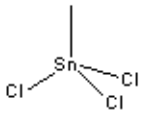
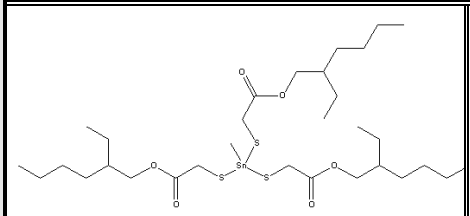
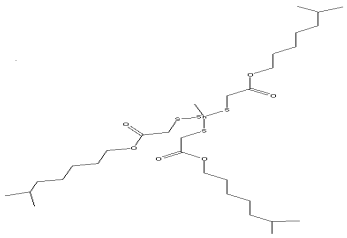
SIDS INITIAL ASSESSMENT PROFILE

Category Name	Monomethyltin chloride, thioglycolate esters, and tall oil ester reaction product	
Structural Formula, Chemical Names and CAS Registry Numbers		Monomethyltin trichloride, MMTC, CASRN 993-16-8
		Monomethyltin tris[2-ethylhexylmercaptoacetate], MMT(EHTG), CASRN 57583-34-3
		Monomethyltin tris[isooctylmercaptoacetate], MMT(IOTG), CASRN 54849-38-6
	This compound is a reaction product; therefore, the molecular structure will vary depending on the precursors (See SIAR)	Methyltin reverse ester tallate reaction product, TERP, CASRN 201687-58-3 201687-57-2; 68442-12-6; 151436-98-5 [mixture of CASRN 13269-74-4; 33397-79-4; 59118-79-5; 67859-63-6; 67859-64-7; 68928-40-5] See note for description of TERP

Note: The CASRN cited in the OECD SIAP for this substance refers to the descriptions of TERP from all national regulatory bodies. Therefore, this SIAP applies to TERP globally, whether described as a reaction product or described as a mixture of components. The CASRN of TERP described as a reaction product are: 201687-58-3; 201687-57-2; 68442-12-6; 151436-98-5. The CASRN of the individual components which, taken together as a mixture, describe TERP are: 13269-74-4; 33397-79-4; 59118-79-5; 67859-63-6; 67859-64-7; 68928-40-5. TERP described as a mixture of Japanese MITI numbers 2-3207 and 2-3208 is also included in the OECD definition of TERP.

The chemical definition of the substance described above is the reaction product of monomethyltin trichloride and dimethyltin dichloride, sodium sulfide (Na2S) and various organic carboxylic acids including oleic acid and tall oil fatty acid (CASRN 8002-26-4), which are within the definition of C13 to C23 fatty acid used by Japan.

SUMMARY CONCLUSIONS OF THE SIAR

Category Rationale

MMTC, MMT(EHTG), MMT(IOTG), and TERP 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 MMTC when placed in simulated mammalian gastric contents [0.07M HCl] under physiological conditions. For the MMT(EHTG) >90% conversion to MMTC occurred within 0.5 hours. For TERP, 68% of the monomethyltin portion of the compound was converted to MMTC within 1 hour. Thus, MMTC is the appropriate surrogate for mammalian toxicology studies via the oral route.

TERP is a reaction product of MMTC and dimethyltin dichloride (DMTC), Na2S, and tall oil fatty acid [a mixture of carboxylic acids, predominantly C-18]. The reaction product is a mixture of carboxylic esters and includes short oligomers of mono/dimethyltins bridged by sulfide groups. Although the tall oil component of TERP is not structurally similar to EHTG, TERP's conversion to MMTC justifies its inclusion. While the contribution of the various ligands to the overall toxicity may vary, the contribution is expected to be small relative to that of the MMTC. Further, the EHTG ligand from MMT(EHTG) is likely to be more toxic than the oleic or linoleic acid from TERP so inclusion of TERP in the category is a rather conservative approach. The other possible degradate of tall oil and EHTG is 2-mercaptoethanol (2-ME), and it is common to both ligands.

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, MMT(EHTG) and MMT(IOTG) will degrade in aqueous solution such that organisms will be exposed to the parent material and their different degradation products. MMTC is not an appropriate surrogate for the thioesters or TERP for the ecotoxicity and environmental fate endpoints.

Analogue Rationale

Data for MMT(EHTG) and MMT(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 MMT(EHTG) and MMT(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 within the OECD HPV Chemicals Program.

Human Health

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

Gastric hydrolysis studies were conducted with TERP and MMT(EHTG) in which simulated gastric fluid [0.07M HCl under physiological conditions] converted these substances to methyltin chloride and the respective organic acids. Based on data for DMTC and DMT esters the dermal penetration of MMTC and its esters is expected to be low.

Acute oral LD_{50} values for MMTC, MMT(EHTG), MMT(IOTG), and TERP indicated low to moderate toxicity; the most reliable data place the LD_{50}s in the range of 1000 mg/kg. Acute dermal LD_{50} values were $\geq$1000 mg/kg bw, and inhalation LC_{50} was >200 mg/L. MMTC was corrosive to skin and assumed corrosive to eyes. MMT(IOTG)/(EHTG) are irritating to skin, but not to eyes. No data on sensitization are available on MMT(EHTG/(IOTG), but the hydrolysis products EHTG or IOTG are sensitizers. No primary irritation data

were available for TERP, but it was a sensitizer in the mouse Local Lymph Node Assay.

There are no repeated-dose studies for the category members via the dermal or inhalation routes.

In a 90-day repeated dose oral study of MMTC, treatment-related changes were limited to the high dose group (750 ppm in diet; 50 mg/kg bw/d with some gender-related variation). Organ weight changes (adrenal, kidney, thymus, spleen, brain, epididymides), haematology, clinical chemistry, and urinalysis changes were noted, but histopathology only confirmed effects in the thymus and brain. The critical toxic effects were neurotoxicity and thymic atrophy. Both sexes had decreased cortex/medulla ratios in the thymus. In the brain there was loss of perikarya of neuronal cells in the pyramidal layer of the Hippocampus CA1/2 in both sexes, and in males there was loss of perikarya in the piriform cortex. The NOAEL was 150 ppm (10 mg/kg bw/d). Another 90-day dietary study using MMTC showed increased relative kidney weights and slight to moderate epithelial hyperplasia of the bladder in females at the lowest dose (NOAEL <20 ppm in diet [<1-3.6 mg/kg bw/d]) and additional effects including increased relative thymus weights in females and urinalysis results in both sexes at higher doses.

A 90-day dietary study with dose levels of 30, 100, 300, and 1000 ppm TERP in the diet resulted in slightly decreased food intake, body and organ weight changes, and decreased specific gravity of the urine at the highest dose. The NOAEL was 300 ppm in diet (equivalent to 15 mg/kg bw/d). A 28-day gavage study using TERP showed changes in clinical chemistry and slight differences in hematology at 150 mg/kg bw/d and higher. The NOAEL was 50 mg/kg bw/d.

The effects of MMT(IOTG) were evaluated in a 90-day dietary study using doses of 100, 500, and 1500 ppm (decreased from 2500 ppm) in the diet. Based on clinical chemistry effects at 500 ppm and other effects at higher doses, the NOAEL was 100 ppm in diet (approximately 6-21 mg/kg bw/d).

The monomethyltin compounds as a class are not mutagenic in the Ames test. TERP was positive in a human lymphocyte assay. MMTC was equivocal for induction of micronucleated polychromatic erythrocytes (MPEs) in an *in vivo* rat micronucleus test (OECD 474). In this study a statistically significant increase in MPE was observed only at 24 h and not at 48 h after treatment and there was no dose-response. Based on these observations the overall conclusion is that MMTC does not have genotoxic potential.

In a limited carcinogenicity study, MMT(EHTG) produced no compound-related macroscopic or microscopic changes in rats fed 100 ppm in the diet for two years.

In the reproductive satellite portion of the 90-day study using MMTC (with dose levels of 30, 150, and 750 ppm in the diet), post-implantation loss, decreased litter size and increased neonatal mortality occurred at 750 ppm (26-46 mg/kg bw/d for females). Maternal gestational body weights were transiently suppressed and other maternal toxicity was inferred from the repeated dose results at this dose. There were no malformations observed at any dose. The NOAEL for maternal toxicity, and reproductive, and fetotoxic effects was 150 ppm in the diet (6-12 mg/kg bw/d).

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.

MMTC is a solid at room temperature and melts at 43°C, boils at 171°C, has a calculated vapor pressure of 1.7 hPa at 25 °C, and is soluble in water (1038 g/L at 20°C). The measured log Kow is -0.9 and MMTC is not readily biodegradable. Atmospheric degradation occurs by photochemical induced hydroxyl radicals, with a half-life of 15.7 days. A Henry's Law constant of 3.83×10^{-7} atm-m^3/mol predicts MMTC will volatilize from surface water (t½ = 99 days and 3 years for model river and lake, respectively). If released to the environment, MMTC is expected to partition primarily into water (54%) and soil (43%).

In water, MMTC undergoes rapid degradation by hydrolysis and is expected to hydrolyze within minutes. It is expected that the chlorines in MMTC will be displaced to form mono-methyltin hydroxide which eventually precipitates as the oxide (the alkyltin moiety (MMT) was hydrolytically stable at pH 4, 7, and 9 (t½ > 1 year at 25°C)).

MMTC has sufficient water solubility that it can be studied in water using analytical methods that involve derivatization. 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.

MMT(IOTG), MMT(EHTG), and TERP are sparingly soluble in water (0.6-10.7 mg/L). In water, these monomethyltin compounds undergo rapid degradation by hydrolysis. Although there is no stability data for MMT(EHTG)/(IOTG) or TERP, data for other organotins [DOTC, DBTL and DBT(EHTG)] indicate that the monomethyltin compounds are expected to hydrolyze within minutes to hours in water. The thioester ligands on MMT(EHTG)/(IOTG) will be rapidly displaced to form mono-methyltin 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 ethylhexanol or isooctanol, respectively.

TERP is a liquid at room temperature, boils at 216°C, and has a calculated vapor pressure of 0.2 hPa at 25°C. TERP is slightly soluble in water (4.4 mg/L), highly hydrophobic (log Kow = 25.5), has low potential for bioaccumulation (log BCF = 2.0), and is readily biodegradable. It is degraded atmospherically by hydroxyl radicals and ozone, with a half-life of 0.5 hours. If released to the environment, TERP is predicted to partition primarily to sediment (99%).

MMT(EHTG) is a liquid at room temperature and has a freezing point of -85 to -65°C, decomposes at ≥260°C, has a derived vapour pressure of 0.02 hPa at 25°C, a calculated log Kow of 10.98, is slightly soluble in water (1.8-6 mg/L), and is readily biodegradable. MMT(EHTG) is also degraded atmospherically, with a half-life of 6.3 hours. A Henry's Law constant of 3.18×10^4 atm-m^3/mol predicts MMT(EHTG) will volatilize from surface water (t½ = 8 hours and 11 days for a model river and lake, respectively). If released to the environment, MMT(EHTG) is expected to partition primarily into sediment (71%) and soil (25%).

In the ecotoxicity tests the organisms were most likely exposed to parent substance as well as hydrolysis/degradation products. MMTC was not acutely toxic to zebra fish (*Brachydanio rerio*) (96-h LC_{50} > 102 mg/L) or *Daphnia magna* (48-h EC_{50} > 101 mg/L). MMTC inhibited the growth (72-h EC_{50} = 0.03 mg/L) and biomass (72-h EC_{50} = 0.02 mg/L) of the green alga *Scenedesmus subspicatus* (NOEC = 0.007 mg/L). MMTC was not acutely toxic to earthworms at nominal concentrations up to 1000 mg/kg. TERP was not acutely toxic to rainbow trout *(Oncorhynchus mykiss)* (96-hr LC_{50} >4.4 mg/L), inhibited *D. magna* survival and mobility (48-h EC_{50} = 0.27 mg/L), and inhibited growth of the freshwater green alga *Pseudokirchneriella subcapitata* was (72-h EC_{50} = 0.64 mg/L; NOEC = 0.28 mg/L). MMT(EHTG) was not acutely toxic to *B. rerio* (LC_{50} > 6 mg/L; NOEC = 3.6 mg/L) and did not inhibit the growth of *S. subspicatus* (72-h EC_{50} > 1.84 mg/L; NOEC = 0.6 mg/L). The 21-d EC_{50} for reproduction in a chronic *Daphnia magn*a study was > 0.134 mg/L (NOEC = 0.134 mg/L).

Exposure

In 2000, worldwide production was estimated at 1,000 to 5,000 metric tons for MMTC, 5,000 to 10,000 MT for MMT(2-EHTG), and 7,500 to 10,000 MT for TERP. MMTC is used as an industrial intermediate in the production of organotin chemicals; there are no commercial applications for this chemical. TERP and MMT(2-EHTG) are used in the production of polyvinyl chloride (PVC) films, sheets, injection moldings, pipes, sidings, and other applications where high thermostability is required. TERP and MMT(2-EHTG) have clearance in many countries for use in potable water pipes, and MMT(2-EHTG) also is approved for use in food contact applications. MMT(2-EHTG)/(IOTG) or TERP are added to PVC and chlorinated polyvinyl chloride (CPVC) as heat stabilizers. After being blended into the PVC and CPVC resin, the stabilizers remain there throughout the subsequent processing steps. Use of MMT(IOTG) has been gradually replaced by MMT(EHTG) over approximately a ten year period.

Consumers may be exposed to monomethyltins from PVC used in potable water pipes and fittings and from PVC used in food packaging applications. Monomethyltin stabilizers are used in the production of PVC water pipes, and these pipes are tested to insure that the amount of monomethyltin leaching into the water meets regulatory requirements Monomethyltin chemicals can either leach out of PVC and CPVC articles, or are released into the atmosphere during the processing. However, monomethyltin compounds that leach out of PVC articles into the environment will be hydrolyzed to the corresponding monomethyltin and associated anions.

Monomethyltins 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 monomethyltins that can be extracted into food and water are controlled.

In Canadian water samples from drinking distribution systems collected in 1996, monomethyltin was detected in 21 of 25 samples at 5.7 to 112 ng/L, and in 28 (100%) samples at concentrations of 2.1 to 129 ng Sn/L. Monomethyltin concentrations in distributed water systems from 5 Canadian municipalities ranged from not detected (< 0.5 ng Sn/L) to 257.4 ng Sn/L. Also, no organotin compounds were seen in raw water or water leaving the treatment plant, which suggests that the source was the distribution system. In the U.S., monomethyltin was found to range from 0.49 to 8.1 ng Sn/L in a limited number of tap water samples from Florida in 1977.

Monomethyltins are removed from wastewater primarily by sedimentation and adsorption onto sewage sludge. Regarding environmental fate, most PVC and CPVC articles will either be recycled or landfilled at end of life. PVC is not usually incinerated, but if other organotin products are incinerated, the organotins present are converted to inorganic tin oxides. Concentrations of organotins in leachate samples from sanitary landfills were found to be in the low micrograms per liter range. If landfill leachate should directly enter the environment, there would be dilution of the leachate entering the environment. The estimated half-lives of monomethyltin in a simulated landfill study ranged from 2 to 6 months.

Monomethyltins have been detected in fresh and marine waters and sediments. Concentrations of monomethyltins in fresh and marine waters are in the low micrograms per liter, and concentrations in sediments range from not detected (< 0.1 mg Sn/kg) to 0.3 mg Sn/kg. It has been found in precipitation in Germany and in limpet in the Mediterranean.

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.

Exposure in the workplace is controlled through equipment design, as well as regular air monitoring, and worker exposure is confined to manual operations, such as material addition, transfer, or sampling.

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, neurotoxicity, and reproductive 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 aquatic invertebrates and algae). Member countries are invited to perform an exposure assessment for the environment, and if necessary a risk assessment.