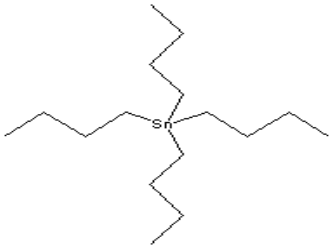
SIDS INITIAL ASSESSMENT PROFILE

CAS No. (Nos.)	1461-25-2
Chemical Name(s)	Tetrabutyltin (TTBT)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Tetrabutyltin (TTBT) was reported to be taken up primarily in the jejunum, liver and the duodenum of rats. Small amounts of absorbed TTBT (0.12-0.16% of dosed amount) were dealkylated in the body and the tributyltin cation (TBT+) metabolite was excreted in the urine and feces of rats. Lipid-soluble TTBT that was not dealkylated was excreted into bile and either further metabolized in the small intestine or reabsorbed there. Additionally, the percentage of an ingested butyltin dose appears to increase as the number of butyltin moieties increases, suggesting that more highly-butylated tin compounds may be absorbed to a greater extent.

The acute oral LD_{50} of TTBT to rats was > 2000 mg/kg bw. Clinical signs included hunched posture, lethargy, ataxia, and piloerection that disappeared by 2 days post-exposure. At 2000 mg/kg, half of the animals showed thickening of the non-glandular region of the stomach. There are no data on acute dermal or acute inhalation toxicity, irritation, or sensitization.

The repeated-dose toxicity of TTBT (96.52% purity) was evaluated in a combined repeated-dose and reproduction/developmental toxicity screening test (OECD TG 422) conducted in rats at doses of 100, 300, and 2,000 mg/kg diet. At 300 mg/kg diet (equivalent to 16-24 mg/kg bw/day), decreased spleen weight and lymphoid depletion in the thymus were observed. At 2000 mg/kg diet (100-130 mg/kg bw/day), the following effects were observed: decreased body weights and food consumption; decreased spleen weights in males and decreased thymus weights (both sexes); increased thrombocytes and decreased prothrombin time; increased gamma glutamyl transferase, cholesterol, and phospholipids; blood in the lymph nodes; and lymphoid depletion. Based on the observed effects in the 300 mg/kg diet group, the NOAEL for sub-chronic toxicity was 100 mg/kg diet (equivalent to 5–8 mg/kg bw/day for both sexes), and the LOAEL was 300 mg/kg diet.

TTBT was negative in all tests for genotoxicity conducted with and/or without metabolic activation, including standard and modified Ames assays using single and multiple strains of *Salmonella typhimurium* and/or *Escherichia coli*, a SOS chromotest and a Rec-assay. TTBT was not clastogenic in an *in vivo* mouse micronucleus test.

In the reproductive/developmental segment of the OECD 422 study, adverse developmental/reproductive effects observed in the high-dose (2000 mg/kg diet) group (LOAEL; equivalent to 100-118 mg/kg bw/day for both sexes) included decreased number of pups, increased pup mortality, decreased pup body weight, increased number of runts, and increased post-implantation loss. The NOAEL for maternal and reproductive/developmental toxicity was 300 mg/kg diet (equivalent to 16-24 mg/kg bw/day). In a limited exposure gavage study in rats, TTBT resulted in malformations (i.e., cleft palate) at ≥ 229 mg/kg bw/day; significant only at 1833 mg/kg bw/day.

Environment

The EPIWIN suite developed by Syracuse Research Corporation, used to predict Henry's Law Constant and partitioning in the environment, has not been validated for chemicals that contain metals in their molecular structure; therefore, there is uncertainty associated with the calculated values and they should be used with caution whenever

they are reported below.

TTBT is a colorless liquid at room temperature. Based on experimental data, the freezing point of TTBT is < -20°C, the boiling point is 196.9 @ 1013.3 hPa, the relative density is 1.05 g/m^3 @ 20°C, and vapour pressure measurements are 0.0014 and 0.0026 hPa @ 25°C. The most reliable measured water solubility value is <0.1 mg/L and the measured octanol-water partition coefficient (log K_{ow}) is >5.07 (calculated log K_{ow} is 9.37). TTBT has a strong tendency to sorb to labware. Additionally, the low solubility of TTBT presents significant challenges to testing and analysis in aqueous solution.

TTBT is not readily biodegradable, but atmospherically degraded by reaction with photochemically produced hydroxyl radicals (t1/2 = 4.5 hours; rate constant of 56.9×10^{-12} cm^3/molecule*second). TTBT is hydrolytically stable, with an estimated half-life of >1 year at 25ºC at both pH 7 and 9. A Henry's Law Constant of 0.0092 atm-m^3/mol was estimated. If released to the environment, TTBT is predicted to partition primarily to soil (68%); partitioning to water and sediment were nearly equal (17 and 14%, respectively). Measured bioconcentration factors of 38 to 97 (log BCFs of 1.8–2) using a concentration of 0.005 mg/L, and 127 to 310 (log BCFs of 2.1–2.5) using a concentration of 0.0005 mg/L were reported for carp (*Cyprinus carpio*) in flow-through tests. The calculated BCF is 3980 (log BCF of 3.6).

Typically the TTBT commercially produced is approximately 96% pure. TTBT contains technical impurities, including tributyltin chloride (TBTC) and dibutyltin dichloride (DBTC). Because of the high toxicity of TBTC and chronic toxicity of DBTC, the level of these impurities (and their degradation products) should be taken into account when assessing the ecotoxicological profile of commercial products.

The 96-h LC/EC_{50} was 0.045 mg/L (based on measured values) for fathead minnows (*Pimephales promelas)* in a flow-through exposure regime. A static study in *Pimephales promelas* using nominal concentrations resulted in a 96-hr LC_{50} of 0.19 mg/L. TTBT also reduced *Skeletonema costatum* growth (72-h EC_{50} = 0.05 mg/L, based on nominal dilutions of a measured stock solution of TTBT).

The acute toxicity (EC_{50}) of TTBT to *Daphnia magna* is estimated to be approximately 0.2 mg/L (based on measured values) at 48 hours. The 21-day LC_{50} for parental survival of *D. magna* was 0.051 mg/L, and the overall LOEC and NOEC were 0.034 and 0.014 mg/L, respectively, based on time-weighted average measured concentrations. The 21-d EC_{50} for reproduction could not be determined; at the highest concentration not resulting in 100 percent parental mortality (0.034 mg/L), reproduction was affected in less than 50% of the surviving daphnids. TTBT was moderately stable (decrease of 10–30% of nominal) between media exchanges in the chronic daphnia reproduction study based on measured concentrations.

Exposure

In 2000, worldwide production of TTBT was estimated at 10,000 to 12,500 metric tonnes per year. TTBT is produced by companies in North America, Europe, and Asia-Pacific. TTBT is used by producers as an industrial intermediate in the production of butyltin chemicals or may be sold to other chemical/industrial manufacturers for conversion to other products.

Releases to the environment could occur as part of the production of this intermediate, or during its conversion to other butyltin chemicals.

Exposure to TTBT in an occupational setting can occur via inhalation and dermal contact. Exposure in the workplace is controlled through equipment design, the use of appropriate personal protective equipment, and regular air monitoring. In the production of TTBT, operations are usually sealed to prevent releases to the atmosphere. Worker exposure is expected to be confined to manual operations such as material addition, transfer, or sampling. For those operations that specifically involved manual handling of organotin stabilizers (not TTBT specifically), the measured exposure potential was 50% to just above the threshold limit value (TLV) of 0.1 mg/m^3.

There are no direct consumer applications for TTBT as a product itself; however, consumers may be exposed to TTBT that may be present as an impurity in products containing other butyltin compounds (e.g. PVC articles) or may be released into the atmosphere during processing. TTBT was not detected (<1 µg/kg) in dust samples collected from Parliament buildings in European countries, or in American private household dust samples. No TTBT was detected

(at a detection limit of 0.03 mg/kg) in a variety of Danish consumer products manufactured wholly or in part from PVC. A small sampling (n = 5) of PVC flooring from the UK contained TTBT at concentrations ranging 0.14 to 12.3 mg/kg.

TTBT was not detected (at 1.4 to 2.6 µg/kg tissue wet weight) in samples of oysters, clams, Dungeness crab, and mussels from Washington State in a screening level study.

In England and Wales, 0.5% of estuarine and coastal water samples had TTBT concentrations >0.1 µg/L, and marine water samples from the Northern Adriatic Sea had TTBT levels ranging from not detected to 6ng/L as Sn. In Germany, river sediments had TTBT concentrations ranging from <1µg/kg dry wt to 14mg Sn/kg, concentrations in zebra mussels (*Dreissena polymorpha*) ranged from <1 to 4µg Sn/kg round weight, and concentrations in brace (*Abramis brama*) muscle tissue ranged from <1 to 13µg Sn/kg round weight. TTBT was not detected in mussels (*Mytilus galloprovincialis*) collected in 2000 from 3 locations in the Adriatic Sea.

A multi-year national monitoring program in the U.S. measured TTBT in water, sediment, and bivalve tissue collected in and around US commercial harbors, shipyards/dry docks, marinas, and ecologically significant areas (ESAs). Across the various media collected, geometric mean TTBT concentrations ranged from not detected to a maximum of 543.4ng/g dry weight in subsurface sediments collected 1995-1996.

Organotins (not further specified) were found in air and water samples collected from current and former hazardous waste sites in the United States. No organotins were found in air or groundwater at these sites; however, organotins (concentrations not reported) were found in surface water at 1 of 8 sites, in sediment at 4 of the 8 sites, and in soil at one site.

Tin is not listed as a hazardous waste constituent by the U.S. EPA; therefore, its disposal is not restricted by federal land disposal restrictions. The preferred method of disposal for organotin compounds is incineration in an approved hazardous waste incinerator, which converts the organotin to inorganic tin.

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

Human Health: This chemical is a candidate for further work. The chemical possesses properties indicating a hazard for human health (repeated-dose and reproduction/developmental toxicity). Member countries are invited to perform an exposure assessment for consumers and workers, and if necessary a risk assessment.

Environment: This chemical is a candidate for further work. The chemical possesses properties indicating a hazard for environment (acute and chronic aquatic toxicity). Member countries are invited to perform an exposure assessment for the environment, and if necessary a risk assessment.