Stannane, tetrabutyl-: Human health tier II assessment

08 March 2019

CAS Number: 1461-25-2

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.

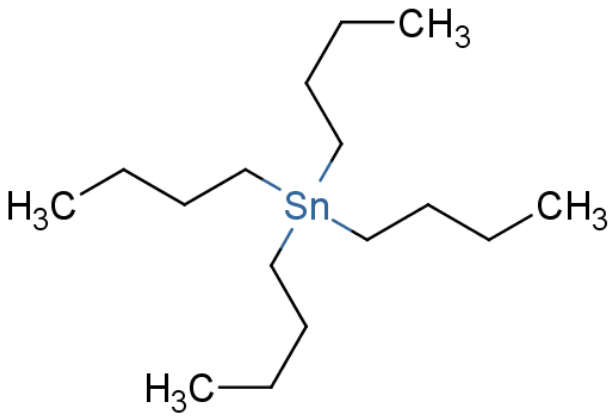
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	tetrabutyltin tetra-n-butyltin
Structural Formula	
Molecular Formula	C16H36Sn
Molecular Weight (g/mol)	347.15
Appearance and Odour (where available)	Clear colourless oily liquid
SMILES	C(CCC)[Sn](CCCC)(CCCC)CCCC

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 uses have been identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; the Organisation for Economic Co-operation and Development (OECD) Screening information data set International Assessment Report (SIAR) (OECD, 2007); and Galleria Chemica.

The chemical has reported site limited uses as:

- an intermediate in the synthesis of other organotin compounds; and
- a constituent of preparations used for water treatment and biocidal products.

Restrictions

Australian

Tin and its compounds—which includes the chemicals 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

Tin compounds (organic)—which includes the chemicals 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;
- 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; 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 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 0.2–0.4 mg/m^3 STEL in different countries such as Bulgaria, Canada (Alberta, British Columbia, Ontario, Quebec, Saskatchewan, Yukon), Chile, Denmark, Egypt, Estonia, France, Greece, Hungary, Malaysia, Mexico, Norway, Philippines, Singapore, South Africa, Spain, Sweden, Taiwan, the United Kingdom and the United States of America (California, Hawaii, Minnesota, Tennessee, Vermont, Washington).

Health Hazard Information

Toxicokinetics

In a non-guideline study, rats and rabbits were used to determine the extent of tetrabutyltin absorption, distribution, metabolism and excretion.

Three male Wistar rats were orally administered the chemical (10 mg/kg bw) dissolved in sesame oil five times at 12 hour intervals. The rats were euthanised and upon examination it was found that the chemical was taken up from the small intestine, and was retained by the kidney and liver. Only trace amounts of the chemical were found in the brain and blood of the rats. Large amounts of the metabolite Bu_3Sn^+ were observed in the small and large intestines, and the brain (OECD, 2007; ATSDR, 2005; REACH).

Three male Wistar rats were subcutaneously administered the chemical (10 mg/kg bw). In the following 3 days post administration a trialkyltin metabolite (Bu_3Sn^+) was identified in the urine (approximately 0.12 % of the dose) and faeces (approximately 0.16 % of the dose). No tetrabutyltin was observed in the urine and faeces suggesting that the tetrabutyltin is dealkylated in the body and the metabolites are excreted (OECD, 2007; ATSDR; 2005; REACH).

Two male Japanese white rabbits were administered the chemical (51 mg) once and their bile was collected in a test tube. The amounts of tetrabutyltin were measured as a function of time after the initial administration. The most lipid soluble tetrabutyltin metabolites that were not initially dealkylated and excreted undergo further metabolism in the presence of the bile and are reabsorbed by the intestines (OECD, 2007; REACH).

Acute Toxicity

Oral

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

The oral median lethal dose (LD50) value for the chemical was reported to be >2000 mg/kg bw in female Sprague Dawley (SD) rats (OECD Test Guideline (TG) 423) (OECD, 2007; REACH).

Other non-guideline studies have reported oral LD50 values from ≥4000 to 6000 mg/kg bw in rats and mice (OECD, 2007; REACH).

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Based on the available in vitro data, the chemical is considered to be a skin irritant, warranting hazard classification (see **Recommendation** section).

In an in vitro skin irritation study (similar to OECD TG 439), reconstructed human epidermis (EPISKIN ™) was topically exposed to 10 µL of the chemical for 15 minutes, and then rinsed before incubation for 42 hours. The relative mean viability of the treated epidermis was 38.5 % and based on the criteria of the assay, it was considered that the chemical is a skin irritant (REACH).

In an in vitro skin corrosion study (according to OECD TG 431), reconstructed human epidermis (EPISKIN ™) was topically exposed to 50 µL for either 3, 60 or 240 minutes. The relative mean viability of the treated epidermis was >90 % for all exposure periods and based on the criteria of the assay, it was considered that the chemical is non-corrosive to the skin (REACH).

Eye Irritation

Based on the available data, the chemical is considered to be an eye irritant, warranting hazard classification (see **Recommendation** section).

In an in vitro/ex vivo eye irritation study (non-guideline), three enucleated (removed or isolated) rabbit eyes were treated with 0.1 mL of the chemical for approximately 10 seconds before being washed with at least 20 mL saline. Assessment of the corneas were made at 60, 120, 180 and 240 minutes after treatment. Observed effects included the presence of corneal opacity at 240 minutes (scored 3/4; equivalent to cloudiness in 51–75 % of the stromal thickness of the cornea); increased fluorescein uptake at 240 minutes (scored 3/4; involving a large portion of the cornea and underlying structures barely visible (but not obliterated) with illumination); corneal swelling from 60 minutes onwards (13–27 % in treated eyes, compared with 3.5–5.1 % in controls); and corneal sloughing in two treated eyes. Based on these results, it was concluded that the chemical has the potential to be a severe ocular irritant (REACH).

Sensitisation

Skin Sensitisation

Based on the available data, the chemical is considered to be a skin sensitiser, warranting hazard classification (see **Recommendation** section).

In a mouse local lymph node assay (OECD TG 429), 25 µL of the chemical was applied topically to the dorsum of both ears of female CBA/J mice (n = 5/dose) at concentrations of 0, 0.25, 0.5 or 1 % v/v in an acetone/olive oil vehicle (4:1 v/v), once daily for three consecutive days. The stimulation index (SI) at a 1 % chemical concentration was greater than three (SI 10.82 at 1 % concentration), indicating that the chemical is a potent sensitiser with an EC3 value <1 % (REACH).

Repeated Dose Toxicity

Oral

Based on the available data, the chemical is considered to cause some spleen (males only) and thymus effects following repeated oral exposure. The effects at lower doses are not sufficient to warrant hazard classification.

In a combined repeated dose toxicity study with the reproduction/development toxicity screening test (OECD TG 422), Wistar rats (n = 4/sex/dose) were administered the chemical at 0, 100, 300 or 2000 mg/kg diet (equivalent to approximately 0, 6–7, 17–20 and 109–130 mg/kg bw/day in males; and 0, 5–8, 16–24 and 100–118 mg/kg bw/day in females during premating, gestation and lactation). Dosing was for 33 days in males and for 2 weeks premating, as well as during mating, gestation, and up to postnatal day (PND) 4 or 5 in females. No mortalities occured during the study. One female in the high dose group had piloerection on gestation days (GD) 21–22, while another female was emaciated during PND 1–5. Significant decreases in food consumption were noted in females in the high dose group during the premating period through to lactation, except during GD 14–21. Average body weight changes in males were significantly decreased in the high dose group from days 21–28. The average body weight change of females in the high dose group was significantly decreased from GD 0–14. Significant increases in thrombocytes, and a shorter prothrombin time (clotting factor), were noted in females in the high dose group compared with controls, at the end of the premating period only. Significant decreases in the absolute thymus weight were noted in males in the high dose group. Non-significant decreases in thymus weight were noted in males in the mid dose group, and in females in the in the mid and high dose groups, compared with the control group. Significant decreases in the relative spleen weight were noted in males in the mid and high dose groups. Histopathological changes include lymphoid depletion in the thymus of females in the mid and high dose groups. Lymphoid decreases were also noted in the paracortex of mesenteric lymph nodes of male and female animals in the high dose group. There were also deposits of haemosiderin (iron) and evidence of erythrophagocytosis (red blood cell removal) in the mesenteric lymph nodes of males and females in the high dose group. The no observed adverse effect level (NOAEL) was determined to be 100 mg/kg diet (approximately 6–7 mg/kg bw/day in males and 5–8 mg/kg bw/day in females), based on decreases in (relative) spleen weight (males only) and thymus effects from 300 mg/kg diet (OECD, 2007; 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 (OECD, 2007; REACH):

- in bacterial gene mutation studies (OECD TG 471) in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, 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;

- in a modified Ames test (non-guideline) in *S.typhimurium* strain TA 100 exposed to the chemical at up to 100 µg/plate for 48 hours without metabolic activation; and
- in a SOS chromotest (non-guideline) in *E.coli* strain PQ37 exposed to the chemical (concentration unknown), without metabolic activation; and
- a Rec-assay (to detect DNA damage; non-guideline) in *Bacillus subtilis* H17 Rec+ and M45 Rec- exposed to 50 µL of the chemical solution, without metabolic activation.

Negative results were obtained in an in vivo micronucleus assay (OECD TG 474) in male Swiss mice (n = 38) exposed to the chemical orally at single doses of 0, 500, 1000 or 2000 mg/kg bw. No mortalities or clinical signs were noted during the study period. When compared 24 and 48 hours after administration, the differences between the number of micronucleated polychromatic erythrocytes (MPE) from bone marrow were not significantly different between the treated groups and the controls (OECD, 2007; REACH).

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Based on the available data, the chemical is considered to cause developmental effects following oral exposure, warranting hazard classification (see **Recommendation** section).

As a part of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test, Wistar rats (n = 4/sex/dose) were administered the chemical at 0, 100, 300 or 2000 mg/kg diet (equivalent to approximately 0, 6–7, 17–20 and 109–130 mg/kg bw/day in males; and 0, 5–8, 16–24, and 100–118 mg/kg bw/day in females; see **Repeated dose toxicity: Oral** section). No statistically significant differences in the precoital time were noted between the groups. The fecundity, fertility, gestation and mating indices were comparable across the groups (75–100 %). The numbers of stillborn pups were comparable across the groups. One female in the high dose group failed to deliver any pups; however, upon necroscopy there were 11 implantations in the uterus. Post implantation loss was 10.1, 11.5, 6.9 and 21.5 % for the control, low, mid and high dose groups, respectively; effects were not significantly different compared with controls. In the high dose group, there was a significant decrease in the number of pups delivered per litter; a significant decrease in the number of live pups on PND 1 and 4; a significant increase in pup mortality on PND 4; and a significant increase in the number of runts on PND 4, compared with the control group. The NOAEL for developmental toxicity was 300 mg/kg diet (approximately 17–20 mg/kg bw/day in males and 16–20 mg/kg bw/day in females) (OECD, 2007; REACH).

In a developmental toxicity study, pregnant Wistar rats (n = 10–12) were orally administered either 0, 330, 660, 1320, 2640 or 5280 µmol/kg diet (approximately equal to 0, 115, 229, 458, 917 and 1833 mg/kg bw/day) once daily from GD 13–15. There was one maternal death in the highest dose group. Maternal body weight gain was reduced on GD 13–16 in rats exposed at ≥660 µmol/kg (≥229 mg/kg bw/day). External malformations (cleft palate) were observed in foetuses exposed to ≥660 µmol/kg (≥229 mg/kg bw/day), and the incidence was significantly increased at the highest dose. There were no significant differences in the incidence of skeletal or internal malformations between the treated and control groups (OECD, 2007; REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (developmental toxicity) and local effects (skin sensitisation). The chemical can also cause skin and eye irritation.

Public Risk Characterisation

Given the uses identified 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 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 local health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise oral, dermal 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]
Irritation / Corrosivity	Not Applicable	Causes serious eye damage - Cat. 1 (H318) Causes skin irritation - Cat. 2 (H315)
Sensitisation	Not Applicable	May cause an allergic skin reaction - Cat. 1B (H317)
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, dermal and ocular 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

Agency for Toxic Substances and Disease Registry (ATSDR) 2005. Toxicological Profile for Tin and Tin Compounds. Accessed December 2018 at https://www.atsdr.cdc.gov/toxprofiles/tp55.pdf

Galleria Chemica. Accessed December 2018 at http://jr.chemwatch.net/galleria/

Globally Harmonized System of Classification and Labelling of Chemicals (GHS) 2009. United Nations. 3rd edition. Accessed December 2018 at http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

National Pollutant Inventory (NPI). Accessed December 2018 at http://www.npi.gov.au/

Organisation for Economic Co-operation and Development (OECD), 2007. SIDS Initial Assessment Report (SIAR) on Tetrabutyltin (CAS No. 1461-25-2). Accessed December 2018 at https://hpvchemicals.oecd.org/ui/Search.aspx

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Dossier. Tetrabutyltin (CAS 1461-25-2). Accessed December 2018 at https://echa.europa.eu/search-for-chemicals

Safe Work Australia (SWA). Hazardous Chemical Information System (HCIS). Accessed December 2018 at http://hcis.safeworkaustralia.gov.au/

Last update 08 March 2019

Share this page