppm (Lee and Parkinson, 1982).

3.4. DERMAL

Consumers and workers who use solvents containing 1,1,2-trichloro-1,2,2-trifluoroethane may be dermally exposed to this chemical. Exposure may be from direct skin contact with the liquid solvent or from contact with vapors and aerosols.

3.5. SUMMARY

1,1,2-Trichloro-1,2,2-trifluoroethane is ubiquitous in the atmosphere. It is entirely derived from anthropogenic sources. Its atmospheric lifetime is extremely long and almost all the pollutant released has accumulated in the atmosphere. As with all inert chemicals that are used as a solvent, refrigerant or blowing agent, essentially all of the chemical produced will eventually be released into the atmosphere. A 7-year monitoring study conducted at seven remote sites around the world reported that concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane in the atmosphere doubled in the last 5 years. As of September 1988, the background concentration of 1,1,2-trichloro-1,2,2-trifluoroethane ranged from 40-50 ppt (Khalil and Rasmussen, 1988). This level appears to increase 14% each year (Borchers et al., 1987). The atmospheric concentration of 1,1,2-trichloro-1,2,2-trifluoroethane in urban and industrial areas may be much higher as 1,1,2-trichloro-1,2,2-trifluoroethane is used in consumer products and as an industrial solvent. The median and maximum concentration of 1,1,2-trichloro-1,2,2-trifluoroethane at 15 selected urban and suburban sites in the United States was 170 and 4100 ppt, respectively (Brodzinsky and Singh, 1982). Of 79 air samples taken from three urban/industrial areas of the United States, 19 were >19 ppb (Pleil et al., 1988).

Many consumer products contain 1,1,2-trichloro-1,2,2-trifluoroethane as a solvent. The use of these products will expose the user and people nearby to 1,1,2-trichloro-1,2,2-trifluoroethane. Exposure will be by inhalation and dermal contact with the vapor; it may also be from skin contact with the liquid solvent. In a 1987 EPA survey of solvents found in household products, 13% of product categories had one or more brands containing 1,1,2-trichloro-1,2,2-trifluoroethane (Weststat, Inc. and Midwest Research

Institute, 1987). The products most likely to contain 1,1,2-trichloro-1,2,2-trifluoroethane were VCR cleaners (71%), video disk cleaners (67%), electric shaver cleaners (25%) and specialized aerosol cleaners (25%). Many of these products were entirely or almost entirely composed of 1,1,2-trichloro-1,2,2-trifluoroethane and not labeled as to their contents.

Since 1,1,2-trichloro-1,2,2-trifluoroethane is used primarily as a solvent and is highly volatile, there is a potential for exposure in the workplace. Exposure will be both by inhalation and dermal contact with the vapor and liquid solvents. NIOSH (1988) estimated that 134,476 workers, including 50,482 women, are exposed to 1,1,2-trichloro-1,2,2-trifluoroethane in the workplace. In other NIOSH surveys, an air sample at one company contained 0.70 ppm of 1,1,2-trichloro-1,2,2-trifluoroethane (Chrostek, 1980) and personal air samples for workers in another plant contained 1,1,2-trichloro-1,2,2-trifluoroethane ranging from 0.2-6.7 ppm (Lee and Parkinson, 1982). A worker died and others were overcome while cleaning out a large vapor degreaser; the concentration of 1,1,2-trichloro-1,2,2-trifluoroethane may have been as high as 374,000 ppm (Anonymous, 1987). A comprehensive survey of 1,1,2-trichloro-1,2,2-trifluoroethane levels in occupational atmospheres in France reported that 1.5% of the workplaces had 1,1,2-trichloro-1,2,2-trifluoroethane of which 10% were between 500 and the TLV value (1000 ppm) and 3% had levels >1000 ppm (Ensminger, 1988).

Results of surveys indicate that the general population may be exposed to 1,1,2-trichloro-1,2,2-trifluoroethane in drinking water derived from surface and underground sources. 1,1,2-Trichloro-1,2,2-trifluoroethane has been found in drinking water in the Great Lakes basin. In a survey in which nine raw and treated Canadian water supplies were sampled once during each of three seasons, and a tenth plant was sampled on 5 consecutive days in

each sampling period (Otson, 1987), 1-3 samples contained ≥0.1 µg/ℓ of 1,1,2-trichloro-1,2,2-trifluoroethane in raw and treated water and an additional 1-11 samples contained trace levels of the pollutant. It has also been found in groundwater (1.3 µg/ℓ) near a municipal solid waste landfill (Sabel and Clark, 1984).

1,1,2-Trichloro-1,2,2-trifluoroethane would tend to partition in air, rather than in soil and water, because of its high volatility; therefore, if 1,1,2-trichloro-1,2,2-trifluoroethane is found in food, it would most likely result from air intake by a plant or animal. 1,1,2-Trichloro-1,2,2-trifluoroethane was found in all eight samples of mothers' milk in a pilot study; the levels were not quantified (Pellizzari, 1982). The infants of these mothers would therefore be exposed to 1,1,2-trichloro-1,2,2-trifluoroethane in their food.

4. ENVIRONMENTAL TOXICOLOGY

4.1. AQUATIC TOXICOLOGY

4.1.1. Acute Toxic Effects on Fauna. Pertinent data regarding the effects of acute exposure of aquatic fauna to 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature in Appendix A.

4.1.2. Chronic Effects on Fauna.

4.1.2.1. TOXICITY -- Pertinent data regarding the effects of chronic exposure of aquatic fauna to 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

4.1.2.2. BIOACCUMULATION/BIOCONCENTRATION -- Pertinent data regarding the bioaccumulation/bioconcentration potential of 1,1,2-trichloro-1,2,2-trifluoroethane in aquatic fauna were not located in the available literature cited in Appendix A.

4.1.3. Effects on Flora.

4.1.3.1. TOXICITY -- Pertinent data regarding the toxic effects of exposure of aquatic flora to 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

4.1.3.2. BIOCONCENTRATION -- Pertinent data regarding the bioconcentration potential of 1,1,2-trichloro-1,2,2-trifluoroethane in aquatic flora were not located in the available literature cited in Appendix A.

4.1.4. Effects on Bacteria. Pertinent data regarding the effects of exposure of aquatic bacteria to 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

4.2. TERRESTRIAL TOXICOLOGY

4.2.1. Effects on Fauna. Pertinent data regarding the effects of exposure of terrestrial fauna to 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

4.2.2. Effects on Flora. Pertinent data regarding the effects of exposure of terrestrial flora to 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

4.3. FIELD STUDIES

Pertinent data regarding the effects of 1,1,2-trichloro-1,2,2-trifluoroethane on flora and fauna in the field were not located in the available literature cited in Appendix A.

4.4. AQUATIC RISK ASSESSMENT

No data were available regarding the effects of exposure of aquatic fauna and flora to 1,1,2-trichloro-1,2,2-trifluoroethane, precluding the development of freshwater and saltwater criteria by the method of U.S. EPA/OWRS (1986).

4.5. SUMMARY

Pertinent data regarding the environmental toxicity of 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

5. PHARMACOKINETICS

5.1. ABSORPTION

Experiments with humans (Morgan et al., 1972), dogs (Trochimowicz et al., 1974) and rats (Andersen et al., 1980) indicate that although vapors of 1,1,2-trichloro-1,2,2-trifluoroethane are poorly absorbed by the pulmonary system, measurable absorption occurs.

Morgan et al. (1972) administered vapors of ^{36}Cl-labeled 1,1,2-trichloro-1,2,2-trifluoroethane to volunteers in single breaths and measured the change in concentration of radioactivity in alveolar air with breath-holding time and the elimination of radioactivity in breath during normal breathing over 30 minutes. The concentration of radiolabel in alveolar air was ~70-80% of the initial concentration after 40 seconds of breath-holding. In contrast, after only 10-20 seconds of breath-holding, concentrations of ^{36}Cl-labeled 1,1,2-trichloroethane in alveolar air had dropped to 10% of the initial concentration. In normal breathing experiments, 80.2% of the radiolabel inhaled in a single breath of 1,1,2-trichloro-1,2,2-trifluoroethane (and held for 5 seconds) was exhaled after 30 minutes, thus indicating that 19.8% of inhaled 1,1,2-trichloro-1,2,2-trifluoroethane was retained in the body. About half of the radiolabel was exhaled during the first minute, reflecting the low rate of absorption (Morgan et al., 1972).

Andersen et al. (1980) could not measure loss of 1,1,2-trichloro-1,2,2-trifluoroethane from the recirculating atmosphere of a closed 31 ℓ chamber containing nine rats and air containing 1,1,2-trichloro-1,2,2-trifluoroethane at unspecified concentrations. This technique allowed measurement of absorption rates of other vapors including trichloroethylene. The results indicate that net pulmonary absorption of 1,1,2-trichloro-1,2,2-trifluoroethane was low, relative to other vapors.

Trochimowicz et al. (1974) measured arterial and venous concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane in conscious beagle dogs during and after 10-minute inhalation exposures to three concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane vapors (1000, 5000 and 10,000 ppm). Blood concentrations increased rapidly during the first 5 minutes of exposure and tended to level off (arterial) or increase less rapidly (venous) thereafter (Figure 5-1). Arterial blood levels of 1,1,2-trichloro-1,2,2-trifluoroethane increased more rapidly than did venous blood levels, and both arterial and venous blood levels increased with increasing exposure levels. The data reinforce the existence of pulmonary absorption of 1,1,2-trichloro-1,2,2-trifluoroethane, indicate that arterial blood levels reached apparent steady-state within 10 minutes and demonstrate that blood levels were proportional to exposure levels.

The U.S. EPA (1983) reviewed unpublished data from Haskell Laboratory (1968) regarding the dermal absorption of 1,1,2-trichloro-1,2,2-trifluoroethane in three human subjects. Liquid 1,1,2-trichloro-1,2,2-trifluoroethane was applied to the scalp for 15 minutes or to the hands and forearms for 30 minutes, and the concentration of 1,1,2-trichloro-1,2,2-trifluoroethane in the breath was measured at various times after termination of exposure. The presence of 1,1,2-trichloro-1,2,2-trifluoroethane in the expired air indicated that dermal absorption of 1,1,2-trichloro-1,2,2-trifluoroethane occurred in the human body, but the data do not allow quantitation of the extent of absorption.

Data regarding the rate and extent of gastric absorption of 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

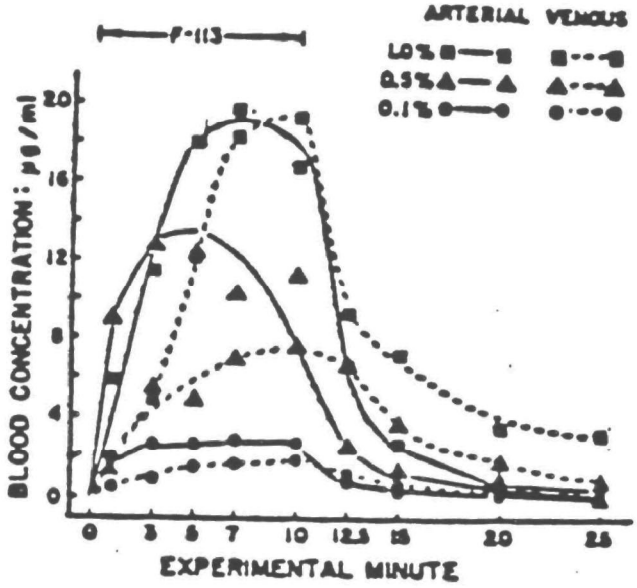

FIGURE 5-1

Fluorocarbon 113 Concentration in Arterial and Venous Blood of Beagle Dogs During and After 10-Minute Exposures to Three Inspired Levels (Four Dogs/Level)

Source: Trochimowicz et al., 1974

5.2. DISTRIBUTION

In the dog experiments by Trochimowicz et al. (1974), concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane in the blood dropped rapidly upon termination of a 10-minute exposure (see Figure 5-1). Arterial blood concentrations returned to control values by 15 minutes after termination of exposure. Concentrations in venous blood decreased less rapidly than arterial levels, but nevertheless were ~80% decreased by 15 minutes after termination of exposure. The data indicate that, during pulmonary exposure, blood contains 1,1,2-trichloro-1,2,2-trifluoroethane, which can be distributed to other parts of the body. The difference between the arterial and venous concentrations both during and after exposure also suggests that 1,1,2-trichloro-1,2,2-trifluoroethane is absorbed from the blood by tissues and subsequently released after exposure.

Carter et al. (1970) determined levels of 1,1,2-trichloro-1,2,2-trifluoroethane in the brain, liver, heart, fat, adrenal and thyroid of rats exposed to 2000 ppm for 7-14 days. The data are presented in Table 5-1. Concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane were much higher in the fat than in the other tissues. Twenty-four and 48 hours following termination of exposure, 1,1,2-trichloro-1,2,2-trifluoroethane could only be detected in fat, but levels in the fat also progressively decreased with time after termination of exposure.

Savolainen and Pfaffli (1980) exposed rats to 1,1,2-trichloro-1,2,2-trifluoroethane at concentrations of 200, 1000 or 2000 ppm 6 hours/day, 5 days/week for 1 or 2 weeks and measured concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane in the brain and perirenal fat. Concentrations in both tissues increased with increasing exposure level, but duration of

TABLE 5-1

Tissue Concentrations of 1,1,2-Trichloro-1,2,2-trifluoroethane from Rats Exposed to Air Containing 2000 ppm[a,b]

Tissue	Exposure		Postexposure	
	7 Days	14 Days	24 Hours	48 Hours
Brain (µg/g)	22.73±1.00	22.65±1.33	none	none
Liver (µg/g)	15.77±0.87	16.40±1.72	none	none
Heart (µg/g)	16.59±2.56	15.03±2.51	none	none
Fat (µg/g)	722.48±71.29	659.24±21.17	108.45±33.62	5.60±2.94
Adrenal (µg)	8.39±2.61	3.47±0.34	none	none
Thyroid (µg)	1.09±0.46	0.94±2.00	none	none

[a]Source: Carterr et al., 1970

[b]Values are means ± standard derivation of determinations from five rats.

exposure (1 week vs. 2 weeks) did not alter tissue concentrations significantly. In agreement with the measurements of Carter et al. (1970), concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane in fat were much larger (~20-fold) than concentrations in brain tissue (Savolainen and Pfaffli, 1980).

5.3. METABOLISM

Data from experiments designed to identify the metabolites of 1,1,2-trichloro-1,2,2-trifluoroethane in humans or animals are not available. The only available information indicating a possible metabolic route is the observation that, in in vitro experiments, 1,1,2-trichloro-1,2,2-trifluoroethane binds to cytochrome P-450 from rat hepatic microsomes, thus suggesting that 1,1,2-trichloro-1,2,2-trifluoroethane may be a substrate for oxidative enzymes associated with P-450 (Vainio et al., 1980).

The observations that 1,1,2-trichloro-1,2,2-trifluoroethane is preferentially partitioned into fatty tissues but rapidly disappears upon termination of exposure (Carter et al., 1970; Savolainen and Pfaffli, 1980; Morgan et al., 1972) has led to the suggestion that 1,1,2-trichloro-1,2,2-trifluoroethane is poorly metabolized in mammals (U.S. EPA, 1983). This suggestion requires more direct evidence for substantiation, but corroborative evidence is provided by inhalation dog studies on the biotransformation and elimination of ^{14}C-labeled homologous chlorofluorocarbons (trichlorofluoromethane and dichlorodifluoromethane). In these studies, dogs were given short-term (6-20 minutes) exposures to known amounts of the ^{14}C-labeled compounds. Exhaled air and urine were collected for 1 hour and 3 days after termination of exposure, respectively, and analyzed for radioactivity. CO_2 was separated from other gases in the exhaled air and analyzed for radioactivity. Essentially all (99-100%) of the administered

radioactivity was accounted for in the exhaled air. Radioactivity in exhaled CO_2 and in urine accounted for only traces (≤1%) of the administered dose (Blake and Mergner, 1974).

5.4. EXCRETION

1,1,2-Trichloro-1,2,2-trifluoroethane is rapidly cleared from the mammalian body, as indicated by its rapid disappearance from rat tissue during postexposure periods (Carter et al., 1970) (see Table 5-1) and the rapid decrease in blood concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane following 10-minute inhalation exposures in dogs (Trochimowicz et al., 1974) (see Figure 5-1).

The appearance of 1,1,2-trichloro-1,2,2-trifluoroethane in the exhaled air of humans subjected to dermal exposures to 1,1,2-trichloro-1,2,2-trifluoroethane (Haskell Laboratory, 1968) indicates that pulmonary exhalation represents a significant route of excretion. Direct analysis of urine and fecal matter for 1,1,2-trichloro-1,2,2-trifluoroethane content following exposure to 1,1,2-trichloro-1,2,2-trifluoroethane is not available, but in dog studies on the elimination of homologous chlorofluorocarbons, only trace amounts of radioactivity were found in the urine following acute inhalation exposures to ^{14}C-labeled compounds (Blake and Mergner, 1974).

5.5. SUMMARY

Inhalation experiments in humans with ^{36}Cl-labeled 1,1,2-trichloro-1,2,2-trifluoroethane (Morgan et al., 1972) indicate that, although pulmonary absorption of 1,1,2-trichloro-1,2,2-trifluoroethane occurs, the rate of absorption is lower than that of other chlorinated hydrocarbons such as trichloroethane. Dermal absorption has also been shown to occur in humans (Haskell Laboratory, 1968), but data regarding gastric absorption of 1,1,2-trichloro-1,2,2-trifluoroethane are not available.

Inhalation studies with dogs (Trochimowicz et al., 1974) and rats (Carter et al., 1970; Salvolainen and Pfaffli, 1980) indicate that absorbed 1,1,2-trichloro-1,2,2-trifluoroethane is rapidly distributed by the blood to various organs and tissues (including the brain, liver, adrenal, heart and thyroid) and is preferentially deposited into fat.

Upon cessation of exposure, 1,1,2-trichloro-1,2,2-trifluoroethane is rapidly cleared from the body. 1,1,2-Trichloro-1,2,2-trifluoroethane could not be detected in the brain, liver, heart, adrenal or thyroid of rats 24 and 48 hours after termination of a 14-day exposure regime, and 1,1,2-trichloro-1,2,2-trifluoroethane-levels in fat were decreased by ~80 and 99% during the same respective periods (Carter et al., 1970).

Human data indicate that pulmonary exhalation is a significant excretory route for 1,1,2-trichloro-1,2,2-trifluoroethane. 1,1,2-Trichloro-1,2,2-trifluoroethane was detected in the exhaled air of humans following dermal administrations of 1,1,2-trichloro-1,2,2-trifluoroethane (Haskell Laboratory, 1968).

Identifications have not been made of *in vivo* metabolites of 1,1,2-trichloro-1,2,2-trifluoroethane in animals or humans. Based upon the demonstration of *in vitro* binding of 1,1,2-trichloro-1,2,2-trifluoroethane to rat hepatic cytochrome P-450, a suggestion has been made that 1,1,2-trichloro-1,2,2-trifluoroethane may be oxidized by enzymes associated with P-450 (Vainio et al., 1980), but reaction products have not been identified.

6.1. SYSTEMIC TOXICITY

6.1.1. Inhalation Exposure.

6.1.1.1. SUBCHRONIC -- Data regarding the toxicity of subchronic exposure to 1,1,2-trichloro-1,2,2-trifluoroethane vapors are limited to a single 84-day rat study. Groups of six male Sprague-Dawley rats were exposed by whole-body inhalation to 0 or 200 ppm 1,1,2-trichloro-1,2,2-trifluoroethane (industrial grade) for 8 hours/night for 84 days. Body weights and urinary catecholamine metabolites were monitored at intervals throughout the treatment period. After 84 days of treatment, the following endpoints were measured: liver and kidney weights, liver cytochrome P-450 content and liver monooxygenase activity (with 7-ethoxycoumarin as substrate). The imposed treatment did not significantly affect any of the measured endpoints (Blohm et al., 1985).

6.1.1.2. CHRONIC -- Trochimowicz et al. (1988) exposed groups of 100 male and 100 female Crl:CDBR rats to 0, 2000, 10,000 or 20,000 ppm 1,1,2-trichloro-1,2,2-trifluoroethane 6 hours/day, 5 days/week for $\leq$24 months. Hematological analysis, chemical analysis of serum (for example, alkaline phosphatase, bilirubin, urea nitrogen, cholesterol and total protein) and urinalysis (e.g., pH, fluoride concentration, blood, protein and bilirubin) were conducted on samples collected from 10 rats/sex/group at 3, 6, 12, 18 and 24 months. Body weights were measured periodically. All major organs including the heart, lungs, brain and nasal turbinates were examined macroscopically and microscopically upon death and, in the control and high-exposure groups, at termination of the experiment. Tissues with gross lesions or masses and nasal turbinates from rats in the low- and intermediate-exposure groups were also examined microscopically at termination of

the experiment. No adverse effects were noted within any of the measured endpoints, with the exception that body weight was decreased relative to that of controls in both sexes receiving the 20,000 ppm treatment and in females treated with 10,000 ppm, especially after the first 50 weeks of treatment. Survival in treated rats was comparable with that of control rats. Some rats developed Cornybacterium kutscheri infections, which resulted in deaths of 3-8% of the females and 20-39% of the males; the data indicated, however, that these infections were not treatment-related (Trochimowicz et al., 1988).

No adverse effects were noted in comparative examinations of 50 male workers frequently exposed to 1,1,2-trichloro-1,2,2-trifluoroethane and 50 unexposed male workers. Average ages were 34 years (range = 23-51) and 37 years (range = 25-63) for exposed and unexposed workers, respectively. Exposed workers worked an average 2.8 years (6 hours/day, 5 days/week) in clean rooms in which 1,1,2-trichloro-1,2,2-trifluoroethane was used daily for general cleaning and degreasing. Samples of air in these rooms indicated that 1,1,2-trichloro-1,2,2-trifluoroethane concentrations ranged from 46-4700 ppm with a mean (n=161) of 699 ppm. Examination of the workers included the following: medical history, blood cell counts, visual profile, electrocardiogram, audiometric test, serum analysis (e.g., cholesterol, bilirubin, BUN, glucose, alkaline phosphatase), chest X-ray and timed lung vital capacity (Imbus and Adkins, 1972).

Epidemiological and case-report studies suggest that subchronic or chronic occupational exposure to 1,1,2-trichloro-1,2,2-trifluoroethane may have neurotoxic or neuropsychological effects, but additional information and research is needed to substantiate these reports. In a questionnaire

study of Danish metal workers, workers exposed to 1,1,2-trichloro-1,2,2-trifluoroethane ("degreasers") more frequently provided positive answers to questions regarding feelings of dizziness and drunkenness at work and irritability at home and work than did unexposed workers (Rasmussen and Sabroe, 1986). Rasmussen et al. (1988) also reported that medical and psychological examinations of 23 degreasers from a Danish metal factory that exclusively used 1,1,2-trichloro-1,2,2-trifluoroethane to clean metals revealed 3 workers with characteristics of what the authors termed slight psychoorganic syndrome. These characteristics included the following: neuropsychological symptoms such as increased irritability, headaches and impaired ability to concentrate and remember appointments and instructions; slight cerebral cortical atrophy in two of the three cases, as indicated by CT scanning; and below-normal performance in various psychological tests (Rasmussen et al., 1988). Raffi and Violante (1981) reported a case of neuropathy in a woman who used liquid 1,1,2-trichloro-1,2,2-trifluoroethane daily to remove spots from clothes during the last 7 of 13 years in which she worked as a laundress. During the previous 6 years she had used tetrachloroethylene. Exposure levels experienced by the woman were not estimated. The woman complained of pain, paresthesia and weakness of the legs, and electromyographic examination revealed diminished motor nerve conduction velocities in the left and right tibialis nerves. The patient was advised to curtail her exposure to 1,1,2-trichloro-1,2,2-trifluoroethane, and she subsequently quit her job. The authors reported that the woman's condition improved after ~4 months without exposure to 1,1,2-trichloro-1,2,2-trifluoroethane, but measured values for motor nerve conduction velocity in the patient's tibialis nerves were still below quoted normal values (Raffi and Violante, 1981).

6.1.2. Oral Exposure.

6.1.2.1. SUBCHRONIC -- Pertinent data regarding the toxic effects of subchronic oral exposure to 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

6.1.2.2. CHRONIC -- Pertinent data regarding the toxic effects of chronic exposures to orally administered 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

6.1.3. Other Relevant Information. Steinberg et al. (1969) reported no adverse effects in studies of dogs, guinea pigs and rats exposed to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane at a concentration of 5100 ppm (6 hours/day, 5 days/week) for 4 weeks. Control and treated groups each included 2 dogs of both sexes, 10 female guinea pigs and 10 rats of both sexes. No differences in the following endpoints were observed between control and treated groups in each species: growth rate; relative weights of liver, spleen, lung and kidneys; and macroscopic and microscopic examinations of liver, kidneys, lungs, trachea, heart and spleen. No treatment-related alterations were observed in plasma lactic dehydrogenase, amylase activity, BUN and values for hematocrit, percent neutrophils and percent lymphocytes in dogs. Rotobar performance and voluntary movement measured by an activity wheel were unaffected by the treatment in rats (Steinberg et al., 1969).

Carter et al. (1970) reported no significant changes in hematological values, clinical chemistries, electroencephalographic findings, body weights or relative organ weights in studies of 4 monkeys, 8 dogs, 40 mice and 50 rats exposed continuously to 2000 ppm 1,1,2-trichloro-1,2,2-trifluoroethane for 14 days. Controls consisted of 4 monkeys, 8 dogs, 20 mice and 25 rats.

Minor changes in liver cell histology, ultrastructure and biochemistry were reported in male Wistar rats (mean weight = 424 g) exposed to 1,1,2-trichloro-1,2,2-trifluoroethane vapors at concentrations $\leq$2000 ppm as compared with sham-exposed controls. Groups of unspecified numbers were exposed to 0, 200, 1000 or 2000 ppm 6 hours/day, 5 days/week for 1 or 2 weeks. Significant ($p<0.01$) changes in liver biochemical parameters (decreased reduced glutathione and activity of NADPH cytochrome c reductase and increased activity of UDP-glucuronosyltransferase) were most prevalent at the highest concentration provided. Light microscopy of liver sections from all rats revealed lipid accumulation that appeared dose-related. The only change revealed by electron microscopy was a "slight to moderate" proliferation and vacuolization of the smooth endoplasmic reticulum in liver cells from rats exposed to either 1000 or 2000 ppm. Exposure to 200 ppm produced no effects associated with the liver (Vainio et al., 1980).

The acute lethality of 1,1,2-trichloro-1,2,2-trifluoroethane is low when administered to animals by either oral or inhalation routes. An oral LD_{50} of 43 g/kg was determined in Sprague-Dawley rats (Michaelson and Huntsman, 1964), but rabbits appeared to be more susceptible (Busey, 1967). Two of eight rabbits died after three oral doses of 1 g/kg/day. When the dose was increased to 5 g/kg/day, half of the rabbits died after one or four doses (Busey, 1967). In inhalation experiments, Desoille et al. (1968) determined 2-hour LC_{50} values to be 95,000, 120,000 and 110,000 ppm for mice, guinea pigs and rats, respectively.

Six-hour exposures of rats and dogs to lower concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane vapors (11,000-13,000 ppm) were not lethal, but caused CNS effects that disappeared after termination of exposure (Steinberg et al., 1969). Clark and Tinston (1982) determined an

EC_{50} value for CNS effects in rats to be 28,000 ppm for 10-minute exposures to 1,1,2-trichloro-1,2,2-trifluoroethane. Minor biochemical changes (for example, increased NADPH-diaphorase activity, decreased cerebral glutathione, increased RNA) were noted in brain preparations from male rats exposed to 1,1,2-trichloro-1,2,2-trifluoroethane concentrations $\leq$2000 ppm 6 hours/day, 5 days/week for 2 weeks (Savolainen and Pfaffli, 1980). The observed changes were not dose-related, however, and the significance of the changes in the CNS effects noted in other studies is unclear.

Although the lethality of acute exposure to 1,1,2-trichloro-1,2,2-trifluoroethane appears to be low, a number of human deaths have been attributed to acute exposure to high concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane and related halogenated hydrocarbons. During the late 1960s, some people in the United States and other countries voluntarily inhaled aerosol products containing halogenated hydrocarbons like 1,1,2-trichloro-1,2,2-trifluoroethane to obtain narcotic effects. The popularity of this practice appears to have been short-lived, perhaps because of the sudden deaths that sometimes occurred. By 1971, ~65 deaths were attributed to this practice (Reinhardt et al., 1971a). The suddenness of death in otherwise healthy individuals, as well as the failure of autopsies to reveal the cause of death, led to the hypothesis that halogenated hydrocarbons at high concentrations cause cardiac arrhythmias, ventricular fibrillation and cardiac arrest (Reinhardt et al., 1971a; Reinhardt and Maxfield, 1973; Zakhari and Aviado, 1982). Accidental exposures to high concentrations of halogenated hydrocarbons have also been reported. May and Blotzer (1984) reported two cases of occupational deaths attributed to 1,1,2-trichloro-1,2,2-trifluoroethane. In both cases, workers were exposed to high levels of 1,1,2-trichloro-1,2,2-trifluoroethane vapors in confined spaces. The

first was exposed to ~128,000 ppm for <45 minutes, but the exposure level for the second worker was not available. The cause of death in both cases was cardiac arrhythmia.

The hypothesis that high concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane vapors can cause adverse cardiovascular effects has received support from a number of animal experiments (Zakhari and Aviado, 1982). When animals are exposed to a halogenated hydrocarbon and given an injection of epinephrine, arrhythmia can occur, as evidenced by electrocardiographical signals. This effect, known as cardiac sensitization, has been observed in unanesthetized dogs (Reinhardt and Maxfield, 1973) and anesthetized mice (Aviado and Belej, 1974). Male beagle dogs were given epinephrine injections (8 μg/kg) 5 minutes before and 5 minutes following initial exposure to 1,1,2-trichloro-1,2,2-trifluoroethane vapors. Exposure to 1,1,2-trichloro-1,2,2-trifluoroethane lasted 10 minutes. Cardiac arrhythmias were observed in 3/4, 10/29 and 0/12 of the animals exposed to respective concentrations of 10,000, 5000, and 2500 ppm (Reinhardt and Maxfield, 1973). Male Swiss mice were exposed to a similar protocol, except that mice were anesthetized with sodium pentobarbital (0.7 mg/10 g bw), exposures were for 6 minutes and epinephrine doses (6 μg/kg) were administered 2 minutes after the start of inhalation. Cardiac sensitization to epinephrine was observed in 3/3 and 1/3 of the mice exposed to 100,000 and 50,000 ppm, respectively (Aviado and Belej, 1974). Unpublished data indicated that, without administration of exogenous epinephrine, cardiac arrhythmia did not occur in dogs exposed to concentrations $\leq$20,000 ppm while running on a treadmill (Mullin et al., 1971) nor in dogs frightened by a loud noise or electric shock and exposed to 10,000 ppm (U.S. EPA, 1983). Clark and Tinston (1973) compared the cardiac sensitizing potency of 14 halogenated hydrocarbons administered by inhalation with conscious beagle dogs.

Epinephrine (5 µg/kg) was administered intravenously during the last 10 seconds of exposure and 10 minutes after exposure. The potency was directly related to the saturated vapor pressures of the compounds, inversely related to their boiling points, but not related to structural features, molecular weights or degree of fluorination. An EC_{50} (concentration at which 50% of the animals could be sensitized to exogenous epinephrine) of 10,000 ppm was determined for 5-minute exposures to 1,1,2-trichloro-1,2,2-trifluoroethane (Clark and Tinston, 1973). In rhesus monkeys anesthetized with sodium pentobarbital (30 mg/kg), 5-minute exposures to 25,000 and 50,000 ppm 1,1,2-trichloro-1,2,2-trifluoroethane caused arrhythmias and dose-related myocardial depressions and tachycardia, without administrations of exogenous epinephrine (Belej et al., 1974).

Aviado and Smith (1975) reported that 5-minute in vivo exposures to 25,000 and 50,000 ppm 1,1,2-trichloro-1,2,2-trifluoroethane decreased the pulmonary resistance and increased the pulmonary compliance in groups of three anesthetized rhesus monkeys. Alarie et al. (1975) reported that in vitro ventilation of excised rat lungs with vapors of 1,1,2-trichloro-1,2,2-trifluoroethane (concentration and period of exposure unspecified) produced changes in pressure-volume relationships (compared with control excised lungs) manifested predominantly by changes in surface tension at the alveolar surface. Both of these studies indicate that acute exposures to high concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane may affect pulmonary function; the authors of the latter report suggested that interactions of 1,1,2-trichloro-1,2,2-trifluoroethane with the normal surfactant of the inner alveolar surface are responsible for surface tension changes that alter pulmonary function (Alarie et al., 1975).

Acute exposure to moderate concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane vapors can alter psychomotor function in humans. Stopps and McLaughlin (1967) administered psychophysiological tests (manual dexterity tests, Necker cube test, card sorting, addition of three single-digit numbers and a clerical task test) to two men during ~2-hour exposures to 1,1,2-trichloro-1,2,2-trifluoroethane at concentrations of 0, 1500, 2500, 3500 or 4500 ppm. Performance was not affected at 1500 ppm, but increasingly declined at concentrations $\geq$2500 ppm. In a subsequent experiment to examine the effects of daily 6-hour exposures to lower concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane, four men were exposed to 0 ppm, 6 hours/day, 5 days/week for 1 week, followed by a week of identical exposures to 500 ppm and then a week of identical exposures to 1000 ppm (Reinhardt et al., 1971b). Performance in psychophysiological tests (Stopps and McLaughlin, 1967) was not affected by exposure to 1,1,2-trichloro-1,2,2-trifluoroethane, and the subjects stated that they were unable to tell when they were being exposed to the compound, except for a transient awareness of odor upon first entering the exposure chamber. In addition, no adverse effects were noted in a battery of examinations including hematological analysis, serum chemistry (for example, alkaline phosphatase, BUN and glucose), urinalysis, chest X-ray and pulmonary function tests (for example, diffusing capacity of lungs and fractional uptake of carbon monoxide) (Reinhardt et al., 1971b).

6.2. CARCINOGENICITY

6.2.1. Inhalation. Data regarding the carcinogenicity of inhalation exposures to 1,1,2-trichloro-1,2,2-trifluoroethane are limited to negative results from the 24-month study of rats exposed to 1,1,2-trichloro-1,2,2-trifluoroethane vapors at concentrations of 0, 2000, 10,000 or 20,000 ppm 6

hours/day, 5 days/week (Trochimowicz et al., 1988). Further experimental details of this study are discussed in Section 6.1.1.2. Major organs and tissues from the control and high-exposure groups were examined microscopically. Microscopic examination of organs and tissues of the low- and intermediate-exposure groups was limited to rats that died or were killed when moribund during the study and to nasal passages and organs in which gross lesions or tissue masses were identified in rats killed at the end of the experiment. Overall tumor incidence and incidences of individual tumor types were similar in all groups, with the exception that a significant increase in pancreatic islet cell adenomas was observed in female rats exposed to 20,000 ppm (Table 6-1). The authors did not consider this incidence compound-related, because the incidence of 5/86 was within historical background levels for their laboratory, and female controls in a separate but concurrent inhalation study showed an incidence of 6/95 for pancreatic islet cell adenomas. Tumors were also observed in the nasal passages of one male rat from the 2000 ppm group and one female and three males from the 10,000 ppm group. The authors argued that this incidence was not compound-related because no two tumors were of the same cell type, there was no dose-related trend and other preneoplastic histological changes were not observed in the nasal passages at any exposure level.

6.2.2. Oral. Pertinent data regarding the carcinogenicity of oral exposures to 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

6.2.3. Other Relevant Information. Other pertinent data regarding the carcinogenicity of 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

TABLE 6-1

Incidence of Tumors in Crl:CDBR Rats Exposed to Vapors of 1,1,2-Trichloro-1,2,2-trifluoroethane for 24 Months[a]

Sex	Exposure Level[b] (ppm)	Tumor Type	Tumor Incidence
Female	0	pancreatic	0/85
	2,000	islet cell	0/36
	10,000	adenomas	0/30
	20,000		5/86
Male	0	pancreatic	2/88
	2,000	islet cell	1/64
	10,000	adenomas	0/58
	20,000		2/87

QUALITY OF EVIDENCE

Strengths of Study: The compound was administered by a relevant route at three levels to both sexes. Adequate numbers of animals and adequate duration of exposure.

Weakness of Study: Some decreased survival in all groups, which is due to respiratory infection.

Overall Adequacy: Study was of adequate design, but data were not positive for carcinogenic effect. Authors reported that incidence for females at the high-exposure level was within historical background incidence level for their laboratory.

[a]Source: Trochimowicz et al., 1988

[b]Rats were exposed 6 hours/day, 5 days/week for 24 months.

6.3. MUTAGENICITY

1,1,2-Trichloro-1,2,2-trifluoroethane was not mutagenic in assays for dominant lethal mutations in mice (Epstein et al., 1972) or in assays for reverse mutations in numerous strains of Salmonella typhimurium (Simmon et al., 1977; Longstaff, 1988; Mahurin and Bernstein, 1988) (Table 6-2).

6.4. DEVELOPMENTAL TOXICITY

The U.S. EPA (1983) presented summaries of three unpublished studies, one rat study (Ward, 1983) and two rabbit studies (Hazelton Laboratories, 1967a,b), regarding the possible teratogenicity of 1,1,2-trichloro-1,2,2-trifluoroethane. Other teratogenicity studies for 1,1,2-trichloro-1,2,2-trifluoroethane were not available. The summarized data indicate that 1,1,2-trichloro-1,2,2-trifluoroethane was not teratogenic in rats at the experimental exposure levels, but conclusions are precluded in the rabbit studies because of marked maternal toxicity and inadequate numbers of animals.

Ward (1983) exposed groups of 24 pregnant rats to 0, 5000, 12,500 and 25,000 ppm 1,1,2-trichloro-1,2,2-trifluoroethane 6 hours/day on days 6-15 of gestation. No macroscopic abnormalities were noted in dams of the treated groups at autopsy. The only maternal effects noted were decreases in body weight gain, food utilization and consumption and signs of hyperactivity in the high-exposure group. The author reported that no evidence was found for embryotoxicity. Increased incidences of fetal ribs were reported at all exposure levels, but the author stated that the incidences were within the control range.

Hazelton Laboratories (1967a) exposed groups of 12 rabbits to 0, 2000 or 20,000 ppm 1,1,2-trichloro-1,2,2-trifluoroethane 2 hours/day on days 8-16 of presumed gestation. The respective groups, however, only contained 4, 4 and

TABLE 6-2

Mutagenicity Testing of 1,1,2-Trichloro-1,2,2-trifluoroethane

Assay	Indicator/ Organism	Compound and/or Purity	Application	Concentration or Dose	Activating System	Response	Comment	Reference
Dominant lethal mutation	ICR/Ha Swiss mice	NR	single intra-peritoneal application	200, 1000 mg/kg	NA	-	7 and 9 males treated at low and high dose, respectively, 8 weeks of mating, incidence of early fetal deaths and preimplanation losses within control limits	Epstein et al., 1972
Reverse mutation	Salmonella typhimurium TA1535, TA1537, TA1538, TA98 TA100	commercial	vapors in closed desiccator, 7-10 hours	NR	NR	-	Tested at ≤ toxic concentration	Simmon et al., 1977
Reverse mutation	S. typhimurium TA1535, TA100	commercial (>99.5%)	vapors in closed system, 72 hours	NR	NR	-	TA1535 tested at concentrations ≤100,000 ppm; TA100 tested at concentrations ≤200,000 ppm	Longstaff, 1988
Reverse mutation	S. typhimurium TA98 and TA100	commercial	NR	NR	±S-9	-	Further details not presented	Mahurin and Bernstein, 1988

NA = Not applicable; NR = not reported

7 rabbits that were actually pregnant. Maternal toxicity, evident in the high-exposure group, was characterized by lowered body weight gain during exposure, eye irritation, premature delivery in one doe and death of another. Examinations were made of the external soft-tissue and skeletons of 19, 8 and 24 fetuses for the control, low- and high-exposure groups, respectively. No differences were noted among the groups of offspring, except that one pup in the low-exposure group and two in the high-exposure group were dead at examination. In an oral study, groups of eight female rabbits were administered 0, 1 or 5 g/kg 1,1,2-trichloro-1,2,2-trifluoroethane by gavage on days 8-11 of presumed gestation (Hazelton Laboratories, 1967b). Pregnancy was obtained, however, in only three, six and four rabbits in the control, low- and high-exposure groups, respectively. Two and three of the pregnant females died in the low- and high-exposure groups, respectively. Maternal toxicity was also indicated by body weight loss and reduced food and water consumption in the high-exposure group. The marked maternal toxicity precluded evaluation of fetotoxicity and teratogenicity data.

6.5. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

6.6. SUMMARY

Adverse systemic effects in animals caused by long-term exposure (subchronic or chronic) to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane at concentrations $\leq$2000 ppm have not been identified, but the data base is limited to two rat studies (Blohm et al., 1985; Trochimowicz et al., 1988).

At concentrations ≥10,000 ppm, adverse body weight changes were observed in rats (Trochimowicz et al., 1988). No adverse changes in body, liver or kidney weights, liver biochemistry or urinary catecholamine metabolites were observed in rats exposed to 1,1,2-trichloro-1,2,2-trifluoroethane vapors at concentrations of 200 ppm for 84 days (Blohm et al., 1985). Chronic exposure (24 months) of rats to 1,1,2-trichloro-1,2,2-trifluoroethane vapors at 2000 ppm caused no adverse changes in blood and urine chemical indices, body and organ weights or in the histology of major organs and tissues (Trochimowicz et al., 1988). The same endpoints were unaffected by higher chronic exposure levels, except for body weight gain, which was decreased in both sexes of rats exposed to 20,000 ppm and in female rats exposed to 10,000 ppm.

No adverse effects were identified in shorter-term studies of dogs, guinea pigs and rats exposed to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane at concentrations of 5100 ppm for ~4 weeks (Steinberg et al., 1969). Carter et al. (1970) also reported no adverse effects in inhalation studies of monkeys, dogs, mice and rats continuously exposed to 2000 ppm for 14 days.

The only report of 1,1,2-trichloro-1,2,2-trifluoroethane-induced systemic effects other than body weight changes in animals exposed to low to moderate concentrations comes from a 2-week inhalation study of rats (Vainio et al., 1980). Light microscopy revealed lipid accumulation and electron microscopy revealed changes in the smooth endoplasmic reticulum in liver cells from rats exposed to concentrations of 1000 or 2000 ppm. Changes were also noted in enzymic activities and reduced glutathione levels in the liver of rats exposed to 2000 ppm (Vainio et al., 1980).

Adverse systemic effects of long-term exposure of humans to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane have not been clearly identified.

In a comparison of chronically exposed human workers with unexposed workers (Imbus and Adkins, 1972), no adverse effects were noted in physical examinations of workers who worked an average 2.8 years in rooms in which average concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane were estimated to be 699 ppm. Epidemiological and case-report studies suggest, however, that long-term occupational exposure to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane may cause neuropsychological effects (Rasmussen and Sabroe, 1986; Rasmussen et al., 1988) or neuropathy (Raffi and Violante, 1981). Further information is needed to substantiate the suggestions of the epidemiological and case-report studies.

Acute exposures (<2 hours) to moderate concentrations (≥2500 ppm) of 1,1,2-trichloro-1,2,2-trifluoroethane vapors altered the performance of volunteers in psychophysiological tests (Stopps and McLaughlin, 1967). Exposure of volunteers to lower concentrations (≤1000 ppm) for a longer duration (6 hours/day, 5 days/week for 2 weeks) did not cause treatment-related changes in performance in psychophysiological tests or in physical examinations (Reinhardt, et al., 1971b).

The acute lethality of 1,1,2-trichloro-1,2,2-trifluoroethane is low when administered to animals by either oral or inhalation routes. An oral LD_{50} of 43 g/kg was determined for rats (Michaelson and Huntsman, 1964), but rabbits appeared more susceptible. Half of a group of eight rabbits died after receiving one to four doses of 5 g/kg/day (Busey, 1967). Two-hour LC_{50} values of 95,000, 120,000 and 110,000 ppm were determined for inhalation exposures of mice, guinea pigs and rats, respectively (Desoille et al., 1968).

Acute exposures to moderate to high concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane caused CNS effects in two animal species. Reversible

CNS effects were seen in dogs and rats given 6-hour exposures to 11,000-13,000 ppm (Steinberg et al., 1969), and an EC_{50} value of 28,000 ppm was determined for CNS effects in rats given 10-minute exposures (Clark and Tinston, 1982). The mechanistic connection between these CNS effects and the observation of minor biochemical effects in brain preparations from rats exposed to concentrations $\leq$2000 ppm for 2 weeks (Savolainen and Pfaffli, 1980) currently is unclear.

Accidental and voluntary human exposures to high concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane vapors caused sudden death generally thought to be due to cardiac arrest (May and Blotzer, 1984; Reinhardt et al., 1971a, 1973; Zakhari and Aviado, 1982). This hypothesis has received support from animal studies in which acute exposures (5-10 minutes) to moderate to high concentrations caused adverse cardiac effects. Cardiac sensitization to epinephrine-induced arrhythmias was observed in dogs at concentrations $\geq$5000 ppm (Reinhardt et al., 1973) and in anesthetized mice at concentrations $\geq$50,000 ppm (Aviado and Belej, 1974). An EC_{50} for cardiac sensitization of 10,000 ppm was determined for 5-minute exposures of dogs (Clark and Tinston, 1973). In anesthetized rhesus monkeys, 5-minute exposures to concentrations $\geq$25,000 ppm caused arrhythmias, myocardial depressions and tachycardia, without administration of exogenous epinephrine (Belej et al., 1974).

Acute 5-minute exposures to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane at concentrations $\geq$25,000 ppm altered pulmonary function in rhesus monkeys (Aviado and Smith, 1975). *In vitro* experiments with excised rat lungs (Alarie et al., 1975) indicated that this effect may involve interaction of 1,1,2-trichloro-1,2,2-trifluoroethane with surfactant on the inner alveolar surface.

Pertinent data regarding the systemic toxicity of chronic or subchronic exposure to orally administered 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

Data regarding the carcinogenicity of 1,1,2-trichloro-1,2,2-trifluoroethane are limited to a 2-year inhalation study in which rats were exposed to concentrations of 0, 2000, 10,000 or 20,000 ppm (Trochimowicz et al., 1988). No treatment-related increases in tumor incidences were reported. 1,1,2-trichloro-1,2,2-trifluoroethane was not mutagenic in assays for dominant lethal mutations in mice (Epstein et al., 1972) nor in assays for reverse mutations in S. typhimurium (Simmon et al., 1977; Longstaff, 1988; Mahurin and Bernstein, 1988).

The U.S. EPA (1983) summarized three unpublished studies (Ward, 1983; Hazelton Laboratories, 1967a,b), which contain the only available data regarding the teratogenicity and other reproductive effects of 1,1,2-trichloro-1,2,2-trifluoroethane. The summarized data indicate that 1,1,2-trichloro-1,2,2-trifluoroethane was not teratogenic in rats exposed to air containing $\leq$25,000 ppm on days 6-15 of gestation (Ward, 1983), but conclusions were precluded in rabbit studies (Hazelton Laboratories, 1967a,b) because of marked maternal toxicity and inadequate numbers of animals.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

The ACGIH (1986) established a TLV-TWA of 1000 ppm (7600 mg/m³) and a TLV-STEL of 1250 ppm (9500 mg/m³) for 1,1,2-trichloro-1,2,2-trifluoroethane. These limits were thought to provide margins of safety against systemic effects and cardiac sensitization such as that observed in dogs given 5-minute exposures to 5000 ppm 1,1,2-trichloro-1,2,2-trifluoroethane (38344 mg/m³) in conjunction with intravenous epinephrine (Reinhardt et al., 1973) (see Section 6.1.3.).

OSHA (1989) established limits of 1000 ppm (7600 mg/m³) as an 8-hour TWA and 1250 ppm (9500 mg/m³) as a 15-minute STEL for 1,1,2-trichloro-1,2,2-trifluoroethane. These limits were established to provide margins of safety against cardiac sensitization as discussed above and to reduce the risk of impaired psychomotor performance such as that reported by Stopps and McLaughlin (1967) to occur in humans during 2-hour exposures to concentrations $\geq$2500 ppm (19,172 mg/m³) (see Section 6.1.3.).

The U.S. EPA (1989) lists a verified RfD of 30 mg/kg/day for oral exposure to 1,1,2-trichloro-1,2,2-trifluoroethane. This RfD is being reconsidered and is pending change. The basis for the RfD is the observation of no adverse effects in humans occupationally exposed to vapors of 1,1,2-trichloro-1,2,2-trifluoroethane at an average concentration of 699 ppm (5358 mg/m³) for an average 2.77 years (Imbus and Adkins, 1972). To derive the RfD, the average exposure concentration was converted to an oral dose equivalent of 273 mg/kg/day, divided by an uncertainty factor of 10 and rounded to 30 mg/kg/day.

7.2. AQUATIC

Pertinent guidelines and standards for the protection of aquatic life from exposure to 1,2,2-trichloro-1,1,2-trifluoroethane were not located in the available literature cited in Appendix A.

8. RISK ASSESSMENT

8.1. CARCINOGENICITY

8.1.1. Inhalation. Data regarding the carcinogenicity of inhaled 1,1,2-trichloro-1,2,2-trifluoroethane in humans were not located. No treatment-related tumorigenic effects were noted in a 24-month inhalation study of rats (Trochimowicz et al., 1988). Groups of 100 Crl:CDBR rats of both sexes were exposed to 0, 2000, 10,000 or 20,000 ppm 1,1,2-trichloro-1,2,2-trifluoroethane (15,328, 76,638, 153,276 mg/m^3) 6 hours/day, 5 days/week.

8.1.2. Oral. Pertinent data regarding the carcinogenicity of oral exposure of humans or animals to 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

8.1.3. Other Routes. Data regarding the carcinogenicity of 1,1,2-trichloro-1,2,2-trifluoroethane by other routes of exposure or other data regarding the carcinogenicity of 1,1,2-trichloro-1,2,2-trifluoroethane were not located in the available literature cited in Appendix A.

8.1.4. Weight of Evidence. No data were available regarding the carcinogenicity of 1,1,2-trichloro-1,2,2-trifluoroethane to humans. A single inhalation experiment using rats (Trochimowicz et al., 1988) provided the only available test for the carcinogenicity of 1,1,2-trichloro-1,2,2-trifluoroethane in animals. According to the EPA classification scheme for carcinogenic risk assessment adopted by the U.S. EPA (1986b), 1,1,2-trichloro-1,2,2-trifluoroethane is assigned to EPA Group D, not classifiable as to human carcinogenicity. Assignment to Group E, evidence for noncarcinogenicity for humans, requires, in the absence of human data, at least two animal tests of two species (U.S. EPA, 1986b), and is therefore inappropriate for 1,1,2-trichloro-1,2,2-trifluoroethane.

8.1.5. Quantitative Risk Estimates.

8.1.5.1. INHALATION -- The only carcinogenicity data located were the negative studies using rats (Trochimowicz et al., 1988). Therefore, quantitative estimation of carcinogenic risk associated with inhalation exposure to 1,1,2-trichloro-1,2,2-trifluoroethane cannot be made.

8.1.5.2. ORAL -- Lack of data precludes quantitative estimation of carcinogenic risk associated with oral exposure to 1,1,2-trichloro-1,2,2-trifluoroethane.

8.2. SYSTEMIC TOXICITY

8.2.1. Inhalation Exposure.

8.2.1.1. LESS THAN LIFETIME (SUBCHRONIC) -- The data base for subchronic inhalation exposure to 1,1,2-trichloro-1,2,2-trifluoroethane contains only an 84-day rat study (Blohm et al., 1985). No adverse effects were observed in body weights, liver and kidney weights, urinary levels of catecholamine metabolites or indices of liver biochemistry in rats exposed to 200 ppm 1,1,2-trichloro-1,2,2-trifluoroethane (1533 mg/m^3) for 8 hours/night for 84 days (Rec. #3). Because of the relative inadequacies of this study (no LOAEL was identified, a single exposure level and small numbers of animals were used, and no histopathological examinations were performed), the chronic RfD of 27 mg/m^3 (Section 8.2.1.2.) is adopted as the RfD for subchronic inhalation exposure to 1,1,2-trichloro-1,2,2-trifluoroethane.

8.2.1.2. CHRONIC -- The data base for chronic inhalation exposure to 1,1,2-trichloro-1,2,2-trifluoroethane includes two studies suitable for use in risk assessment: a 24-month inhalation study of rats (Trochimowicz et al., 1988) and an epidemiological study of human workers frequently exposed to 1,1,2-trichloro-1,2,2-trifluoroethane (Imbus and Adkins, 1972).

No adverse effects were noted in comparative physical examinations of 50 male workers exposed to 1,1,2-trichloro-1,2,2-trifluoroethane and 50 unexposed workers (Imbus and Adkins, 1972). Exposed workers worked an average 2.8 years (6 hours/day, 5 days/week) in rooms containing air with an average 1,1,2-trichloro-1,2,2-trifluoroethane concentration of 699 ppm (5357 mg/m^3), as indicated by 161 air samplings. Thus, 5357 mg/m^3 represents a NOEL in this study, but a LOAEL was not identified (Rec. #4).

The rat study (Trochimowicz et al., 1988) provides a more suitable basis for derivation of an RfD for chronic inhalation exposure to 1,1,2-trichloro-1,2,2-trifluoroethane because: more precisely defined, multiple exposure levels were employed; the duration of exposure was an entire lifetime; histopathological examinations were conducted; and both a NOEL and a LOAEL were identified (Recs. #1, 2). Rats were exposed to 0, 2000, 10,000 or 20,000 ppm 1,1,2-trichloro-1,2,2-trifluoroethane (15,328, 76,638 and 153,276 mg/m^3) 6 hours/day, 5 days/week for $\leq$24 months. No adverse effects were noted at any exposure level in hematological and blood chemical indices, urinalysis and histopathological examinations of all major organs. Decreased body weight gain was noted in both sexes receiving the 153,276 mg/m^3 treatment and in females exposed to 76,638 mg/m^3 (Rec. #2). The 76,638 mg/m^3 level thus represents a LOAEL for decreased body weight in female rats and the 15,328 mg/m^3 level represents a NOEL (Rec. #1).

In studies of dogs given 10-minute exposures to 1,1,2-trichloro-1,2,2-trifluoroethane (Trochimowicz et al., 1974), apparent steady-state levels of 1,1,2-trichloro-1,2,2-trifluoroethane were reached in arterial blood within 10 minutes of the start of exposure (see Section 5.1. and Figure 5-1). Therefore, assuming that a steady state is attained in the blood during 6-hour/day exposures and that the blood/gas partition coefficient for

1,1,2-trichloro-1,2,2-trifluoroethane is the same in rats and humans, the rat NOEL of 15,328 mg/m³ following exposure for 6 hours/day, 5 days/week is the HEC associated with no effects. Adjusting for intermittent exposure and applying an uncertainty factor of 100 (10 to extrapolate between species and 10 to protect the most sensitive individuals) yields an RfD of 27 mg/m³ for chronic inhalation exposure to 1,1,2-trichloro-1,2,2-trifluoroethane. This concentration is well below the lowest levels associated with cardiac sensitization to exogenous epinephrine in dogs (5000 ppm or 38,319 mg/m³ for 10 minutes) (Reinhardt et al., 1973) and those associated with human psychomotor impairment (2500 ppm or 19,160 mg/m³ for 2 hours) (Stopps and McLaughlin, 1967) in acute studies (Recs. #20, 25).

Confidence in the key study is high. More than adequate numbers of animals were exposed to multiple concentrations, multiple endpoints were measured and both a LOAEL and NOEL were identified. Confidence in the data base is medium. Human acute experimental exposure studies (Stopps and McLaughlin, 1967; Reinhardt et al., 1971a,b) and an occupational exposure study (Imbus and Adkins, 1972) found no adverse effects at concentrations lower than the chronic rat NOEL. Although microscopy revealed minor histological and ultrastructural changes in liver cells of rats exposed to concentrations of 1000 and 2000 ppm (7664 and 15,328 mg/m³) for 2 weeks (Vainio et al., 1980) (Rec. #12), the key study identified (with light microscopy) no histopathological liver effects upon much longer duration of exposure and at concentrations $\leq$20,000 ppm (153,276 mg/m³). Summarized data from a rat study indicate that 1,1,2-trichloro-1,2,2-trifluoroethane was not teratogenic (Ward, 1983), but the data were not available for review, and adequate supporting studies of the reproductive and teratogenic effects of 1,1,2-trichloro-1,2,2-trifluoroethane are not available. Reflecting confidence in the data base, confidence in the RfD is medium.

8.2.2. Oral Exposure.

8.2.2.1. LESS THAN LIFETIME (SUBCHRONIC) -- Data were not located regarding toxicity following subchronic oral exposure to 1,1,2-trichloro-1,2,2-trifluoroethane in humans or animals. Lacking sufficient data, the RfD of 3 mg/kg/day for chronic oral exposure to 1,1,2-trichloro-1,2,2-trifluoroethane is adopted for subchronic oral exposure. Confidence in this RfD is low, as explained in the next section.

8.2.2.2. CHRONIC -- Data were not located regarding the chronic toxicity of 1,1,2-trichloro-1,2,2-trifluoroethane in humans following oral exposure. The chronic inhalation study of rats (Trochimowicz et al., 1988), in which a LOAEL of 10,000 ppm (76,638 mg/m^3) and a NOEL of 2000 ppm (15,328 mg/m^3) 6 hours/day, 5 days/week were identified, may serve as the basis for an RfD for chronic oral exposure to 1,1,2-trichloro-1,2,2-trifluoroethane.

An equivalent dose of 1713 mg/kg/day is estimated by expanding the rat NOEL concentration of 2000 ppm (15,328 mg/m^3) to continuous exposure, multiplying the result by the inhalation rate for rats of 0.231 m^3/day estimated according to U.S. EPA (1980), and dividing by the time-weighted average body weight of 0.369 kg for females exposed to 2000 ppm, estimated from graphic data in the published report (Trochimowicz et al., 1988). An equivalent absorbed dose of 343 mg/kg/day is estimated by multiplying the equivalent dose by an absorption factor of 0.2. The absorption factor is based upon breath-holding experiments with humans (Morgan et al., 1972) (see Section 5.1.), which indicated that ~20% of the 1,1,2-trichloro-1,2,2-trifluoroethane inhaled in a single breath and held for 30 seconds was absorbed by the pulmonary system, and the assumption of 100% gastric absorption of

1,1,2-trichloro-1,2,2-trifluoroethane. The absorption factor for inhalation exposure is likely to be an overestimate, because it was obtained under nonsteady-state conditions.

The estimated equivalent absorbed dose is divided by an uncertainty factor of 100 (10 to extrapolate between species and 10 to protect the most sensitive individuals) to derive an RfD of 3 mg/kg/day or 210 mg/day for a 70 kg human for chronic oral exposure to 1,1,2-trichloro-1,2,2-trifluoroethane. Confidence in this RfD is low because of the uncertainty associated with route-to-route extrapolation.

9. REPORTABLE QUANTITIES

9.1. BASED ON SYSTEMIC TOXICITY

The toxicity of 1,1,2-trichloro-1,2,2-trifluoroethane was discussed in Chapter 6. The only observation of an adverse effect caused by subchronic or chronic exposure to nonlethal concentrations of 1,1,2-trichloro-1,2,2-trifluoroethane comes from the 24-month inhalation study of rats (Trochimowicz et al., 1988) in which decreased body weights relative to controls were observed in rats exposed to either 20,000 ppm (both sexes) or 10,000 ppm (females only) for 6 hours/day, 5 days/week. The dose-effect data for the lower of the two exposure levels associated with this response are summarized in Table 9-1. A CS is calculated for each study and presented in Table 9-2. Although a CS of 4 has been calculated for both studies in Table 9-2, the study in which female rats were exposed to 10,000 ppm was chosen to represent the chronic toxicity of 1,1,2-trichloro-1,2,2-trifluoroethane because of its lower MED value (Table 9-3).

9.2. BASED ON CARCINOGENICITY

As reviewed in Chapter 6, carcinogenicity data for 1,1,2-trichloro-1,2,2-trifluoroethane are limited to the negative inhalation studies of rats (Trochimowicz et al., 1988). In Chapter 8, 1,1,2-trichloro-1,2,2-trifluoroethane was assigned to EPA Group D, not calssificable as to human carcinogenicity. Because of lack of positive data, quantitative estimates of cancer risks cannot be derived; therefore, hazard ranking based on carcinogenicity is not possible for 1,1,2-trichloro-1,2,2-trifluoroethane.

TABLE 9-1

Inhalation Toxicity Summary for 1,1,2-Trichloro-1,2,2-Trifluoroethane[a,b]

Sex	No. at Start	Average Body Weight (kg)	Exposure	Transformed Animal Dose[c] (mg/kg/day)	Equivalent Human Dose[d] (mg/kg/day)	Response
F	100	0.369[e]	20,000 ppm (153,276 mg/m³) 6 hours/day, 5 days/week, for 24 months	17,134	2982	Decreased body weight relative to controls
F	100	0.369[e]	10,000 ppm (76,638 mg/m³) 6 hours/day, 5 days/week, for 24 months	8,567	1491	Decreased body weight relative to controls

[a]Source: Trochimowicz et al., 1988

[b]The vehicle/physical state was vapor and the purity of the compound was 99.89%.

[c]Calculated by multiplying the exposure concentration in mg/m³ by 6 hours/24 hours x 5 days/7 days x rat inhalation rate [0.231 m³/day for a rat weighing 0.369 kg (U.S. EPA, 1980)]

[d]Animal dose is scaled to the human dose by a surface area scaling factor (body weight 2/3).

[e]Average of body weights at 10, 30, 50, 70 and 90 weeks for females exposed to 20,000 ppm

TABLE 9-2

Inhalation Composite Score for 1,1,2-Trichloro-1,2,2-Trifluoroethane Using the Rat[a]

Dose/ Duration (mg/kg/day)	Chronic Human MED[b] (mg/day)	RV_d	Effect	RV_e	CS	RQ
17,134	208,740	1	Decreased body weight relative to controls	4	4	5000
8,567	104,370	1	Decreased body weight relative to controls	4	4	5000

[a]Source: Trochimowicz et al., 1988

[b]Calculated by multiplying the equivalent human dose (expressed as mg/kg/day) by 70 kg, the reference human body weight

TABLE 9-3

1,1,2-Trichloro-1,2,2-trifluoroethane

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	inhalation
Species/Sex:	rat/female
Dose*:	104,370 mg/day
Duration:	24 months
Effect:	decreased body weight relative to controls
RV_d:	1
RV_e	4
CS:	4
RQ:	5000
Reference:	Trochimowicz et al., 1988

*Equivalent human dose

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APPENDIX A

LITERATURE SEARCHED

This HEED is based on data identified by computerized literature searches of the following:

CHEMLINE
TSCATS
CASR online (U.S. EPA Chemical Activities Status Report)
TOXLINE
TOXLIT
TOXLIT 65
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP
NTIS
Federal Register
CAS ONLINE (Chemistry and Aquatic)
HSDB
SCISEARCH
Federal Research in Progress

These searches were conducted in April, 1989, and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Documentation of the Threshold Limit Values and Biological Exposure Indices, 5th ed. Cincinnati, OH.

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Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. 2878 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-1984. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., Littleton, MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. IARC, WHO, Lyons, France.

Jaber, H.M., W.R. Mabey, A.T. Lieu, T.W. Chou and H.L. Johnson. 1984. Data acquisition for environmental transport and fate screening for compounds of interest to the Office of Solid Waste. EPA 600/6-84-010. NTIS P884-243906. SRI International, Menlo Park, CA.

NTP (National Toxicology Program). 1987. Toxicology Research and Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, I.N. 1984. Dangerous Properties of Industrial Materials, 6th ed. Van Nostrand Reinhold Co., NY.

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USITC (U.S. International Trade Commission). 1986. Synthetic Organic Chemicals. U.S. Production and Sales, 1985, USITC Publ. 1892, Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under Contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Serv. Res. Publ. 137, Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California, State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. Prepared for the U.S. EPA, Washington, DC. PB-269605.

Schneider, B.A. 1979. Toxicology Handbook. Mammalian and Aquatic Data. Book 1: Toxicology Data. Office of Pesticide Programs, U.S. EPA, Washington, DC. EPA 540/9-79-003. NTIS PB 80-196876.

APPENDIX B

Summary Table for 1,1,2-Trichloro-1,2,2-trifluoroethane

	Species	Exposure	Effect	RfD or q_1^*	Reference
Inhalation Exposure					
Subchronic	rat	10,000 ppm (76,638 mg/m³) 6 hours/day, 5 days/week for 24 months	decreased body weight relative to controls in females; observed also in males at higher exposure concentration	27 mg/m³	Trochimowicz et al., 1988
Chronic	rat	10,000 ppm (76,638 mg/m³) 6 hours/day, 5 days/week for 24 months	decreased body weight relative to controls in females; observed also in males at higher exposure concentration	27 mg/m³	Trochimowicz et al., 1988
Carcinogenicity	ID	ID	ID	ID	ID
Oral Exposure					
Subchronic	rat	10,000 ppm (76,638 mg/m³) 6 hours/day, 5 days/week for 24 months	decreased body weight relative to controls in females; observed also in males at higher exposure concentration	3 mg/kg/day	Trochimowicz et al., 1988
Chronic	rat	10,000 ppm (76,638 mg/m³) 6 hours/day, 5 days/week for 24 months	decreased body weight relative to controls in females; observed also in males at higher exposure concentration	3 mg/kg/day	Trochimowicz et al., 1988
Carcinogenicity	ID	ID	ID	ID	ID
REPORTABLE QUANTITIES					
Based on Chronic Toxicity:		5000			Trochimowicz et al., 1988
Based on Carcinogenicity:		ID			

ID = Insufficient data

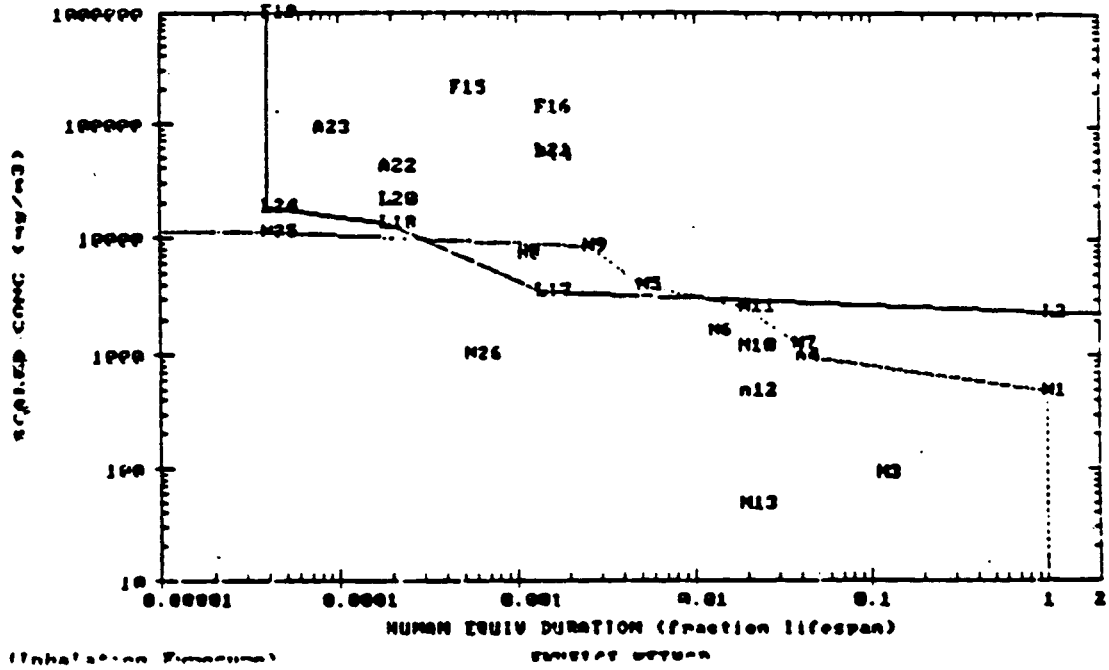
APPENDIX C

DOSE/DURATION RESPONSE GRAPHS FOR EXPOSURE TO 1,1,2-TRICHLORO-1,2,2-TRIFLUOROETHANE

C.1. DISCUSSION

Dose/duration-response graphs for inhalation exposure to 1,1,2-trichloro-1,2,2-trifluoroethane generated by the method of Crockett et al. (1985) using the computer software by Durkin and Meylan (1988) developed under contract to ECAO-Cincinnati are presented in Figures C-1 and C-2. Data used to generate these graphs are presented in Section C.2. In the generation of these figures, all responses are classified as adverse (FEL, AEL or LOAEL) or nonadverse (NOEL or NOAEL) for plotting. For inhalation exposure, the ordinate expresses concentration as the experimental concentration expressed as mg/m³ multiplied by the time parameters of the exposure protocol (e.g., hours/day and days/week) and is presenteq as expanded experimental concentration [expanded exp conc (mg/m³)]. For oral exposure, the ordinate expresses dose as human equivalent dose. The animal dose, in mg/kg/day is multiplied by the cube root of the ratio of the animal:human body weight to adjust for species differences in basal metabolic rate (Mantel and Schneiderman, 1975). The result is then multiplied by 70 kg, the reference human body weight, to express the human equivalent dose as mg/day for a 70 kg human.

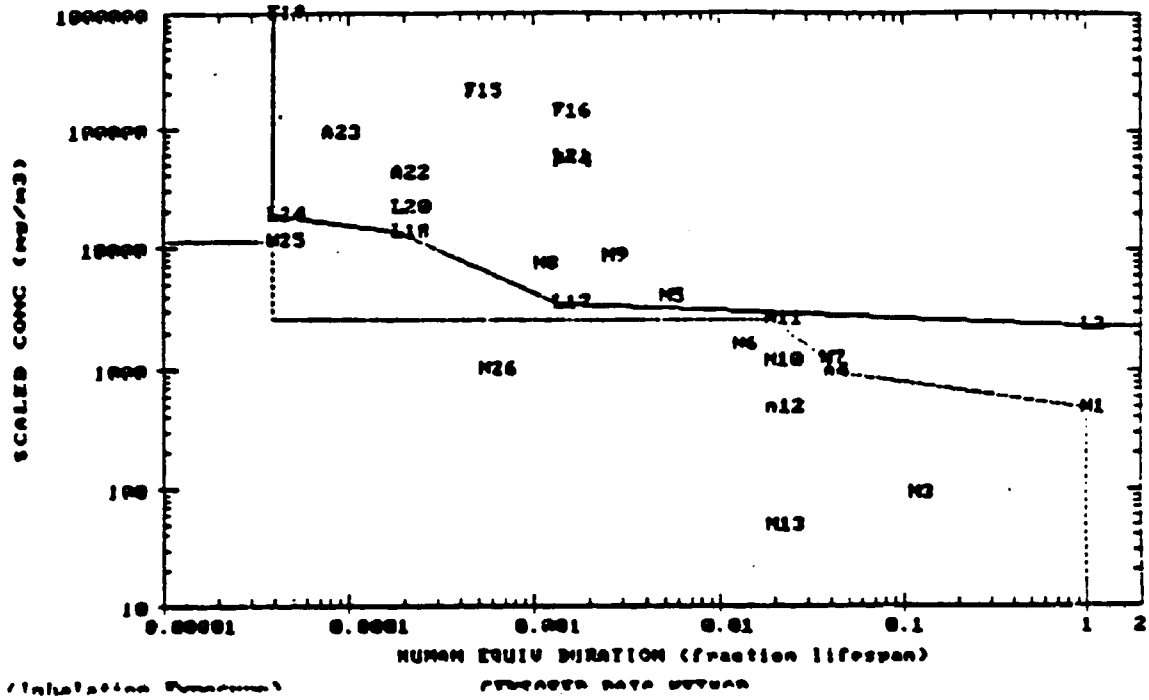
The boundary for adverse effects (solid line) is drawn by identifying the lowest adverse effect dose or concentration at the shortest duration of exposure at which an adverse effect occurred. From this point, an infinite line is extended upward, parallel to the dose axis. The starting point is then connected to the lowest adverse effect dose or concentration at the next longer duration of exposure that has an adverse effect dose or concentration equal to or lower than the previous one. This process is continued



F = FEL
L = LOAEL
n = NOAEL
N = NOEL
A = AEL

FIGURE C-1

Dose/Duration-Response Graph for Inhalation Exposure to 1,1,2-Trichloro-1,2,2-trifluoroethane (Envelope Method)



F = FEL
L = LOAEL
n = NOAEL
N = NOEL
A = AEL

FIGURE C-2

Dose/Duration-Response Graph for Inhalation Exposure to
1,1,2-Trichloro-1,2,2-trifluoroethane (Censored Envelope Method)

to the lowest adverse effect dose or concentration. From this point, a line is extended to the right, parallel to the duration axis. The region of adverse effects lies above the adverse effects boundary.

Using the envelope method, the boundary for no adverse effects (dashed line) is drawn by identifying the highest no adverse effects dose or concentration. From this point, a line parallel to the duration axis is extended to the dose or concentration axis. The starting point is then connected to the next lower or equal no adverse effect dose or concentration at a longer duration of exposure. When this process can no longer be continued, a line is dropped parallel to the dose or concentration axis to the duration axis. The no adverse effects region lies below the no adverse effects boundary. At either ends of the graph between the adverse effects and no adverse effects boundaries are regions of ambiguity. The area (if any) resulting from intersection of the adverse effects and no adverse effects boundaries is defined as the region of contradiction.

In the censored data method, all no adverse effect points located in the region of contradiction are dropped from consideration and the no adverse effect boundary is redrawn so that it does not intersect the adverse effects boundary and no region of contradiction is generated. This method results in the most conservative definition of the no adverse effects region.

The graph in Figure C-1 was generated using the envelope method. The adverse effects boundary is defined by four data points: the LOAEL for impaired psychomotor function (Stopps and McLaughlin, 1967) in humans exposed to 2500 ppm for 2 hours (Rec. #24); two LOAELs for reversible CNS effects observed during 6-hour exposures (Steinberg et al., 1969) of dogs to 13,000 ppm (Rec. #18) and of rats to 11,000 ppm (Rec. #17); and the LOAEL for decreased body weight in female rats (Rec. #2) exposed to 2000 ppm 6

hours/day, 5 days/week for 2 years (Trochimowicz et al., 1988). The no adverse effects boundary in Figure C-1 is defined by: NOELs for body weight decreases in dogs (Rec. #9) and mice (Rec. #10) from the 2-week inhalation study by Carter et al. (1970); NOELs for body weight decreases in dogs (Rec. #5) and in rats (Rec. #7) from a 4-week study (Steinberg et al., 1969); a NOAEL (Rec. #4) for physical examinations of occupationally exposed workers (Imbus and Adkins, 1972); and the NOEL for weight decreases in rats (Rec. #1) from the 2-year study by Trochimowicz et al. (1988). A region of contradiction is defined in Figure C-1. The rat data (Recs. #1, 2) from the study by Trochimowicz et al. (1988) were the basis for the chronic RfD for inhalation exposure derived in Chapter 8. The region of contradiction disappears in Figure C-2, in which Recs. #9 and 5 are not included in the defining of the no adverse effects boundary.

C.2. DATA USED TO GENERATE GRAPH

Chemical Name: 1,1,2-Trichloro-1,2,2trifluoroethane
CAS Number: 76-13-1
Document Title: Health and Enviromental Effects Document for 1,1,2-Trichloro-1,2,2-trifluoroethane
Document Number: pending
Document Date: pending
Document Type: HEED

==========

RECORD #1:
Species: Rats
Sex: Both
Effect: NOEL
Route: Inhalation
Dose: 2737.000
Duration Exposure: 24.0 months
Duration Observation: 24.0 months

Number Exposed: 200
Number Responses: 0
Type of Effect:
Site of Effect:
Severity Effect: 3

Comment: Concentrations studied: 2000, 10,000, 20,000 ppm 6 hours/day, 5 days/week. See following record.

Citation: Trochimowicz et al., 1988

RECORD #2:

Species:	Rats	Dose:	13685.000
Sex:	Female	Duration Exposure:	24.0 months
Effect:	LOAEL	Duration Observation:	24.0 months
Route:	Inhalation		

Number Exposed:	100
Number Responses:	NR
Type of Effect:	WGTDC
Site of Effect:	BODY
Severity Effect:	4

Comment: See previous record. Decreased body weight gain in males at higher concentration.

Citation: Trochimowicz et al., 1988

RECORD #3:

Species:	Rats	Dose:	511.000
Sex:	Male	Duration Exposure:	84.0 days
Effect:	NOEL	Duration Observation:	84.0 days
Route:	Inhalation		

Number Exposed:	6
Number Responses:	0
Type of Effect:	
Site of Effect:	
Severity Effect:	1

Comment: Experimental concentration: 200 ppm 8 hours/day. No treatment-related changes in liver, kidney or body weights, urinary catecholamine metabolites or liver cytochrome P-450.

Citation: Blohm et al., 1985

RECORD #4:

Species:	Humans	Dose:	957.000
Sex:	Male	Duration Exposure:	2.8 years
Effect:	NOEL	Duration Observation:	2.8 years
Route:	Inhalation		

Number Exposed:	50
Number Responses:	0
Type of Effect:	
Site of Effect:	
Severity Effect:	4

Comment: Occupational exposure study: workers averaged 2.8 years (6 hours/day,5 days/week) in rooms with mean concentration of 699 ppm (conc. range=46-4700 ppm). No adverse effects in physical examinations.

Citation: Imbus and Adkins, 1972

RECORD #5:

Species:	Dogs	Dose:	6980.000
Sex:	Both	Duration Exposure:	4.0 weeks
Effect:	NOEL	Duration Observation:	4.0 weeks
Route:	Inhalation		

Number Exposed: 0
Number Responses: 0
Type of Effect:
Site of Effect:
Severity Effect: 3

Comment: Experimental concentration: 5100 ppm 6 hours/day, 5 days/ week. No adverse effects on body weight, organ weights, macro or microscopic exam of major organs.

Citation: Steinberg et al., 1969

RECORD #6:

Species:	Guinea pigs	Dose:	6980.000
Sex	Female	Duration Exposure:	4.0 weeks
Effect:	NOEL	Duration Observation:	4.0 weeks
Route:	Inhalation		

Number Exposed: 10
Number Responses: 0
Type of Effect:
Site of Effect:
Severity Effect: 3

Comment: See record #5.

Citation: Steinberg et al., 1969

RECORD #7:

Species:	Rats	Dose:	6980.000
Sex:	Both	Duration Exposure:	4.0 weeks
Effect:	NOEL	Duration Observation:	4.0 weeks
Route:	Inhalation		

Number Exposed: 20
Number Responses: 0
Type of Effect:
Site of Effect:
Severity Effect: 3

Comment: See record #5. Also, no effects on rotobar performance and voluntary movement on activity wheel.

Citation: Steinberg et al., 1969

RECORD #8:

Species:	Monkeys	Dose:	15328.000
Sex:	NR	Duration Exposure:	14.0 days
Effect:	NOEL	Duration Observation:	14.0 days
Route:	Inhalation		

Number Exposed:	4
Number Responses:	0
Type of Effect:	
Site of Effect:	
Severity Effect:	3

Comment: Experimental concentration: 2000 ppm continuous exposure. No significant changes in hematology, clinical chemistry, EEG, body or organ weights.

Citation: Carter et al., 1970

RECORD #9:

Species:	Dogs	Dose:	15328.000
Sex:	NR	Duration Exposure:	14.0 days
Effect:	NOEL	Duration Observation:	14.0 days
Route:	Inhalation		

Number Exposed:	8
Number Responses:	0
Type of Effect:	
Site of Effect:	
Severity Effect:	3

Comment: See record #8.

Citation: Carter et al., 1970

RECORD #10:

Species:	Mice	Dose:	15328.000
Sex:	NR	Duration Exposure:	14.0 days
Effect:	NOEL	Duration Observation:	14.0 days
Route:	Inhalation		

Number Exposed:	40
Number Responses:	0
Type of Effect:	
Site of Effect:	
Severity Effect:	3

Comment: See record #8.

Citation: Carter et al., 1970

RECORD #11:

Species:	Rats	Dose:	15328.000
Sex:	NR	Duration Exposure:	14.0 days
Effect:	NOEL	Duration Observation:	14.0 days
Route:	Inhalation		

Number Exposed:	0
Number Responses:	0
Type of Effect:	
Site of Effect:	
Severity Effect:	3

Comment: See record #8.

Citation: Carter et al., 1970

RECORD #12:

Species:	Rats	Dose:	2737.000
Sex:	Male	Duration Exposure:	2.0 weeks
Effect:	NOAEL	Duration Observation:	2.0 weeks
Route:	Inhalation		

Number Exposed:	NR	NR
Number Responses:	NR	NR
Type of Effect:	ENZYM	HISTO
Site of Effect:	LIVER	LIVER
Severity Effect:	1	3

Comment: Concentrations: 200, 1000, 2000 ppm 6 hours/day, 5 days/week. Altered enzyme activity; light microscopy no effects; electron microscopy slight to moderate changes in endoplasmic reticulum in liver cells.

Citation: Vainio et al., 1980

RECORD #13:

Species:	Rats	Dose:	274.000
Sex:	Male	Duration Exposure:	2.0 weeks
Effect:	NOEL	Duration Observation:	2.0 weeks
Route:	Inhalation		

Number Exposed:	NR
Number Responses:	0
Type of Effect:	
Site of Effect:	
Severity Effect:	1

Comment: See record #12.

Citation: Vainio et al., 1980

RECORD #14:

Species:	Mice	Dose:	728061.000
Sex:	NR	Duration Exposure:	1.0 days
Effect:	FEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	NR
Number Responses:	NR
Type of Effect:	DEATH
Site of Effect:	BODY
Severity Effect:	10

Comment: Two-hour LC_{50} value = 95000 ppm.

Citation: Desoille et al., 1968

RECORD #15:

Species:	Guinea pigs	Dose:	919656.000
Sex:	NR	Duration Exposure:	1.0 days
Effect:	FEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	NR
Number Responses:	NR
Type of Effect:	DEATH
Site of Effect:	BODY
Severity Effect:	10

Comment: Two-hour LC_{50} value = 120,000 ppm.

Citation: Desoille et al., 1968

RECORD #16:

Species:	Rats	Dose:	843018.000
Sex:	NR	Duration Exposure:	1.0 days
Effect:	FEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	NR
Number Responses:	NR
Type of Effect:	DEATH
Site of Effect:	BODY
Severity Effect:	10

Comment: Two-hour LC_{50} value = 110,000 ppm.

Citation: Desoille et al., 1968

RECORD #17:

Species:	Rats	Dose:	21075.000
Sex:	NR	Duration Exposure:	1.0 days
Effect:	LOAEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	NR
Number Responses:	NR
Type of Effect:	BEHAV
Site of Effect:	CNS
Severity Effect:	7

Comment: Reversible CNS effects observed during 6-hour exposure to 11,000 ppm.

Citation: Steinberg et al., 1969

RECORD #18:

Species:	Dogs	Dose:	24907.000
Sex:	NR	Duration Exposure:	1.0 days
Effect:	LOAEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	NR
Number Responses:	NR
Type of Effect:	BEHAV
Site of Effect:	CNS
Severity Effect:	7

Comment: Reversible CNS effects observed during 6-hour exposure to 13,000 ppm.

Citation: Steinberg et al., 1969

RECORD #19:

Species:	Humans	Dose:	980967.000
Sex:	Male	Duration Exposure:	1.0 days
Effect:	FEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	1
Number Responses:	1
Type of Effect:	DEATH
Site of Effect:	CARDV
Severity Effect:	10

Comment: Occupational accident report. Worker exposed to about 128,000 ppm for less than 45 minutes died due to cardiac arrest.

Citation: May and Blotzer, 1984

RECORD #20:

Species:	Dogs	Dose:	38319.000
Sex:	NR	Duration Exposure:	1.0 days
Effect:	LOAEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	29
Number Responses:	10
Type of Effect:	FUND
Site of Effect:	CARDV
Severity Effect:	7

Comment: Cardiac arrhythmias observed in unanesthetized dogs given injections of epinephrine with 10-minute exposure to 5000 ppm, "cardiac sensitization."

Citation: Reinhardt et al., 1973

RECORD #21:

Species:	Mice	Dose:	766380.000
Sex:	NR	Duration Exposure:	1.0 days
Effect:	LOAEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	3
Number Responses:	3
Type of Effect:	FUND
Site of Effect:	CARDV
Severity Effect:	7

Comment: Cardiac arrhythmias in anesthetized mice given 6-minute exposure to 100,000 ppm and injections of epinephrine.

Citation: Aviado and Belej, 1974

RECORD #22:

Species:	Dogs	Dose:	76638.000
Sex:	NR	Duration Exposure:	1.0 days
Effect:	AEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	NR
Number Responses:	NR
Type of Effect:	FUND
Site of Effect:	CARDV
Severity Effect:	7

Comment: EC_{50} value of 10,000 ppm for cardiac sensitization to epinephrine: 5-minute exposure.

Citation: Clark and Tinston, 1973

RECORD #23:

Species:	Monkeys	Dose:	191595.000
Sex:	NR	Duration Exposure:	1.0 days
Effect:	AEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	NR
Number Responses:	NR
Type of Effect:	FUND
Site of Effect:	CARDV
Severity Effect:	7

Comment: Five-minute exposures to 25,000 ppm caused cardiac arrhythmias, myocardial depressions and tachycardia without exogenous epinephrine.

Citation: Belej et al., 1974

RECORD #24:

Species:	Humans	Dose:	19160.000
Sex:	Male	Duration Exposure:	1.0 days
Effect:	LOAEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	2
Number Responses:	2
Type of Effect:	MOTOR
Site of Effect:	CNS
Severity Effect:	7

Comment: Impaired psychomotor function during 2-hour exposure to concentrations at or above 2500 ppm.

Citation: Stopps and McLaughlin, 1967

RECORD #25:

Species:	Humans	Dose:	11496.000
Sex:	Male	Duration Exposure:	1.0 days
Effect:	NOEL	Duration Observation:	1.0 days
Route:	Inhalation		

Number Exposed:	2
Number Responses:	0
Type of Effect:	
Site of Effect:	
Severity Effect:	7

Comment: See Record #24.

Citation: Stopps and McLaughlin, 1967

RECORD #26:

Species:	Humans	Dose:	992.000
Sex:	Male	Duration Exposure:	2.0 weeks
Effect:	NOEL	Duration Observation:	2.0 weeks
Route:	Inhalation		

Number Exposed:	4
Number Responses:	0
Type of Effect:	
Site of Effect:	
Severity Effect:	4

Comment: Exposure protocol: 500 ppm, 6 hours/day, 5 days/week for 1 week, then 1000 ppm, 6 hours/day, 5 days/week for 1 week. Estimated dose is average expanded conc. No effects on psychomotor function or physical exam.

Citation: Reinhardt et al., 1971b

NR = Not reported