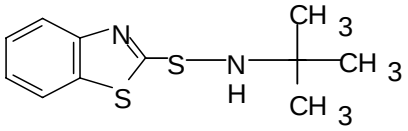
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	95-31-8
Chemical Name	N-tert-butylbenzothiazole-2-sulphenamide
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

There is no information on toxicokinetics. Based on the available data, it can be concluded that the chemical or its hydrolysis products can be absorbed by oral dermal or inhalation routes. Toxicity may be via the hydrolysis products. Hepatic metabolism of the parent material or the hydrolysis products is likely. Excretion is most likely via the kidney.

The oral LD50 (rat) was greater than 2000 mg/kg [OECD TG 423]. The dermal LD50 (rabbit) was greater than 7940 mg/kg. The substance shows signs of mild irritation in the skin and eyes of rabbits but is not considered to be a skin or eye irritant. A hydrolysis product, mercaptobenzothiazole, is a strong skin sensitiser. This is further supported by animal testing (Buehler assay) and human patch tests with the parent chemical reported in the secondary literature.

In a combined oral repeat dose reproductive/developmental toxicity screening test [OECD TG 422] rats were dosed by gavage at 40, 200 and 1000 mg/kg bw/day. Toxicologically significant effects were identified in liver (hepatocyte hypertrophy), kidneys (vacuolar degeneration) and erythrocytes (haemolytic anaemia).The LOAEL was 40 mg/kg/day for males, based on anaemia (female data unavailable). In a 90 day oral toxicity study, which cannot be validated, females showed increased liver and kidney weight at 1000 mg/kg/day together with increased cholesterol and urine specific gravity. Bodyweight was reduced in males at 300 mg/kg/day and 1000 mg/kg/day. The NOAEL was 100 mg/kg/day. A 28 day repeated exposure inhalation study (5 days per week exposure) has been conducted but cannot be validated. The highest exposure level, 0.084 mg/L, produced a decrease in bodyweight and effects to liver and lymph nodes. The NOAEL was 0.029 mg/L.

Based on these studies the LOAEL for repeated dose toxicity (oral) is considered to be 40 mg/kg/day for males, based on anaemia (female data unavailable). The NOAEL for repeated dose toxicity (inhalation) is 0.029 mg/L (non-validated data).

The chemical was not mutagenic in bacteria [OECD TG 471 and 472] and in several *in vitro* mammalian gene mutation assays. Positive responses, however, were seen in several mouse lymphoma assays in the presence of exogenous metabolic activation. It also induced chromosomal aberrations in mammalian cells *in vitro* in the presence of an exogenous metabolic activation system [OECD TG 473]. Because the chemical was non-mutagenic in bacteria and mammalian cells and clastogenic in mammalian cells, the positive response in the mouse lymphoma assays seemed to be derived from chromosomal aberrations. The chemical was negative in the mouse micronucleus assay [OECD TG 474] tested up to 2000 mg/kg. Accordingly this chemical was clastogenic *in vitro* but not *in vivo*.

For the above mentioned reproduction/developmental toxicity screening test [OECD TG 422], the chemical was given for 42 days in males and from 14 days before pregnancy to day 3 of lactation in females. No adverse effects were observed in terms of fertility, delivery and nursing in parent animals. The viability and body weight of offspring were unaffected and no malformations were detected. Both male and female reproductive tissues were well examined and

no abnormalities were observed. Changes in fertility index were observed at 40 and 1000 mg/kg bw/day, but not at 200 mg/kg bw/day.

In a developmental toxicity study reported in the secondary literature, female rats were dosed with the chemical at up to 500 mg/kg bw/day between days 6-15 of gestation. No effects were seen, either in females or offspring, at any dose level and under the conditions of the test the chemical was considered to have no effect on reproduction. No further details of the study could be obtained. The NOAEL for developmental toxicity was 500 mg/kg bw/day.

Environment

The chemical has a log Pow of 3.9 at room temperature, a vapour pressure of less than 0.0000021 hPa at 25°C and a water solubility of 0.345 mg/L at 20°C. Fugacity model Mackay level III calculations suggest that the majority of the chemical would distribute to soil if released to the air or soil compartments and to water if released to the water compartment. The chemical is not ionised at environmental pHs ($pKa_{(1)}$ 1.75, $pKa_{(2)}$ –3.43, conjugate acid). The chemical is not readily biodegradable (0%) but it does hydrolyse in less than 1 day at pH 9 or less (t1/2 = 1.7h at pH 4, 1.8h at pH 7 and 21.5h at pH 9). The identified hydrolysis products are mercaptobenzothiazole, di(benzothiazoyl-2)disulfide, t-butylamine, and benzothiazole. These hydrolysis products have been tested and shown to have a low potential for bioaccumulation. Based on these findings, the chemical is judged to have low potential for bioaccumulation also. Indirect photo-oxidation by hydroxy radicals is predicted to occur with a half-life estimated at 2.8 hours. The substance does not inhibit the action of wastewater treatment microorganisms EC50 (3h) > 10000 mg/L. The hydrolysis products, such as mercaptobenzothiazole, di(benzothiazoyl-2)disulfide and benzothiazole, are non-volatile and not readily biodegradable in the environment.

In an acute fish toxicity study (OECD TG 203, *Oryzias latipes*, 96h) a LC50 = 0.345 mg/L (limit of water solubility) was reported. In Daphnia magna, an acute toxicity value of 48h EC50 = 0.345 mg/L (limit of water solubility) was reported. The results in algae (OECD TG 201) were an E_rC50 = 0.071 mg/L, a $NOEC_b$ (0 to 72 h, biomass) = 0.011 mg/L and a $NOEC_r$ (24 to 72 h, growth rate) = 0.023 mg/L (measured concentrations). In a prolonged fish toxicity study (OECD TG 204, *Oryzias latipes*) a 14d LC50 = 0.345 mg/L (limit of water solubility) and a 14d NOEC = 0.15 mg/L were presented. The chronic toxicity to *Daphnia magna* (OECD TG 211) was a NOEC (14d, reproduction) = 0.042 mg/L (measured) and NOEC (21d, parental) = 0.068 mg/L (measured).

Some of the degradation products of N-tert-butylbenzothiazole-2-sulfenamide, and especially mercapto-benzothiazole, show similar levels of aquatic toxicity compared to the parent compound.

Exposure

The production volume of the chemical in 2000 is 16,000 – 20,000 t/y worldwide, with production in Japan being 4,000 – 4,500 t/y. The chemical is an accelerator for the vulcanization of rubber. Due to the chemical transformation processes involved in vulcanization, the finished rubber products only contain small amounts of the chemical in addition to substances produced from the synthesis, such as benzothiazole, 2-mercaptbenzothiazole and 2-mercaptobenzothiazole disulfide. The substance and its degradation products may be released to the environment during the use of rubber products, such as tyres.

Occupational hygiene measurements suggest that occupational exposure is 0.64 mg/m^3. Personal Protective equipment (dust masks, goggles, protective clothing, gloves) is worn during operations. Consumer exposure is minimal.

RECOMMENDATION

The chemical is a candidate for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical possesses properties indicating a hazard for the environment. Also some of the degradation products show similar hazards to the environment. The substance and its degradation products are present in many rubber products and a release to the environment is possible. An exposure assessment, and if necessary a risk assessment for the environment of the chemical and its degradation products should be performed. The currently on-going assessment of di(benzothiazoyl-2)disulfide (CAS No 120-78-5) and of N-cyclohexylbenzothiazole-2-sulfenamide (CAS No 95-33-0) should be taken into account.

The chemical also possesses properties indicating a hazard for human health (sensitisation and anaemia). An exposure assessment and, if necessary, a risk assessment for human health should be performed.