1-Chloro-1,1-difluoroethane; CASRN 75-68-3

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the IRIS assessment development process. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the guidance documents located on the IRIS website.

STATUS OF DATA FOR 1-Chloro-1,1-difluoroethane

File First On-Line 07/01/1995

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	yes	07/01/1995*
Carcinogenicity Assessment (II.)	not evaluated	

*A comprehensive review of toxicological studies was completed 01/05/05 - please see section I.B.6 for more information.

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — 1-Chloro-1,1-difluoroethane
CASRN — 75-68-3
Primary Synonym — HCFC-142b

Not available at this time.

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — 1-Chloro-1,1-difluoroethane
CASRN — 75-68-3
Primary Synonym — HCFC-142b
Last Revised — 07/01/1995

The inhalation Reference Concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory effects). It is expressed in units of mg/cu.m. In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Inhalation RfCs were derived according to the Interim Methods for Development of Inhalation Reference Doses (EPA/600/8-88/066F August 1989) and subsequently, according to Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (EPA/600/8-90/066F October 1994). RfCs can also be derived for the noncarcinogenic health effects of substances that are carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.B.1. Inhalation RfC Summary

Critical Effect	Exposures*	UF	MF	RfC
No adverse effects **2-Year Rat Inhalation Study** **Seckar et al., 1986**	NOAEL: 82,620 mg/cu.m (20,000 ppm) NOAEL(ADJ): 14,710 mg/cu.m NOAEL(HEC): 14,710 mg/cu.m LOAEL: None LOAEL(ADJ): None LOAEL(HEC): None	300	1	5E+1 mg/cu.m

* Conversion Factors and Assumptions: MW = 101. Assuming 25 C and 760 mmHg, NOAEL (mg/cu.m) = NOAEL (ppm) x MW/24.45 = 82,620. NOAEL(ADJ) = 82,620 x 6 hours/24 hours

x 5 days/7 days = 14,710 mg/cu.m. The NOAEL(HEC) was calculated for a gas:extrarespiratory effect assuming periodicity was attained. Because the b:a lambda values are unknown for the experimental animals species (a) and humans (h), a default value of 1.0 is used for this ratio. NOAEL(HEC) = 14,710 x (b:a lambda(a)/b:a lambda(h)) = 14,710 mg/cu.m.

I.B.2. Principal and Supporting Studies (Inhalation RfC)

Seckar, J.A., H.J. Trochimowicz, G.K. Hogan. 1986. Toxicological evaluation of hydrochlorofluorocarbon 142b. Fund. Chem. Toxicol. 24(3): 237-240.

Groups of 110 Sprague-Dawley rats/sex were whole-body exposed for 6 hours/day, 5 days/week for 104 weeks to 0, 1000, 10,000, or 20,000 ppm 1- chloro-1,1-difluoroethane (HCFC-142b) (99.85-99.99% pure), which corresponds to 0, 4130, 41,310, or 82,620 mg/cu.m, respectively. The corresponding duration-adjusted concentrations were 0, 738, 7380, or 14,710 mg/cu.m, respectively. The animals were observed for clinical signs of toxicity. Body weight was measured weekly during the first 14 weeks and biweekly through week 80. Hematological, clinical chemistry, and urinalysis evaluations were conducted on 10 animals/sex/group at 12, 18, and 24 months. Organ weights were recorded for all animals sacrificed after 1 year of exposure. Gross and microscopic tissue examination of over 45 tissues, including sectioning of brain and lungs, was performed on the animals in the control and high-exposure groups only. It is not clear to what extent the nasal tract tissues were examined. The HCFC-142b vapor was generated by evaporating the liquid test material in a stream of metered air. The test atmosphere concentration was assayed 6 times/day by gas-liquid chromatography. Mean daily chamber concentrations were found to be within 10% of the nominal concentrations.

There were no exposure-related effects on mortality, clinical signs, food consumption, body weight, behavior, ocular characteristics, hematology, clinical pathology, urinalysis, organ weights, or gross or microscopic pathology. Nonneoplastic effects were similar for both treated and control animals and were limited to typical age-related degenerative changes. Bronchopneumonia was evident in some treated and control animals. The study NOAEL is 20,000 ppm [NOAEL(HEC) = 14,710 mg/cu.m]; a LOAEL was not achieved.

I.B.3. Uncertainty and Modifying Factors (Inhalation RfC)

UF — An uncertainty factor of 10 is used to protect unusually sensitive individuals. A full factor of 10 is also applied for database deficiencies, due to lack of reproductive studies and the absence of chronic information on a second species. A partial uncertainty factor of 3 is used for interspecies extrapolation. The total uncertainty is 300.

MF — None

I.B.4. Additional Studies/Comments (Inhalation RfC)

A 90-day toxicity study was performed on groups of 27 male and female ChR- CD rats and 4 male beagle dogs/group that were whole body-exposed to 0, 1000, or 10,000 HCFC-142b (99.7% pure) for 6 hours/day, 5 days/week (Kelly, 1976). These concentrations corresponded to 0, 4130, or 41,310 mg/cu.m., respectively (duration-adjusted values = 0, 738, or 7380 mg/cu.m, respectively). The experimental protocol was similar to that described above for the chronic study, except that hematology, urinalysis, and clinical chemistry determinations were conducted at approximately monthly intervals in 10 rats/sex/group and in all dogs. Approximately 35-40 tissues were examined microscopically (it is not clear whether the nasal cavity was examined). There were no deaths, clinical signs of toxicity, or treatment-related effects on body weight, hematology, urinalysis, clinical chemistry, or gross or microscopic pathology. The lack of a significant increase in urinary fluoride indicates that HCFC-142b was not metabolized to any significant degree. This study demonstrates a NOAEL of 10,000 ppm [NOAEL(HEC) = 7380 mg/cu.m] under these exposure conditions; a LOAEL was not achieved.

A 13-week cytogenetics study in male rats was conducted concurrently with the 2-year study (Bio/dynamics, 1983; Seckar et al., 1986). In this study, 10 rats/group were exposed as in the principal study. No treatment-related effects on mortality, body-weight gain, or gross pathology were noted.

The lack of toxicity of HCFC-142b also was demonstrated in a 2-week study conducted by Moore (1976). In this study, ChR-CD rats (10 males/group) exposed to 0 or 20,000 ppm HCFC-142b for 6 hours/day, 5 days/week exhibited no exposure-related effects on survival, body weight gain, hematology, clinical chemistry, urinalysis, or gross or microscopic pathology. Salivation was noted in the animals during exposure to HCFC-142b. This concentration corresponds to 82,620 mg/cu.m and becomes 14,710 mg/cu.m when duration adjusted.

In rats, short-term (single or repeated) exposures to relatively high concentrations of HCFC-142b result in reversible CNS depression. The 4-hour lethal concentration in the rat is about 126,000 ppm (Wier, 1962). High exposures cause signs of pronounced CNS depression such as labored breathing and unconsciousness. At all, except very high doses, CNS depression is fully reversible, with no clinical sequelae being noted after repeated exposures and continued observation.

Lester and Greenberg (1950) conducted whole-body exposures in 10 rats (sex and strain unspecified) to 100,000 ppm (413,100 mg/cu.m) for 16 hours/day. All animals died within nine exposures: 6 in 7 days, 2 in 8 days, and 2 in 9 days. All animals were examined grossly, and sections of lung and liver were examined for histopathology. Lungs of all animals showed signs of severe irritation, having extensive consolidation and advanced lobar pneumonia. In a

subsequent experiment, five rats were exposed to 10,000 ppm (41,310 mg/cu.m), 16 hours daily for a period of 2 months, with no apparent effects. The lungs of 2/5 of these animals revealed evidence of inflammation, but sufficient information is not given to conclude that this effect was treatment related. These studies have a number of significant experimental (apparently no control animals were used) and reporting deficiencies that preclude their use in quantitative risk assessment.

Culik and Kelly (1976) exposed 25 pregnant ChR-CD rats/group to 0, 1000, or 10,000 ppm HCFC-142b (0, 4130, or 41,300 mg/cu.m, respectively) for 6 hours/day; 13 females were exposed on gestation days 4-13, and 12 females were exposed on gestation days 6-15. The rationale given for these two treatment regimes was that the former corresponded to the time before implantation and the latter to the period of organogenesis; however, the two groups were combined for evaluation of all parameters. Dams were examined for the numbers of corpora lutea, implantation sites, the number and location of live and dead fetuses and late and early resorptions, and the weight and crown-rump length of all live fetuses. All fetuses were examined for external anomalies, and approximately half of the fetuses from each litter were examined for skeletal abnormalities. Except for increased preimplantation losses noted in both exposure groups, no adverse effects were noted. This effect was not concentration-related and difficult to interpret because, as already mentioned, the dams exposed to HCFC-142b after implantation were not listed separately in the study. No maternal toxicity was described in the study. Because of the procedural and reporting inadequacies in this study, no effect levels were assigned.

Damske et al. (1978) exposed 20 pregnant CRL:COBS CD (SD) BR rats to 0, 3259, or 9420 ppm HCFC-142b (0, 13,460, or 38,905 mg/cu.m, respectively) for 6 hours/day on gestation days 6-15. Dams were sacrificed on day 20, and the fetuses were weighed, sexed, and examined for external malformations. One- third of the fetuses from each litter were examined for internal malformations, and the remainder were examined for skeletal abnormalities. There were no clearly exposure-related maternal effects that resulted from exposure to HCFC-142b, nor were there exposure-related embryotoxicity, variation in sex ratio, effects on fetal growth, or incidence of visceral defects. Some skeletal variations described by the study authors were classified as "commonly encountered" or "unusual skeletal variations", but no further information is given. Reduced ossification was described for several areas, including the interparietal and supraoccipital bones of the skull and the hyoid bone, although no concentration-related trends in incidence were apparent. Although these results are suggestive of developmental toxicity, no clear effect levels could be assigned from this study.

Cardiac sensitization was tested in a stress challenge test with 12 healthy male dogs. After a 5-minute inhalation of 50,000 ppm (206,500 mg/cu.m) stress (noise) elicited marked responses (a life-threatening cardiac arrhythmia) in five (41.7%) of the dogs.

The metabolism of HCFC-142b was studied in male Sprague-Dawley and Fischer 344 rats (Dodd et al., 1993). Groups of eight animals were exposed (nose-only) to room air or to 10,000 ppm HCFC-142b for 2 hours. Immediately after the termination of exposure, four exposed animals and one control animal were sacrificed, and samples of liver, kidney, heart, lung, muscle, skin, fat, testes, and blood were processed for analysis. The remaining animals were placed in metabolism cages for 24 hours, and urine and feces were collected. The parent compound was found in the tissues assayed immediately after exposure but not in tissue samples assayed 24 hours after exposure, indicating complete elimination of the compound within 24 hours. A carboxylic acid metabolite of HCFC-142b, chlorodifluoroacetic acid, was measured in the urine. The presence of this metabolite indicates that HCFC-142b is oxidatively metabolized.

The ozone depleting and global warming potential of this compound relative to other chlorofluorocarbon substitutes is discussed by Jarabek et al. (1994).

I.B.5. Confidence in the Inhalation RfC

Study — Medium
Database — Medium
RfC — Medium

The principal study was well conducted but failed to identify a LOAEL. The lack of toxicological response of this compound at the upper concentration used in the principal study demonstrates this compound is without adverse effects, although only for the endpoints examined and only in a single species. The database is given a medium to low level of confidence because a chronic inhalation study exists in only one species, and there are no reproductive toxicity studies. The developmental toxicity following inhalation exposure has been studied but is not considered totally adequate. A medium to low confidence in the RfC follows.

I.B.6. EPA Documentation and Review of the Inhalation RfC

Source Document — This assessment is not presented in any existing U.S. EPA document.

This assessment was peer reviewed by external scientists. This review was completed on 05/18/1995. Their comments have been carefully evaluated and considered in the revision and finalization of this IRIS summary. A record of these comments is included in the IRIS documentation files.

Other EPA Documentation — None

Agency Work Group Review — 09/24/1992

Verification Date — 09/24/1992

A comprehensive review of toxicological studies published through 2004 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing RfC for 1-Chloro-1,1-difluoroethane and a change in the RfC is not warranted at this time. For more information, IRIS users may contact the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

I.B.7. EPA Contacts (Inhalation RfC)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 1-Chloro-1,1-difluoroethane
CASRN — 75-68-3
Primary Synonym — HCFC-142b

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — 1-Chloro-1,1-difluoroethane
CASRN — 75-68-3
Primary Synonym — HCFC-142b

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

Bio/dynamics. 1983. A study in the rat of the cytogenetic effect of inhalation of fluorocarbon 142b, with attachment and cover letter dated March 27, 1992. EPA/OTS Doc. No. 86-920000865. NTIS/OTS 0535423.

Culik, R. and D.P. Kelly. 1976. Embryotoxic and teratogenic studies in rats with inhaled chlorodifluoroethane (FC 142b). E.I. Du Pont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine. EPA/OTS Doc. No. 86-890000866. NTIS/OTS 0520981.

Damske, D.R., F.J. Mecler and R.P. Beliles. 1978. Teratology study in rats. Isotron 142b. Monochlorodifluoroethane. Litton Bionetics, Kensington, MD. LBI Project No. 20890.

Dodd, D.E., W.T. Brashear and A. Vinegar. 1993. Metabolism and pharmacokinetics of selected Halon replacement candidates. Toxicol. Lett. 68: 37-47.

Jarabek, A.M., J.W. Fisher, R. Rubenstein, et al. 1994. Mechanistic insights aid the search for CFC substitutes: Risk assessment of HCFC-123 as an example. Risk Analysis. 14(3): 231-250.

Kelly, D.P. 1976. Ninety-day inhalation exposure of rats and dogs to vapors of 1-chloro-1,1-difluoroethane (FC-142b). E.I. Du Pont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine. Haskell Laboratory Report No. 469-76.

Lester, D. and L.A. Greenberg. 1950. Acute and chronic toxicity of some halogenated derivatives of methane and ethane. Arch. Ind. Hyg. Occup. Med. 2: 335-344.

Moore, B.L. 1976. Subacute (two-week) inhalation toxicity. Chlorodifluoroethane. E.I. Du Pont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine. EPA/OTS Doc. No. 86-890000864. NTIS/OTS 0520979.

Seckar, J.A., H.J. Trochimowicz and G.K. Hogan. 1986. Toxicological evaluation of hydrochlorofluorocarbon 142b. Fund. Chem. Toxicol. 24(3): 237-240. (Several volumes of the original study were consulted and are part of the literature file for this compound.)

Wier, J. 1962. Inhalation toxicity test-acute. 1-Chloro-1,1-difluoroethane (K-142b) distillation residue. E.I. Du Pont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine. Haskell Laboratory Report No. 30-62.

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — 1-Chloro-1,1-difluoroethane
CASRN — 75-68-3
Primary Synonym — HCFC-142b

Date	Section	Description
07/01/1995	I.B.	Inhalation RfC summary on-line
12/03/2002	I.B.6.	Screening-Level Literature Review Findings message has been added.
03/03/2005	I.B.6	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

VIII. Synonyms

Substance Name — 1-Chloro-1,1-difluoroethane
CASRN — 75-68-3
Primary Synonym — HCFC-142b
Last Revised — 10/01/1992

- 75-68-3
- Ethane, 1-chloro-1,1-difluoro-
- FREON 142B
- Hydrochlorofluorocarbon 142b
- 1-chloro-1,1-difluoroethane
- alpha-CHLOROETHYLIDENE FLUORIDE
- CFC 142b
- CFC 1426

- Chlorodifluoroethane
- Chlorofluorocarbon 142b
- FC 142b
- FC142b
- Freon 142
- Freon 142b
- Genetron 101
- Genetron 142b
- Gentron 142B
- HSDB 2881
- Propellant 142b
- R 142b
- 1,1-DIFLUORO-1-CHLOROETHANE
- HCFC-142b