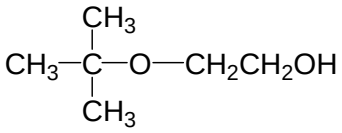
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7580-85-0
Chemical Name	Ethanol, 2-tert-butoxy-
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

There is no available information on toxicokinetics.

In an acute oral toxicity study [OECD TG 401, now deleted] with ethanol, 2-tert-butoxy- (ETB), Crj:CD (SD) IGS rats (five animals/sex/dose) were given ETB by gavage at 0, 500, 1000, or 2000mg/kg bw. No deaths occurred in any groups. Anemia and chromaturia at 500 mg/kg bw and higher, abnormal gait at 1000 mg/kg bw, and adoption of a prone position, decreased locomotor activity and irregular respiration at 2000 mg/kg bw were observed. No abnormalities were observed in body weights or necropsy findings. The oral LD_{50} values were more than 2000 mg/kg bw for both sexes. In an acute oral toxicity study of ETB in male ddY mice (four animals/dose), the LD_{50} was 1328 mg/kg bw.

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422], Crj:CD (SD) IGS rats (12 animals/sex/dose) were given ETB by gavage at 0, 4, 20, or 100 mg/kg bw/day. Males were dosed for 37 days from day 14 before mating and females were dosed for 42-47 days from day 14 before mating to day 4 of lactation throughout the mating and pregnancy period. There were no deaths in any groups. Reddish urine was apparent in all animals at 100 mg/kg bw/day. No effects of ETB on body weight, food consumption, or urinalysis were observed. In the hematological examination, decreases in erythrocyte count, hemoglobin, hematocrit, mean corpuscular hemoglobin concentration (MCHC) and leukocyte count, and increases in mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and reticulocytes at 100 mg/kg bw/day were observed in males. Decreases in erythrocyte count, hemoglobin and MCHC, and increases in MCV and reticulocytes at 20 and 100 mg/kg bw/day, and increase in MCH at 100 mg/kg bw/day were found in females. Absolute and relative weights of the spleen were increased in males and females at 100 mg/kg bw/day. Increase in hematopoietic cells, erythrocyte cells, in the bone marrow and hemosiderin deposition in Kupffer cells of the liver and tubular epithelium of the kidney were observed in males and females at 100mg/kg bw/day. Hemosiderin deposition in the spleen was observed in males at 100 mg/kg bw/day. Extramedullary hematopoiesis in the liver was found in females at 100mg/kg bw/day. Extramedullary erythropoietic hematopoiesis in the spleen was found in males at 100 mg/kg bw/day and females at 20 mg/kg bw/day and higher. The NOAELs for repeated dose toxicity were 20 mg/kg bw/day in males and 4 mg/kg bw/day in females.

In a reverse gene mutation assay [OECD TG 471], ETB was not mutagenic in *Salmonella typhimurium* TA100, TA1535, TA98, TA1537 or *Escherichia coli* WP2 *uvr*A with or without an exogeneous metabolic activation. In a chromosomal aberration test [OECD TG 473], ETB did not induce structural chromosomal aberrations or polyploidy with or without an exogeneous metabolic activation in cultured Chinese hamster lung (CHL/IU) cells. Based on these findings, ETB is not anticipated to be genotoxic *in vivo*.

The above-mentioned combined study [OECD TG 422] showed that the reproductive/developmental parameters, i.e., estrous cycle, copulation index, fertility index, gestation length, or number of corpora lutea, or implantations in dams or number, sex ratio, body weight, or viability of pups, were not affected by administration of ETB up to 100 mg/kg bw/day. No external or internal malformations were noted in pups of any groups. The NOAEL for reproductive/developmental toxicity was 100 mg/kg bw/day in rats.

No information is available for irritation, sensitization, or carcinogenicity.

Environment

ETB is a colourless liquid with a water solubility of 100 g/l at 25 °C and a vapour pressure of 1.03 hPa at 25 °C. Based on a measured log Kow of 0.36, bioaccumulation is not expected. Environmental distribution estimated by a level III Fugacity model indicates that almost all of the ETB partitions into water and soil. A ready biodegradation study showed that ETB was not mineralised (6% by BOD) but about 70% of ETB was transformed to 1-tert-butoxy acetic acid (OECD TG 301C). The degradation products may have similar physical chemical properties and less ecotoxicity to ETB. A study on hydrolysis indicates that ETB is stable in water. In the atmosphere ETB is indirectly photodegraded by reaction with OH radicals with a half-life of 0.849 days.

Ecotoxicity data on this substance were available in aquatic species from three trophic levels. In an algal growth inhibition test (OECD TG 201, *Selenastrum capricornutum*, open system, 72 h), acute toxicity was > 866 mg/L for both ErC_{50} and EbC_{50}. For daphnids, a 48 h EC_{50} of > 891 mg/L was reported (OECD TG 202, *Daphnia magna*, semi-static). For fish (OECD TG 203, *Oryzias latipes*, semi-static) a 96 h LC_{50} > 100 mg/L was available.

Regarding chronic toxicity to algae, a 72 h NOEC (growth rate and biomass) of 291 mg/L (OECD TG 201, *Selenastrum capricornutum*, open system) was reported. For daphnids, a 21 d EC_{50} of > 94.2 mg on reproduction and a 21 d NOEC of 94.2 mg/L on reproduction were reported (OECD TG 211, *Daphnia magna*, semi-static).

Exposure

ETB is produced by a single Japanese manufacturer at one production site. Annual production volume in 2003 was 4,000-5,000 metric tonnes in Japan. ETB is synthesised from butene, isobutylene and ethylene glycol. ETB is used primary as a solvent for dyes and a raw material of inks but also there are many applications including end use products. Exposure to the environment can occur primary through evaporation at production and user sites. Exposure to the general public is expected through dermal contact and inhalation of vapour. This chemical is produced in a closed system in Japan, but used to formulate various products, occupational exposure through inhalation and dermal route is possible in both production and user sites.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is a candidate for further work. The chemical possesses properties indicating a hazard for human health (repeated dose toxicity by oral route). Exposure to the general public is expected through dermal contact and inhalation of vapour. This chemical is produced in a closed system in Japan, but used to formulate various products, occupational exposure through inhalation and dermal route is possible in both production and user sites. Therefore, an exposure assessment and, if necessary, risk assessment for workers and consumers are recommended.

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