# 2-CHLORO-1,1,1,2-TETRAFLUOROETHANE

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## I. IDENTIFICATION

Chemical Name: 2-Chloro-1,1,1,2-Tetrafluoroethane
Synonyms: Chlorotetrafluoroethane; HCFC-124; HFA 124; Fluorocarbon 124; G124; Genetron 124.
CAS Number: 2837-89-0
Common Name: HCFC-124
Molecular Formula: $C2HClF_4$
Structural Formula: CF,—CFC1H

## II. CHEMICAL AND PHYSICAL PROPERTIESI[1,~1]

Physical State: Colorless gas
Molecular Weight: 136.48 g/mol
Conversion Factors: 1 ppm = 5.58 mg/m$^3$;
1 mg/m$^3$ = 0.18 ppm
Boiling Point: -11°C (12.2°F) at 760 mmHg
Vapor Pressure: 68 psia (3517 mmHg) at 25°C (77°F)
Odor: Faint ethereal odor
Flash Point: Nonflammable
Specific Gravity Liquefied Gas: 1.364 at 20OC (68°F)
Reactivity: Unreactive under most conditions

## III. USES

HCFC-124 is one of the substances under development as a replacement for the current chlorofluorocarbons (CFCs). It is being evaluated as a propellant and refrigerant.

## IV. TOXICITY DATA

A. Acute Toxicity

1. *Oral Toxicity*

No data are available because HCFC-124 is a gas at room temperature.

B. Eye Toxicity

There are no data identified on the ocular toxicity of HCFC-124 gas.

C. Skin Toxicity

There are no data identified on the dermal effects of HCFC-124 gas.

D. Inhalation Toxicity

Rat:
6-hour exposure to 360,000 ppm was nonlethal.(3)
Approximate lethal concentration =
230,000 ppm (4-hour exposure).")
15-min $LC_{50}$— 570,000 ppm.$^0$)

E. Other

The cardiac sensitization potential of HCFC 124 was evaluated in beagle dogs exposed to various concentrations for approximately 5 minutes, given an intravenous injection of adrenalin, and monitored for cardiac arrhythmias. This resulted in a lowest observable adverse effect level (LOAEL) of 25,000 ppm and a no observable adverse effect level (NOAEL) of 10,000 ppm.(5)

B. Genotoxicity

*In vitro,* HCFC-124 vapor was negative in the Ames assay using *Salmonella typhimurium* strains TA97, TA98, TA100, TA1535, TA1537, TA1538 and in *Escherichia coli* WP2 uvrA either with or without S-9 metabolic activation.(610 It was also inactive in chromosome aberration studies using human lymphocyteso$^9$) and Chinese hamster ovary cells.(1o)

*In vivo,* HCFC 124 was not active in a mouse micronucleus assay at exposure levels up to 99,000 ppm!'"

C. Metabolism

Male Fisher 344 rats exposed to 10,000 ppm HCFC-124 for 2 hours excreted both inorganic fluoride anion and trifluoroacetic acid (TFA) in

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the urine. In vitro studies with rat liver microsomes indicated that HCFC-124 was metabolized to Trifluoroacetic acid (TFA) by cytochrome P450 2E.[12]

D. Developmental and Reproductive Studies

Teratology studies were conducted in rats and rabbits. In the rat study,[13,14] groups of pregnant animals were exposed to HCFC-124 levels of 0, 5000, 15,000, and 50,000 ppm during Gestational Days 7 through 16. No developmental effects were seen in this study. A decrease in maternal body weight gain was observed during Gestation Days 7 through 9. This was the only evidence for maternal toxicity. In the second study,[14,15] groups of pregnant white rabbits were also exposed to HCFC-124 levels of 0, 5000, 15,000, and 50,000 ppm on Days 7 to 19 of gestation. No treatment-related developmental or teratogenic effects were seen in this study. The only suggestion of maternal toxicity was an occasional decrease in food consumption at 50,000 ppm. Also, these rabbits may have been less alert during the exposures, compared to rabbits in the lower levels and control group.

E. Subacute/Subchronic Toxicity

Groups of 10 male ChR-CD rats each were exposed to levels of 0 or 100,000 ppm for 6 hours/day, 5 days/week, for 2 weeks. No signs of toxicity were seen in hematological, blood chemistry, or urinalysis results, either immediately following the study or 14 days postexposure. A mild anesthetic effect was observed during the inhalation exposure that was reversible within 15–30 minutes of exposure.[16,17]

A 4-week inhalation toxicity study was conducted with 5 groups of 10 male and 10 female Crl:CD®R rats.[18] The animals were exposed 6 hours/day, 5 days/week, for approximately 4 weeks, at target concentrations of 0, 500, 2000, 10000, or 50000 ppm. There were no compound-related effects on body weight, food consumption, mortality, hematology, clinical chemistry parameters, organ weights, or histopathology. Urine fluoride levels were significantly elevated in all exposure groups, except in females exposed to 500 ppm HCFC-124. These high urine fluoride levels are considered to be a marker of exposure rather than a sign of toxicity, and are consistent with the previously demonstrated HCFC-124 metabolism in rats reported by Olson et al (1991). During their daily exposure period the rats exposed to 50,000 ppm appeared to be lethargic and uncoordinated. However, at the end of the daily exposure when the animals were removed from their chambers, no evidence of lethargy or uncoordination was observed. For this study, a NOAEL of 10,000 ppm was established on the basis of the observation of lethargic, uncoordinated movement occurring during exposure at 50,000 ppm.

In a subsequent study[14,19] in the same laboratory, groups of 20 male and 20 female Crl:CD®R rats were exposed to levels of 0, 5000, 15000, and 50000 ppm of HCFC-124, 6 hours per day, 5 days per week, for 13 weeks. The study involved complete clinical chemistry, hematology, and histopathological evaluation of more than 40 tissues per animal. Also, a functional observational battery (FOB) was included at Weeks 4, 8, and 13. There were no compound-related effects on survival, body weight, food consumption, organ weights, hematology, or tissue morphology. The NOAEL was set at 5000 ppm for males based on lower serum triglyceride levels seen at the 45-day interval at 15,000 and 50,000 ppm (this was not seen at the end of the study), and also a transient decreased arousal rate noted during the FOB evaluation in 4 of 10 males exposed to 15,000 ppm. For the females, a NOAEL of 15,000 ppm was based on an increase in alkaline phosphatase at 50,000 ppm (otherwise 50000 ppm could be considered the NOAEL). The authors considered the effects observed in both male and female animals to be of minimal biological significance.

In a similar study, groups of 20 male and 20 female Crl:CD-1(ICR)BR mice were exposed to levels of 0, 5000, 15000, and 50000 ppm of HCFC-124, 6 hours/day, 5 days/week, for 13 weeks.[14] Clinical chemistry was examined at 7 and 13 weeks and following a 1-month recovery period. Complete histopathology and hepatic beta-oxidation were examined at 13 weeks and at 1-month postexposure. Body weight changes in male mice were observed; however, they were deemed unrelated to HCFC-124 concentration. There was a transient decrease in the serum triglycerides of male mice exposed to 15,000 and 50,000 ppm HCFC-124 at 13 weeks that was reversed 1 month after exposure. Hepatic beta-oxidation activity in all exposed male mice was twice that observed in control animals at 13 weeks, and returned to control levels at 1 month postexposure. While the observed two-fold increase in beta-oxidation was statistically significant, there was no concentration-response relationship, and the control results between the

time points demonstrated a variability of 1.5-fold. Also, the two-fold increase in beta-oxidation is considered small when compared to classic inducers such as clofibrate and tibricacid.

F. Chronic Toxicity

A chronic toxicity study was conducted by exposing male and female Crl:CD®BR rats to 0, 2000, 10000, or 50000 ppm HCFC-124 for 6 hours/day, 5 days/week for 2 years.([8]) In this study, neither male nor female rats at any HCFC-124 exposure level demonstrated adverse effects on body weight, food consumption, survival, clinical signs of toxicity, ophthalmoscopically observable ocular lesions, serum hormone levels, or clinical pathology parameters during the course of the study. There were no HCFC-124-induced changes in organ weights, gross organ observations, or microscopic findings in either the male or female rats at any exposure concentration. HCFC-124 did not demonstrate any carcinogenicity in either sex of rats after inhalation exposures at concentrations up to 50,000 ppm, therefore, the NOAEL for both male and female rats.

## V. HUMAN USE AND EXPERIENCE

There is no toxicity information available. It is being considered as a potential replacement for CFC-12 in certain applications.

## VI. RATIONALE

Acute toxicity studies in rats have shown HCFC-124 to be practically non-toxic by the inhalation route of exposure. The acute lethal level for HCFC-124 exceeds 230,000 ppm for a 4-hour exposure, and a 13-week study (6 hours/day, 5 days/week) demonstrated only transient decreases in serum triglycerides and arousal rates in male rats exposed to >15,000 ppm. A recently published 2-year study has shown HCFC-124 to be practically non-toxic by the inhalation route; both male and female rats exposed to concentrations up to 50,000 ppm demonstrated no evidence of carcinogenicity or toxicity in numerous testing endpoints. HCFC-124 was not active in a series of *in vitro* and *in vivo* mutagenicity studies, and did not cause developmental or teratogenic effects in rats or rabbits exposed to concentrations up to 50,000 ppm. The threshold for cardiac sensitization in dog studies is 25,000 ppm, with 10,000 ppm reported as the NOAEL. None of the newly published data indicate the need for a change in the current OEL. The 1000 ppm OEL should provide an ample margin of safety to prevent cardiac sensitization and/or systemic injury.

## VII. RECOMMENDED OEL GUIDE

8-hour time-weighted average (TWA): 1000 ppm

## VIII. REFERENCES


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