Stannane, chlorotrioctyl-: Human health tier II assessment

08 March 2019

CAS Number: 2587-76-0

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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.

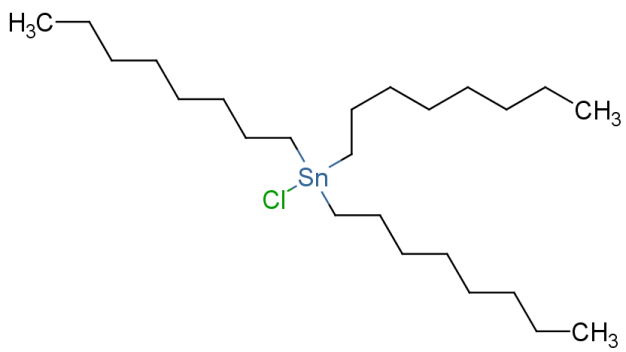
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	trioctyltin chloride TOTC TOTCl
Structural Formula	
Molecular Formula	C24H51ClSn
Molecular Weight (g/mol)	493.83
Appearance and Odour (where available)	Colourless liquid
SMILES	C(CCCCCCC)[Sn](Cl)(CCCCCCCC)CCCCCCCC

Import, Manufacture and Use

Australian

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

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

The following site limited uses were identified for organotin compounds by the NPI in 2016–17:

- glass and glass product manufacturing; and
- polymer product manufacturing.

International

The following international use has been identified through Galleria Chemica and the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers.

The chemical has reported site-limited use as an intermediate in the manufacture of fine chemicals.

Restrictions

Australian

Tin and its compounds—which includes the chemical in this assessment—are listed in 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' (Galleria Chemica).

International

Tri-substituted organostannic compounds—which includes the chemical in this assessment—are listed on Annex XVII to REACH Regulations (Galleria Chemica):

'(a) Tri-substituted organostannic compounds such as tributyltin (TBT) compounds and triphenyltin (TPT) compounds shall not be used after 1 July 2010 in articles where the concentration in the article, or part thereof, is greater than the equivalent of 0.1 % by weight of tin'; and

'(b) Articles not complying with point (a) shall not be placed on the market after 1 July 2010, except for articles that were already in use in the Community before that date' (European Parliament and Council 2006).

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

- Council of Europe Resolution AP (92) 2 on the control of aids to polymerisation for plastic materials and articles—Limits for finished articles—a limit of 0.05 mg/kg (as Sn);
- Council of Europe Resolution ResAP(2008)1 on requirements and criteria for the safety of tattoos and permanent make-up (PMU)—Table 3 Maximum allowed concentrations of impurities in products for tattoos and PMU—a limit of 50 ppm tin (Sn) applies;
- 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 sticky toy material, dry or brittle or powder like material, and scraped-off toy material, respectively; and
- Under Section 84 of the Canadian Environmental Protection Act, 1999, notifiers must comply with specific conditions relating to the application of the chemical, its use, potential environmental release, and its disposal. The notifiers must also meet specific information and record keeping requirements. Before dealing with the chemical the notifier must also produce a written confirmation that they understand, and will meet, the terms of the Ministerial Condition that they now operate under.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is covered by a general entry for 'trioctyltin compounds' on the Hazardous Chemical Information System (HCIS) and is classified as hazardous, with the following hazard categories and hazard statements for human health (Safe Work Australia):

- Eye irritation - Category 2 - H319 (Causes serious eye irritation)
- Skin irritation - Category 2 - H315 (Causes skin irritation)
- Specific target organ toxicity (single exposure) - Category 3 - H335 (May cause respiratory irritation)

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).

Health Hazard Information

Within the class of trialkyltin compounds, the smaller alkyl variants such as trimethyltin and triethyltin are highly toxic. Increases to the n-alkyl chain length results in a reduction in mammalian toxicity. As such, trioctyltin compounds are considered less toxic compared with the shorter chained homologues (Snoeij et al., 1987).

Toxicokinetics

Trioctyltin compounds—which includes the chemical in this assessment—are lipophilic, which may limit absorption or metabolism (Snoeij et al., 1987).

In an *in vitro* metabolism study—(not done according to OECD Test Guidelines)—using rat liver microsomes, the chemical (Oct_3SnCl) was metabolised to trace amounts of a dioctyltin compound only (Oct_2SnX_2) (Kimmel et al., 1977).

Acute Toxicity

Oral

Based on the available data, trioctyltin chloride (hereafter referred to as 'the chemical') has low acute oral toxicity.

The following oral median lethal dose (LD50) values were reported (REACH):

- >4000 mg/kg bw in male and female rats (strain not specified); and
- 28642 mg/kg bw in male Wistar rats.

Observed sub-lethal effects included lethargy, reduced appetite and respiratory distress.

Dermal

No data are available.

Inhalation

Based on the available data, the chemical is considered to be toxic following acute inhalation, warranting hazard classification (see **Recommendation** section).

A median lethal concentration (LC50) of 250 mg/m^3 (0.25 mg/L) was reported in male and female specific pathogen free (SPF) rats exposed (nose only) to the chemical as an aerosol mist for 4 hours (REACH).

Observed sub-lethal effects included lethargy, cyanosis (bluish skin/lips), lateral position (lying on one side) and ruffled fur. Signs of respiratory irritation in surviving animals include dyspnoea (laboured breathing), and lung haemorrhages in the animals that died (REACH).

Corrosion / Irritation

Respiratory Irritation

Trioctyltin compounds are classified as hazardous with hazard category ‘Specific target organ toxicity (single exposure) – Category 3’ and hazard statement ‘May cause respiratory irritation’ (H335) in the HCIS (Safe Work Australia). No data are available to evaluate the classification. However, signs of respiratory irritation were noted in an acute inhalation toxicity study (see **Acute toxicity: Inhalation** section) and there were lung haemorrhages in the animals that died (REACH).

Skin Irritation

Trioctyltin compounds are classified as hazardous with hazard category ‘Skin irritation – Category 2’ and hazard statement ‘Causes skin irritation’ (H315) in the HCIS (Safe Work Australia). The available data showed only slight irritation following dermal exposure. In the absence of more comprehensive information, there is insufficient evidence to amend the current classification.

In an in vivo skin irritation study (according to the Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics (1959) of the US Association of Food and Drug Officials (AFDO)), New Zealand White (NZW) rabbits (n = 3/sex) were exposed (occlusive) to 0.5 mL of the chemical on one intact and one abraded site for 24 hours and monitored for 72 hours. An erythema score of 1 was attributed to 4 of the 6 animals, with reactions on both the intact and abraded sites after 24 hours. Oedema reactions were observed in 2 of the 6 animals, on both intact and abraded skin. Three of the reactions were scored as a 1, while one abraded site was scored as a 2. Within 72 hours, the erythema and oedema effects were reversed (REACH).

Eye Irritation

Trioctyltin compounds are classified as hazardous with hazard category ‘Eye irritation – Category 2’ and hazard statement ‘Causes serious eye irritation’ (H319) in the HCIS (Safe Work Australia). The available data showed only slight irritation following

eye exposure. In the absence of more comprehensive information, there is insufficient evidence to amend the current classification.

In an in vivo eye irritation study (according to the Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics (1959) of the United States Association of Food and Drug Officials (AFDO)), NZW rabbits (n = 3/sex) were exposed to 0.1 mL of the chemical in the conjunctival sac of the left eye, which was held open for a few seconds after application. The eyes of the female rabbits were washed with water 30 seconds after application. The animals were observed for 7 days after application. No corneal or iridial effects were observed in any of the animals during the study period. Mild irritation (mainly conjunctival redness, chemosis and discharge) was observed in 5/6 animals (3 with rinsed eye and 2 with unrinsed eye) 1 day after application, but this had reversed in 4/5 animals by day 2. The last animal (unrinsed eye) fully recovered by day 3. On day 1, all three female animals had conjunctivitis with scores ranging from 3–5, and 2 of the males had conjunctivitis scores of 4 and 5. By day 2, a single male had a conjunctivitis score of 6. For conjunctival effects, the average scores were 1.33 for females (rinsed eye) and 1.67 for males (unrinsed eye) for the initial 72 hr observation period (REACH).

Sensitisation

Skin Sensitisation

No data are available.

Repeated Dose Toxicity

Oral

Based on the available data, the chemical is not considered to cause severe effects within the classifiable range.

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 422), Wistar rats (n = 12/sex/dose) were administered the chemical at 0, 300, 750 or 4000 mg/kg diet (approximately equal to 0, 20, 49 and 221 mg/kg bw/day). Males were fed the diet for 30 days and females for a period of 2 weeks prior to mating, throughout mating, gestation and up to post-natal day (PND) 4 or 5. There were no mortalities reported during the study. The mean food intake in males in the high dose group was statistically significantly decreased from days 0–7 and 7–13. Food intake information could not be gathered from days 21–28, as some males remained caged with the females for mating. The mean food intake in females in the high dose group was statistically significantly decreased during the premating (days 0–7), gestation (days 0–21) and postnatal (days 1–4) periods. In females in the mid-dose group there was a statistically significant decrease in food consumption during gestation days 7–14 only. In males in the highest dose group, average body weight was statistically significantly reduced from day 7 onwards compared with controls. Statistically significant lower body weight was noted in females in the high dose group during the premating (days 7 and 13), gestation (days 7, 14 and 21) and postnatal (days 1 and 4) periods. The terminal body weight for males and females in the high dose groups was statistically significantly decreased. In high dose females, the reduced growth was reported to have contributed to reduced body temperature and reduced limb grip strength at the end of the study. The absolute and relative thymus weight of males and females in the high dose groups was statistically significantly decreased. Females in the high dose group also had a statistically significant decrease in the absolute weight of the adrenals. Histopathological changes included thymus lymphoid depletion in high dose males (5/5) and females (4/4). Paracortical lymphoid depletion and macrophage clusters were also noted in the mesenteric lymph nodes of 3 males and 3 females in the high dose group, and 1 female in the mid dose group. Treatment related haematological changes included decreased white blood cell count in males in the high dose group and decreased monocyte count in males in the mid and high dose groups. The no observed adverse effect level (NOAEL) for repeated dose toxicity is 300 mg/kg diet (equivalent to approximately 20 mg/kg bw/day) based on thymus effects seen at higher doses (REACH).

In studies in male weanling rats exposed to the chemical at up to 150 ppm in the diet for 2 or 4 weeks, there were no mortalities or signs of toxicity (Snoeij et al., 1985). However, the highest administered dose in these studies was less than the NOAEL for repeated dose toxicity identified in the study above.

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the limited available studies, the chemical is not expected to be genotoxic.

Negative results were obtained in an in vitro bacterial reverse mutation assay (OECD TG 471) in *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537, and *Escherichia coli* WP2 uvr A, exposed to the chemical at up to 5000 µg/plate for 48–72 hours, with and without metabolic activation (REACH).

Negative results were obtained in an in vivo mammalian erythrocyte micronucleus test (OECD TG 474) in bone marrow from male Swiss mice (n = 5–10/dose) administered the chemical once by oral gavage at 0, 500, 1000 or 2000 mg/kg bw/day. Micronucleated polychromatic erythrocytes were counted after 24 hours in 5 animals from each dose group, and after 48 hours in the remaining 5 animals in the control and high dose groups. There was no chromosomal damage in treated animals compared with controls at any time point (REACH).

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Based on the available data, the chemical causes reproductive toxicity at the highest tested dose, and developmental toxicity effects at a lower dose thus warranting hazard classification (see **Recommendation** section).

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422), Wistar rats (n = 12/sex/dose) were administered the chemical at 0, 300, 750 or 4000 mg/kg diet (approximately equal to 0, 20, 49 and 221 mg/kg bw/day) during the premating, mating, gestation and lactation periods. There was no mortality in the F0 animals. In the high dose group, treatment related reproductive effects included increased pre-coital time, decreased gestation index, prolonged gestation duration and increased post-implantation loss. In the high dose group, treatment related developmental effects included decrease in the number of dams with live born pups, increase in the number of dams with stillborn pups/only stillborn pups, decrease in the number of live born pups, increase in the number of still born pups, increase in the number of runts by PND 1 and increase in pup mortality by PND 4. In the mid-dose group there was a statistically significant decrease in the number of live born pups per litter and significantly increased number of stillborn pups per litter. Pups born to dams from the high dose group also had significantly reduced body weight gain from PND1–4. The NOAEL for reproductive toxicity was 750 mg/kg diet (approximately 49 mg/kg bw/day), while the NOAEL for developmental toxicity was 300 mg/kg diet (approximately 20 mg/kg bw/day) (REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (reproductive and developmental toxicity), systemic acute effects (acute toxicity from inhalation exposure). The chemical can also cause local effects such as skin, eye and respiratory irritation.

Public Risk Characterisation

Given the identified use for the chemical, it is unlikely that the public will be exposed. Hence, the public risk from this chemical is not considered to be unreasonable.

Occupational Risk Characterisation

During product formulation, oral, dermal, inhalation 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 chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long-term and systemic acute health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise oral, dermal, inhalation and ocular exposure are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

The data available support an amendment to the hazard classification in the HCIS (Safe Work Australia) (see **Recommendation** section).

NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Work Health and Safety

The chemical is recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Not Applicable	Fatal if inhaled - Cat. 2 (H330)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Not Applicable	Causes serious eye irritation - Cat. 2A (H319)* Causes skin irritation - Cat. 2 (H315)* May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)*
Reproductive and Developmental Toxicity	Not Applicable	May damage the unborn child. Suspected of damaging fertility - Cat. 1B (H360Df)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from oral/dermal/ocular/inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minmising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

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 08 March 2019

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