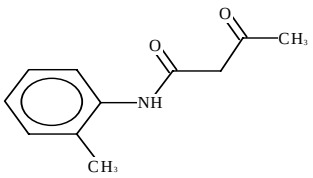
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	93-68-5
Chemical Name	o-Acetoacetotoluidide
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The oral LD50 of o-Acetoacetotoluidide (AAOT) in rats was 1854 mg/kg in males and 1945 mg/kg in females [OECD TG401]. Toxicological effects such as decreased locomotor activity, adoption of a prone position, hypotonia, ptosis, deep respiration, piloerection, hypothermia, lacrimation and pale skin were observed at 819 mg/kg and higher in both sexes in a dose dependent manner.

In addition, the following data was available, although they were insufficient for adequate assessment. AAOT caused slight irritation to the rabbit eyes, and caused slight to moderate irritation to the guinea pig skin. There was a potential for it to induce contact sensitization to guinea pig. Erythema was found in one of ten guinea pigs.

In a Combined Repeat Dose and Reproduction/Developmental Toxicity Screening Test in rats [OECD TG422], AAOT was administered by gavage at the dose levels of 0, 8, 25, 80 and 250 mg/kg/day.
The blood findings in males in the 250 mg/kg/day group were: decreases of erythrocyte count, hemoglobin concentration and hematocrit value, also increases of mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), reticulocyte count, methemoglobin concentration, bilirubin and potassium. Other findings in the 250 mg/kg/day group were: increase of pituitary weight in males; increases of weight of spleen, weight of liver, extramedullary hematopoiesis and congestion in spleen, also blackening of spleen and hemosiderin deposit in liver and spleen in both sexes.
The blood findings in males in the 80 mg/kg/day group were: decrease of erythrocyte count and increase of MCV and bilirubin. Other findings in the 80 mg/kg/day group were: increase of congestion in spleen in females, blackening of spleen and hemosiderin deposit in liver and spleen in both sexes.
In all dose groups up to 250 mg/kg/day, no changes in mortality, behavior or toxic effects on the body weight and food consumption were observed in any sexes. No toxic effects were observed in any dose groups up to 25 mg/kg/day.
Based on these results, the NOAEL for repeat dose toxicity is considered to be 25 mg/kg/day in both sexes.

AAOT was not mutagenic in bacteria up to 5,000 ug/plate [OECD TG471, 472]. Although AAOT showed marginal response in induction of chromosomal aberrations in CHL/IU cells at 2.5 or 5.0 mg/mL, the response was observed only at concentration levels higher than 10 mM (1.91 mg/mL) [OECD TG473]. Therefore, the response was regarded as a biologically irrelevant phenomenon under unphysiological (high osmolality) culture condition. Both the unscheduled DNA synthesis test in rat CD-1 cells and HGPRT assay in CHO cells were negative. Considering all of the *in vitro* studies available, AAOT is not genotoxic.

For reproduction/developmental toxicity, AAOT was administered in the above described screening test [OECD TG422] for 44 days in males and 41 – 45 days (from 14 days before mating to 3 days after parturition) in females. No toxic effects were observed in the following test parameters in parental animals; copulation index, fertility index, gestation index, number of corpora lutea or implantations, implantation index, gestation index and maternal behavior, at up to 250 mg/kg/day.
As for pups; no compound-related effects on the number of pups, delivery index, sex ratio, body weight and viability index were observed in any dose groups. No pups with malformations were found in any groups. No changes in histopathological findings were observed in offspring.
Based on these results, the NOAEL for reproduction/developmental toxicity is considered to be 250 mg/kg/day.

Environment

AAOT is soluble in water (3.0 g/L at 25°C) and the vapour pressure is low (0.00066 Pa at 20°C by calculation) [MPBPWIN v1.40]. AAOT is inherently biodegradable with pre-adapted inoculum (78.5% on DOC after 7 days incubation) [OECD TG302B]. AAOT is stable to hydrolysis in water at pH 4, 7 and 9 [OECD TG111]. The bioaccumulation potential is estimated to be low (BCF = 3.2: calculated from log Pow = 0.85 [OECD TG107]). If AAOT is released into the atmosphere, it will react with photo-chemically produced hydroxyl radicals and will be decreased with a half-life of 8.0 hours. The Fugacity Model [Mackey level III] suggests that if released to water, the majority of the substance would remain in the water compartment, if released into air, 41 % would distribute to water and 58 % distribute to soil compartment, and if released to soil, 36 % would distribute to water and 64 % remain in soil compartment.

In acute toxicity tests with algae, daphnids and fish [OECD TG201, 202, 203 and other methods], the EC50 for algae (*Selenastrum capricornutum*) was 383 mg/L (0 - 72hr biomass) and 654 mg/L (24 - 72hr growth rate), the EC50 for daphnids was 931 mg/L (*Daphnia magna*, 48hr) and the LC50s for fish were > 100 mg/L (*Oryzias latipes*, 96hr limit test), 316.2 mg/L (*Pimephales promelas*, 96hr) and > 500 mg/L (*Brachydanio rerio*, 96hr).

In chronic toxicity tests with daphnids and algae [OECD TG211, 201], the NOEC for daphnids was 10 mg/L (*Daphnia magna*, 21 days reproduction), and the NOEC for algae (*Selenastrum capricornutum*) was 95.3 mg/L (0 - 72hr biomass) and 171 mg/L (24 - 72hr growth rate).

Exposure

The production volume of AAOT in 2001 is estimated to be 1,000 - 1,500 tons/year in Japan and ca. 4,000 tonnes/year in the world. The production countries are Germany, India, Japan, P.R. China, Switzerland, U.S.A and maybe in Eastern Europe. In total there are about 15 manufacturing sites and about 55 use sites in the world.

AAOT is produced in closed systems, and the packing process is performed in semi-closed or open systems. The user may use it in semi-closed systems. The only recognized use is an industrial intermediate in the synthesis of organic pigments. These pigments are utilized in ink, paint and coloring of various materials. There are no known direct uses of AAOT in any consumer product.

The concentration of non-reacted AAOT in the pigments is unknown. However, migration of the pigments is expected to be very limited and there are no adverse health reports from such exposure. Therefore, significant consumer exposure is not expected.

Because of its use limited to the pigment industry, the releases to the environment are estimated to be low.

A survey of users and producers show that the chemical is usually used in well controlled processes and therefore worker exposure is likely to be low.

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 potential hazard for human health. Based on data presented by the Sponsor country, exposure to humans and the 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 by the Sponsor country.