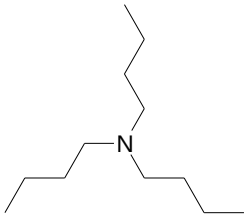
SIDS INITIAL ASSESSMENT PROFILE

CAS No(s).	102-82-9
Chemical Name(s)	TRIBUTYLAMINE (**TBA**)
Structural Formula(s)	

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Rationale

Toxicokinetic data were not located for **TBA.** However, data were located for tributylammonium chloride (CAS No. 6309-30-4), a salt of TBA. In this case, testing the salt of TBA avoids damage to the gastrointestinal tract following gavage administration due to the caustic mode of action. Repeated-dose toxicity data for **TBA** are limited. In addition, reproductive toxicity data were not located. Therefore, read-across to di-n-butylamine (DBA; CAS No 111-92-2) for repeated dose and reproductive (fertility) toxicity endpoints is appropriate because both compounds have similar chemical structures and because **TBA** is partially deaminated to DBA derivatives *in vivo* and is excreted in the urine. Furthermore, for both compounds, the acute and repeated-dose inhalation effects are generally related to local effects. Although the water solubilities of TBA and DBA are different (0.08 and 3.8 g/L, respectively), the acute oral LD50 values are in the same range (420 and 550 mg/kg bw, respectively, for male rats). For ecotoxicity purposes, dibutylamino ethanol (CASRN 102-81-8) is used as an analogue to support the TBA data for acute fish and algae toxicity endpoints; data for acute and chronic invertebrates are also presented for comparative purposes. This approach is appropriate because both compounds have similar chemical structures (i.e., both classified as tertiary amines with a central nitrogen atom bearing an unshared pair of electrons that underlies their similar chemical behavior) and physico-chemical properties. According to the acute aquatic toxicity classification of OASIS (MOA profiler in QSAR Toolbox) for the mode of action, both TBA and dibutylaminoethanol are considered to be narcotic amines.

Read Across Strategy

Mammalian toxicity			Ecotoxicity
Toxicokinetics	Repeated dose	Reproductive toxicity	Acute and chronic aquatic toxicity
TRIBUTYLAMMONIUM CHLORIDE	DBA	DBA	DIBUTYLAMINOETHANOL

Physical-chemical Properties

TBA is a liquid with a measured melting point of $\leq$- 90 °C, a measured boiling point of 208 °C at 1013 hPa and a measured vapour pressure of 0.18 hPa at 20 °C. The measured octanol-water partition coefficient (log K_{ow}) is 3.34 at 20 °C, the estimated log K_{oc} (25°C) is 1860 and 18900 for the neutral and for the ionized molecule (pH 7) respectively, and the water solubility is 0.08 g/L at 20 °C. A pH of 10.2 was measured at 0.1 g/L and 25 °C.

The pKa value of the conjugate acid of **TBA** in water is 10.89 (measured). The pKa value of dibutylamino

ethanol is 10.3 (measured).

Human Health

TBA is expected to be absorbed by the dermal, oral and inhalation routes of exposure. Following oral exposure to tributylammonium chloride, a salt of **TBA**, the majority of excretion is expected in the urine; urinary metabolites identified were chain hydroxylation (60%), deamination to di-n-butylamine derivatives (ca. 33%), in addition to unchanged (10%) and unidentified (14%) of the administered dose.

The acute 4 hour inhalation LC50 of **TBA** in rats is 0.5 – 0.69 mg/L [similar/same as OECD TG 403 or a standard acute inhalation study design]. Clinical signs of toxicity included irritation (not specified), abnormal respiration and rales, restlessness, symptoms of respiratory tract irritation, closed eyelids, excessive salivation, tremor and convulsions. The acute dermal LD50 of **TBA** was 195 mg/kg bw (rabbits; use of vehicle not specified) to > 2000 mg/kg bw (rats; 40% in vehicle) [similar to OECD TG 402 or a standard acute dermal study design]. Clinical signs of toxicity included slight edema and erythema at the application site and transient convulsions, spastic gait, dyspnea, apathy and poor general state. Each of the acute oral studies have some limitations and are considered reliability 4; a weight-of-evidence analysis is applied to these and all results are reported. The acute oral LD50 of **TBA** in rats ranged from 420 - 780 mg/kg bw [similar to OECD TG 401 or a standard acute oral study design]. Clinical signs of toxicity included salivation, rapid respiration, lethargy, slight staggering, ataxia, tremor, twitching, seizures, lateral or abdominal position, imbalance, dyspnea and dilated pupils. These clinical effects were signs of animal suffering at high doses/concentrations of the corrosive chemical. The acute oral LD50s in other species are >39 mg/kg bw (cat, sex not reported), >390-<708 mg/kg bw (rabbit, sex not reported), 615 mg/kg bw (rabbit, male and female), 114 mg/kg bw (mouse, male and female), 888 mg/kg bw (mouse, sex not reported), and 350 mg/kg bw (guinea pig, male and female) (no guideline specified). **TBA** was corrosive to rabbit skin in a short term patch test (no guideline specified). Although **TBA** was not irritating to the rabbit eye in an OECD TG 405 study, vapour concentrations did likely cause eye irritation in an acute inhalation toxicity study. **TBA** is a respiratory tract irritant in acute inhalation studies in rats [similar to OECD TG 403 or a standard acute inhalation study design]. **TBA** was negative for skin sensitization in a Buehler Test with guinea pigs [similar to OECD TG 406].

Repeated-dose toxicity data were limited for **TBA** to a single inhalation toxicity study. Rats were exposed to **TBA** via inhalation (whole-body) at concentrations up to 0.923 mg/L 6 h/day, 5 days/wk for a total of 19 exposures (RL=4, no guideline specified). These animals exhibited nasal irritation, some loss of muscular control, lethargy, tremors and lack of weight gain. In a study similar to OECD TG 413, repeated nose-only inhalation study, rats were exposed to the analogue substance DBA at 0.051, 0.142, and 0.448 mg/L for 6 h/day, 5 days/wk for 90 days. At the highest dose, convulsions were seen in some rats within the first three days, and a decrease in body weight and food consumption was also observed. At 0.448 mg/L, nasal irritation and hyperplasia, hemorrhage and inflammatory cell infiltration were most pronounced during the first three days, indicating that some adaptation occurred. Mucous cell hyperplasia was also observed at the two lower doses. Some hyperplasia of lymphoid tissues surrounding the respiratory tract was seen at all doses, without statistical significance. The Lowest Observed Adverse Effect Concentration (LOAEC) for local irritation following 90 day repeated dose inhalation exposure to DBA was 0.051 mg/L; this LOAEC is considered applicable to **TBA**.

TBA did not induce mutations in a bacterial reverse mutation assay [similar to OECD TG 471] or an in vitro mammalian gene mutation assay at the HPRT locus in mouse lymphoma L5178Y cells [OECD TG 476]. In addition, **TBA** did not induce micronuclei in bone marrow of mice at 150 mg/kg bw [OECD TG 474]. Based on these studies, there is no evidence that **TBA** is genotoxic.

No data are available for the carcinogenicity of **TBA**.

Effects on fertility data were not located for **TBA*;*** read across to analogue substance DBA is used to fill this endpoint. Test substance-related microscopic changes were not observed in the reproductive organs of either males or female rats exposed by inhalation for 91 days (similar to OECD TG 413) to analogue substance DBA at concentrations up to 0.448 mg/L (highest concentration tested); a similar lack of effect on reproductive oragns is expected for **TBA**. For developmental toxicity of **TBA**, when administered to 20 pregnant rats by oral gavage on gestation days 6-15 at doses of 0, 15, 45 and 135 mg/kg bw/day [OECD TG 414], **TBA** caused systemic

toxicity (mortality, transient reductions in body weight gain) at 135 mg/kg bw/day resulting in a maternal NOAEL of 45 mg/kg bw/day; the developmental NOAEL was 135 mg/kg bw/day (the highest dose tested). There were no embryotoxic or fetotoxic effects except a slight and dose-related increase in fetal body weight gain, which was significant at the highest dose. The treatment did not produce malformations.

TBA possesses properties indicating a hazard for human health [acute and repeated-dose toxicity, skin corrosion, respiratory tract irritation andpotential for eye irritation]. Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

TBA is expected to be hydrolytically stable in the natural environment and to exist as a cation in water at environmentally relevant pH. It should be noted, however, that EPISuite predicts certain environmental fate endpoints in their neutral forms (Phototransformation in air, adsorption/desorption and Level III fugacity model). Therefore, there will be some differences between predicted and actual results.

A standard hydrolysis study was not located for **TBA**; due to the structural properties of the substance, hydrolysis is not expected under environmental conditions.

In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 1.2 hours. Two OECD TG 301B studies with **TBA** resulted in ≥80% biodegradation after 28 days (readily biodegradable) and an OECD TG 302 B (activated sludge from industrial WWTP) resulted in 98% biodegradation in 15 days (6% after 3 h) (inherently biodegradable). Based on TOC measurements in a screening test, **TBA** has been found to be stable for 28 days in test solutions (no significant loss, nearly 100%) in an abiotic elimination control according to OECD TG 301B. Considering the tests in total, **TBA** is readily biodegradable under aerobic conditions.

A level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments suggests that **TBA** (in the neutral form), will distribute mainly to the soil (75%) and water (24%) compartments with minor distribution to the air (0.5%) and sediment compartments (1%). However, as the model does not take into account the charged form of the molecule at environmental relevant pH-values (pH 5-9), the model may underestimate distribution of **TBA** into water. An estimated pH-corrected Henry's law constant (pH 7.0; charged molecule) of 0.006 $Pa.m^3$/mole at 25 °C suggests that volatilization of **TBA** from the water phase is not expected to be high.

TBA is not expected to bioaccumulate in the aquatic environment based on a measured bioconcentration factor of 3.2-47 (10 µg/L); 7.3 (100 µg/L) [OECD TG 305C; test species: *Cyprinus carpio*]. The analogue chemical dibutylamino ethanol (CASRN 102-81-8) is also not expected to bioaccumulate in the aquatic environment based on a measured bioconcentration factor of < 5 (0.2 mg/L); < 39 (0.02 mg/L) [OECD TG 305C; test species: *Cyprinus carpio*].

Acute ecotoxicity data with dibutylamino ethanol is used to support the TBA data for the fish and algae acute toxicity endpoint; data for invertebrates are also presented for comparative purposes, as not all tests for **TBA** include measurements of stability. It is demonstrated that the toxicity of **TBA** and dibutylamino ethanol are in the same range, however, **TBA** seems to be slightly more toxic than dibutylamino ethanol. Based on TOC measurements in a screening test, **TBA** has been found to be stable in test solutions (>80% for 96 and 48 hours, respectively) according to OECD TG 201 and 202 (without organisms). The following acute toxicity test results have been determined for aquatic species, e.g.:

Fish
TBA:
Danio rerio 28 d LC_{50} >10 mg/L (nominal; semi-static; not neutralized, pH 7.1-8.3) [OECD TG 204]
Oryzias latipes 96 h LC_{50} = 16.3 mg/L (nominal; semi-static; not neutralized, pH 8.1 - 8.7) [OECD TG 203]

Dibutylamino ethanol:
Oryzias latipes 96 h LC_{50} = 29.2 mg/L (measured; semi-static; pH 7.4-8.9) [OECD TG 203]
Leuciscus idus 96 h LC_{50} = 31.6 mg/L (nominal; not neutralized pH 7.3 to 9.6, geometric mean; static); > 100

–< 500 mg/L (neutralized; pH 7.3-7.7; nominal; static) [DIN 38412, part 15]

Invertebrate
TBA:
Daphnia magna 48 h EC_{50} = 8 mg/L (measured; semi-static; not neutralized, pH 7.9-8.0) [OECD TG 202]
Daphnia sp. *2*4 h EC_{50} = 18 mg/L (not specifed, static; not neutralized, pH not reported) [DIN 38412, part 11]

Dibutylamino ethanol:
48 h EC_{50} = 81.7 (nominal; semi-static; not neutralized, pH 7.8 to 8.0 (highest concentration)) [similar to OECD TG 202]
48 h EC_{50} > 108 mg/L (measured; pH 7.9-9.6) [OECD TG 202]

Algae
TBA:
[*Desmodesmus subspicatus*] 72 h EbC_{50} = 3.6 mg/L; 72 h EbC_{10} = 1.5 mg/L (not specified; static; not neutralized, pH not reported);
72 h EbC_{50} = 8.2 mg/L; 72 h EbC_{10} = 1.4 mg/L (not specified; neutralized, pH not reported) [DIN 38412, part 9]

Dibutylamino ethanol:
[*Pseudokirchnerella subcapitata*] 72-h EbC_{50} = 9 mg/L; 72-h $NOEbC_{50}$ = 1.65 mg/L (measured; static; not neutralized, pH 7.8 - 10.2);
72-h ErC_{50} = 21 mg/L; 72-h $NOErC_{50}$ = 3.2 mg/L (measured; static; not neutralized, pH 7.8 - 10.2)

In a chronic aquatic toxicity study in *Daphnia magna* with dibutylamino ethanol, the 21-d EC_{50} for reproduction = 9 mg/L (21-d NOEC for reproduction = 4.4 mg/L) (measured; not neutralized, pH 7.4 - 9.5) .

TBA possesses properties indicating a hazard for the environment (acute aquatic toxicity values between 1 and 100 mg/L). TBA is readily biodegradable and has a low bioaccumulation potential. Adequate screening-level data are available to characterize the hazard to the environment for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

TBA is commercially produced with an annual production volume of 454 < 4,536 tonnes in the United States [sponsor country]. Global production volume was also estimated to be approximately 454-4536 tonnes/year in year 2010. These values are provided as ranges to protect confidential business information.

TBA is used as a proton scavenger in a variety of chemical processes and to produce quaternary ammonium compounds (e.g. tributylmethyl and tetrabutyl ammonium bromide, chloride or bisulphate) which are used as phase transfer catalysts, and to produce phosphonium salts. **TBA** is also used commercially as an acid acceptor and used as directly as a catalyst in phenolic resins, polycarbonates, polyesters, and engineered plastics.

TBA is produced in closed systems by producer sponsor companies. It is not known whether other producers might use other (e.g., open) systems of manufacturing. Inhalation and dermal exposure may be possible during occupational use. Procedures are recommended for ensuring that emissions and exposures are well controlled during production and use. In production, **TBA** is handled in closed systems by ACC Amines panel producers. Necessary engineering controls during production include proper ventilation, containment, safety equipment and actual hardware designed to minimize exposure through splashing or exposure to the air. Transfer of these materials is in closed pipe systems rather than in open systems to minimize loss. There may be low level losses in process waters, which are discharged to a waste water treatment system. Limited potential exists for release of material to a publicly-owned treatment works (POTW) or a body of water after primary biological

treatment on site. **TBA** is stored in closed tanks and transported in tank cars and tank trucks, and smaller amounts are transported in drums or Intermediate Bulk Containers (IBCs).

Consumer exposures have not been reported for **TBA**.