SIAM 23, 17-20 October 2006

US/ICCA

SIDS INITIAL ASSESSMENT PROFILE

Chemical Category	Dibutyltin dichloride and selected thioglycolate esters	
Structural Formula, Chemical Names and CAS Registry Numbers	SI CI	Dibutyltin dichloride DBTC, CASRN 683-18-1
		Dibutyltin dilaurate DBTL, CASRN 77-58-7
		Dibutyltin maleate DBTM, CASRN 78-04-6
	SN SN	Dibutyltin oxide DBTO, CASRN 818-08-6
		Dibutyltin bis(2-ethylhexylthioglycolate) DBT(EHTG), CASRN 10584-98-2
		Dibutyltin bis(isooctylthioglycolate) DBT(IOTG), CASRN 25168-24-5

SUMMARY CONCLUSIONS OF THE SIAR

Category Rationale

DBTC, DBTL, DBTM, DBTO, and DBT(EHTG) are considered one category of compounds for mammalian toxicology studies via the oral route. The justification for this category is based on structural similarities and the simulated gastric hydrolysis studies of DBTL, DBTM, DBTO, and DBT(EHTG) demonstrated that these dibutyltin compounds readily converted (> 80% to 100%) to DBTC within < 0.5 to 3.5 hours under physiological conditions (pH 1 to 2). Thus, DBTC is an appropriate anchor compound and a valid surrogate for the mammalian toxicology endpoints of repeated dose, reproduction, developmental, and *in vivo* genetic toxicity, when they are assessed using oral administration.

Sensitization, irritation and *in vitro* genotoxicity are not covered under the category approach and the results of the mammalian *in vivo* tests via the oral route with the representative chloride cannot be extrapolated to the dermal or inhalation routes. However, the esters have much higher molecular weight and lower volatility than the chlorides, reducing the possibility of toxicity via inhalation and dermal routes.

The category approach was not used for the ecotoxicity and environmental fate endpoints. The considerable differences in the structures of the labile ligands cause differences in water solubility between the alkyltin chloride and the thioesters and carboxylates affecting their respective bioavailabilities and distribution in the environment. Furthermore, DBT thioesters or carboxylates will degrade in aqueous solution such that organisms will be exposed to the parent material and their different degradation products. DBTC is not an appropriate surrogate for the thioesters and carboxylates for the ecotoxicity and environmental fate endpoints.

Analogue Rationale

Data for DBT(EHTG) and DBT(IOTG) are used interchangeably because they are isomers, differing only slightly in the structure of the C-8 alcohol of the mercaptoester ligand. In addition, the breakdown products of DBT(EHTG) and DBT(IOTG) are the thioglycolate esters (EHTG and IOTG), which have the common degradates, thioglycolic acid and C-8 alcohols (either 2-ethylhexanol or isooctanol). EHTG and IOTG also have similar physicochemical and toxicological properties.

EHTG (CAS No. 7659-86-1) and IOTG (CAS No. 25103-09-7) form the Thioglycolic Acid Esters B Category, assessed at the OECD HPV Chemicals Program.

Human Health

The majority of toxicology studies were conducted with commercial mixtures having high dialkyltin to monoalkyltin ratios. Toxicokinetic data were not available for these substances. For DBTC, DBTL, DBTM, DBTO, and DBT(EHTG)/(IOTG), acute rat oral LD₅₀ values ranged from 58 (DBTC) to > 5000 (DBT[EHTG]) mg/kg bw, rat acute inhalation LC₅₀ values ranged from 59 (DBTC) to > 22,000 (DBT[IOTG]) mg/m³, and acute rat dermal LD₅₀ values ranged from 777 (DBT[EHTG]) to \geq 2000 (DBTO) mg/kg bw.

The dibutyltin compounds tested ranged from slightly irritating (DBTO) to highly irritating/corrosive [DBT(EHTG), DBT(IOTG), and DBTC] to the skin of rabbits and slightly [DBTO, DBT(EHTG), and DBT(IOTG)] to severely DBTC) irritating to the eyes of rabbits. DBT(EHTG)/(IOTG) blends are skin sensitisers in guinea pigs. Absorption through human epidermis was slow (0.210 to 0.002 μ g/cm²/h) at non-irritating, environmentally relevant concentrations [500 μ g/cm² DBTC and 21,120 μ g tin/cm² as DBT(EHTG)].

Multiple repeated dose studies have been conducted with DBTC and its related esters. The critical study for hazard assessment was the 90-day dietary study in rats using DBTC (99.7% purity). In this study, the concentrations were 10, 20, 40, or 80 ppm in the diet. The NOAEL was 40 ppm (~2 mg/kg bw-day) and the LOAEL was 80 ppm (~7.5 mg/kg bw-day) based on reduced body weight and food consumption, hematological effects (significant decrease in hemoglobin concentrations in males and females), and decreased absolute kidney weight (males). In the repeated dose screening study to assess reproductive/developmental effects, immunotoxicity with thymus atrophy and severe lymphoid depletion were noted in the parental animals. The

NOAEL was 0.3-0.4 mg DBTC /kg bw/day

DBTC, DBTL, DBTM, DBTO, and DBT(EHTG)/(IOTG) were not mutagenic in standard Ames assays with multiple strains of *Salmonella typhimurium*, conducted both with and without metabolic activation. However, DBTC produced evidence of mutagenic or clastogenic effects in 5/7 *in vitro* studies reviewed, including an SOS chromotest, Rec-assay, HGPRT assay, and a chromosomal aberration test conducted with and without activation. In mouse micronucleus assays, DBTC was not clastogenic in one study and was clastogenic in the other at a dose that also caused some lethality. DBTC showed a potential to cause clastogenic effects. Overall, this category is considered to be genotoxic.

In a rat reproduction/developmental toxicity screening test of DBTC (OECD Test Guideline (TG) 421) dietary concentrations were 5, 30, or 200 ppm (ca. 0.4, 2, or 12 mg/kg bw/day). Absolute and relative thymus weights of the mid and high dose dams were decreased and accompanied by moderate to severe lymphoid depletion. Treatment-related post implantation losses, increased number of stillborn pups and decreased pup weights and increased number of runts, and pup mortality were confined to the high dose group. The maternal NOAEL was 5 ppm (0.3–0.4 mg/kg bw/day). The NOAEL for reproduction/ developmental effects was 30 ppm (ca. 2 mg/kg bw/day).

Multiple developmental toxicity studies also have been done with DBTC and its related esters. In one study [with DBTC(?)] in rats, craniofacial malformations, ankyloglossia and cleft jaw, were observed. The DBT moiety produced developmental toxicity in several additional rat studies using an oral route of administration. In these studies, a classical developmental response pattern was observed and gestation day 8 was determined to be the most sensitive day, with other periods refractory to the teratogenic effects of DBT. In rat developmental toxicity studies of DBTC, NOAELs for maternal toxicity were established at 1 and 5 mg/kg bw/day, and NOAELs for developmental toxicity and teratogenicity were 2.5 and 5 mg/kg bw/day, respectively.

There were no carcinogenicity studies for this category of compounds.

Environment

The EPIWIN suite developed by Syracuse Research Corporation 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.

At room temperature, DBTC, DBTO and DBTM are solids or powders, and DBT(EHTG)/(IOTG) are oily liquids. DBTL can be produced as either an oily liquid or as a solid material. DBTC, DBTL, DBTM, DBTO, and DBT(EHTG) have melting points ranging from -80°C ([DBT(EHTG)] to 110°C (DBTM), and boiling points ranging from 113.6°C (DBTC) to ≥ 260 °C [decomposition of DBT(EHTG)]. Measured and calculated vapour pressures range from 5.4e-11 hPa (DBT(EHTG)) to 0.0016 hPa at 25°C (DBTC). Measured vapor pressure values for the organotins are difficult to obtain. Similar problems exist for measuring vapor pressure as for water solubility and partition coefficient. The lower molecular weight impurities in the named substance will volatilize more readily and, therefore, influence the measured vapor pressure. In order to confirm that the vapor pressure is completely attributable to the named substance, a derivitization method to analyze the organotins would have to be used. This method involves ligand exchange and currently there is no analytical method available to quantify the entire organotin compound with its associated ligands. Therefore, only calculated vapor pressure values are provided. The water solubilities of the dibutyltin compounds range from relatively insoluble (0.07 mg/L for DBTL) to moderately soluble (320 mg/L for DBTC). Log Kow values range from 0.97 (DBTC) to 11.43 [DBT(EHTG)]. Log BCFs of -0.9 to 2.13 for DBTC, 1.5 to 2.0 for DBTL, 2.0 for DBTM, and 2.0 for DBT(EHTG) indicate a low potential for bioaccumulation; however, a log BCF of 4.80 indicates that DBTO may bioaccumulate in the tissues of aquatic organisms.

None of the dibutyltin compounds are readily biodegradable. However, they are atmospherically degraded by photochemically-induced hydroxyl radicals; half-lives range from 4.7 hours [DBTL, DBT(EHTG), DBT(IOTG)] to 9.0 hours (DBTC and DBTO). DBTM may also be degraded by atmospheric ozone ($t_{1/2} = 6.6$ days).

In water, DBTC undergoes rapid degradation by hydrolysis and is expected to hydrolyze within minutes. It is expected that the chlorines in DBTC will be displaced to form dibutyltin hydroxide which eventually precipitates as the oxide (DBTO) which will precipitate.

In water, DBT(EHTG)/(IOTG), DBTL, undergo rapid degradation by hydrolysis ($t_{1/2} = 10 - 12$ hrs and < 38 minutes, respectively.) Although there is no stability data for DBTM, data for DBTL and DBT(EHTG)) indicate that DBTM is expected to hydrolyze within minutes to hours. Maleic acid and lauric acid are the hydrolysis products of DBTM and DBTL, respectively. Similarly, the thioester ligands on DBT(EHTG)/(IOTG) will be rapidly displaced. It is also possible that the labile ligands can be displaced by other anions in the medium. The displaced thioester ligands, EHTG/IOTG, can also undergo further hydrolysis of the ester linkage to form thioglycolic acid and either ethylhexanol or isooctanol, respectively.

DBTL, DBTM, DBTO, and DBT(EHTG)/(IOTG) are sparingly soluble in water, from estimated values of 0.07 mg/L at 20°C (DBTL) to 8 mg/L (DBTM). The low solubility and occurrence of hydrolysis reactions present significant challenges to testing and analyzing organotin compounds in aqueous solution. The named substance contains a certain percentage of impurities and the lower molecular weight impurities will hydrolyze more readily in solution. These organotin impurities, including hydrolysis reaction products, will be present in solution along with the named substance. At least some of these impurities are often more soluble in water than the named substance and, therefore, confound the reported solubilities.

Based on the results of the Level III distribution modelling, DBTC and DBTM are expected to partition primarily to water (43–44%) and soil (55–56%), and DBTO, DBT(EHTG) and DBT(IOTG) are expected to partition primarily to soil (25–57%) and sediment (30–73%). For DBTL, the results of the distribution modelling (using a measured log Pow of 3.12) indicated that DBTL would partition primarily to water (79.4%). However, DBTL is relatively insoluble in water (ca. 0.07 mg/L). The results of distribution modelling using the calculated log Pow of 10.64 indicate that DBTL is expected to partition primarily to the soil (30.4%) and sediment compartments (65.9%).

DBTC contains technical impurities, including tributyltin chloride (TBTC). Because of its high toxicity, the level of this impurity should be taken into account when assessing the ecotoxicological profile of commercial products. Typically, the DBTC commercially produced contains less than 1% TBTC by weight. Also, in the ecotoxicity tests, the organisms were most likely exposed to parent substance as well as hydrolysis/degradation products.

The acute 96 hr LC₅₀ toxicity values to zebra fish (*Brachydanio rerio*) ranged from >3 mg/L (DBTC, DBTL, DBTO) to ≥ 11 mg/L [DBT(EHTG)] based on measured concentrations. The acute 48-h toxicity values to *Daphnia magna* ranged from 0.21 mg/L (DBTM) to 2.52 mg/L (DBTL) based on measured concentrations. For freshwater algae, 72-h ECr50 values ranged from 0.56 mg/L [DBT(EHTG)] to 8.0 mg/L (DBTC), and the 72 h ECb50 values ranged from 2.5 mg/L (DBT(EHTG)) to 5.9 mg/l (DBTM). NOECs ranged from 0.19 to 2.8 mg/L. Other studies with lower toxicity values but not considered to be key studies are also mentioned in the SIAR.

DBTC (containing 0.12% (w/w) TBTC) reduced parental growth in chronic *D. magna* studies. The 21-d EC50 was > 0.08 mg/L (as DBTC), and the NOEC and LOEC were 0.015 and 0.03 mg DBTC/L, respectively. The NOEC and LOEC in a 110-d survival and growth test with rainbow trout (*O. mykiss*) fry were 0.04 and 0.2 mg/L, respectively, based on nominal concentrations of DBTC. The overall NOEC and LOEC were 0.098 and 0.574 mg/L, respectively, in a chronic *D. magna* toxicity study of DBT(EHTG).

Exposure

In 2000, worldwide production was 10,000 to 15,000 tonnes of DBTC, 1000 to 5000 tonnes each of DBTL and DBTO, 500 to 1000 tonnes of DBTM, and 7500 to 12,500 tonnes of DBT(EHTG). DBTC, DBTL, DBTM, and DBTO are used as industrial intermediates and/or reaction catalysts in the production of organotin chemicals or are sold to chemical and coating/coating formulation manufacturers. DBT(EHTG) and DBT(IOTG) are used commercially as heat stabilizers and are added to polyvinyl chloride (PVC) and chlorinated polyvinyl chloride (CPVC) as heat stabilizers intended to preserve the polymeric structure and properties of the resins during the

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final stages of fabrication into finished articles. However, over the past several years, the IOTG product has been gradually replaced by the EHTG version due to raw material availability, cost, and customer preference. After being blended into the PVC and CPVC resin, the stabilizers remain there throughout the subsequent processing steps. All systems are designed and maintained to ensure that moisture is kept away from the resin compound, because the presence of water creates significant problems during processing. Therefore, losses to water during blending and melt processing are low, as these are designed to be "dry" processes.

Over a period of approximately ten years, use of DBT(IOTG) has gradually decreased, and DBT(EHTG) is being used instead.

Dibutyltin chemicals either leach out of PVC and CPVC articles or are released into the atmosphere during processing. The dibutyltin compounds that leach out of PVC articles into the environment will be hydrolyzed to the dibutyltin cations and associated anions. When tested, PVC water pipes showed an initial release of dibutyltins, which is followed by decreased releases until lower levels of release are reached. Other articles that have dibutyltin stabilizers, such as window profiles and building siding, will show the same type of leaching behavior, i.e., initial level falling to lower levels.

DBT concentrations in drinking water passed through new CPVC pipe at two temperatures initially ranged from 1.9-5.9 ng Sn/g and 31.2-100.4 ng Sn/g at 24 and 65° C, respectively, and declined to 0.5-0.8 ng Sn/g and 1.3-3.7 ng Sn/g, respectively, over a period of 20 repetitive extractions. DBT concentrations measured in potable water in Canada range from non-detected (< 0.5 ng Sn/L) to 52 ng Sn/L. In the U.S., organotins are on the contaminant candidate list (published in February 2005) because they are known or anticipated to occur in public drinking water systems and are of sufficient concern to warrant further investigation.

Consumers may also be exposed to DBT compounds in fish/fishery products, and DBT levels in cultured fish products were higher than levels found in marine products (maximum values: 65.5 ng/g vs. 6.12 ng/g). Wholebody DBT levels in freshwater fish range from non-detected (0.00097 μ g/g detection limit) to a maximum of 0.221 μ g/g. DBT levels reported in mussels and other bivalves ranged from not detected to 2.6 μ g Sn/g wet weight. DBT also has been reported in a small number (4 of 95 items) of household items in Japan; the maximum concentration measured was 33.7 μ g/g. Average concentrations of DBT found in household dust in two studies were 0.25 μ g/g (United States) and 0.56 μ g/g (United Kingdom).

Exposure in the workplace is controlled through equipment design and administrative controls such as the use of personal protective equipment. Based on an air monitoring survey in 2003, workers in PVC processing facilities that manually handled the stabilizer had exposures ranging from 50 percent of the threshold limit value (TLV) to equal to the TLV.

Most PVC and CPVC articles will either be recycled or landfilled at end of life. A portion of the PVC products entering the total solid waste stream will be incinerated, which destroys organotins and converts them to inorganic tin oxides. Landfill leachate may directly enter the environment; tests have shown that organotin leaches out from PVC at μ g/L levels. If landfill leachate should directly enter the environment, the leachate would likely be more dilute, resulting in lowered environmental concentrations.

Organotins detected in untreated wastewater were primarily associated with suspended solids and 80-98% was removed from wastewater primarily by sedimentation and adsorption into sewage sludge. In soil, dibutyltins have a half-life of approximately 5 months.

A multi-year (1992–1998) national monitoring program that measured butyltins in water, sediment, and bivalve tissue collected in and around US commercial harbors, shipyards/dry docks, marinas, and ecologically significant areas (ESAs) found that butyltin concentrations have been generally steadily declining over time. In 1999, mean DBT concentrations ranged from ≤ 3.2 –7.8 ng/L in surface waters regardless of depth, 9.6–16 ng/g in surface sediments, 9.1–19 ng/g in deep sediments, and 38–145 ng/g in bivalve tissue.

Several monitoring studies were conducted in areas where antifouling paints have been used. In U.S. freshwaters, a concentration of 160 ng/L was found in North Carolina. Other data on sediments showed similar results, although some have shown higher maximum levels. For instance, a maximum dibutyltin concentration of 0.71 mg Sn/kg tissue was found in a survey of freshwater estuaries in Spain. Also, in the St. Lawrence River in Canada, a

maximum dibuyltin sediment concentration of 1.00 mg Sn/kg tissue was found. A maximum dibutyltin concentration of 345 ng Sn/g mussel tissue was found off the coast of Portugal in a recent study.

Tin is not listed as a hazardous waste constituent by the EPA; therefore, its disposal is not restricted by federal land disposal restrictions. The recommended method of disposal is incineration in an approved hazardous waste incinerator. This method converts the organotin to inorganic tin. Most PVC and CPVC articles will either be recycled or landfilled at end of their use.

Exposure and risk assessments specific to several countries are available. These assessments were performed in countries that produce dibutyltins for use in PVC.

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

Human Health: The chemicals in this category are candidates for further work. The chemicals possess properties indicating a hazard for human health (acute, repeated-dose, corrosivity, immunotoxicity, genotoxicity and reproduction/developmental toxicity). Member countries are invited to perform an exposure assessment for consumers and workers, and if necessary a risk assessment.

Environment: The chemicals in this category are candidates for further work. The chemicals possess properties indicating a hazard for the environment (toxicity to fish, aquatic invertebrates and algae). Member countries are invited to perform an exposure assessment for the environment, and if necessary a risk assessment.