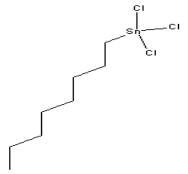
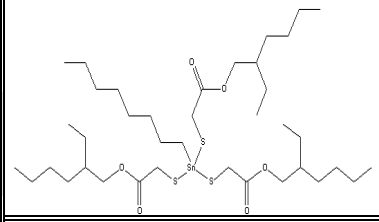
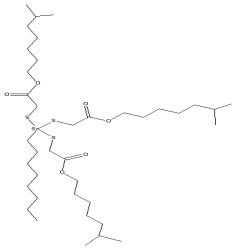
SIDS INITIAL ASSESSMENT PROFILE

Chemical Category	Mono-octyltin trichloride and selected thioglycolate esters
Structural Formula, Chemical Names and CAS Registry Numbers	 Mono-octyltin chloride [MOTC], CASRN 3091-25-6
	 Mono-octyltin tris[2-ethylhexyl thioglycolate] [MOT(EHTG)], CASRN 27107-89-7
	 Mono-octyltin tris[isooctyl thioglycolate] [MOT(IOTG)], CASRN 26401-86-5

SUMMARY CONCLUSIONS OF THE SIAR

Category Rationale

MOTC, MOT(EHTG), and MOT(IOTG) 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 demonstrated rapid conversion of the thioesters to MOTC when placed in simulated mammalian gastric contents [0.07 M HCl] under physiological conditions. For MOT(EHTG), 88% conversion to MOTC occurred within 0.5 hours. Thus, MOTC is the appropriate surrogate for mammalian toxicology studies via the oral route.

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

Analogue Rationale

Data for MOT(EHTG) and MOT(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 MOT(EHTG) and MOT(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 monoalkyltin to dialkyltin ratios.

Toxicokinetic data are not available for the monooctyltins. However, a study was conducted with MOT(EHTG) and in which simulated gastric fluid [0.07 M HCl under physiological conditions] converted MOT(EHTG) to MOTC and the respective organic acids. Within 0.5 hr, 88% of the MOT(EHTG) was converted to MOTC. This was a primary basis for creating the chemical category. In vitro data for DOTC and DOT(EHTG) indicate the dermal penetration of MOTC and MOT(EHTG)/(IOTG) is low.

There are no data on the acute dermal or inhalation toxicity of the monooctyltin compounds. Acute oral toxicity studies have been conducted with MOTC, MOT(EHTG) and MOT(IOTG). Acute oral LD50 values are >2000 mg/kg bw in rats [MOTC and MOT(EHTG)], 980-5000 mg/kg bw in rats for MOT(IOTG), and 1500 mg/kg bw in mice for MOT(EHTG). MOTC is slightly irritating to skin and severely irritating to the eyes of rabbits; MOT(EHTG)/(IOTG) are skin irritants. No sensitization data on MOTC were available; MOT(EHTG) is a sensitizer in animal studies. The signs of irritation and sensitization are in keeping with the expectations based on the data for the hydrolysis products, MOTC and EHTG/IOTG.

There are no repeated dose studies for MOTC, MOT(EHTG) or MOT(IOTG) via the dermal or inhalation routes. Two repeated dose oral studies of MOTC were reported. The NOAELs from the two 90-day sub-chronic oral (dietary) studies of MOTC were < 30 ppm diet and 100 ppm diet. In the critical GLP study (OECD TG 408), treatment-related changes were limited to the high dose group (500 ppm in diet) and included increased ALP levels, organ weight changes (liver, thymus), thymic atrophy, and moderate to severe lymphoid depletion in the thymus of 9/10 females. Histopathology confirmed lymphoid depletion was characterized by a decrease in the size of the thymic lobules due to an extensive loss of cortical and medullary small lymphocytes. In severe cases, the cortex was very small or partially absent. Based on decreased thymic weights and associated histopathological findings in animals of the 500 ppm group, the NOAEL for sub-chronic toxicity was placed at 100 ppm in the diet (~7 mg/kg bw/day in males and females), and the LOAEL was ~32 mg/kg bw/day in males and females. In the second, non-GLP study, a definitive NOAEL could not be determined and the LOAEL was 30 ppm diet (~1.5-4.8 mg/kg bw/day in males and females). In this study, treatment-related effects included a dose-related decrease in relative thymus weights at ≥30 ppm diet in females and ≥100 ppm in males; decreased body weights; changes in hematology, clinical chemistry and urinalysis; and organ weight changes (thymus, liver, heart, spleen). A contributor to the differential toxicity seen in these two 90-day dietary studies is likely the age (size) of the exposed animals. In the GLP study, 7-week old rats (mean body weights: 122.4 and 135.1 g) were fed experimental diets of 10, 100 or 500 mg MOTC/kg diet for 13 weeks. In the non-GLP study, weanling rats (mean body weights: 59 and 64 g) were fed diets containing 30, 100, 300 or 1000 mg MOTC/kg diet for 13 weeks. Additionally, the critical GLP study contained ~10% (mass/mass) DOTC, and test diets were stable at room temperature (confirmed by analysis). No (or limited) data on test diet preparation and stability are available for the second 90-day study; however, it was reported to contain ~6% (mass/mass) DOTC.

The monooctyltin compounds were not mutagenic in standard in vitro Ames assays conducted with and without metabolic activation. MOTC also was negative in an in vitro HGPRT assay, and in an in vivo mouse micronucleus test. These materials are not considered genotoxic.

In the reproduction/developmental screening study (OECD TG 421), MOTC administered in the diet was maternally toxic at 100 and 500 ppm diet, and embryo-toxic to the developing fetus at 500 ppm diet. Maternal toxicity was manifest as decreased absolute and relative thymus weights (300 and 500 ppm), and moderate to severe lymphoid depletion, which was characterized by severe thymic atrophy. Reproduction and fertility changes were limited primarily to the high dose (500 ppm diet) group and included slight decreases in gestation, live birth, fertility, and viability indices; increased post-implantations loss (41.3% vs. 6.4% in controls); increased number of stillborn pups (16 vs. 0 in controls); and decreased number of liveborn pups (46 vs. 104 in controls). The NOAEL for maternal toxicity was 10 ppm diet (0.5-0.7 mg/kg bw/day), and the NOAEL for reproductive effects was 100

ppm diet (6.4 mg/kg bw/day in males, 4.8-7.7 mg/kg bw/day in females). The decreased incidence of pregnancy/lactation involution seen in animals of the 500 ppm group is likely due to the presence of overt treatment-related lymphoid depletion, which obscured the lactation-related involution. No developmental toxicity was observed in the OECD 421 study of MOTC.

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. This could be especially pertinent to estimation of the BCF. This is being investigated in other assessment foray.

All of the category members are liquids at room temperature. MOTC is always manufactured as a mixture with DOTC. MOTC melts at < 10°C, boils at 150–159°C at 13 hPa, and has a calculated vapor pressure of 0.005 hPa at 25°C, and a relative density of 1.41-1.45 g/cm3 at 20°C. MOT(EHTG)/(IOTG) melts at -80 to -70°C and decomposes at ≥ 250°C.

MOT(EHTG)/(IOTG) have an estimated vapor pressure of 0.04 hPa at 25°C and a relative density of 1.08 g/cm3 at 20°C. MOTC and MOT(EHTG)/(IOTG) are not readily biodegradable, but are atmospherically degraded by photochemically induced hydroxyl radicals; half-lives are 12.9 hours for MOTC and 4.3-4.5 hours for MOT(EHTG)/IOTG). Calculated log Kow values for MOTC and MOT(EHTG)/(IOTG) are 2.14 and 14.1-14.4, respectively, indicating that MOT(EHTG)/(IOTG) is hydrophobic. Calculated log BCFs of approx. 1 (MOTC) and 2 [MOT(EHTG)/(IOTG)] should be seen with caution (refer to the EPIWIN discussion above).

MOTC and MOT(EHTG)/(IOTG) are sparingly soluble in water, with estimated values of 0.33 mg/L at 20°C (MOTC) and 0.5-2.7 mg/L [MOT(EHTG)/(IOTG)]. In water, MOTC and MOT(EHTG)/(IOTG) undergo rapid degradation by hydrolysis. Although there is no stability data for MOTC or MOT(EHTG)/(IOTG), data for other organotins [DOTC, DBTL and DBT(EHTG)] indicate that the monooctyltin compounds are expected to hydrolyze within minutes to hours in water. It is expected that the chlorine in MOTC will be displaced to form mono-octyltin hydroxide which eventually precipitates as the oxide. The thioester ligands on MOT(EHTG)/(IOTG) will be similarly 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.

Based on Level III distribution modeling, MOTC is predicted to partition primarily to water (69%) and soil (20%); MOT(EHTG)/(IOTG) are predicted to partition primarily to sediment (74-84%) and soil (15-22%). Under environmental conditions these compounds hydrolyze very quickly in water; therefore, the calculated partition coefficients may not be precise, but they do provide a reasonable estimation as to which compartments the named substance will migrate.

In ecotoxicity tests, the organisms were most likely exposed to the parent substance as well as hydrolysis/degradation products. A filtered, saturated solution of MOTC prepared at a loading rate of 100 mg/L was not toxic to zebra fish (*Brachydanio rerio*) (96-h LC50 > 0.33 mg MOTC/L) or to *Daphnia magna* (48-h EC50 > 0.33 mg MOTC/L). MOTC inhibited the growth (72-h EC50 = 0.22 mg MOTC/L) and biomass (72-h EC50 = 0.13 mg MOTC/L) of the freshwater green alga *Pseudokirchneriella subspicatus* (formerly known as *Scenedesmus subspicatus)* (NOEC = 0.045 mg MOTC/L).

A 100% Water-Accommodated Fraction (WAF) of MOT(EHTG) induced no visible effects in zebra fish (*B. rerio*) (96-h LC50 >2.3 mg MOT(EHTG)/L). The 48-h EC50 for MOT(EHTG) for *D. magna* is 1.0 mg MOT(EHTG)/L, based on nominal concentrations. The 9.9% Water Soluble Fraction (WSF) inhibited *P. subspicatus* growth (72-h EC50 >0.44 mg MOT(EHTG)/L, NOEC = 0.007 mg MOT(EHTG)/L) and biomass (EC50 = 0.18 mg MOT(EHTG)/L).

In a 21-day *D. magna* study, the LC50 for parental survival was 0.23 mg MOT(EHTG)/L, the EC50 for reproduction was >0.34 MOT(EHTG)/L, and the overall NOEC and LOEC were 0.036 and 0.16 mg MOT(EHTG)/L, respectively. MOT(EHTG) and MOT(IOTG) are analogs and ecotoxicity data for MOT(EHTG) are representative of MOT(IOTG).

Exposure:

In 2000, global production was estimated at 1,000-5,000 metric tonnes (MT) for MOTC, and 2,500-7,500 MT for MOT(EHTG). Production of MOT(IOTG) ceased approximately 10 years ago and no production numbers are available for this compound.

MOTC [always manufactured as a mixture with DOTC] used as an industrial intermediate in the production of organotin chemicals such as MOT(EHTG); there are no commercial applications for MOTC. MOT(EHTG) [always manufactured as a mixture with DOT(EHTG)] is added to PVC and CPVC as a heat stabilizer intended to preserve the polymeric structure and properties of the resins during the final stages of fabrication into finished articles. After being blended into the PVC and CPVC resin, the stabilizers remain there throughout the subsequent processing steps. Mono-octyltin mercaptoacetate-based stabilizers are widely used in the production of films including indirect food contact applications, sheets, injection moldings, pipes, sidings, and other rigid PVC applications where high thermostability is required. All systems are designed and maintained to ensure that moisture is kept away from the resin compound, since the presence of water creates significant problems during processing. Therefore, losses to water during blending and melt processing are very low, as these are designed to be "dry" processes. Furthermore, water is not used on a regular basis to clean equipment, wash out vessels, etc., and no wastewater is generated. Compounded PVC and CPVC material is solid and any spillage is cleaned up by vacuum or sweeping. Once the PVC or CPVC is melt processed into a final part, most of the mono-octyltin chemicals are strongly held within the resin and are highly resistant to leaching although some leaching of monooctyltin compounds may occur from some PVC products.

Mono-octyltin chemicals either leach out of PVC and CPVC articles, or are released into the atmosphere during processing. Releases from production facilities are low, and are regulated in many countries. There are a range of organotin chemicals that are in the PVC after processing which might leach out; however, the organotins will be hydrolyzed to the constituent alkyltin (MOT) and the relevant anion. Leaching of mono-octyltins from commercially available PVC products is low, and regulatory bodies that have approved of the use of mono-octyltins in potable water systems set limits on the amount of tin that can migrate, and in some cases, the time over which such migration must fall to a small number, for example ANSI/NSF Standard 60. When tested, PVC water pipes showed an initial release of mono-octyltins, which is quickly followed by decreased released until low levels of release are reached. No octyltins were detected in Canadian drinking water samples at concentrations above the detection limit of 0.5 ng Sn/L. No octyltins were detected in water passed through new CPVC pipe at 24 and 65°C under static and repetitive extractions. In the U.S., organotins were placed on the drinking water contaminant candidate list in 1998 partly because mono- and di-organotins used in chlorinated PVC pipes were of sufficient concern to warrant further investigation (63 FR 10273). Organotins remain on the contaminant candidate list (published in February 2005) because they are known or anticipated to occur in public drinking water systems (70 FR 9071). Other articles, such as window profiles and building siding that have mono-octyltin stabilizers will show the same type of leaching behavior, i.e., initial level falling to a very low level quite rapidly.

Exposure from food packaging also is regulated, with limits on either the amount of migrated mono-octyltin or the amount of mono-octyltin the food packaging material can contain. MOT levels extracted from olive oil packaged in PVC packaging materials were well below the specific migration limit (SML) established for mono-octyltins (1.2 mg/kg as Sn). Consumers may be exposed to octyltins in food products shipped in PVC containers or transportation tanks. MOT was detected in 5 of 15 edible oils (i.e., sunflower, peanut, corn, canola, soya, olive) at concentrations of 5.7 to 26.9 ng/g. MOTC was only found in 1 of 90 samples of blended wines from France, Greece, Italy, Germany, USA, China, and Canada at a concentration of 2.41 ng/mL. A variety of store-bought fruit juices were analyzed for organotins; MOT was detected in 5 of 42 samples at a maximum concentration of 16.3 ng/cm3.

In Japan, monooctyltins were found in 16 of the 54 kitchen utensils, food packages and toys examined at a maximum concentration of 775 µg/g (PVC food container). PVC flooring was found to contain MOT at concentrations ranging from not detected (< 0.4 µg/g) to 91 mg/kg.

Individuals may be exposed to mono-octyltins from indoor dust. MOT was found in dust samples collected from private homes and business in the U.K. at a mean concentration of 0.45 µg/g dust, and from private homes in Germany at a maximum concentration of 0.04 µg/g. Possible sources were from stabilizers in PVC. Dust samples from other European countries showed a similar pattern.

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 just at the TLV. For general work in and around extruders, measured exposure levels were <0.0001 to 0.034 mg/m3.

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 of organotins is incineration in an approved hazardous waste incinerator, which converts the organotin to inorganic tin. Most PVC and CPVC articles will either be recycled or landfilled at end of life. Although landfill leachate may directly enter the environment, tests have shown that very little organotin leaches out from PVC. Concentration of organotins in leachate samples from sanitary landfills were found to be in the low micrograms per liter range. In addition, it is expected that most leachate would be treated at on-site water treatment facilities or released into a municipal sewer. If landfill leachate should directly enter the environment, there would be dilution of the leachate resulting in substantially lowered environmental concentrations.

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 (skin and eye irritation, skin sensitization, repeated-dose, 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.