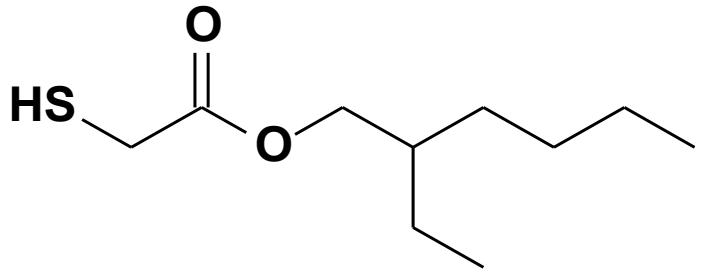
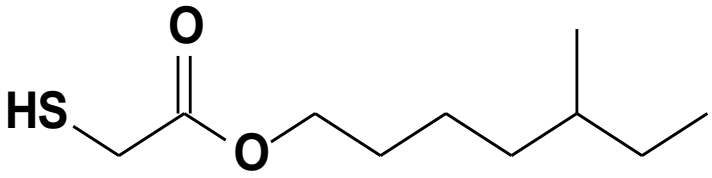
SIDS INITIAL ASSESSMENT PROFILE

Chemical Category	**ESTERS OF THIOGLYCOLIC ACIDS**
CAS Numbers and Chemical Names	**7659-86-1 Ethylhexyl Thioglycolate (EHTG)** **25103-09-7 Isooctyl Thioglycolate (IOTG)**
Structural Formula	EHTG:  IOTG (iso-octanol is a mixture of C-8 alcohol isomers: methylheptanols with methyl at 3, 4, or 5 carbon, methyl at 5 shown; and dimethylhexanols, no structure shown): 

SUMMARY CONCLUSIONS OF THE SIAR

Category/Analog Justification:

This category contains two octyl [C-8] esters of thioglycolic acid ethylhexyl thioglycolate (EHTG) and isooctyl thioglycolate (IOTG). The thioglycolate segment of the molecules is identical as is the ester linkage. Both EHTG and IOTG are hydrolytically unstable, and have a common degradate, thioglycolic acid (TGA; CAS No. 68-11-1). The other hydrolysis product for EHTG is 2-ethylhexanol (CAS No. 104-76-7), an 8-carbon alcohol and for IOTG it is iso-octanol. The iso-octanol in this case is a mixture of 8-carbon alcohols, the major isomers being methylheptanols, and dimethylhexanols. Melting point, boiling point, vapor pressure and water solubility values are consistent, as expected for close structural analogs. Partition coefficients further suggest that their kinetic behavior in mammalian and aquatic biological systems would not be markedly different. These similarities suggest that the two compounds would be toxicologically similar. Therefore, biodegradation and acute fish toxicity data for IOTG are used to address these endpoints for EHTG. Similarly, acute aquatic toxicity to alga, in vivo mammalian genetic toxicity, reproductive and developmental toxicity data for EHTG are considered to be representative of IOTG.

Human Health

Toxicokinetics data are not available. Acute toxicity studies have been conducted with EHTG and IOTG by the dermal, inhalation and oral routes of exposure. Acute dermal and inhalation toxicity is low, with inhalation LC50 values in rats ranging from 0.4 mg/L (IOTG) to >0.51 mg/L (EHTG) and dermal LD50 values in rats or rabbits greater than 2000 mg/kg bw for both substances. The acute oral toxicity values indicate moderate toxicity, with LD50 values in rats ranging from 303 – 334 mg/kg bw (EHTG) to 485 mg/kg bw (IOTG). EHTG and IOTG are slightly irritating to the skin. EHTG has no to slight eye irritation potential, similar signs of eye irritation are seen with IOTG.

In animals, EHTG is a skin sensitizer while IOTG showed a weak response.

Repeated inhalation of up to 3.2 ppm IOTG did not cause any clinical signs of irritation or toxicity. There were no

exposure-related effects on hematology, urinalysis, clinical chemistry, organ and terminal body weights for male and female rats. There were no exposure-related lesions observed in any rats at necropsy. The No Observed Adverse Effect Level (NOAEL) for repeated inhalation of IOTG was 3.2 ppm (0.38 mg/m^3; the highest concentration tested). The administration of up to 0.2% EHTG in the diet of rats for 28 days did not lead to a proliferation of hepatic peroxisomes, and did not produce any treatment-related effects. The 28 day NOAEL was 0.2% EHTG in the diet (the highest dose tested; 168 mg/kg bw for males; 173 mg/kg bw for females). The administration of up to 150 mg/kg bw EHTG by gavage to rats for 7 days did not produce any treatment-related effects. Higher doses (up to 250 mg/kg bw/d) produced mortality but no other effects that could be unequivocally attributed to the treatment. The 7 day NOAEL was 150 mg/kg bw. In an OECD guideline 421 study, groups of male and female rats were exposed to doses of EHTG of 0, 10, 50 and 150 mg/kg bw /day by gavage. Systemic toxicity was observed in the 150 mg/kg/day group. It was characterized by mortality, moribundity, decreased mean body weight gain, decreased consumption of feed, increased liver and kidney weight, or hepatocellular vacuolization in at least one sex of the F0 animals. The systemic NOEL was established at 50 mg/kg/day based on the hepatocellular effects at 150 mg/kg/d.

In an *in vivo* micronucleus assay, EHTG was not considered to be an inducer of micronuclei in male and female mice or rats up to 700 or 900 mg/kg bw, respectively. In *in vitro* bacterial mutation assays EHTG and IOTG did not induce mutagenicity in *Salmonella* bacterial strains with or without metabolic activation.

In an OECD guideline 421 study, groups of male and female rats were exposed to doses of EHTG of 0, 10, 50 and 150 mg/kg bw/day by gavage. Parental systemic toxicity was observed in the 150 mg/kg/day group. It was characterized by: mortality, moribundity, decreased mean body weight gain, decreased consumption of feed, increased liver and kidney weight, or hepatocellular vacuolization in at least one sex of the F0 animals. Increased mucification of the cervical and vaginal epithelium were noted in post-partum F0 dams. Decreased viability and growth of the F1 animals through post-partum day 4 also occurred at the 150 mg/kg bw/day dose. At doses producing maternal mortality, EHTG is considered to have a reproductive effect (dystocia in the 150 mg/kg/day group was considered test article-related). EHTG also reduced post-natal survival at 150 mg/kg bw/d but was not teratogenic. It is possible that maternal toxicity and direct neonatal exposure contributed to decreased viability and growth of F1 animals. Within the limits of the experimental design, a dosage level of 50 mg/kg bw/day was considered to be a NOAEL for reproductive or developmental effects, neonatal toxicity and systemic (maternal) toxicity resulting from exposure to EHTG when administered orally by gavage to rats.

Environment

The melting point of EHTG and IOTG is <-50°C and the boiling points are 119.5-171.1 °C at 1013 hPa and 117.5 – 161.8 °C at 1013 hPa, respectively. The vapor pressure for EHTG is 0.966 hPa at 25 °C; the vapor pressure of IOTG is 0.191 hPa at 25 °C. The water solubility of EHTG is 4.73 mg/L at 20°C; the water solubility for IOTG is 10.6 mg/L at 20°C. The partition coefficient (log Kow) of EHTG is 2.4; the partition coefficient (log Kow) for IOTG is 3.68 to 3.96 (at 25 °C; both values estimated). The overall OH rate constant for EHTG and IOTG is 45 x 10^{-12} cm^3/molecule-sec with half-lives of 2.8 hrs (EHTG) and 2.9 hrs (IOTG). The hydrolysis t1/2 of EHTG and IOTG at pH 7 and at 25 °C are12 and 7.2 hrs, respectively. Hydrolysis of IOTG produces a mixture of C8 alcohols, with the major products being methylheptanols and dimethylhexanols. Hydrolysis of EHTG produces 2-ethylhexanol. Level III Fugacity modeling, using loading rates for Air, Soil, and Water of 1000 kg/h for each media, shows the following percent distribution for EHTG: Air = 3.84%; Soil = 49%; Water = 45.6%; Sediment = 1.57%; for IOTG the values are Air = 1.83%; Soil = 68.2%; Water = 29%; Sediment = .995%. However, EHTG and IOTG are unlikely to be found in the environment, as these materials are hydrolytically unstable. IOTG is not readily biodegradable (18% degradation after 26 d; 45% degradation after 28 d). EHTG is also expected to be not readily biodegradable. Based on modeling results, bioconcentration is likely to be low for both materials (BCF = 136). The Henry's Law Constant for both EHTG and IOTG is 4.6 Pa m3/mole.

The 96-hr LC50 of IOTG in fathead minnows was 4.4 mg/L under static conditions. Acute fish aquatic toxicity data for IOTG are considered to be representative of EHTG. The 48 hr EC50 for EHTG to *Daphnia magna* was 0.38 mg/L under static conditions. The 48 hr EC50s for IOTG are 0.39 mg/L and 2.4 mg/L, both under static conditions. The 72 hr ErC50 for EHTG to *Pseudokirchneriella subcapitata* was 0.91 mg/L; the 72 hr EbC50 was 0.41 mg/L. Acute aquatic toxicity to alga data for EHTG are considered to be representative of IOTG. Based on the hydrolysis of these substances, the test organisms were most likely exposed to both parent substance and hydrolysis/oxidation products.

Exposure

There is no direct environmental exposure to EHTG or IOTG as a commercial end-products because they are mainly used to produce organotin stabilizers for polyvinylchloride (PVC). These stabilizers are used in processing of PVC and are strongly held by the resin so very little is released into the environment. EHTG and IOTG are also used as

chain length transfer agents during polymerization to control molecular weight. IOTG was used in permanent wave solutions in the past, but it is no longer sold for that application or other personal care/cosmetic applications. In production, EHTG and IOTG are handled in closed systems. Air streams and waste water are treated prior to release to the environment. Air emissions from manufacturing processes are controlled by a 99% efficient Thermal Oxidizer. Odors from the manufacturing process are controlled by a Sodium Hypochlorite scrubber. Wastewater from the process area is treated on site in a biological wastewater treatment system using primary and secondary treatment.

Personal protective equipment is recommended for use during production to minimize exposure. Potential routes of exposure to workers during manufacture include dermal and inhalation routes, however low vapor pressure diminishes the potential for inhalation exposure. EHTG and IOTG are stored at ambient temperature and atmosphere in bulk storage tanks with atmospheric vents, drums and rail cars. These materials are transported from the manufacturer by road, marine, rail and air in several container types and sizes.

At the industrial consumer level, EHTG and IOTG are handled in closed systems. Engineering controls and personal protective equipment are recommended for use by the industrial consumer to minimize exposure. Exposure to EHTG or IOTG is possible during handling at the industrial consumer level (sampling raw materials or charging drummed material into reactors). Potential routes of exposure to industrial consumer workers during use include dermal and inhalation routes. While inhalation exposure may be possible, the vapor pressures are very low. Because water is not used in PVC processes there are no water emissions of EHTG or IOTG in PVC processing.

There are no direct consumer exposures to EHTG or IOTG as end-products. The primary use for these materials is to be reacted with organotins to produce PVC heat stabilizers for PVC extrusion. Use as chain length transfer agents during polymerization is also a significant application. None of these are consumer products.

RECOMMENDATION 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 sensitization potential, acute, repeated-dose/reproductive/neonatal 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.