Stannane, bis[(2-ethyl-1-oxohexyl)oxy]dioctyl-: Human health tier II assessment

12 December 2019

CAS Number: 24577-34-2

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.

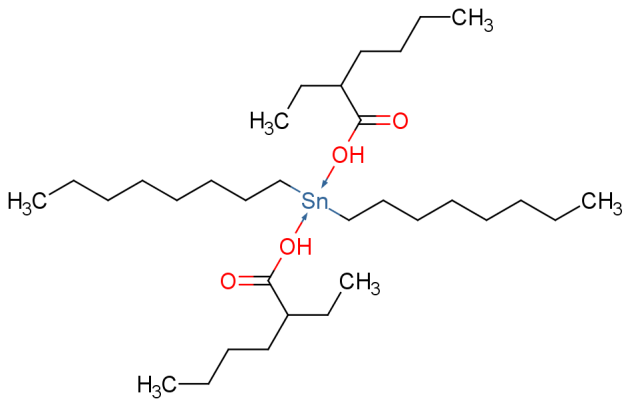
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	Dioctyltin bis[2-ethylhexanoate Bis[(2-ethyl-1-oxohexyl)oxy]dioctylstannane
Structural Formula	
Molecular Formula	C32H64O4Sn
Molecular Weight (g/mol)	631.56
Appearance and Odour (where available)	Colourless turbid solid
SMILES	C(=O)(C(CCCC)CC)O[Sn](CCCCCCCC)(CCCCCCCC)OC(=O)C(CCCC)CC

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 as sources of organotin compounds by the NPI in 2017–18:

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

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers.

The chemical has site limited use, including in the manufacture of:

- plastic products;
- rubber products;
- pulp and paper products;
- fine chemicals;
- fabricated metal products;
- electronic and electrical equipment;
- furniture; and
- building and construction material.

Restrictions

Australian

Tin and its compounds are listed in Schedule 10 of the model Work Health and Safety Regulations (2019) 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

Dioctyltin compounds—which includes the chemical in this assessment—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).
- Part 1 of Annex I to Regulation (EU) No 649/2012 of the European Parliament and of the Council concerning the export and import of hazardous chemicals—a severe restriction applies for the industrial chemical for public use.

- 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—which includes the chemical in this assessment— are listed on the following:

- 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.

- 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.

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) (Safe Work Australia).

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

The contain a dioctyltin (Oct2Sn-) group, and 2 labile ligands (X). Data available indicate that the chemical is hydrolysed to release 2-ethylhexanoic acid (2-EHA, CAS No. 149-57-5) (see **Toxicokinetics** section). Although there is no evidence that the chemical is hydrolysed to dioctyltin dichloride—DOTC (CAS No. 3542-36-7), the systemic toxicity of dioctyltin compounds is similar (NICNASa; NICNASb; NICNASc; NICNASd). Therefore when data for the chemical being assessed are not available, health hazard information for 2-EHA and dioctyltin compounds including DOTC, dioctyltin oxide—DOTO (CAS No. 870-08-6) and dioctyltin laurate—DOTL (CAS No. CAS No. 3648-18-8) have been included in this report for read across for systemic toxicity endpoints.

The Tier II assessment reports for the dioctyltin compounds and 2-ethylhexanoic acid are available at https://www.nicnas.gov.au. These reports should be read in conjunction with this Tier II assessment.

Toxicokinetics

In a hydrolysis study (OECD Test Guideline (TG) 111), using ^{119}Sn-NMR, the chemical was hydrolytically stable at pH 4 and 7. Under simulated gastric conditions, the chemical hydrolysed to form dioctyltin chloro 2-ethylhexanoate, the monochloroester of the chemical. This would mean the release of 2-ethylhexanoic acid. In contrast to DOTL, the dimeric distannoxane (ClOct2SnOSnOct2Cl) was not detected. No DOTC was formed under the conditions of the study (REACH).

Dioctyltin compounds have minimal dermal absorption (NICNASa; NICNASb; NICNASc; NICNASd).

Acute Toxicity

Oral

The chemical has low acute toxicity based on results from an animal test (OECD TG 420) following oral exposure. The median lethal dose (LD50) in rats is >2000 mg/kg bw. Observed sub-lethal effects included hunched posture and ataxia. All animals had recovered by day 1 (REACH).

The finding of low toxicity is supported by data for other dioctyltin compounds (NICNASa; NICNASb; NICNASc; NICNASd).

Dermal

No data are available. The chemical is expected to have low acute dermal toxicity based on the reported oral LD50, limited expected dermal absorption (see **Toxicokinetics** section) and data for other diotyltin compounds (NICNASa; NICNASb; NICNASc; NICNASd).

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

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

In an in vitro skin corrosion, reconstructed human epidermis (RHE) test (OECD TG 431), duplicate tissues were treated with the chemical for exposure periods of 3 and 60 minutes. The relative mean viabilities for the test material treated tissues were 96.4 and 90.8 % after 3 and 60 minute exposure times, respectively. Based on this finding it was concluded that the chemical was not irritating (REACH).

In an in vitro skin irritation, reconstructed human epidermis (RHE) test (OECD TG 439), triplicate tissues were treated with the chemical; for an exposure period of 15 minutes. At the end of the exposure period each tissue was rinsed before incubating for 42 hours. The relative mean viability of the test material treated tissues was 104.4 % after the 15 minute exposure period and 42 hours post exposure incubation period. Based on this finding it was concluded that the chemical was not irritating REACH).

Eye Irritation

Based on the limited available data the chemical is considered to be at most slightly irritating to eyes.

In an in vitro bovine corneal opacity and permeability (BCOP) test (OECD TG 437) the chemical was applied at a concentration of 20% w/v in 0.9% w/v sodium chloride solution for 240 minutes. An in vitro irritancy score (IVIS) of 12.2 was reported. This is outside the range for which a prediction of eye irritation can be made (REACH).

Another related dioctyltindocarboxylate ester, DOTL, was slightly irritating in an eye irritation study in rabbits (OECD TG 405) (NICNASc)

Sensitisation

Skin Sensitisation

No data are available. In general dioctyltin compounds (with the exception of dioctyl tin alkyl mercaptoacetates) are not considered to be skin sensitisers (NICNASa; NICNASb; NICNASc; NICNASd).

Repeated Dose Toxicity

Oral

No data are available for the chemical.

Based on the available data for the dioctyltin compounds DOTC (NICNASa), DOTO (NICNASb) and dioctyltin alkyl mercaptoacetates (NICNASd), the chemicals in this group are expected to cause serious health effects in the thymus following repeated oral exposure, warranting hazard classification (see Recommendation section). Effects observed at doses <10 mg/kg bw/day included reduced thymus weights with associated lymphoid depletion.

The metabolite, 2-EHA, has reported lowest adverse effect levels (LOAEL) of 917 mg/kg bw/day and 1040 mg/kg bw/day in two 90-day dietary studies in rats. Reported effects included reduced body weight gain and reduced food consumption (NICNASe).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

No data are available for the chemical. Based on the available data for DOTC (NICNASa), DOTO (NICNASb), dioctyltin alkyl mercaptoacetates (NICNASd) and 2-EHA (NICNASe) the chemical is not considered to be genotoxic.

Dioctyltin compounds produced negative results in in vivo genotoxicity tests with mostly negative results in vitro (NICNASa; NICNASb; NICNASd).

The metabolite, 2-EHA, gave some positive results in vitro (negative in a bacterial reverse mutation assay, induced DNA damage in rat hepatocytes, and increased frequency of sister chromatid exchange in CHO cells). In vivo 2-EHA was negative in a mouse micronucleus assay.

Carcinogenicity

No data are available for the chemical. Limited data available using mixtures containing dioctyltins are insufficient to derive a conclusion on carcinogenicity (NICNASa).

Reproductive and Developmental Toxicity

No data are available for the chemical. Based on the available data for dioctyltin compounds and the hydrolysis product 2-EHA, the chemical may cause developmental and reproductive effects, warranting classification (see **Recommendation** section).

The hydrolysis product, 2-EHA, is classified as hazardous with the hazard category 'Toxic to reproduction' (Category 2), with the hazard statement ‘Suspected of damaging fertility or the unborn child’ (H361) in the HCIS (Safe Work Australia).

2-EHA, was reported in several studies to cause developmental toxicity in rats following treatment via the oral route (NICNASe). These effects, including foetal skeletal variations, malformations, reduced foetal body weights and early foetal deaths, were noted in the absence of signs of maternal toxicity. The lowest observed adverse effect level (LOAEL) for developmental toxicity was reported to be 100 mg/kg bw/day. Effects on the male reproductive system (reduction in sperm motility) and fertility were also observed at 100 mg/kg bw/day.

Developmental effects were observed with dioctyltin compounds DOTC (skeletal malformations; see NICNASa), DOTO (pup mortality in rats; see NICNASb) and dioctyltin alkyl mercaptoacetates (increased post implantation loss, depressed foetal weight, increased pup mortality) (NICNASd).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects from repeated oral exposure (reproductive and 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, a group tolerable daily intake (TDI) of 0.1 µg/kg bw (as Sn) for tributyltins, triphenyltins, dibutyltins and dioctyltins has been established (EFSA, 2004). Based on an impact assessment report conducted in Europe (European Commission, 2009), the chemicals with their identified uses are not considered to significantly contribute to the overall TDI. Organotins have not been found in Australian drinking water (NWQMS, 2011). In addition, the dominant contribution to human intake of organotins (mainly tributyltin compounds) is via the consumption of fish. Hence, the public risk from these chemicals 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 may 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 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 fertility or the unborn child - Cat. 2 (H361fd)

[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 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;
- 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;
- 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.

References

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