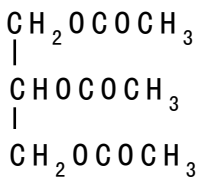
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	102-76-1
Chemical Name	Triacetin
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Triacetin is readily hydrolyzed to free glycerol and acetic acid, when incubated with rat intestine *in vitro*. The chemical infused in dogs undergoes intravascular hydrolysis and the majority of the resulting acetate is oxidized nearly quantitatively.

The acute oral and dermal toxicity of triacetin are very low: in an oral acute toxicity study in rats [OECD TG 401], a limit dose of 2,000 mg/kg bw caused no mortality and no signs of systemic toxicity during the 14-day observation period. The LD_{50} in rats by gavage is determined to be >2,000 mg/kg bw for both sexes, and dermal LD_{50} in rabbits and guinea pigs were >2,000 mg/kg bw. Acute inhalation toxicity is considered to be very low, since the LC_{50} in an acute inhalation toxicity study in rats was >1,721 mg/m^3 for both sexes [OECD 403] and repeated daily exposure of rats to 73,700 mg/m^3 produced no sign of toxicity after 5 days.

In an oral study in rats by the OECD combined repeated dose and reproductive/developmental toxicity screening test [OECD TG 422], animals received gavage doses of 0 - 1,000 mg/kg bw/day of triacetin for 44 days from 2 weeks prior to mating for males and for 41 - 48 days from 14 days before mating to day 3 postpartum for females. Triacetin had no effects on clinical signs, body weight, food consumption, and organ weight or necropsy findings. No histopathological changes ascribable to the compound were observed in either sex. There were no abnormalities in haematological or blood chemical parameters in males. The NOAEL for repeated dose oral toxicity is thus considered to be 1,000 mg/kg bw/day for both sexes.

An inhalation study was conducted in rats given triacetin for 90 days at a dose of 249 ppm (2,220 mg/m^3) under non-GLP condition. No toxic signs were noted during the exposure. The NOAEL is considered to be 249 ppm (2,220 mg/m^3) for 90 days. Although the inhalation study is considered to be useful, it does not fully comply with the current testing protocol.

The combined repeated dose and reproductive/developmental toxicity study in rats at doses of 0 - 1,000 mg/kg bw/day [OECD TG 422] showed no statistically significant adverse effects on reproductive parameters including the mating index, fertility index, gestation length, numbers of corpora lutea and implantations, implantation index, gestation index, delivery index, parturition and maternal behavior at delivery and lactation. In addition, there were no significant differences in numbers of offspring or live offspring, the sex ratio, the live birth index, the viability index or body weight. Developmental toxicity, clinical signs of toxicity, and change in necropsy findings were not found in offspring. Therefore, the NOAEL is considered to be 1,000 mg/kg bw/day for parental animals and offspring.

Triacetin did not induce gene mutation in bacteria at concentrations up to 5,000 ug /plate (OECD TG 471 and 472).

Induction of chromosome aberrations, however, was observed in the Chinese hamster cultured cells only at the highest concentration (2.2 mg/mL, 10 mM) in the presence of an exogenous metabolic activation system (OECD TG 473). Because of high toxicity (75 %) that might be caused by low pH (4.9) at the end of the treatment, the chromosomal aberration observed might not be biological relevant. Under un-physiological culture condition, such as low pH, it was reported that the frequency of chromosomal aberrations could be increased. Polyploidy was not induced under any of the conditions tested. Taking all data into consideration, triacetin could be considered to be non-genotoxic.

Triacetin is not irritating to skin [OECD TG 404] and to eyes [OECD TG 405] in rabbits. There is no skin sensitisation in guinea pigs by triacetin. In the tests using human volunteers, triacetin induced no skin irritation or skin sensitization. However, one case concerning allergic contact eczema caused by triacetin has so far been reported in a cigarette factory.

Based on the available data and anticipated daily intake (7.8 mg/day/adult), triacetin and a group of related triglyceride did not represent a hazard to human health (JECFA, 1975, Commission, 1992 and SCF, 1995). Triacetin was given GRAS status by FEMA (1965) and is approved by the FDA for human food use.

Environment

Triacetin is a liquid with a boiling point of 258 °C and vapour pressure of 0.003306 hPa at 25°C. It is soluble in water (70 g/L at 25°C) and miscible with alcohols, aromatic hydrocarbons and diethyl ether.

The generic fugacity model (Mackay Level III Fugacity Model) shows that triacetin will be distributed mainly to water if it is released into water, whereas approximately one third and two third of the chemical will stay in water and soil, respectively when released at equal amounts to water, soil and sediment (1:1:1). An estimated Henry's law constant of 1.23×10^{-8} atm m^3/mol indicates that the compound is essentially non-volatile from water.

The rate constant for the vapour-phase reaction with photochemically produced hydroxyl radicals has been estimated to be 7.81×10^{-12} cm^3/molecule sec at 25°C, which corresponds to an atmospheric half-life of about 48 hours at an atmospheric concentration of 5×10^5 hydroxy radicals/cm^3.

Triacetin is readily biodegradable (OECD TG 301C: 77 % after 14 days based on BOD, OECD TG 301B: 93 % after 28 days based on $ThCO_2$, OECD TG 301D: 79 % after 30 days based on BOD). The chemical is expected to have a low potential for bioaccumulation based on a low Log Pow (0.21).

The half-lives in water at pH 7 and 9 are estimated to be 60.4 days and 16.5 hours at 25 °C, respectively, whereas no hydrolysis at pH 4 occurs at 50 °C in 5 days. Triacetin is expected to have high soil mobility and may leach readily in soil based on Koc value of 10.5 from a regression-derived equation. Therefore, aqueous hydrolysis may be a major degradation process for triacetin in moist alkaline soils.

The 72-h toxicity of triacetin to alga (growth inhibition, *Selenastrum capricornutum*) is > 1,000 mg/L for EC_{50} and 556 mg/L for NOEC [OECD TG 201]. In *Daphnia magna*, EC_{50} values (48 h) for acute toxicity [OECD TG 202] are 768 mg/L, 810.9 mg/L and 380 mg/L, while the NOEC (21-d reproduction) for chronic toxicity [OECD TG 211] is 100 mg/L. The acute toxicity to fish is > 100 mg/L (Medaka; *Oryzias latipes*) and 165.3 mg/L (Fathead minnow; *Pimephales promelas*) for 96 h LC_{50} [OECD TG 203]. The prolonged toxicity to fish (Medaka; *Oryzias latipes*) is 100 mg/L for 14 d LC_0 [OECD TG 204].

Exposure

Triacetin is manufactured in a closed reaction system. The production volume in Japan is approximately 5,000 tonnes/year, while the estimated global production is 10,000-50,000 tonnes/year. Commercially available triacetin contains less than 0.1 % of diacetin and 0.01 % of monoacetin. Since triacetin produced in Japan is used industrially in a variety of applications including a solvent for basic dyes, fixative in perfumery, food additive, pharmaceuticals, CO_2 remover from natural gas and in manufacture of cigarette filters, celluloid, photographic films etc., in consumer products as well as at industrial sites, both workplace and consumer exposure has to be assumed according to the

following three scenarios.

(1) Occupational exposure: inhalation and dermal route during operations such as cleaning of strainers, sampling, analysis and drum filling.
(2) Consumer exposure: intake and dermal/inhalation route in food additive and topical antifungal or perfume fixative and cigarette filter.
(3) Environmental exposure: emission to aquatic compartment from waste water and evaporative emissions associated with its use in the perfume and cosmetic industries and its use as a solvent and CO_2 remover from natural gas, and disposal of consumer products containing triacetin.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical is currently of low priority for further work because of its low hazard potential.