Monooctyltin alkyl mercaptoacetates: Human health tier II assessment

12 December 2019

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Acetic acid, 2,2',2''-[(octylstannylidyne)tris(thio)]tris-,triisooctyl ester	26401-86-5
8-Oxa-3,5-dithia-4-stannatetradecanoic acid, 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-octyl-7-oxo-, 2-ethylhexyl ester	27107-89-7
8-Oxa-3,5-dithia-4-stannadocosanoic acid, 4-octyl-7-oxo-4-[[2-oxo-2-(tetradecyloxy)ethyl]thio]-, tetradecyl ester	74162-83-7

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS

already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals monooctyltin tris(2-ethylhexylmercaptoacetate) (MOT(2-EHMA), CAS No. 27107-89-7), monooctyltin tris(isooctylmercaptoacetate) (MOT(IOMA), CAS No. 26401-86-5) and monooctyltin tris(tetradecylmercaptoacetate (MOT(TDMA), CAS No. 74162-83-7) are structurally similar and are expected to have similar physicochemical and toxicological properties (OECD, 2007a; OECD, 2007b).

Mono-substituted organotin compounds have the general formula RSNX3. The toxicity of organotin compounds depends largely on the organotin moiety (R group), with the anionic ligand (X) mostly influencing physico chemical properties and local toxicity. In some cases, release of the anionic ligand may contribute to systemic toxicity. These chemicals are grouped together for risk assessment due to their similar end uses and expected toxicity profiles.

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified for the chemicals.

The National Pollutant Inventory (NPI) holds data for all sources of organotin compounds in Australia.

The following site limited uses were identified as sources of organotin compounds by the NPI in 2017–18:

- Glass and glass product manufacturing.
- Polymer product manufacturing.

International

The following uses have been identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers (REACHa; REACHb); Galleria Chemica; the Organisation for Economic Co-operation and Development (OECD) Screening information data set (SIDS) dossiers (OECD, 2007a; OECD, 2007b); the World Health Organization (WHO) Concise International Chemical Assessment Document 73 (WHO, 2006); and the Substances in Preparations in Nordic Countries (SPIN) database.

The chemicals MOT(2-EHMA) and MOT(IOMA) have reported site limited use as intermediates in the production of organotin stabilisers for polyvinylchloride (PVC).

The chemicals are always manufactured as a mixture with their dioctyltin equivalents (i.e. dioctyltin(isooctylmercaptoacetate) (DOT-IOMA), CAS No. 26401-97-8 or dioctyltin bis(2-ethylhexyl mercaptoacetate) (DOT(2-EHMA), CAS No. 15571-58-1), either as an aqueous solution or as a solid material, and may contain 5–80 % of the respective monooctyltin by weight. Mixtures with greater than 50 % monooctyltin are considered to be monooctyltin substances, whereas mixtures with less than 50 % monooctyltin are considered to be dioctyltin substances (OECD, 2007a; OECD, 2007b).

No use information were identified for MOT(TDMA).

Restrictions

Australian

Tin and its compounds are listed in Schedule 10 of the Work Health and Safety Regulations (2016 revision) as restricted hazardous chemicals—the restricted use is 'abrasive blasting at a concentration of greater than 0.1 % as tin' (Safe Work Australia, 2019).

International

Tin compounds—which includes the chemical in this assessment—are listed on the following (Galleria Chemica):

- Council of Europe Resolution AP (92) 2 on control of aids to polymerisation for plastic materials and articles intended to come into contact with foodstuffs—Limits for finished articles; a limit of 0.05 mg/kg (as Sn) applies to tin compounds organic (Council of Europe, 1992)
- Europe Directive 2009/48/EC of the European Parliament and of the Council on the safety of toys—Maximum Migration Limits; limits of 0.2, 0.9 and 12 mg/kg of organic tin applies in liquid or sticky toy material, dry or brittle or powder-like or pliable toy material, and scraped-off toy material, respectively (European Parliament and Council, 2009)
- Council of Europe Resolution ResAP(2008)1 on requirements and criteria for the safety of tattoos and permanent make-up —Table 3 Maximum allowed concentrations of impurities in products for tattoos and PMU; a limit of 50 ppm tin (Sn) applies.

Organostannic compounds—which includes the chemical in this assessment—are listed in Annex XVII to the REACH regulations with restrictions relating to biocide and water treatment uses (ECHA).

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

'Tin, organic compounds (as Sn)' have an exposure standard of 0.1 mg/m^3 time weighted average (TWA) and 0.2 mg/m^3 short-term exposure limit (STEL).

International

The following exposure standards are identified for 'Tin, organic compounds (as Sn)' (Galleria Chemica).

An exposure limit of 0.1 mg/m^3 TWA and 0.2 mg/m^3 STEL in different countries such as Bulgaria, Canada (Alberta, British Columbia, Ontario, Quebec, Saskatchewan, Yukon), Chile, Denmark, Egypt, Estonia, France, Greece, Malaysia, Mexico, Norway, Philippines, Singapore, South Africa, Spain, Sweden, Taiwan, the United Kingdom and the United States of America (California, Hawaii, Minnesota, Tennessee, Vermont).

The American Conference of Government Industrial Hygienists (ACGIH) recommends a threshold limit value (TLV) of 0.1 mg/m TWA for Tin, organic compounds, as Sn 'to minimize the potential for adverse effects on immune function and the central nervous system.' and 0.2 mg/m STEL 'to minimize acute symptoms such as eye and upper respiratory tract irritation, headache, and nausea.' (ACGIH, 2011).

Health Hazard Information

Data available indicate that the chemicals are hydrolysed to release mercaptoacetate moieties when placed in a simulated mammalian gastric environment (refer **Toxicokinetics** section). Two of the mercaptoacetate hydrolysis products 2-ethylhexyl mercaptoacetate (EHMA, CAS No. 7659-86-1) or isooctyl mercaptoacetate (IOMA, CAS No. 25103-09-7 are isomers and have similar physiochemical and toxicological properties (NICNASd). Although no toxicological data were identified tetradecylmercaptoacetate (TDMA, CAS No. 57414-16-1), it is expected to be toxicologically similar to the other mercaptoacetates. Although there is limited evidence that the chemicals are hydrolysed to monooctyltin dichloride—MOTC (CAS No. 3542-36-7), the systemic toxicity of monooctyltin compounds is similar.

Therefore when data for the chemical being assessed are not available, health hazard information for EHMA, IOMA and MOTC has been included in this report for read across for systemic toxicity endpoints. The Tier II assessment reports for these chemicals (NICNASa; NICNASb) are available at **https://www.nicnas.gov.au**. These reports should be read in conjunction with this Tier II assessment.

Toxicokinetics

Sulfur or carboxylate based ligands in organotin compounds are easily displaced at low pH conditions (OECD, 2007a; REACHa).

Under simulated gastric conditions, 9.2 mg/L of a 61 %:36 % MOT(2-EHMA):DOT(2-EHMA) mixture in 0.07 M HCl (pH 1–2, 37 °C), rapidly converted (approximately 88 %) to MOTC and released the EHMA ligand within 0.5 hours (OECD, 2007a; REACHa). The same is expected to occur for DOT(IOMA).

A more direct analysis method of the hydrolysis products of MOT(2-EHMA) (by NMR-spectroscopy; according to standardised OECD Test Guideline (TG) 111), using 1 g of MOT(2-EHMA) in excess 0.1 M HCl (pH 1.2, 37 °C), indicated that instead of the complete loss of the mercaptoacetate ligands from the tin ion to form MOTC, some ligands remained attached forming a mono-chloro ester of the chemical (REACHa; REACHb).

In the above in vitro studies, a greater concentration of starting chemical was used in the second study which may have affected the position of the equilibrium. No data are available on the in vivo metabolism of the chemicals.

Acute Toxicity

Oral

Based on the weight of evidence of the available data, the chemicals are considered to have low acute oral toxicity. This is based primarily on the outcomes of guideline studies, where experimental details are included. While there is some data suggesting moderate acute toxicity for these chemicals, information about the chemicals compositions and/or study method are lacking for these.

The following oral median lethal dose (LD50) values were reported for MOT(2-EHMA) (OECD, 2007a; REACHa):

- 1500 mg/kg bw in male and female white mice (strain H) using a 'pure sample' of chemical (according to the 'standard acute method');
- 2177 mg/kg bw in male and female Tif:RAI rats using a a 70:30 % MOT(2-EHMA):DOT(2-EHMA) mixture (similar to OECD TG 401) ;
- 3400 mg/kg bw in rats (chemical composition, and animal sex and strain not specified; non-guideline study); and
- 2000–5000 mg/kg bw in female SD rats using a 97.7 % pure MOT(2-EHMA) (OECD TG 423).

The following oral LD50 values were reported for MOT(IOMA) (OECD, 2007b; REACHb):

- 1190 mg/kg bw in male and 1250 mg/kg bw in female Wistar rats using a MOT(IOMA):DOT(IOMA) mixture (proportions not specified; guideline not specified);
- 1700 mg/kg bw in male and female Sprague Dawley (SD) rats (chemical composition not specified; similar to EPA OPP 81-1);
- approximately 2400 mg/kg bw (based on 2.85 mL/kg bw) in male Wistar rats (chemical composition not specified; similar to OECD TG 401);
- >4000 mg/kg bw in male Wistar rats (chemical composition not specified; similar to OECD TG 401); and
- 5000 mg/kg bw in male and female Tif:RAI rats (chemical composition not specified; similar to OECD TG 401).

Observed sub-lethal effects included ataxia (lack of muscle control), prostration, decreased activity, discharge (oral, nasal and ocular), soft stool, faecal and urinary staining, unkempt coats and weight loss.

Dermal

Based on the available data for the chemical MOT(2-EHMA), both chemicals in this group are considered to have low acute dermal toxicity. Low acute dermal toxicity is also supported by the data for the chemicals EHMA and IOMA (NICNASb).

The dermal LD50 value for MOT(2-EHMA) was reported to be >2000 mg/kg bw in male and female Wistar rats (OECD TG 402) (REACHa; REACHb).

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Based on the available data for MOT(2-EHMA), the chemicals in this group are considered to cause slight skin irritation, but effects were not sufficient to warrant hazard classification. Lack of skin irritation is also supported by the data for the chemicals EHMA and IOMA (NICNASb).

In an in vivo skin irritation study (according to OECD TG 404), female New Zealand White (NZW) rabbits (n = 3) were exposed (occlusive) to 0.5 mL of a 70:30 % MOT(2-EHMA):DOT(2-EHMA) mixture on shaved skin for 4 hours and monitored for 10 days after patch removal. At 24, 48 and 72 hours after patch removal the average erythema score for the animals was 2/4 and the average oedema score was 1/4. At the end of the 10 day observation period the skin reactions were fully reversible (REACHa; REACHb).

Eye Irritation

Based on the available data for MOT(2-EHMA), the chemicals in this group are not considered to cause eye irritation. Lack of eye irritation is also supported by the data for the chemicals EHMA and IOMA (NICNASb).

In an in vivo eye irritation study (according to OECD TG 405), NZW rabbits (n = 3) were exposed to 0.1 mL of MOT(2-EHMA) (97.9 %) in 1 eye each and the treated eye held shut for 1 second. The untreated eye served as the control. The treated eyes were not rinsed and rabbits were monitored for 72 hours. No signs of irritation were observed. The average scores for cornea/iris/conjunctivae (redness)/conjunctivae (discharge) were given as 0/4, 0/2, 0/3 and 0/3, respectively over the 72 hour observation period (REACHa; REACHb).

In an in vitro eye irritation study (according to OECD TG 438), fresh chicken eyes were exposed to 30 µL of MOT(2-EHMA) (97.9 %) for 10 seconds before being rinsed off with 20 mL saline solution. The eyes were monitored for 4 hours after being rinsed. The average scores for cornea opacity after 4 hours were 0.5/4, for eye swelling after 30 minutes were 2.33/32, for fluorescein after 30 minutes were 0.5/3, and for opacity after 30 and 75 minutes were 0.16/4 and 0.5/4, respectively. Based on the scores obtained in this assay, the chemical was considered to not be irritating to the eye (REACHa; REACHb).

Sensitisation

Skin Sensitisation

Based on the available data for MOT(IOMA), the chemicals are not considered to be skin sensitisers.

In a mouse local lymph node assay (LLNA) study (OECD TG 442B), female CBA:J mice (n = 4/dose) were tested using concentrations of 2.5, 5 or 10 % of MOT(IOMA) in acetone/olive oil (4:1 v/v). The animals were administered a 25 µL dose of the chemical daily for 3 consecutive days. On day 4 no dosing occurred. On day 5, 10 mg/mL of BrdU staining solution was injected intraperitoneally to all the animals. On day 6 the animals were euthanised. No mortality or clinical signs were observed during the treatment period. No erythema was observed in any dose groups. No statistically significant changes in mean ear thickness was observed between the control and test groups. The stimulation index (SI) scores were 0.6, 0.6 and 0.9 for the 2.5, 5 and 10 % groups respectively. As the SI values were all below 3, the chemical was deemed not to be a skin sensitiser (REACHb).

In a guinea pig maximisation test (OECD TG 406), Pirbright White guinea pigs (n = 10/sex/dose) were induced intradermally with a 1 % concentration of a 70:30 % MOT(2-EHMA):DOT(2-EHMA) mixture, and then epidermally with a 100 % concentration

by occlusive exposure over the injection site 1 week later for 48 hours. The first challenge was performed 3 weeks after the second induction, under occlusive epidermal conditions using a 50 % concentration of the test mixture with petrolatum for 24 hours. The sites were monitored for up to 48 hours after the patches were removed. In the treated group 18/20 of the animals showed skin reactions while 6/10 of the controls showed similar reactions at 24 and 48 hours after patch removal. A second epidermal challenge was performed using a lower concentration of 20 % of the test mixture incorporated with Vaseline and applied occlusively for 24 hours. The sites were monitored for up to 48 hours after the patches were removed. In the treated group there were 0/20 reactions at 24 hours and 2/20 reactions at 48 hours, while 2/10 animals in the control group had positive reactions at 24 hours and 0/10 had positive reactions at 48 hours. It was concluded that the chemical has very weak sensitisation potential which does not warrant classification (OECD, 2007a; REACHa; REACHb).

Repeated Dose Toxicity

Oral

Based on the available data for MOT(IOMA), the chemicals are not considered to cause serious health effects following repeated oral exposure. Observed organ effects were not consistent between sexes and across studies. The effects in the thymus reported in studies with MOTC (NICNASa) were not observed for the chemicals in the group. Limited data indicate that IOMA and EHMA did not cause damage to health from repeated oral exposure (NICNASb).

In a 13 week study (according to OECD TG 408), Wistar rats (n = 10/sex/dose) were administered MOT(IOMA) (purity unknown) at 0, 200, 500 or 1250 mg/kg diet (equivalent to approximately 0, 13, 32 and 82 mg/kg bw/day in males; and 0, 14, 37 and 91 mg/kg bw/day in females). No mortality, treatment related clinical signs, changes in haematological and urinalysis parameters, body weight differences or organ weight differences were observed during the study. The no observed adverse effect level (NOAEL) was determined to be 1250 mg/kg diet (approximately 82–91 mg/kg bw/day) (REACHa; REACHb).

In a 13 week study (similar to OECD TG 408), Wistar rats (n = 5/sex/dose) were administered MOT(IOMA) (purity unknown) at 0, 30, 100, 300 or 1000 ppm in diet (equivalent to approximately 0, 1.5, 5, 15 and 50 mg/kg bw/day). No mortality occurred during the study. No significant changes in body weight and food consumption were noted between the treated and control groups. Slightly increased blood urea nitrogen (BUN) levels were noted in the 30 ppm group at week 6 of the study, and in the 30 and 100 ppm groups at week 13 of the study. Slight increases in relative kidney weights and decreased relative liver weight were noted in males in the 1000 ppm group compared with the control group. An increase of tin content in the kidneys was noted in the 300 and 1000 ppm groups, but overall kidney function was not affected. No significant changes in thymus weight were noted across the treated groups. The NOAEL was determined to be 300 ppm (approximately 15 mg/kg bw/day), based on treatment related changes to the relative organ weights in males in the high dose group (OECD, 2007b; REACHb).

In a 13 week study (similar to OECD TG 408), Wistar rats (n = 5/sex/dose) were administered MOT(IOMA) (purity unknown) at 0, 300, 1000 or 3000 ppm in diet (equivalent to approximately 15, 50 and 150 mg/kg bw/day). No mortality occurred during the study. No changes in food consumption were noted between the treated groups and the controls. No changes in body weight were noted between the treated groups and the controls except for males in the high dose group during weeks 8–13. A non-significant decrease in haemoglobin levels were noted in males in the high dose group at week 6, while neutrophil counts were slightly raised in males in the mid-dose group at week 12. Significant increases in BUN levels were noted in males at weeks 6 and 12 of the study. Urinalysis results indicated a higher incidence of epithelium cells and urinary crystals in males in the high dose group at week 6. Significant increases in relative kidney weight were noted in males in all the treated groups and in females in the high dose group. Slight increases in the relative liver weight were noted in males in the high dose group. Dose dependent decreases in thymus weight were noted across all treated groups, but this was only significantly decreased in males in the high dose group. Upon necroscopy, small white spots were found on the kidneys of males in the high dose group, and a green discolouration in kidneys of males in the mid-dose group. Overall, there was tubular nephrosis (kidney disease) in treated males and a large amount of proteinaceous material was present in the dilated tubules in the lower cortex of males at ≥1000 ppm. An NOAEL could not be determined. The LOAEL was 300 ppm (approximately 15 mg/kg bw/day), based on a significant increase in relative kidney weight and histopathological changes in males in this group (OECD, 2007b).

In a 90 day study (similar to OECD TG 409), beagle dogs (n = 4/sex) were administered MOT(IOMA) (purity unknown) at 0, 100, 300 or 1000 ppm in diet (equivalent to 0, 5, 15 and 50 mg/kg bw/day). There was no mortality, or significant changes in average body weight and food intake between the groups. Non-significant decreases in haemoglobin content, haematocrit volume and erythrocyte count were noted in week 13 for animals in the high dose group. The mean absolute and relative weights of the heart and ovaries were slightly higher in females in treated groups compared with the control group; however, this was not dose

related. The mean absolute and relative spleen weights were slightly lower in the high dose group compared with the control group. Necroscopy of the animals did not identify any abnormalities associated with consumption of the test substance. The NOAEL was determined to be 300 ppm (approximately 15 mg/kg bw/day), based on a slight decrease in spleen weight and slight decreases in a few haematological endpoints in the highest dose group (OECD, 2007b; REACHb).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the available data, the chemicals are not considered to be genotoxic (OECD, 2007a; OECD, 2007b; REACHa; REACHb).

Ambiguous to positive results were obtained in 1 study using the chemicals in vitro (REACHa). In a mammalian cell gene mutation assay (OECD TG 476), mouse lymphoma L5178Y cells were exposed to MOT(2-EHMA) at up to 55 µg/ mL for 4 hours with metabolic activation and generated ambiguous results. At up to 32 µg/ mL for 4 hours without metabolic activation, positive genotoxicity results were observed. Under the conditions of the study, MOT(2-EHMA) is considered mutagenic at the TK-locus of mouse lymphoma L5178Y cells.

Negative results were obtained using the chemicals in vitro:

- In a bacterial reverse mutation assay (similar to OECD TG 471), *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, and *Escherichia coli* strain WP2 uvrA were exposed to the chemical (67:33 % of MOT(2-EHMA):DOT(2-EHMA)) at up to 5000 µg/0.1 mL for between 48–60 hours, with and without metabolic activation;
- In a bacterial reverse mutation assay (similar to OECD TG 471), *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to the chemical (60:40 % of MOT(IOMA):DOT(IOMA)) at up to 50 µL/plate for between 48–72 hours, with and without metabolic activation; and
- In a mammalian chromosome aberration test (OECD TG 473), human lymphocytes were exposed to the chemical MOT(2-EHMA) at up to 2000 µg/ mL for 4 hours, with and without metabolic activation. The chemical failed to induce a statistically significant increase in the number of chromosomal aberrations in all dose groups.

Negative results were obtained using MOT(2-EHMA) (97.7 %) in vivo in a mammalian erythrocyte micronucleus test (OECD TG 474) in male Wistar rats (n = 5/dose) orally administered 250, 500 or 1000 mg/kg bw of the chemical (MOT(2-EHMA)) twice over 2 days. The animals were euthanised 24 hours after the final treatment and bone marrow analysed for chromosomal damage. No statistically significant increase in the mean number of micronucleated polychromatic erythrocytes per 2000 polychromatic erythrocytes was observed in any of the treated groups, indicating that the chemical did not cause damage to the chromosomes or mitotic spindles at the doses tested.

The chemicals MOTC, IOMA and EHMA were not considered to be genotoxic based on the available data (NICNASa; NICNASb).

Carcinogenicity

No data are available. The limited data for the metabolites do not indicate a concern for carcinogenicity (NICNASa; NICNASb).

Reproductive and Developmental Toxicity

Although there is evidence of fertility and developmental effects for the metabolites MOTC and EHMA (NICNASa; NICNASb), based on the available data, the chemicals are not considered to cause reproductive and developmental effects following long term oral exposure. However, the chemical MOT(2-EHMA) (concentrations from <50 % to ≥99 %) is listed on the European Chemicals Agency (ECHA) Community Rolling Action Plan (CoRAP) as a potential endocrine disruptor, that may be subject to further evaluation (ECHA, 2018).

In a 2 generation reproduction toxicity study (OECD TG 416), SD rats (n = 25/sex/dose) were administered MOT(IOMA) at 0 or 300 ppm for up to 13 weeks for males and >13 weeks for females (through lactation period) for the F0, and 17 weeks for males and >17 weeks for females (through lactation period) for the F1 generation. In the F0 group, the average dose of the chemical was 20 mg/kg bw/day for males and 30 mg/kg bw/day for females. In the F1 generation, the average dose of the chemical was 21 mg/kg bw/day for males and 31 mg/kg bw/day for females. No mortality, histopathological changes, pup malformation or significant organ weight changes occurred in any of the F0 animals in the study. A slight significant increase in maternal body weight gain was noted in treated rats during the gestation and lactation period, but food and water intake were similar across all groups. Reproductive parameters (e.g. pre-coital time, duration of pregnancy, number of pups (live and dead), sex of pups, number of pup malformations, number of runts and the number of stillbirths) were not affected by administration of the chemical. One dam that did not become pregnant, and another that had 4 stillbirths, were not considered to be treatment related. No macroscopic pathological findings and no notable deviation in the number of implantations were noted in treated rats compared with controls. In the F1 group there was no variation in the sex, organ and body weight of the treated pups compared with the control group. One male pup from a treated dam showed signs of dyspnoea (laboured breathing), haemorrhagic snout (bloody nose) and reduced motility, and was euthanised. The number of stillbirths (9) and runts (1) were not considered treatment related as this was similar to that of the control group (6 stillbirths, 0 runts). The surviving animals did not have any macroscopic treatment related pathological findings. In treated dams, the number of implantations was comparable to the control group. Slight significant increases in the relative thymus weight in males and the relative spleen and thymus weights in females were noted; however, the differences were within historical control ranges. In the F2 group, there were no variations in the body weight, sex distribution or viability index of pups when compared with the control group. A slight decrease in the lactation index (proportion of pups alive at 4 days that survive the 21 day lactation period) was noted in the treated group compared with the control. No differences in functional tests or morphological landmarks was noted in the treated groups when compared with the control. Pup organ weights were also similar when compared with the control group. Overall no teratogenic effects were observed during the study (OECD, 2007b; REACHb).

In a reproduction/developmental toxicity screening test (OECD TG 421), Wistar rats (n = 12/sex/dose) were administered MOT (2-EHMA) at 200, 500 or 1250 mg/kg diet (equivalent to approximately 11, 29 and 72 mg/kg bw/day in males; and 15, 38, 96 mg/kg bw/day in females) for 28 days in the males, and at least 6 weeks in the females. No mortality or significant clinical signs were noted in the parental animals. The parental body weights were comparable between the treated and control groups throughout the study. No treatment related effects were observed in the fertility, gestation and mating indices in the treated groups. The absolute and relative organ weights for the epididymis, testes and thymus in the male animals were comparable across all parental groups. Significant decreases in the absolute and relative thymus weight were observed in the females in the ≥500 groups; however, it was noted that the control group had an unusually high thymus weights that were greater than the historical control range. Microscopic evaluation of various sampled organs from the animals in the high dose group did not show any treatment related histopathological changes. The NOAEL for reproductive toxicity was determined to be 1250 mg/kg diet (approximately 72 and 96 mg/kg bw/day in males and females, respectively). No pup malformations or abnormalities were noted in the treated groups. The development of the pups during the lactation period was not affected by administration of the chemical in any of the treated groups. The NOAEL for developmental toxicity was determined to be 1250 mg/kg diet (approximately 72 and 96 mg/kg bw/day in males and females, respectively)(REACHa; REACHb).

In a prenatal developmental toxicity study (OECD TG 414), Wistar rats (n = 24 mated females/group) were administered MOT (2-EHMA) at 500, 1250 or 3000 mg/kg diet (equivalent to approximately 36, 89 and 208 mg/kg bw/day) for 14 days (gestation day 6 through to 19). No mortality were noted in the animals during the study. In the high dose group, body weight gain and food intake were significantly lower from GD6–10, and food intake remained significantly lower from GD10–14, compared with controls. Mean terminal body weights were similar between all groups. The absolute and relative thymus weight in the maternal treated groups showed a non-significant but dose related decreases in the mid and high dose groups—overall, this was considered to be treatment related. Ovary, uterus and placental weights were similar between groups. The pre- and post implantation loss values, and the total number of early and late resorptions in the treated groups were comparable to the control group. No dead foetuses were noted during the study and the number of implantation sites and live foetuses were comparable across the treated and control groups. The weight of the foetuses was statistically significantly lower at ≥1250 mg/kg compared with the control group; however, this was not considered to be treatment related as the foetal weight of the control group was higher than the historical control values and the foetal weight from treated animals was within the historical control values range. No significant variations in the incidence of skeletal or visceral malformations occurred in the treated groups compared with the

control group. The NOAEL for maternal toxicity was determined to be 500 mg/kg diet (approximately 36 mg/kg bw/day) while the NOAEL for developmental toxicity was 3000 mg/kg diet (approximately 208 mg/kg bw/day) (REACHb).

Risk Characterisation

Critical Health Effects

No critical health effects associated with these chemicals have been established.

Public Risk Characterisation

Given the uses identified for these chemicals, it is unlikely that the public will be directly exposed and the available data do not indicate any hazards associated with exposure to these chemicals. Hence, the public risk from these chemicals is not considered to be unreasonable.

The chemicals with their identified uses are not considered to significantly contribute to the overall public exposure via the environment to organotin compounds. The dominant contribution to human intake of organotins (mainly tributyltin compounds) is via the consumption of fish. In addition, based on the available data, monooctyltin compounds are of lower toxicity compared to dialkyl- and tri alkyl- tin compounds. Hence, the public risk from the chemical is not considered to be unreasonable. If data becomes available indicating specific uses in Australia that could significantly contribute to the overall exposure for organotins, further evaluation of the chemicals may be required.

Occupational Risk Characterisation

During product formulation, oral, dermal and ocular exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemicals at lower concentrations could also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the lack of critical health effects, the risk to workers from these chemicals is not considered to be unreasonable. Information in this report can be used by a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) to determine the appropriate controls. The chemicals currently have no hazard classification for worker health and safety; this is considered appropriate based on the available data.

NICNAS Recommendation

Current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety, and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

Regulatory Control

Work Health and Safety

These chemicals are not recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). This does not consider classification of physical hazards and environmental hazards.

Advice for industry

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

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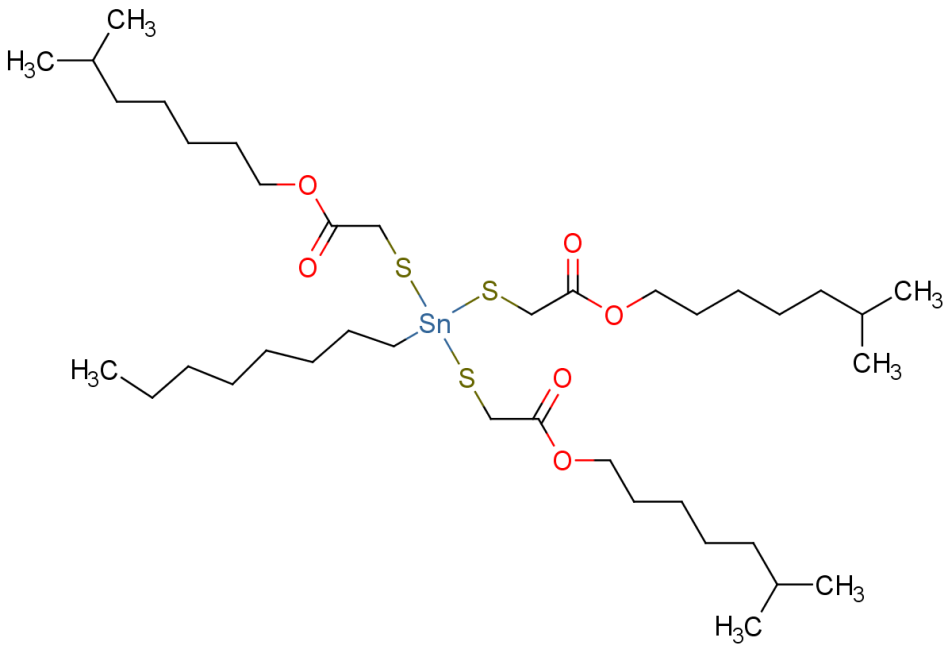
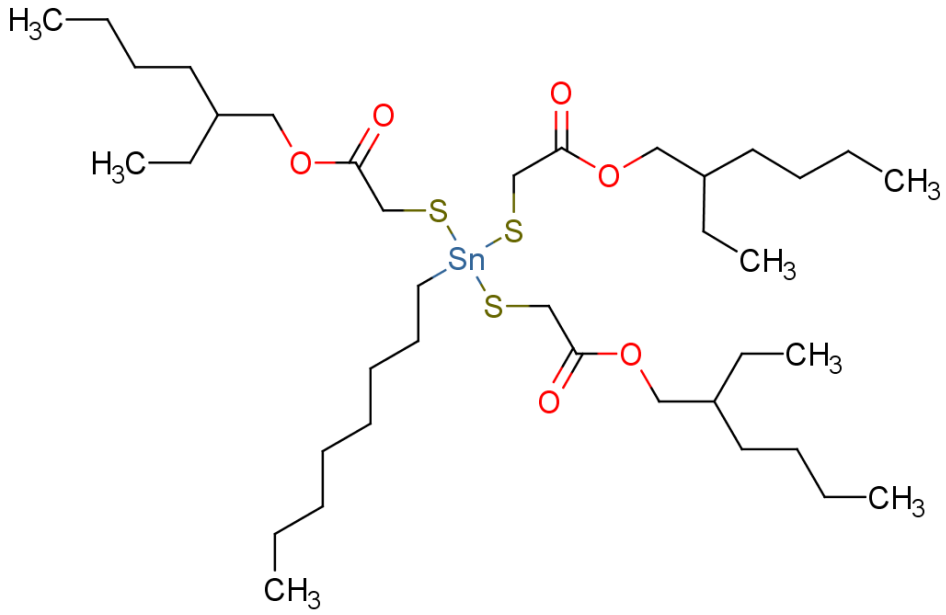
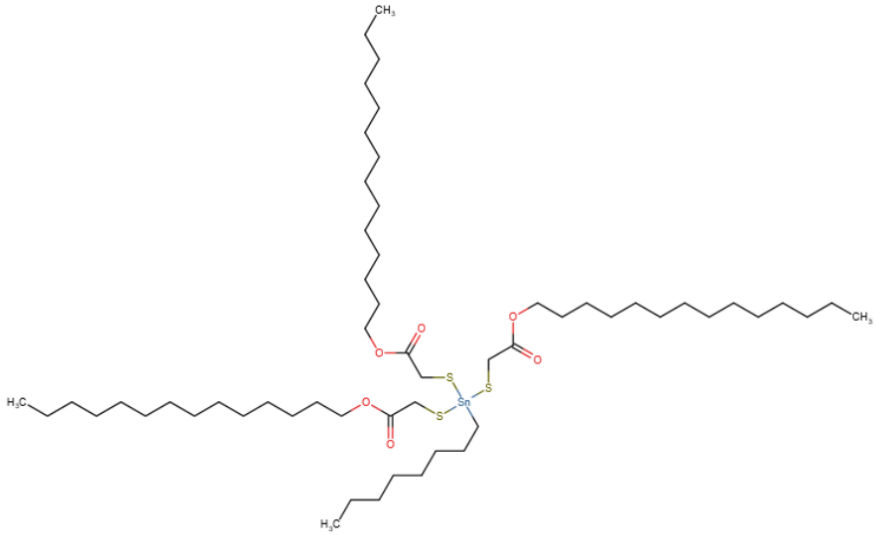
Last Update 12 December 2019

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Acetic acid, 2,2',2''-[(octylstannylidyne)tris(thio)]tris-,triisooctyl ester** triisooctyl 2,2',2''-[(octylstannylidyne)tris(thio)]triacetate monooctyltin tris(isooctylthioglycollate) monooctyltin tris(isooctylmercaptoacetate) MOT(IOMA)
CAS Number	26401-86-5
Structural Formula	
Molecular Formula	C38H74O6S3Sn
Molecular Weight	841.89

Chemical Name in the Inventory and Synonyms	**8-Oxa-3,5-dithia-4-stannatetradecanoic acid, 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-octyl-7-oxo-, 2-ethylhexyl ester** 2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-octyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate octyltintris[2-ethylhexyl mercaptoacetate mono-n-octyltin tris(2-ethylhexyl thioglycolate) monooctyltin tris(2-ethylhexylmercaptoacetate) MOT(2-EHMA)
CAS Number	27107-89-7
Structural Formula	
Molecular Formula	C38H74O6S3Sn
Molecular Weight	841.89

Chemical Name in the Inventory and Synonyms	**8-Oxa-3,5-dithia-4-stannadocosanoic acid, 4-octyl-7-oxo-4-[[2-oxo-2-(tetradecyloxy)ethyl]thio]-, tetradecyl ester** tetradecyl 4-octyl-7-oxo-4-((2-oxo-2-(tetradecyloxy)ethyl)thio)-8-oxa-3,5-dithia-4-stannadocosanoate monooctyltin tris(tetradecylmercaptoacetate (MOT(TDMA))
CAS Number	74162-83-7
Structural Formula	

	
Molecular Formula	C56H110O6S3Sn
Molecular Weight	

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