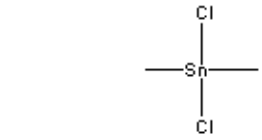
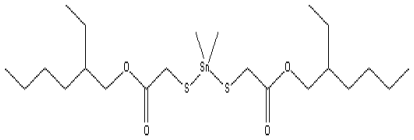
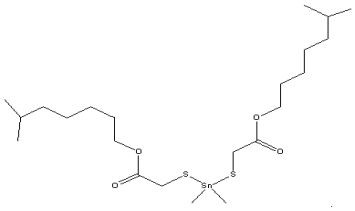
SIDS INITIAL ASSESSMENT PROFILE

Chemical Category	Dimethyltin chloride and selected thioglycolate esters	
Structural Formula Chemical Names and CAS Registry Numbers		**Dimethyltin dichloride (DMTC), CASRN 753-73-1**
		**Dimethyltin bis[2-ethylhexyl thioglycolate] [DMT(EHTG)], CASRN 57583-35-4**
		**Dimethyltin bis[isooctyl thioglycolate] [DMT(IOTG)], CASRN 26636-01-1**

SUMMARY CONCLUSIONS OF THE SIAR

Category Rationale

DMTC, DMT(EHTG), and DMT(IOTG) are considered one category of compounds for mammalian studies via the oral route. The justification for this category is based on structural similarities and the demonstrated rapid conversion of all of the esters to the DMTC when placed in simulated mammalian gastric contents [0.07M HCl] under physiological conditions. The data from the simulated gastric reaction study of DMT(EHTG) shows that essentially all DMT(-EHTG) is converted to DMTC at pH 1.5 within 0.5 hours. Thus, DMTC is the appropriate surrogate for mammalian toxicology studies via the oral route.

Acute toxicity, 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 difference in the structures of the labile ligands causes differences in water solubility between the alkyltin chloride and thioesters affecting their respective bioavailabilities and distribution in the environment. Furthermore, DMT(EHTG) and DMT(IOTG) will degrade in aqueous solution such that organisms will be exposed to the parent material and their different degradation products. DMTC is not an appropriate surrogate for the thioesters for the ecotoxicity and environmental fate endpoints.

Analogue Rationale

Data for DMT(EHTG) and DMT(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 DMT(EHTG) and DMT(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 in the OECD HPV Chemicals Program.

Human Health

The majority of toxicology studies were conducted with commercial mixtures having high dialkyltin to monoalkyltin ratios.

No toxicokinetic data are available for DMTC, however studies were conducted with DMT(EHTG) in which simulated gastric fluid (0.07M HCl under physiological conditions) converted this substances to dimethyltin chloride and the respective organic acid. *In vitro* data for DMTC and DMT esters indicate the dermal penetration of these compounds is low. Published data indicate that dimethyltin can cross the placenta.

Acute oral LD50s for the dimethyltin compounds have a wide range, but the most reliable data place the LD50 at approximately 400 mg/kg for DMTC and approximately 1200 mg/kg for the thioglycolates. The most reliable inhalation LC50 values range from 115 (4-h aerosol exposure) for DMTC to 132,000 mg/m3 for DMT(IOTG) and comparisons are complicated by inadequate descriptions of the aerosol in some studies. Dermal LD50 values in rabbits ranged from 380 to >2000 mg/kg for DMTC and >1050 to >3100 mg/kg for the thioglycolates. Again, study comparisons are complicated by inadequate descriptions of the tested compounds.

DMTC is corrosive to skin and eyes. DMT(EHTG)/(IOTG) are slightly to moderately irritating to skin and minimally to not irritating to eyes. DMTC is not a sensitizer. Data on DMT(2-EHTG) and DMT(IOTG) suggest that the DMT thioesters are weak sensitizers and the hydrolysis products, EHTG or IOTG, are sensitizers.

There are two repeated-dose oral studies of DMTC (90-day drinking water and 90-day feeding). The results are consistent and they are considered in tandem. DMTC had a NOAEL of 15 ppm in feed (~1.0 mg/kg/d). The critical toxic effect in both studies was neurotoxicity; tremors and convulsions were observed in a dose-related manner. Histopathology (feed study) confirmed neuronal death in the cerebellum and lesions in the hippocampal region, the piriform, entorhinal, and perirhinal cortices, the amygdala, the olfactory nuclei and the tenia tecta. The NOAEL was 15 ppm (feed) and the LOAEL was 25 ppm (water; ~2.2 mg/kg bw day).

DMTC was negative in two Ames tests, with and without metabolic activation, but was positive in Salmonella typhimurium strain TA100 without metabolic activation in another test. DMT(EHTG) was negative in a standard Ames assay. Although DMTC was positive in an in vitro chromosomal aberrations assay with metabolic activation, it was negative in an in vivo mouse micronucleus test. Based on these observations the overall conclusion is that DMTC does not have genotoxic potential.

Data from DMTC repeated dose studies with rats indicated no gross or histopathological effects on the reproductive organs of either sex. In separate studies, DMTC was administered to rats from days 7 to 17 of gestation at doses of 5, 10, 15, and 20 mg/kg bw/day. The NOAEL for developmental toxicity was 10 mg/kg-bw/day, with reduced fetal weight observed at 15 mg/kg-bw/day, and fetal death, cleft palate and other effects observed at 20 mg/kg bw/day, which also resulted in severe maternal toxicity (20% deaths, vaginal bleeding, tremors and other effects). In the same study, DMTC was also administered at 20 and 40 mg/kg bw/day at 4 different time periods during gestation (all 3-day intervals). Effects included increased numbers of fetuses with skeletal variations, cervical ribs, and/or splitting of first cervical vertebral arch at 40 mg/kg bw/day in the protocols where DMTC was administered on days 7-9 or 13-15 of gestation. At 40 mg/kg bw/day and days 16-17 of gestation, the number of fetuses with kinked ureters were statistically increased. Maternal toxicity in this portion of the study was limited to the gestation day 10-12 protocol at both 20 and 40 mg/kg bw/day. DMTC was fetotoxic at maternally toxic doses.

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.

DMTC is a solid at room temperature and melts at 90°C, boils at 188-190°C, has a calculated vapor pressure of 0.25 hPa at 25°C , and is soluble in water (823 g/L). The log Kow is -2.18, and is not likely to bioaccumulate (log BCF=0.5). DMTC is not readily biodegradable, but atmospheric degradation occurs by photochemical induced hydroxyl radicals, with a half-life of 7.9 days. If released to the environment, DMTC is expected to partition primarily into water (51.6%) and soil (47.3%).

In water, DMTC undergoes rapid degradation by hydrolysis and is expected to hydrolyze within minutes. It is expected that the chlorines in DMTC will be displaced to form di-methyltin hydroxide which eventually precipitates as the oxide. (The alkyltin moiety (DMT) was hydrolytically stable at pH 4, 7, and 9 (t1/2 > 1year at 25°C)).

DMTC has sufficient water solubility that it can be studied in water using analytical methods that involve derivitization. This analysis method only measures the amount of the alkytin moiety, and can determine if the alkyltin itself is degrading. This method does not identify the other ligands attached to the tin, and thus hydrolysis of the chloride on tin to the hydroxide is NOT detected using this method. DMT(EHTG) is a liquid at room temperature, has a freezing point of -75 to -65°C, decomposes at ≥ 290°C, and a calculated vapor pressure of 0.004 hPa at 25°C. DMT(EHTG) is slightly soluble in water (0.1–4.9 mg/L), hydrophobic (log Kow = 8.48), and has a moderate potential to bioaccumulate (log BCF = 2.7). DMT(EHTG) is not readily biodegradable, but is atmospherically degraded by hydroxyl radicals and UV radiation. If released to the environment, DMT(EHTG) is predicted to partition to sediment (68%) and soil (28%), with smaller amounts in water (3.8%) and air (0.3%). DMT(IOTG) is predicted to partition into sediment (70.4%) and soil (27.5%), with smaller amounts in water (1.9%) and air (0.13%).

DMT(IOTG) and DMT(EHTG) are sparingly soluble in water as shown by the data for DMT(EHTG) that estimates solubility as 0.1-4.9 mg/L. In water, DMT(EHTG)/IOTG undergo rapid degradation by hydrolysis. Although there is no stability data for DMT(EHTG)/(IOTG), data for other organotins [DOTC, DBTL, and DBT(EHTG)] indicate that the dimethyltin compounds are expected to hydrolyze within minutes to hours in water. . The thioester ligands on DMT(EHTG)/(IOTG) will be rapidly displaced to form dimethyltin hydroxide which eventually

precipitates as the oxide. 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.

In the ecotoxicity tests the organisms were most likely exposed to parent substance as well as hydrolysis/degradation products.
DMTC was not acutely toxic to *B. rerio* at 100 mg/L. The 96-h LC50 for *P. promelas* was reported to be 320 mg/L. The 48-h EC50 to *D. magna* was 17 (12–24) mg/L. The 72-h EC50 (growth rate) for *S. subspicatus* was reported as 37 mg/L.

Acute aquatic toxicity data for DMT(EHTG) are available for fish, daphnia, and algae; and chronic aquatic toxicity data are available for daphnia. A 96-h LC50 for *P. promelas* was reported to be >1000 mg/L. The 48-h EC50 for *D. magna* was 32 mg/L. The 72-h EC50 for *P. subcapitata* on growth and cell density values are 270 mg/L and 120 mg/L, respectively. In a 21-day *D. magna* reproduction study, LC50 for parental survival was 1.0 mg/L; however, a clear dose-response relationship was not observed. The overall NOEC and LOEC were 0.46 mg/L (10% WAF) and 2.3 mg/L (50% WAF), respectively.

Exposure

DMTC is primarily used as an intermediate in the synthesis of organotin chemicals and, to a lesser extent, as a coating on glass. In 2000, worldwide production of DMTC was estimated at 1,000 to 5,000 metric tons [MT]. DMT(EHTG) is used in the production of films, sheets, injection moldings, pipes, sidings, and other applications where high thermostability is required. DMT(EHTG) has clearance in many countries for use in potable water pipes, and also is approved for use in food contact applications. In 2000, worldwide production of DMT(EHTG) was estimated at 5,000 to 10,000 MT. Use of DMT(IOTG) has been gradually replaced by DMT(EHTG) over approximately a ten year period.

DMT(EHTG)/(IOTG) is added to polyvinyl chloride (PVC) and chlorinated polyvinyl chloride (CPVC)as a heat stabilizer. After being blended into the PVC and CPVC resin, the stabilizers remain there throughout the subsequent processing steps. Dimethyltins may also be used in other PVC articles, such as window profiles, house siding, fences and decking. The amounts of stabilizer that can be used in the PVC, or the levels of dimethyltins that can be extracted into food and water are controlled. In one study, levels of dimethyltin extracted from PVC packaging materials by food simulants were below the specific migration limit established for methyltin compounds (0.18 mg Sn/kg).

Maximum dimethyltin concentrations of 400 ng Sn/L and 0.27 µg Sn/kg dry weight were reported in water and freshwater and marine sediment, respectively. Dimethyltin stabilizers occur occasionally in raw waste water; however, some research has shown that about 80% of organotins detected in untreated wastewater is associated with suspended solids and are removed from wastewater primarily by sedimentation and adsorption into sewage sludge. Studies have shown that dimethyltins have a half life of about 6 months in the environment.

Dimethyltin was not detected in saltwater in Western Florida or the Gulf of Mexico but was detected in Baltimore Harbor in Maryland with a maximum concentration of 0.1 µg/L. In a Canadian marina (freshwater), a maximum of 0.4 µg/L was found. In U.S. rivers, a mean of 0.004 µg/L was found; in German rivers a maximum of 0.26 µg/L, and in Florida lakes, ponds, and rivers none was detected (<0.008 µg/L).

In Turkey, the maximum sediment concentration of dimethyltin was 0.01 µg/L; in Great Bay, NW, the maximum sediment concentration was 0.06 µg/L, and in San Diego Bay, the maximum

concentration in sediment was 0.003 µg/L. Dimethyltin has been found in fresh water, seawater, and sediment in Canada in about 10 percent of all waters sampled.

In the Mediterranean, dimethyltin has been found in limpet (*Patella caerulea)* at 0.0002 mg Sn/kg in the shell and 0.009 mg Sn/kg in soft parts. In a forested area in Germany, dimethyltin compounds were detected in precipitation.

Dimethyltin compounds have been detected in Canadian drinking water at up to 49.1 ng Sn/L in one survey and up to 6.5 ng Sn/L in another study. In the United States, dimethyltin was found to range from 0.40 to 2.2 ng Sn/L in a limited number of tap water samples from Florida in 1977.

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. Concentrations of organotins in leachate samples from sanitary landfills were found to be in the low micrograms per liter range.

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 (corrosivity, skin sensitization (EHTG/IOTG), neurotoxicity, and fetotoxicity at maternally toxic doses). 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 aquatic invertebrates and algae). Member countries are invited to perform an exposure assessment for the environment, and if necessary a risk assessment.