SIDS INITIAL ASSESSMENT PROFILE

CAS No.	79-38-9
Chemical Name	Chlorotrifluoroethylene (CTFE)
Structural Formula	ClFC=CF2

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Rationale

Two tetrahalotehylenes, tetrafluoroethylene (TFE; CAS No. 116-14-3) and tetrachloroethylene (TCE; CAS No. 127-18-4), are used as analogues for CTFE. TCE data are used for aquatic toxicity endpoints and TFE is used to supplement the genetic toxicity endpoint.

All three chemicals have similar structures, physicochemical properties and fate characteristics. They have high vapor pressures indicating that they will reside in the atmosphere. The distribution is further supported by fugacity modeling. These chemicals also are not subject to hydrolysis or photolysis. However, the major metabolic pathways of TCE and CTFE differ and therefore, human-health related endpoints are addressed only with TFE data. TFE data are considered appropriate because the kidney is a common target organ of both CTFE and TFE.

Human Health

CTFE is metabolized via glutathione and cysteine conjugation pathways, as demonstrated *in vitro* in rat liver hemogenate. Isolated rabbit renal tubule suspensions also show biotransformation of CTFE to the glutathione conjugate.

Most recent (1981) acute inhalation toxicity data indicate a rat LC50 of greater than 540 ppm. Degeneration of the renal tubules was seen at 220 and 345 ppm (1,048 and 1,644 mg/m^3) and diuresis at 100 ppm (476 mg/m^3) following 4 hour exposures. Clinical signs include proximal tubular necrosis, increase in serum BUN/creatinine, urinary fluoride, and urinary LDH activity. These effects were reversible. Older data show a 3-hr LC50 of 8000 ppm (38,109 mg/m^3) in mice, a 4-hr LC50 of 1000 ppm (4,764 mg/m^3) in rats, and a 2-hr LC50 of 5040 ppm (24,009 mg/m^3) in rats and rabbits. An oral LD50 of 268 mg/kg bw has been demonstrated in mice using a CTFE solution in olive oil. No data are available for skin and eye irritation or dermal sensitization.

In repeated-dose inhalation studies in the rat with CTFE exposure durations of 6 hours/day, 5days/week for periods from 2 to 13 weeks, the no-observable-adverse-effect-level was 29 ppm (138 mg/m^3). The higher exposure levels of 62 and 121 ppm (295 and 576 mg/m^3) induced dilated tubules in the kidneys. The effects seen at 62 ppm were reversible 2 weeks after exposure. In a study conducted in the mid 1950's, dogs, rats, guinea pigs, and rabbits were exposed to up to 18 4-hour exposures of CTFE at 300 ppm (1,429 mg/m^3). The following effects were observed: mortality (guinea pigs and rabbits), degenerative changes in renal tubules (rats) loss of body weight (guinea pigs) and encephalopathy, intermittent leucopenia and granulocytopenia (dogs). In a subsequent study which lasted 14 months, rats, rabbits, guinea pigs, and dogs were exposed for 6 hours/day, 5days/week to progressively higher levels of CTFE (15, 30, 50, 100, and 150 ppm; 72, 143, 238, 476, and 715 mg/m^3). Neither the guinea pigs nor the rabbits were adversely affected. The rats developed degenerative changes in the renal tubules. In the dog, exposure at 100 ppm (476 mg/m^3) (and possibly 50 ppm – 238 mg/m3), resulted in significant

hematological changes. Neurological disturbances and degenerative changes in the nervous system were observed at 150 ppm (715 mg/m^3).

Overall CTFE did not present toxicologically significant genotoxic activity *in vitro* and *in vivo*. It was not active in an Ames test with exposure levels up to 50% in the air above the cultures. It also was not active in two *in vivo* sister chromatid exchange studies, one with rabbits and the other with rats. Both used an exposure level of 204 ppm (972 mg/m^3). TFE data were also used as supplemental information. TFE showed no toxicity in a gene mutation study at the HPRT locus in Chinese hamster ovary (CHO) cells without activation but was inconclusive in a study with activation; negative results were obtained after conducting a subsequent study with metabolic activation. In a study of structural chromosomal aberrations using TFE in CHO cells, no increase in frequency of aberrations was observed at any dose up to 100% nominal concentration in air either with or without metabolic activation. In an *in vivo* micronucleus assay conducted using peripheral blood erythrocytes from mice exposed to 0, 1250, 2500 or 5000 ppm via inhalation for 90 days; no increases in micronuclei were observed.

Reproductive organs were evaluated in the 13-week inhalation study of CTFE. No adverse effects were observed after full histopathological examination of the tissues from the testes, epididymides, ovaries, and uterus at exposures up to 121 ppm (576 mg/m^3) for 6 hours/day for 5 days/week. Other subchronic studies also did not result in adverse effects on reproductive organs.

In a limited developmental study, pregnant rats were exposed to 33, 61, 119, or 241 ppm (157, 291, 567, or 1,148 mg/m^3) of CTFE. At 119 ppm (567 mg/m^3) and above, slight reductions in maternal body weight gain were seen. No effects were seen at or below 61 ppm (291 mg/m^3). There was no evidence of developmental toxicity at any exposure level. In a subsequent developmental toxicity study, groups of 25 time-mated female rats were exposed to levels of 0 (control), 31, 89 or 187 ppm (148, 424, 891 mg/m^3). The NOAEL for the dams was 31 ppm. At 89 ppm the dams showed body weight gain depressions. At 187 ppm the exposures were terminated after 7 exposures due to dam body weight loss. The NOAEL for the pups was 89 ppm. At 187 ppm, reduced pup weight and reduced ossification were observed. There were no other test material increases in variations or abnormalities in the offspring.

Environment

CTFE is a gas with a melting point of -157.5 °C, a boiling point of - 27.9 °C, a water solubility of 804 mg/L, and vapor pressure of 537 kPa. It exhibits slow indirect photolysis that is primarily attributed to hydroxyl radicals (with a half-life of approximately 50 days), and very slow direct photolysis. The compound does not have hydrolysable groups, and therefore, will not undergo hydrolysis in water. The low octanol/water partition coefficient (log K_{ow} = 1.65) indicates a low potential for bioaccumulation. Most estimates available from EPIWIN indicate that CTFE generally does not rapidly (or readily) biodegrade. Studies using the analog TCE generally showed no biodegradation under aerobic conditions but suggest biodegradation under anaerobic conditions.

Estimates for the toxicity of CTFE have been calculated with the ECOSAR program in the EPIWIN model. For fish, the 96-hr LC_{50} was estimated to be 4.123 mg/L; for daphnids, the 48-hr EC_{50} was estimated to be 242 mg/L; and for green algae, the 96-hr EC_{50} was estimated to be 44 mg/L. To supplement these results, data using the analog TCE show that in fish, the lowest 96-hr LC_{50} is 4.8 mg/L (measured in rainbow trout). The lowest 48-hr EC_{50} in the invertebrate *Daphnia magna* is 8.5 mg/L. In algae, the 72-hr EC50 is 3.64 mg/L.

Exposure

CTFE has been produced for over 25 years and the estimated worldwide production in 2000 was estimated to be 1,000 to 5,000 tonnes. There is one production site in the U.S. and there are two sites that use CTFE in the U.S. CTFE is one of a series of halogenated ethylenes used as a monomer for the production of chlorofluorocarbon polymers. It is also used as a starting material in the manufacture of fire suppressants and pharmaceuticals such as Halothane. Since it is a gas (BP –27.9°C) at room temperature, it is used in

sealed systems. Exposure levels have been determined from workplace monitoring studies. Eighty-two percent of air samples from employee breathing zones during maintenance operations were below the threshold limit value of 5 ppm (25 mg/m^3) in one U.S. plant; all personal air samples were below 5 ppm in another U.S. plant. Less than 0.5% of samples were above 5 ppm when sampling areas from all parts of the plant in 2003. No adverse effects have been reported.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical possesses properties indicating a possible hazard for the environment (aquatic toxicity between 1 and 100 mg/L based on data for CTFE and for the supporting substance TCE) and human health (acute, repeated-dose and developmental toxicity). Data presented by the Sponsor country indicate that CTFE is an industrial intermediate, that workplace exposures are controlled, that CTFE has no consumer uses, and that the chemical will partition to the atmosphere. These data indicate that exposure to humans and the aquatic environment is anticipated to be low, and therefore, this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented in the Sponsor country.