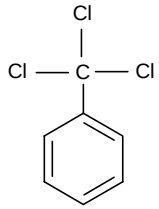
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	98-07-7
Chemical Name	α,α,α-Trichlorotoluene (Trichloromethylbenzene)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

α,α,α-Trichlorotoluene hydrolyzes to hydrochloric acid and benzoic acid upon contact with moisture. It is readily absorbed from the gastrointestinal tract, distributed within the body, and excreted after metabolic transformation to hippuric acid mainly via the urine. The 4-hour inhalation LC_{50} in rats was 530 mg/m^3 for females, and >600 mg/m^3 for males. 5 of 6 rats died after a 4-hour exposure to about 1,000 mg/m^3. Clinical signs included ocular and respiratory tract irritation, dyspnea, and weight loss. The dermal LD_{50} value for rats was greater than 5,000 mg/kg bw, with sedation and poor general health from days 1 to 10 after exposure. Depending on the vehicle used, the acute oral LD_{50} values in rats were between about 700 mg/kg bw (when applied in corn oil) and 2,200 mg/kg bw (when applied as aqueous suspension). Clinical signs like sedation, dyspnea, polyuria, and weight loss were observed for several days after the oral administration of the chemical.

Under occlusive conditions, α,α,α-trichlorotoluene was irritating to the skin of rabbits. The chemical may cause severe eye irritation. The vapors are irritating to the respiratory tract.

In mice, the repeated inhalation of α,α,α-trichlorotoluene (12.8 mg/m^3 for 12 months) resulted in a high incidence of bronchitis and bronchopneumonia. In rats, repeated inhalation exposure to concentrations ≥ 48.2 mg/m³ for 4 weeks led to death, depressed weight gain, dyspnoea and gasping. Microscopically, inflammation and/or squamous metaplasia of the cells lining the nasal, tracheal, bronchial and bronchiolar epithelia were observed. No significant changes occurred in the 5.1 mg/m³ group (NOAEL). Skin irritation up to necrosis was seen after dermal treatment of rabbits with 50, 100 or 200 mg/kg bw/day of the undiluted chemical for three weeks. Histopathologically, an increased incidence of portal inflammatory cell infiltrates in the liver, and, at 200 mg/kg bw/day, bile duct proliferation was found. Pathological changes were also seen in the seminiferous tubules at 100 and 200 mg/kg bw/day. Irritation of the eyes, the skin and the respiratory tract were the main clinical signs after repeated painting of mice skin with α,α,α-trichlorotoluene. In a 28-day feeding study on rats, a NOAEL could not be determined, as mild histopathological effects on liver, kidney and the thyroid gland were still present at the lowest test concentration of 0.5 ppm in the diet (corresponding to about 0.05 mg/kg bw/day).

α,α,α-Trichlorotoluene has demonstrated a genotoxic potential in bacterial and mammalian cell systems. In non-standard *in vivo* tests, the chemical induced micronuclei in bone marrow cells of mice. Chromosomal aberrations in bone marrow cells and sister chromatid exchanges in peripheral lymphocytes have been reported in rats after repeated inhalation exposure.

α,α,α-Trichlorotoluene has induced lung tumors, skin tumors, leukemia and lymphomas in animals by the inhalative, dermal and oral routes of exposure. The available human data for α,α,α-trichlorotoluene are limited because the studies included small numbers of cancer deaths and were confounded by exposure to mixtures of chlorinated compounds. Based on the limited human data and sufficient evidence from animal studies, the combined exposures to α-chlorinated toluenes and benzoyl chloride are probably carcinogenic to humans (IARC Group 2A).

There were no fertility studies available. In a 3-week dermal study on rabbits, degeneration of the tubules in seminiferous ducts, and an increased incidence of multinucleated giant cells in the seminiferous tubules were reported at dose levels of 100 and 200 mg/kg bw/day, but not for 50 mg/kg bw/day. Pathological changes in reproductive organs were not reported in any of the carcinogenicity studies. Sufficient documentation with regard to the scope of the examinations relating to the reproductive organs was however not available, and therefore a lack of effect cannot be deduced from these studies. The effects on male reproductive organs observed in the 3-week dermal study in rabbits give some indications that α,α,α-trichlorotoluene might be toxic to reproduction. As results from further testing would not affect the most stringent exposure control measures already in place, no further tests are warranted.

In a poorly documented study, developmental effects were reported in rats at non-maternally toxic dose levels (LOAEL, fetal development = 12.5 mg/kg bw/day; NOAEL maternal toxicity = 12.5 mg/kg bw/day). Further testing is not warranted because exposure to the chemical is already strictly controlled due to its mutagenic and carcinogenic properties. Although not fully tested for reproductive and developmental toxicity, α,α,α-trichlorotoluene should be regarded as potentially toxic to reproduction because it is a genotoxic carcinogen.

Environment

α,α,α-Trichlorotoluene is a moisture/water sensitive fluid with a melting point of -4.8 °C, a boiling point of 220.7 °C, and a density of 1.37 g/cm³ at 20 °C. The vapour pressure of the substance is 0.2 hPa at 20 °C. The log Kow cannot be determined due to hydrolysis. The solubility in water is 0.1 g/l at 20 °C. The flash point is ca. 108 °C, the auto flammability (ignition temperature) 420 °C. An atmospheric half-life of about 45 days is estimated due to the reaction with hydroxyl radicals.

α,α,α-Trichlorotoluene reacts completely with water within a few minutes at 20 °C, forming benzoic acid and hydrochloric acid. Any emission into the air or into the terrestrial compartment would be affected by humidity and also results in the formation of the hydrolysis products. However, several aquatic toxicity tests have been undertaken with α,α,α-trichlorotoluene. The observed toxicity effects in these studies can be attributed to the degradation products benzoic acid and hydrochloric acid. For assessment of the environmental impact of the hydrolysis products it is referred to the validated results of the hazard assessments on benzoates and hydrochloric acid within the OECD SIDS-Program.

Hydrochloric acid is a strong mineral acid that dissociate readily in water to the hydrated protons. Hydrochloric acid will not adsorb on particulate matters or surfaces and will not accumulate in living tissues. Benzoic acid is not expected to hydrolyse.

The hydrolysis products benzoic acid and hydrochloric acid have been tested with aquatic species. Especially hydrochloric acid caused a pH shift in water which determined the impact on aquatic life. The tolerance of water organisms towards pH margin and variation is diverse. Recommended pH values for test species listed in OECD guidelines are between 6.0 and almost 9. Acute testing with fish showed 96h-LC50 at about pH 3.5 (equals about 20 mg α,α,α-trichlorotoluene), chronic testing with early life stages of fish NOECs at pH 6.0 and 5.56. Benzoic acid is not toxic (LC50 or EC50 >100 mg/l) towards aquatic organisms. The substance is readily biodegradable and non-bioaccumulative.

Acute toxicity of α,α,α-trichlorotoluene to fish (*Leuciscus idus*) was 4140 mg/l (48 h-LC_{50}) . With *Daphnia magna* an EC_{50} (24 h) of > 100 mg/l was determined. For the blue-green alga *Microcystis aeruginosa* an 8 day-EC_3 of 34 mg/l was obtained in a cell multiplication inhibition test (test solution was not neutralized). It is not expected that an algal EC_{50} obtained in a neutralized test solution would be lower than the EC_{50} for *Daphnia*. Since there are acute tests for α,α,α-trichlorotoluene from three trophic levels, an assessment factor of 1000 is applied according to EU

Technical Guidance Document to the lowest acute effect concentration (*Daphnia magna*, 24 h-EC50 of 100 mg/l). The following value is obtained: $PNEC_{aqua}$ = 0.1 mg/l

Exposure

In 2000, the world wide production capacity of α,α,α-trichlorotoluene is estimated to 80,000 metric tons by about 10 producers: Western Europe 56,000 t/a, USA 16,000 t/a, Japan 5,500 t/a, and others 2,400 t/a. α,α,α-Trichlorotoluene is an intermediate, used exclusively in the industrial production of other intermediates such as benzoylchloride, benzotrifluoride, 2,4-dihydroxybenzophenone. These intermediates are further used in the synthesis of pesticides, dyestuffs, UV absorbers and pharmaceuticals.

At the sponsor company α,α,α-trichlorotoluene is manufactured and processed in closed systems. The exhausts from manufacturing and processing (including filling) of α,α,α-trichlorotoluene are connected to absorbing units, thermal exhaust purification plants and air washing units. Thus, at the sponsor company during production and processing virtually no α,α,α-trichlorotoluene is emitted into the atmosphere. Due to the water-free production and processing processes emissions into the wastewater were not detected. The exposure of workers is below the German Technical Exposure Limit (TRK) value of 0.012 ppm (0.1 mg/m³) for α,α,α-trichlorotoluene.

A direct use of α,α,α-trichlorotoluene is not known, and α,α,α-trichlorotoluene is not listed in the Nordic and Swiss product registers as being contained in consumer products. Exposure of consumers to α,α,α-trichlorotoluene is considered negligible.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health:

The chemical possesses properties indicating a hazard for human health (e.g. acute and repeated dose toxicity, irritation, mutagenicity, carcinogenicity, reproduction and developmental toxicity). In the sponsor country, the substance is solely used as an isolated intermediate with controlled transport, and exposure in occupational settings is controlled. There is no exposure of consumers. Countries may desire to investigate any exposure scenarios that were not presented by the sponsor country.

Environment:

The chemical is currently of low priority for further work due to its low hazard profile. The degradation products benzoic acid and hydrochloric acid have already been assessed within the OECD SIDS-Program.