Pentasiloxane, dodecamethyl-: Human health tier II assessment

26 October 2018

CAS Number: 141-63-9

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

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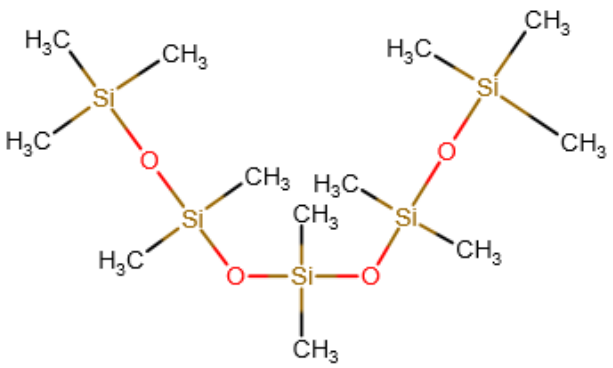
Acronyms & Abbreviations

Chemical Identity

Synonyms	dodecamethylpentasiloxane (L5) pentasiloxane, 1,1,1,3,3,5,5,7,7,9,9,9-dodecamethyl- dimethicone dimethyl silicone L5
Structural Formula	
Molecular Formula	C12H36O4Si5
Molecular Weight (g/mol)	384.84
Appearance and Odour (where available)	liquid
SMILES	C[Si](C)(C)O[Si](C)(C)O[Si](C)(C)O[Si](C)(C)O[Si](C)(C)C

Import, Manufacture and Use

Australian

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

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; US Department of Health and Human Services and Household Products Database (US HPD); and the Compilation of Ingredients Used in Cosmetics in the United States (CIUCUS).

The chemical has reported cosmetic uses as anti-foaming, skin protectants and skin conditioning agents in a wide range of personal care products including body and hand preparations, such as baby and aftershave lotions, colognes, deodorants, bath oils and soaps, cleansing products, foundations, eye makeup preparations, hair dyes, shampoos and conditioners and indoor tanning preparations.

The chemical has reported commercial and potential domestic use in non-metal-surface treatment products, lubricants and greases.

The chemical has reported site-limited uses, including as an intermediate in the preparation of speciality organic chemicals and polymers (i.e. silicone polymers) used in a range of industrial, medical and consumer products.

The chemical has reported non-industrial use in therapeutics as a formulation ingredient in sunscreen lotions (available in liquid and aerosol/pump spray forms at concentrations of <10 % as listed on the US HPD).

Restrictions

Australian

No known restrictions have been identified.

International

No known international restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Chemicals Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific international exposure standards are available.

Health Hazard Information

The chemical dodecamethylpentasiloxane (also known as L5) is an organosilicon compound, containing an alternating silicon-oxygen backbone and it is a member of the volatile methyl siloxanes group. It is a mixture of fully methylated linear siloxane polymers end blocked with trimethylsiloxy units (Personal Care Products Council). The chemical is mainly used as an ingredient in the preparation of a wide range of personal care products and polymers (CIUCUS, 2011; Personal Care Products Council; REACH).

Linear siloxanes (L2 to L5) are expected to have similar physico-chemical properties including high log Kow (increasing with chain length) and low water solubility (REACH). Thus, animal and human data for other structurally relevant linear siloxanes including hexamethyldisiloxane (L2) (CAS No. 107-46-0), octamethyltrisiloxane (L3) (CAS No. 107-51-7), and decamethyltetrasiloxane (L4) (CAS No. 141-62-8) are considered relevant as analogue data (NICNASa; NICNASb; NICNASc) and will be used for read-across where hazard data for L5 are lacking.

Toxicokinetics

In vivo toxicokinetic data are available for linear siloxanes including dodecamethylpentasiloxane (L5) and hexamethyldisiloxane (L2). An in vitro dermal absorption study is available for decamethyltetrasiloxane (L4), showing minimal absorption. L5 is reported to be a relatively low volatile liquid (vapour pressure of 73 Pa at 25 °C), insoluble in water (0.00007 mg/L at 23 °C) and highly lipophilic (with a reported octanol-water partition coefficient value of 9.4 at 25 °C). Minimal human exposure is expected through the oral, inhalation or dermal routes (REACH).

Absorption/administration:

Oral

The chemical L5 is expected to have low oral absorption due to its high molecular weight, highly lipophilic nature and low water solubility. A non-guideline in vivo oral toxicokinetics study on L5 reported that absorption following oral administration (single dose) of 600 mg/kg bodyweight (bw) to 2 Sprague-Dawley (SD) male rats was approximately 25 %. Due to its lipophilic nature and low water solubility, oral absorption of L5 from the gastrointestinal tract is expected to occur via micellar solubilisation. In a repeated dose oral study in rats, oral absorption of L5 based on pathological changes in the liver was also reported (see **Repeated dose toxicity: Oral** section) (REACH).

Dermal

The chemical L5 is expected to have low dermal absorption as its insolubility in water reduces its ability to partition from the stratum corneum into the epidermis. There was no evidence of absorption in the acute dermal toxicity and skin irritation studies (see **Acute toxicity: Dermal** and **Skin irritation** sections). An in vitro dermal penetration study (in accordance with Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 428 (skin absorption: in vitro method), using L4 reported almost all (99.9 %) of recovered ^{14}C-decamethyltetrasiloxane volatilised from the surface of human skin while a small amount of the applied dose (0.06 %) was reported to be on the surface of skin 24 hours post-exposure or remained in the skin after washing and tape stripping (0.03 %). It was estimated that 0.001 % of the applied dose of L4 penetrated through the skin into the receptor fluid and 0.03 % of applied dose was retained in the skin (NICNASc; REACH).

Inhalation

If inhaled, L5 is expected to be absorbed by micellar solubilisation. Based on an in vivo inhalation toxicokinetics study (in accordance with OECD TG 417 (Toxicokinetics)) on L2, it was reported that 3 % of the dose was retained in females rats exposed to L2 vapours (5000 ppm) for 6 hours (NICNASa; REACH).

Distribution

Minimal distribution of L5 to tissues and organs is expected. L5 is reported to be rapidly processed through the liver and expired from the lungs based on an oral gavage study in rats where a single dose of L5 (600 mg/kg bw) was administered by oral gavage and measurements taken 96 hours post-administration. As a result, minimal concentrations of L5 were detected in the tissues and organs of rats (REACH).

Metabolism

Based on a non-guideline in vivo oral toxicokinetics study on L2, linear siloxanes are reported to be extensively metabolised to a number of metabolites following hydroxylation of methyl groups, Si-O hydrolysis and demethylation at the silicon-methyl bond.

Major metabolites of L2 identified in rat urine were $Me_2Si(OH)_2$, $HOMe_2SiCH_2OH$, $HOCH_2Me_2SiOSiMe_2CH_2OH$ (predominant),

$HOCH_2Me2SiOSiMe_3$, $HOMe_2SiOSiMe_3$, Me_3SiOH. The presence of $Me_2Si(OH)_2$ was reported to demonstrate demethylation at the silicon-methyl bonds. In an in vivo inhalation toxicokinetics study (in accordance with OECD TG 417) using L2, the major metabolites reported included 1,3-bis(hydroxymethyl)tetramethyldisiloxane (combined with an unknown metabolite) (61 %), hydroxymethyldimethylsilanol (14 %), dimethylsilanediol (14 %), and trimethylsilanol (6 %) (NICNASa; REACH).

Excretion

In a non-guideline in vivo oral toxicokinetics study, L5 was reported to be rapidly eliminated from 2 male rats, where approximately 74 % of the dose was excreted in faeces, 23 % was eliminated in expired air, and 2.2 % was excreted in urine. It was reported that 65 % and 97 % of the applied dose was eliminated within 24 and 48 hours, respectively (REACH).

In an in vivo inhalation toxicokinetics study (in accordance with OECD TG 417), the majority of systemically absorbed L2 (3 % of the applied dose) was eliminated in urine or as expired volatiles (71 % as mainly L2), while urinary excretion is reported to be of polar metabolites. To a lesser extent (due to low vapour pressure compared to L2), L5 is reported to be expired as volatiles through the lungs, with excretion of metabolites in urine as the major routes of excretion (NICNASa; REACH).

Acute Toxicity

Oral

No data are available for the chemical. Based on the available analogue data for hexamethyldisiloxane (L2) (CAS No. 107-46-0) and octamethyltrisiloxane (L3) (CAS No. 107-51-7), the chemical is expected to have low acute oral toxicity.

It is reported that L2 and L3 have low acute toxicity following oral administration (median lethal dose (LD50) values of >12160 and >2000 mg/kg bw in rats, respectively) (NICNASa; NICNASb).

Dermal

The chemical has low acute dermal toxicity based on the results from a guideline rat study (in accordance with OECD TG 402 (acute dermal toxicity)). The dermal LD50 was reported to be >2000 mg/kg bw in female and male SD rats. No mortality or significant treatment-related effects were reported (REACH).

Inhalation

No data are available for the chemical. Based on the available analogue data for hexamethyldisiloxane (L2) (CAS No. 107-46-0), octamethyltrisiloxane (L3) (CAS No. 107-51-7) and decamethyltetrasiloxane (L4) (CAS No. 141-62-8), the chemical is considered to have low acute inhalation toxicity.

It is reported that L2 and L3 have low acute toxicity following inhalation (median lethal concentration (LC50) values of $>$106000 mg/m^3 (equivalent to >15956 ppm) and $>$22600 mg/m^3 (equivalent to >2350 ppm in rats), respectively, following 4 hours exposure (NICNASa; NICNASb).

Low acute inhalation toxicity was reported in an extrapolated rat study (in accordance with OECD TG 440 (Uterotrophic bioassay in rodents: A short-term screening test for oestrogenic properties)) designed to evaluate anti-oestrogenic activity of L4. An LC50 value of 5080 mg/m^3 (equivalent to >400 ppm) in female SD rats was reported following 6 hour exposure (NICNASc).

Corrosion / Irritation

Skin Irritation

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

In a study conducted in accordance with OECD TG 404 (acute dermal irritation/corrosion), 0.5 mL of the undiluted chemical (unspecified purity) was applied to the shaved skin of New Zealand White (NZW) rabbits (3 animals/group) for 4 hours under semi-occlusive patches with a 4 day observation period (observations at 24, 48, and 72 hours) after patch removal. No treatment-related dermal effects were reported (erythema and oedema mean scores of 0 were noted) (REACH).

Eye Irritation

No data are available for the chemical. Based on the available analogue data for hexamethyldisiloxane (L2) (CAS No. 107-46-0) and decamethyltetrasiloxane (L4) (CAS 141-62-8), the chemical is not considered to be an eye irritant.

L2 and L4 were found to be non-irritating to the eyes of NZW rabbits (NICNASa; NICNASc).

Sensitisation

Skin Sensitisation

No data are available for the chemical. Based on the available animal and human analogue data (see **Sensitisation: Observation in humans** section) for hexamethyldisiloxane (L2) (CAS No. 107-46-0) and octamethyltrisiloxane (L3) (CAS No. 107-51-7), the chemical is not considered to be a skin sensitiser.

L2 and L3 were not reported to be skin sensitisers according to guinea pig maximisation tests (NICNASa; NICNASb).

The chemical structures did not give protein binding alerts for skin sensitisation or respiratory sensitisation as profiled by the OECD Quantitative Structure–Activity Relationship (QSAR) Toolbox v3.4 (OECD Toolbox).

Observation in humans

No evidence of skin sensitisation in human volunteers was reported in a human patch test where 100 subjects were exposed to an induction and challenge dose of 0.2 mL of undiluted hexamethyldisiloxane (L2) under semi-occlusive conditions. There was no evidence of skin sensitisation under the conditions of this study (NICNASa).

In a human patch test, 103 subjects of both sexes were exposed to octamethyltrisiloxane (L3) on the infrascapular region of the back under semi-occlusive conditions. The induction phase consisted of 9 consecutive patch applications of 0.2 mL of undiluted L3 (unspecified purity) at the same site every 48 hours. Patches were removed 24 hours after application. After a 12 to 14 day rest period, the subjects were then challenged, using the same method described for the induction phase, on previously unexposed sites. At 24 and 48 hours following removal of patches, no dermal responses were observed (NICNASb).

Repeated Dose Toxicity

Oral

Based on the available data, the chemical is not expected to cause severe adverse health effects following repeated oral exposure.

In a repeated dose 28-day oral gavage rodent study (in accordance with OECD TG 407), the chemical did not produce systemic toxicity in male and female SD rats (n=5/sex/dose; except at the highest dose where n=10/sex to allow for a recovery group) following repeated oral exposure at doses of 0, 25, 250 or 1000 mg/kg bw/day. No treatment-related signs of systemic toxicity were reported (mortality or significant effects on body weight, food consumption or motor activity). Increased liver weight (likely an adaptive change) was reported in both sexes at doses ≥250 mg/kg bw/day and regressed within the 14 day recovery period. Hepatocellular hypertrophy was observed in animals at the highest dose only. It was reported that after the 14 day recovery period, dose-dependent perilobular fatty change and hepatocellular hypertrophy, considered an adaptive change due to enzyme induction, in the liver were reversible. Increased levels of alpha-2μ-globulin in the kidneys of male rats (an effect not considered relevant to humans) was reported in males at doses ≥250 mg/kg bw/day. A no observed adverse effect level (NOAEL) of ≥1000 mg/kg bw/day was reported for both sexes, based on a lack of toxicologically significant treatment-related effects reported at any dose (REACH).

Dermal

No data are available for the chemical. Based on the available analogue data for hexamethyldisiloxane (L2) (CAS No. 107-46-0), the chemical is not expected to cause severe adverse health effects following repeated dermal exposure (NICNASa).

Inhalation

No data are available for the chemical. Based on the available analogue data for octamethyltrisiloxane (L3) (CAS No. 107-51-7) and decamethyltetrasiloxane (L4) (CAS No.141-62-8), the chemical is not expected to cause severe adverse health effects following repeated inhalation exposure (NICNASb; NICNASc).

Genotoxicity

Whilst no in vivo data are available, based on the weight of evidence from in vitro studies and analogue data for hexamethyldisiloxane (L2) (CAS No. 107-46-0), octamethyltrisiloxane (L3) (CAS No. 107-51-7) and decamethyltetrasiloxane (L4) (CAS No. 141-62-8), the chemical is not expected to be genotoxic.

Several in vitro assays using the chemical gave negative results in (REACH):

- bacterial reverse mutation assays (in accordance with OECD TG 471) in *Salmonella typhimurium* strains TA 98, TA 100, TA1535 and 1537, with or without metabolic activation with S9, at concentrations up to 5000 μg/plate;
- bacterial reverse mutation assays (in accordance with OECD TG 471) in *Escherichia coli* WP2 uvr A strain, with or without metabolic activation with S9, at concentrations up to 5000 μg/plate;
- chromosomal aberration assays (in accordance with OECD TG 473) in Chinese hamster ovary (CHO) V79 cells, with or without metabolic activation with S9, at concentrations up to 10mM (unspecified concentration conversion to μg/mL); and
- mammalian cell gene mutation assay (in accordance with OECD TG 476) in mouse lymphoma L5178Y (TK+/TK-) cells, with or without metabolic activation, at concentrations up to 200 μg/mL.

No in vivo studies are available; however, the chemical structures did not give DNA binding alerts for genotoxicity as profiled by the QSAR Toolbox v3.4 (OECD Toolbox).

L2, L3 and L4 are reported to be non-genotoxic based on in vitro and in vivo studies (NICNASa; NICNASb; NICNASc).

Carcinogenicity

No data are available for the chemical. Based on the available genotoxicity data (see **Genotoxicity** section) and analogue data for hexamethyldisiloxane (L2) (CAS No. 107-46-0), the chemical is not considered likely to be carcinogenic.

L2 is not considered to be carcinogenic based on a 2-year combined chronic inhalation toxicity/carcinogenicity study (in accordance with OECD TG 453) in Fischer 344 rats (NICNASa).

The chemical structures did not contain an alert for genotoxic carcinogenicity as profiled by the OECD QSAR Toolbox v3.4 (OECD Toolbox).

Reproductive and Developmental Toxicity

No data are available for the chemical. Based on the available analogue data for hexamethyldisiloxane (L2) (CAS No. 107-46-0) and decamethyltetrasiloxane (L4) (CAS No. 141-62-8), the chemical is not expected to cause reproductive or developmental toxicity (NICNASa; NICNASc).

Risk Characterisation

Critical Health Effects

The chemical does not have any critical health hazards giving rise to potential health risks under any expected exposure scenarios.

Public Risk Characterisation

In the absence of Australian use information for the chemical, international information indicate potential cosmetic and domestic uses (see **Import, manufacture and use** section). However, based on its hazard profile, the chemical is unlikely to pose a risk to the public.

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 while cleaning and maintaining equipment. Worker exposure to the chemical at low 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.

Based on its hazard profile, the chemical is unlikely to pose a risk to workers. Information in this report can be used by a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) to determine the appropriate controls.

NICNAS Recommendation

The risk to workers and public from this chemical is not considered to be unreasonable. No recommendations or further assessment is required.

Regulatory Control

Public Health

No specific controls are required.

Work Health and Safety

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

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.

Advice for industry

Obligations under workplace health and safety legislation

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

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical is 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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