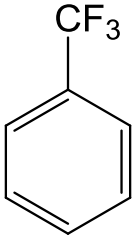
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	98-08-8
Chemical Name	Trifluoromethylbenzene
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Physical-chemical properties

Trifluoromethylbenzene is a colourless liquid at standard temperature and pressure with aromatic odour. Melting point and boiling point are -28.95 °C and 102.1 °C respectively. Vapour pressure is 5.14 kPa at 25 °C and a partition coefficient between octanol and water (Log K_{ow}) is 3.01. Water solubility is 192 mg/L at 20 °C. Trifluoromethylbenzene is highly flammable.

Human Health

Although no toxicokinetic information was identified for absorption, metabolism, distribution or excretion, trifluoromethylbenzene is considered to be absorbed from the gastrointestinal tract and well distributed throughout the rat body based on observations in the combined repeated dose toxicity and reproductive/developmental toxicity test by oral administration of this chemical.

The dermal LD_{50} value was above 2000 mg/kg bw for male and female rats in the acute study following OECD TG 402 (exposure time: not specified but 24 hr in the guideline). No toxic effects were observed at 2000 mg/kg bw. No reliable studies were available for acute oral and inhalation toxicity. Although the quality of data is not robust, trifluoromethylbenzene seems to be slightly toxic after single exposure via oral and inhalation routes. Indeed, the inhalation LC_{50} values were reported to be 70.81 mg/l (4 hrs) for rats and 92.24 mg/l (2 hrs) for mice, and the oral LD_{50} to be 15000 mg/kg bw for rats and 10000 mg/kg bw for mice.

In the skin irritation test conducted in accordance with OECD TG 404, undiluted trifluoromethylbenzene caused very mild edema and mild to moderate erythema up to 72 hrs after 4-hr application to the rabbit skin. While the erythema and edema had almost completely disappeared by the end of the 14-day observation period, the skin surface remained dry and rough, and was parchment-like and flaky in parts. The average irritation value was 2.0 for erythema and eschar formation and 0.2 for edema formation. In the eye irritation test conducted according to OECD TG 405, trifluoromethylbenzene exerts some irritating effects (injected vessels, and carmine-colored and slightly swollen conjunctivae) one hour after instillation into the eye of rabbits, but these effects were no longer observed at other examination times. Therefore, trifluoromethylbenzene was considered to be a skin irritant but not an eye irritant in rabbits. No information regarding the respiratory tract irritancy of trifluoromethylbenzene was available.

No information was available for sensitisation.

The repeated toxicity of trifluoromethylbenzene has been investigated in a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [according to the procedures of OECD TG 422, except for limited haematological and clinical chemistry examination in only male]. The substance was

administered via gavage to male and female rats at 0, 20, 100 or 500 mg/kg bw/day. The duration of treatment in males was 49 days including a 14-day pre-mating period. Females were dosed for a 14-day pre-mating period, during mating and gestation periods, and until day 3 of lactation. One female died after delivery on day 23 of gestation in the 500 mg/kg bw/day group. No other treatment-related clinical signs of toxicity were observed. No effects were found on body weight and food consumption. Hematological and blood biochemical examination performed in males only revealed a decrease in glucose and increases in total protein, albumin, total cholesterol, phospholipid and calcium at 500 mg/kg bw/day. The absolute and/or relative liver weight increased in males in the 100 mg/kg bw/day group and in both sexes in the 500 mg/kg bw/day group, and histopathological examination revealed centrilobular hypertrophy of hepatocytes at 100 and 500 mg/kg bw/day in both sexes. In males, increased absolute and relative kidney weights were also found in the 500 mg/kg bw/day group, and microscopic changes in the kidney (hyaline droplets, epithelial necrosis, dilatation and basophilic changes in the epithelium of proximal tubules) were observed at 100 and 500 mg/kg bw/day. Based on histopathological changes in the liver and kidneys, the NOAEL for repeated dose oral toxicity was considered to be 20 mg/kg bw/day for both sexes.

In an Ames test conducted in accordance with OECD TG 471 and 472, trifluoromethylbenzene was negative in multiple strains of *Salmonella typhimurium* (TA100, TA1535, TA1537, TA98) and *Escherichia coli* (WP2 uvrA) both with and without metabolic activation. Other bacterial reverse mutation studies with *Salmonella typhimurium* (TA100, TA1535, TA1537, TA97, TA98) and *Escherichia coli* (pkM101) also showed negative results with and without metabolic activation. An *in vitro* chromosome aberration test (OECD TG 473) using cultured Chinese hamster lung (CHL/IU) cells with 24-hr and 48-hr continuous exposures without metabolic activation, and 6-hr short term exposure with and without metabolic activation was negative. Negative results were also obtained in a rec assay for DNA damage with *Bacillus subtilis* and mitotic crossover and the gene conversion assay with *Saccharomyces cerevisiae*. Based on these results, trifluoromethylbenzene is considered to be non genotoxic *in vitro*. There was no *in vivo* study on mutagenicity.

No information on carcinogenicity for trifluoromethylbenzene was identified.

In a combined repeated dose toxicity study with the reproductive/developmental toxicity screening test [the modified OECD TG 422, repeated-dose portion described above], trifluoromethylbenzene was administered via gavage to male and female rats at 0, 20, 100 or 500 mg/kg bw/day. The duration of treatment for males was 49 days including a 14-day pre-mating period. Females were dosed for a 14-day pre-mating period, during mating and gestation periods, and until day 3 of lactation. In the 500 mg/kg bw/day group, one dam died after delivery on day 23 of gestation, which was considered due to dystocia. No adverse effects on reproductive parameters (estrous cycle, copulation, fertility and gestation index, precoital and gestational days, and the number of corpora lutea, implantation sites, live newborns and stillborns) were observed up to the highest dose tested. There were also no changes in the weight and histopathology of reproductive organs in either sex. Therefore, the NOAEL for reproductive toxicity was considered to be 100 mg/kg bw/day. For developmental effects, there were no treatment-related changes in the number of live pups born, nor in the sex ratio. No dose-related abnormality was found in gross external and internal findings in pups. In all treatment groups lower body weights of pups were found at day 0 (<10%), which did not recover at day 4 (16% maximum). The toxicological relevance of this observation is unclear as no other signs of developmental toxicity were observed. Therefore, the substance is not considered to be a developmental toxicant. Nevertheless as the body weight reduction was statistically significantly different at the lowest dose tested the overall LOEL of this study is considered to be 20 mg/kg bw/day. The NOAEL for maternal toxicity was 20mg/kg bw/day.

Trifluoromethylbenzene may present a hazard to human health (skin irritation, repeated dose toxicity). Adequate screening level data are available to characterize the human health hazard for the purposes of the OECD HPV Chemicals Programme.

Environment

In the atmosphere, trifluoromethylbenzene is expected to be degraded by hydroxyl radicals. A calculated half-life time of 27.3 days is obtained by AOPWIN (version 1.92) for the indirect photo-oxidation by reaction with hydroxyl radicals in air.

Trifluoromethylbenzene is not hydrolysed due to the lack of hydrolysable functional groups. A hydrolysis test according to OECD test guideline 111 showed that trifluoromethylbenzene was stable in water at pH 4, pH 7 and

pH 9 at 50 °C for five days.

An OECD Guideline 301D test was conducted with trifluoromethylbenzene with sludge for four weeks. The concentrations of trifluoromethylbenzene in the test system were 2.4 mg/L and 11.9 mg/L. The test result showed 0 % degradation by BOD after four weeks cultivation period for both treatments. BIOWIN estimation (version 4.10) predicts that trifluoromethylbenzene is not ready biodegradable. According to these results, trifluoromethylbenzene is considered to be not-readily biodegradable.

In a study performed according to a protocol equivalent to OECD Guideline 305 with carp exposed to trifluoromethylbenzene, bio-concentration factors of 26–54 were obtained for the concentration of 100 μg/L and 31–58 for the concentration of 10 μg/L for six weeks exposure period. In this test, the lipid content value of the test fish was 4.9 %. Taking into account the octanol-water partition coefficient, a bio-concentration factor can be calculated as 45 according to a log K_{ow} of 3.01 by BCFBAF (version 3.00). Trifluoromethylbenzene is not expected to bioaccumulate.

Fugacity level III calculations show that trifluoromethylbenzene is mainly distributed to the water compartment (45.0 %) and air compartment (43.6 %) if equally and continuously released to the air, soil and water. A Henry's law constant of 4.74×10^3 $Pa.m^3$/mole at 25 °C suggests that volatilization of trifluoromethylbenzene from water is rapid. A soil adsorption coefficient of Log K_{oc} = 2.6 indicates trifluoromethylbenzene has moderate sorption to soil and sediment.

The following acute toxicity test results have been determined for aquatic species;

Fish [*Oryzias latipes*, OECD-TG 203]: 96 h LC_{50} = 19 mg/L (measured)

Daphnid [*Daphnia magna*, OECD-TG 202]: 48 h EC_{50} = 3.1 mg/L (measured)

Algae[*Pseudokirchneriella subcapitata*, OECD-TG 201]:

72 h ErC_{50} = 5.4 mg/L (measured, growth rate)

72 h EbC50 = 3.0 mg/L (measured, area under growth curve)

The following chronic toxicity test results have been determined for aquatic species:

Daphnid [*Daphnia magna*, OECD-TG 211]: 21 d LOEC = 1.9 mg/L (measured)

21 d NOEC = 0.59 mg/L (measured)

Algae[*Pseudokirchneriella subcapitata* OECD-TG 201]:

72 h NOErC and 72 h NOEbC 1.5 mg/L (measured)

Trifluoromethylbenzene possesses properties indicating a hazard for the environment (acute aquatic toxicity values between 1 and 100 mg/L for fish, invertebrate and algae and chronic toxicity less than 1 mg/L for invertebrate). This chemical is considered not readily biodegradable and is not expected to have bioaccumulation potential. Adequate screening-level data are available to characterize the hazard to the environment for the purposes of the OECD HPV Chemicals Programme.

Exposure

According to the notification obligation of the amount of manufacture/import based on the Chemical Substances Control Law in Japan (sponsor country), no production was reported and import was less than 1 tonne/year in fiscal year 2007. Although the reporting is obligatry to manufacturers/importers dealing with the substance at more than 1 kg/year, the production volume and/or import volume of trifluoromethylbenzene in Japan seems to be almost zero. Information of the production volume in other areas is not obtained.

As trifluoromethylbenzene seems not to be manufactured in Japan, no detailed information is available on the production method and use patterns. Trifluoromethylbenzene is produced by the reaction of hydrogen fluoride on benzotrichloride, or reaction of antimony trifluoride on benzotrichloride. Trifluoromethylbenzene is used as an intermediate for pharmaceutical products and pesticides. This chemical is also used in dye chemistry, in the manufacturing of substituted trifluoromethylbenzene containing an ethylenic group, in high polymer chemistry,

and in dielectric fluids, such as transformer oils. Other uses are solvent, vulcanizing agents and insecticides.

Occupational exposure to trifluoromethylbenzene through inhalation of vapour and via the dermal route is anticipated from its physical properties. No OEL's are established for this chemical.

As trifluoromethylbenzene is not used in the general consumer products, no consumer exposure is expected. No more detailed information is available for the consumer exposure.