Chlorotrifluoroethylene

Document History
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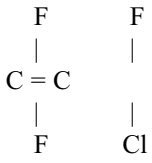
I. IDENTIFICATION

Chemical Name: 2-Chloro-1, 1, 2-trifluoroethylene
Synonyms: Chlorotrifluoroethylene; CTFE; Fluorocarbon 1113; 1, 1, 2-Trifluoro-2-chloroethylene; Trifluorovinylchloride
CAS Number: 79–38–9
Molecular Formula: C_2C1F_3
Structural Formula:



II. CHEMICAL AND PHYSICAL PROPERTIES[1, 2]

Physical State and Appearance: Colorless gas
Odor Description: Faint, ethereal odor
Odor Threshold: No data available
Molecular Weight: 116.47
Conversion Factor: 1 ppm = 4.75 mg/m^3
Boiling Point: -27.9°C (-18.22°F)
Vapor Pressure: 5.22 atm at 21.1°C (70°F)
Flash Point: -27.8°C (-18°F), closed cup
Flammability Limits in Air (by volume):
Lower explosive limit: 16%
Upper explosive limit: 34%
Specific Gravity (Water = 1): 1.30
Reactivity and Incompatibilities: Incompatible with oxidizing agents. Reacts readily in liquid phase with oxygen to form peroxides, followed by sudden release of energy. Peroxide in the presence of water will form chlorofluoroacetic acid, phosgene, carbonyl fluoride, hydrogen fluoride, and hydrogen chloride.

III. USES

Chlorotrifluoroethylene is one of a series of halogenated ethylenes used as a monomer for the production of chlorofluorocarbon polymers.[3]

IV. ANIMAL TOXICITY DATA

A. Acute Toxicity and Irritancy

1. *Oral Toxicity*

   Mice: LD_{50} = 268 mg/kg (administered as a 3.5% solution in olive oil)[4]

2. *Eye Irritation*

   No data available

3. *Skin Absorption*

   No data available

4. *Skin Irritation*

   No data available

5. *Skin Sensitization*

   No data available

6. *Inhalation Toxicity*

   Mice: 3-hr LC_{50} = 8000 ppm[3]

   Rabbits: 2-hr LC_{50} - 5040 ppm[5]

   Rats: 2-hr LC_{50} = 5040 ppm[5]

   Rats: 4-hr LC_{50} = 1000 ppm[5]

   Acute exposure of rats to 220 ppm or 395 ppm for 4 hr resulted in degenerative change in renal tubules. Acute exposure of rats to 100 ppm for 4 hr resulted in diuresis.[6,7] These effects were reversible.

7. *Other Toxicity*

   Mice: Intraperitoneal injections, administered as a 3.5 solution in olive oil, resulted in an LD_{50} of 175mg/kg[4]

B. Subacute Toxicity

Rats were exposed to 0, 33, 61, 119, and 241 ppm CTFE 6 hr/day 5 days/week for 2 weeks. Reduction in body weight gain and necrosis in the renal tubules were reported at the 241 ppm exposure level. No effects were observed at or below 119 ppm.[8]

Male Fisher-344 rats were exposed via inhalation to 395 ppm CTFE 4 hr/day for 5 consecutive days. Within 1 day the rats exhibited diuresis, increased water intake, decreased urine osmolality, increased urinary lactic dehydrogenase activity and increased plasma creatinine and urea nitrogen. During subsequent days of exposure these values returned to control levels, indicating an adaptive response. Necrosis of the kidney was observed. This effect reached a maximum 3 days into the exposure. Again, regeneration and recovery was observed during the latter part of the exposure phase of the study.[6]

C. Subchronic Toxicity

Male and female rats were exposed to 0, 29, 62, and 121 ppm CTFE 6 hr/day 5 days/week for 13 weeks. Exposure to 62 ppm and 121 ppm resulted in large dilated tubules lined by large epithelial cells in the kidneys in both sexes. At 62 ppm, these effects seemed to be reversible within 2 weeks of the final exposure.[8]

In a study conducted in the mid-1950s dogs, guinea pigs, rabbits, and rats were involved in a series of up to 18 4-hr exposures at 300 ppm CTFE. The following effects were reported: mortality (guinea pigs and rabbits); degenerative changes in renal tubules (rats); loss of body weight (guinea pigs); and encephalopathy, intermittent leucopenia, and granulocytopenia (dogs).[5]

In a subsequent study that lasted approximately 14 months dogs, guinea pigs, rabbits, and rats were given 6-hr exposures 5 days/week to progressively high levels of CTFE (15, 30, 50, 100, and 150 ppm). Neither the guinea pigs nor the rabbits were adversely affected. The rats developed degenerative changes in the renal tubules. In the dog study, exposure at 100 ppm (and possibly 50 ppm) resulted in significant hematological changes. Neurological disturbances and degenerative changes in the central nervous system were observed at 150 ppm. However, the results of the dog study have not been repeated in subsequent investigations.[5]

In one other study[5], rabbits were exposed to 500 ppm CTFE 4 hr/day 6 days/week for 58 days. After three rabbits died, the exposure was lowered to 250 ppm and exposure time increased to 6 hr. After an additional 72 days of exposure, the animals showed a decrease in rate of body weight gain, depressed alkalkine phosphatase, and elevated cholinesterase levels, and widespread congestion of the liver, spleen, and kidneys. In a second study[5] by the same investigator, rabbits were exposed to 250 ppm CTFE 4 hr/day for a period of 70–110 days. Weight gain was again retarded, and there were changes in several hematological parameters. These hematological findings, however, have not been reported in subsequent investigations.

Male rats were exposed to 0, 100, and 200 ppm CTFE 5 hr/day 5 days/week for 17 weeks. Proteinurea, elevated lactic acid dehydrogenase, and urinary fluoride and lowered body weight gain were reported at both levels. Necrosis and degenerative changes were observed in the kidney tubules.[9]

D. Chronic Toxicity/Carcinogenicity

No data available.

E. Reproductive/Developmental Toxicity

In a probe teratology study, groups of 5 pregnant rats were exposed to 0, 33, 61, 119, and 241 ppm CTFE 6 hr/day on days 6 through 19 of gestation. At 119 ppm, slight body weight reductions were observed in the pregnant rats, but no effects were seen at or below 61 ppm. There were no indications of feto- or embryotoxicity or teratogenicity at any exposure level tested.[8]

F. Genotoxicity/Mutagenicity

CTFE was nonmutagenic in the Ames *Salmonella typhimurium* assay at exposure levels as high as 50% (v/v).[10] It was also negative in an *in vivo* sister-chromatid exchange (SCE) study with rabbits using exposure levels up to 204 ppm.[11]

G. Metabolism/Pharmacokinetics

The *in vivo* formation of cysteine conjugates has been postulated to account for the nephrotoxiciry of CTFE. Initially, the glutathione conjugate is formed; it is then cleaved to form the cysteine conjugate [S-(2-chloro-1,1,2-trifluoroethylo)-L-cysteine][12,13] This reaction proceeds in both rat and isolated human liver sections at similar rates.[14,15] Isolated rabbit renal tubule suspensions were also used to demonstrate the biotransformation of CTFE by glutathione conjugation to form the nephrotoxic metabolite. *In vivo* and *in vitro* evidence supported metabolism of chemically synthesized glutathione conjugates to the nephrotoxic

cysteine conjugate.[16] The mechanism of toxic action is believed to proceed through inhibition of readsorption of glucose in the proximal tubules in the kidney.[17]

V. HUMAN USE AND EXPERIENCE

CTFE has been produced for more than 35 years. Exposure levels have tended to be at or below 20 ppm as a time-weighted average (TWA), and no adverse effects have been reported.

The recommended maximum permissible concentration in a report published in the former Soviet Union was 5 mg/m^3, or approximately 1 ppm.[18]

VI. RATIONALE

The most significant toxic effect seems to be degenerative changes in the kidney with rats. Most studies report these effects following CTFE exposure to levels of 10 ppm or greater. In one 13-week study, reversible effects were reported at 62 ppm, while 29 ppm seemed to represent a no observable effect level (NOEL).[8] Even when exposures continued, with levels up to 395 ppm, the effects were reversible.

No adverse health effects were found during routine employee physical examinations, when exposures have tended to be at or below 20 ppm.

VII. RECOMMENDED OEL

8-hr TWA: 5 ppm

VIII. REFERENCES

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NOTE: The following databases were searched in developing this 2009 revision of the Chlorotrifluoroethylene WEEL Guide:

MEDLINE (1989 – 2008)
IPA (1970 – 2008)
CURRENT CONTENTS (1990 – 2008)
CAB (Global Health) (1973 – 2008)
CINAHL (1982 – 2008)
TOXNET (2005 – January 2010)