Stannane, dioctyloxo-: Human health tier II assessment

02 March 2018

CAS Number: 870-08-6

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	di-n-octyltin oxide dioctyloxostannane tin, dioctyloxo- DOTO
Structural Formula	
Molecular Formula	C16H34OSn
Molecular Weight (g/mol)	361.15
Appearance and Odour (where available)	Off-white odourless powder
SMILES	C(CCCCCCC)[Sn](=O)CCCCCCCC

Import, Manufacture and Use

Australian

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

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 2015–16:

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

International

The following international uses have been identified through Galleria Chemica; the European (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossier; and the Substances in Preparations in Nordic Countries (SPIN) database.

The chemical has reported site limited uses, including as:

- an intermediate in the production of organotin stabilisers for polyvinylchloride (PVC); and
- a component of formulations with mono-n-octyltin trichloride (MOTC), mono-n-octyltin hydroxide (MOTO) and di-n-octyltindichloride (DOTC)—the formulations are used to produce substances that are in turn used as coatings, plasticisers and synthetic lubricants.

No evidence of the presence of this chemical in consumer products was found in available North American databases (Household Products Database and Personal Care Council), indicating that the chemical is not likely to be widely available for domestic or cosmetic uses. The chemical has reported domestic use in the Substances and Preparations in Nordic countries (SPIN) database. However, it should be noted that SPIN does not distinguish between direct use of the chemical, or use of the materials that are produced from chemical reactions involving the chemical.

Restrictions

Australian

Tin and its compounds 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

Dioctyltin compounds are listed on the following (Galleria Chemica):

- Annex XVII to REACH Regulations—dioctyltin compounds shall not be used after 1 January 2012 in several articles for supply to, or use by, the general public, where concentration in the article, or part thereof, is greater than the equivalent of 0.1 % by weight of tin. Organostannic compounds are also restricted for biocide and water treatment uses (European Parliament and Council, 2006); and
- Council of Europe Resolution AP (92) 2 on the control of aids to polymerisation for plastic materials and articles intended to come into contact with foodstuffs—Limits for finished articles; a limit of 0.02 mg/kg (as Sn) applies for di-n-octyltin.

Tin compounds (organic) are listed on the:

- 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 material, and scraped-off toy material, respectively (Galleria Chemica).

Existing Work Health and Safety Controls

Hazard Classification

The chemical is 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).

Health Hazard Information

The oxygen bridges in the chemical are considered to be labile, and data on related dioctyltin compounds (including dioctyltin dichloride—DOTC, CAS No. 3542-36-7) (NICNAS) are used where needed for read across for systemic toxicity endpoints.

Toxicokinetics

Absorption of the chemical is expected to occur mainly through the oral route, with little to no absorption through the dermal route. Distribution of the chemical throughout the body occurs at high doses, with the target organs being the thymus, liver and reproductive system. Data regarding the metabolism of the chemical is not available; however, due to the length of the alkyl chain and the fact that it is insoluble in in water and in organic solvents, it is not expected to undergo significant metabolic changes. Elimination of the largely unmetabolised chemical is expected to occur via the faeces (REACH).

Acute Toxicity

Oral

Based on the available data, the chemical has low acute oral toxicity.

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

- 1900 mg/kg bw in rats (sex and strain unspecified);
- 1933–2816 mg/kg bw in male Wistar rats;
- 2220 mg/kg bw in rats (sex and strain unspecified);
- 2334–2350 mg/kg bw in rats (sex and strain unspecified);
- 2500 mg/kg bw in male rats (strain unspecified);
- 2500 mg/kg bw in rats (sex and strain unspecified);
- >4000 mg/kg bw in male and female rats (strain unspecified);
- 5250 mg/kg bw in rats (sex and strain unspecified);
- >6000 mg/kg bw in male and female Tif RAI rats; and
- >8000 mg/kg bw in rats (sex and strain unspecified).

Observed sub-lethal effects include dyspnoea (laboured breathing), exophthalmos (protrusion of eyeball/s), sedation and ruffled fur. Although there were some animal mortalities, the other animals recovered fully within 7 days.

Dermal

Based on the available data, the chemical is considered to have low acute dermal toxicity.

A dermal LD50 value of >2000 mg/kg bw was reported in male and female Wistar rats (REACH).

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Based on the available data, the chemical is not considered to be a skin irritant following dermal exposure.

In an ex vivo / in vitro skin irritation study (according to the Organisation for Economic Co-operation and Development (OECD) Test Guidelines (TG) 439), the chemical (10 mg) was applied topically to reconstructed human epidermis for 15 minutes before being rinsed. The relative mean viability of the treated epidermis was 66.7 % and based on the criteria for this assay, it was concluded that the chemical was not irritating (REACH).

In an in vitro skin irritation study (OECD TG 431), reconstructed human epidermis was topically treated with 20 mg of the chemical for 3, 60 or 240 minutes. The relative mean viability of the treated epidermis was >100 % for all three time periods. Based on these results it was concluded that the chemical was not corrosive (REACH).

Eye Irritation

Based on the available data, the chemical is not considered to be irritating to the eyes.

In an in vivo eye irritation study (OECD TG 405), two male New Zealand White (NZW) rabbits were treated with to 0.1 mL chemical in one eye each, and then assessed for a period of 7 days. There were no effects on the cornea. At 24 hours, minor iris irritation was noted in one of the treated eyes. At 24 hours, one of the treated eyes had moderate conjunctival irritation, while the other treated eye had mild conjunctival irritation. Both treated eyes had fully recovered at 7 days after administration (REACH).

In an in vitro eye irritation study (non-guideline), 30 mg of the chemical was administered onto a reconstructed human corneal model (SkinEthic) for 10 minutes and cell viability assessed. The relative mean viability of the treated test material after a 10 minute exposure was >100 %. Based on this result it was concluded that the chemical was not irritating to eyes (REACH).

Sensitisation

Skin Sensitisation

Based on the available data, the chemical is not considered to be a skin sensitiser.

In a local lymph node assay (OECD TG 429) 25 µL of the chemical was administered to female CBA mice (n = 4/dose) at concentrations of 5, 10 or 25 % w/w in propylene glycol vehicle once a day for three consecutive days on the dorsal surface of each ear. The stimulation indices induced by the chemical at all concentrations were less than three (0.92, 0.89 and 1.77 at 5, 10, and 25 %, respectively), indicating that it is not a skin sensitiser in this concentration range (REACH).

Repeated Dose Toxicity

Oral

Based on the available data, the chemical is considered to cause serious thymus effects following repeated oral exposure, warranting hazard classification (see **Recommendation** section). Thymus toxicity was also reported in studies using DOTC (NICNAS).

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422), Wistar rats (n = 52/sex/dose) were administered the chemical at 0, 5, 25 or 250 mg/kg diet (equivalent to approximately 0, 0.3–0.4, 1.5–2.4 and 11.2–17.4 mg/kg bw/day) for 28 days. Average body weight change and food intake were significantly decreased in the high-dose rats compared with controls. No changes in haematology were reported in this study. Statistically significant, treatment-related changes to clinical chemistry included an increase in alkaline phosphatase levels in high-dose males, and an increase in bilirubin in high-dose females. In males in the mid- and high-dose groups, the absolute thymus weights were significantly decreased. In the high-dose female group, there was a significant decrease in the absolute and relative thymus weights, while in the mid-dose group there was a statistically significant decrease in only the relative thymus weight. Histopathological assessment of the thymus identified severe lymphoid depletion in females in the mid dose group, and all animals in the high-dose groups. There was a statistically significant decrease in the relative kidney and liver weights in the high-dose females. It was concluded that the NOAEL was 5 mg/kg diet (equivalent to 0.3–0.4 mg/kg bw/day for males and 0.3–0.5 mg/kg bw/day for females), based on the thymus effects seen at higher doses (REACH).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the available data, the chemical is not considered to be genotoxic.

Negative results were obtained using the chemical in vitro (REACH):

- in bacterial gene mutation studies (OECD TG 471) in *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537, and *Escherichia coli* strain WP2 uvrA exposed to the chemical at up to 5000 µg/plate for between 48–72 hours, with and without metabolic activation; and
- in a mammalian cell gene mutation assay (OECD TG 476) in L5178Y cells exposed to the chemical for 4–24 hours at up to 20 µg/mL without metabolic activation, and up to 112 µg/mL with metabolic activation.

Negative results were obtained for the chemical, in an in vivo mammalian erythrocyte micronucleus test (OECD TG 474) in bone marrow from male Swiss mice exposed to the chemical once by oral gavage at up to 2000 mg/kg bw.

Carcinogenicity

No data are available for the chemical. Limited data are available using mixtures containing dioctyltin compounds and; therefore, are insufficient to derive a conclusion on carcinogenicity (NICNAS).

Reproductive and Developmental Toxicity

Based on the data available, the chemical does not show specific reproductive toxicity. However, developmental effects were observed (pup mortality in rats), warranting hazard classification (see **Recommendation** section). Developmental toxicity (skeletal malformations) was also reported in studies using DOTC (NICNAS).

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422), groups of Wistar rats were administered the chemical at 0, 5, 25 or 250 mg/kg diet (equivalent to approximately 0, 0.3–0.4, 1.5–2.4 and 11.2–17.4 mg/kg bw/day) for 28 days (see also **Repeated dose toxicity** section). A single pregnant female in the high-dose group died on gestation day (GD) 24 and 11 stillborn foetuses were found in the uterus. No significant effects on the mating index, fertility rates or fecundity were noted. Gestation duration in the low- and medium-dose groups was similar to the control group; however, in the high-dose group there was a significant increase in gestation duration. Compared with the control group, there was a statistically significant decrease in the number of live born, and increase in stillborn pups born to dams from the highest dose group. An increase in post implantation losses was observed in the high-dose group compared with controls. There was a statistically significant increase in pup mortality on post-natal day (PND) 4 in the high-dose group. On PND 1 and 4 a statistically significant decrease in pup body weight was reported in the high-dose group (REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects from repeated oral exposure (developmental toxicity and thymus effects).

Public Risk Characterisation

Based on the available use information, the chemical is not likely to be available for domestic or cosmetic uses. Hence, the public risk from direct use of the chemical is not considered to be unreasonable.

Internationally, the tolerable daily intake (TDI) of 0.1 µg/kg bw (as Sn) for a group comprising tributyltins, triphenyltins, dibutyltins and dioctyltins has been established (EFSA, 2004). Based on an impact assessment report conducted in Europe (European

Commission, 2009), the chemical with its identified uses is not considered to significantly contribute to the overall TDI. In addition, the dominant contribution to human intake of organotins (mainly tributyltin compounds) is via the consumption of fish. Hence, the public risk from this chemical is not considered to be unreasonable.

If data becomes available indicating specific uses in Australia that could significantly contribute to the overall TDI for organotins, further assessment of the chemical may be required.

Occupational Risk Characterisation

During product formulation, 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 health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise 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]
Repeat Dose Toxicity	Not Applicable	Causes damage to the immune system through prolonged or repeated exposure - Cat. 1 (H372)
Reproductive and Developmental Toxicity	Not Applicable	Suspected of damaging the unborn child - Cat. 2 (H361d)

[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 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;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising 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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