Trisiloxane, octamethyl-: Human health tier II assessment

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CAS Number: 107-51-7

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.

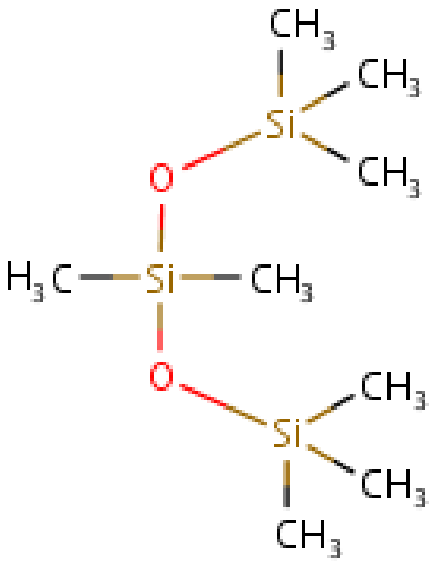
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	octamethyltrisiloxane trisiloxane, 1,1,1,3,3,5,5,5-octamethyl- pentamethyl(trimethylsiloxy)disiloxane L3 MDM
Structural Formula	
Molecular Formula	C8H24O2Si3
Molecular Weight (g/mol)	236.53
Appearance and Odour (where available)	liquid
SMILES	C[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; the Organisation for Economic Co-operation and Development (OECD) Screening information data set International Assessment Report (SIAR); Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; the US Department of Health and Human Services, Household Products Database (US HPD) and various international assessments (Health Canada, 2015).

The chemical is used in industrial products such as cleaning and degreasing products, lubricants, diluents and solvents, and in cosmetics including personal care products. The chemical may also be added in its pure form to cosmetics and may be present as an impurity as a result of polydimethylsiloxane (PDMS) processing (Health Canada, 2015).

The chemical has reported cosmetic use including:

- in antiperspirants and deodorants (in aerosol or gel forms at concentrations of 1–5 % as listed on the US HPD); and
- as anti-foaming and skin conditioning agents in body and hand preparations, colognes, eye lotions, eye makeup preparations, foundations, hair conditioners, and in indoor tanning preparations.

The chemical has reported domestic use including in:

- adhesives (binding agents);
- surface treatments and cleaning products; and
- paints, lacquers and varnishes.

The chemical has reported commercial use including:

- in petroleum oil anti-foaming agents;
- in construction materials;
- as a conductive agent;
- in solvents; and
- in lubricants and additives.

The chemical has reported site-limited use including:

- as an intermediate in the preparation of speciality chemicals including polydimethylsiloxane (PDMS) polymers, oligomers and mixtures as formulation components used in a range of industrial, medical and consumer products.

The chemical has reported non-industrial use as an excipient in therapeutics.

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 octamethyltrisiloxane (also known as L3 or MDM) is an organosilicon compound, substances containing an alternating silicon-oxygen backbone and a member of the volatile methyl siloxanes (VMS) group. The chemical is mainly used as an ingredient in the preparation of PDMS polymers or mixtures (Health Canada, 2015).

Acute Toxicity

Oral

The chemical has low acute oral toxicity based on the results from a guideline rat study (equivalent to OECD TG 423 (acute oral toxicity: Acute toxic class method)). The oral median lethal dose (LD50) was reported to be >2000 mg/kg bw in female Crl:CD Sprague-Dawley (SD) rats. No mortality or significant treatment-related effects were reported (OECD, 2010; Health Canada, 2015; REACH).

Dermal

The chemical has low acute dermal toxicity based on the results from a guideline rat study (equivalent to 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 (OECD, 2010; Health Canada, 2015; REACH).

Inhalation

The chemical has low acute inhalation toxicity based on the results from a guideline rat study (equivalent to OECD TG 403 (acute inhalation toxicity)). The median lethal concentration (LC50) was reported to be >22600 mg/m^3/4 hours (equivalent to >22.6 mg/L or 2350 ppm) in female and male Crl:CD SD rats following whole-body inhalation exposure to the chemical vapour. No mortality or significant treatment-related effects were reported (OECD, 2010; Health Canada, 2015; REACH).

Corrosion / Irritation

Skin Irritation

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

In a guideline study (EPA OPPTS 870.2500 (acute dermal irritation)), 0.5 mL of the undiluted chemical (as a liquid (>99.9 % purity)) was applied to the intact, clipped skin of 3 female New Zealand White (NZW) rabbits for 4 hours, under a semi-occlusive patch. Animals were observed at 60 minutes and at 24, 48, and 72 hours after patch removal. No treatment-related effects were reported. A primary irritation index (PII) score of 0 was reported (OECD, 2010; Health Canada, 2015; REACH).

In a study conducted similarly to OECD TG 404 (acute dermal irritation/corrosion), 0.5 mL of the undiluted chemical (unspecified purity) was applied to the shaved skin of NZW rabbits (3 animals/group) for 4 hours under semi-occlusive patches with a 4 day observation period (at 24, 48, and 72 hours) after patch removal. Erythema and oedema mean scores of 0 were reported (REACH).

Eye Irritation

No data are available.

Sensitisation

Skin Sensitisation

Based on the available animal and human data (refer to **Sensitisation: Observation in Humans** section), the chemical is not considered to be a skin sensitiser.

In a guinea pig maximisation test (GPMT) conducted according to OECD TG 406 (skin sensitisation), male and female IbM GOHI guinea pigs (10/dose) were intradermally induced with a 5 % (v/v) solution of the chemical in olive oil. The animals were topically induced with 100 % of the chemical 1 week later under occlusive conditions. A concentration of 50 % (in olive oil) was used in the topical challenge phase (occlusive epicutaneous application) 2 weeks after topical induction. Negative results for sensitisation were reported (0/10 animals had adverse reactions at 24 and 48 hours post-challenge) (REACH).

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.

Observation in humans

In a human patch test, 103 subjects (male and female) were exposed to the chemical on the infrascapular region of the back under semi-occlusive conditions. The induction phase consisted of nine consecutive patch applications of 0.2 mL of the undiluted chemical (unspecified purity) at the same site every 48 hours. Patch removal 24 hours post-exposure. After a 12 to 14 day rest period, the subjects were then challenged, using the same dose method described for the induction phase, on previously unexposed sites. At 24 and 48 hours following patch removal, no dermal responses were reported in subjects (OECD, 2010; Health Canada, 2015; REACH).

Repeated Dose Toxicity

Oral

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

In a repeat dose 28-day oral gavage study conducted according to OECD TG 407, the chemicals did not produce severe systemic toxicity in male and female SD rats (n = 5/sex/dose) following repeated oral exposure at doses of 0, 5, 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 and motor activity). Increased liver weight was reported in both sexes at doses ≥250 mg/kg bw/day. Hepatocellular hypertrophy and protoporphyrin accumulation with associated bile duct proliferation and periportal chronic inflammation was observed in males at the two highest doses and in females at the highest dose only. It was reported that after the 14 day recovery period, hepatocellular hypertrophy in the liver regressed; however, protoporphyrin accumulation and periportal chronic inflammation was still present in both sexes at the highest dose. An increase in incidence and severity of hyaline droplets and higher levels of alpha-2μ-globulin in the kidneys of male rats (not considered relevant to humans) was reported in males at doses ≥25 mg/kg bw/day. Hyaline deposits showed complete regression post recovery period. Thyroid follicular cell hypertrophy was reported at the highest dose for both sexes. No observed adverse effect levels (NOAEL) of 25 and 250 mg/kg bw/day were reported for males and females, respectively, based on liver and kidney effects (OECD, 2010; Health Canada, 2015; REACH).

Dermal

No data are available.

Inhalation

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

In a repeated dose 90-day inhalation toxicity study conducted according to OECD TG 413, SD rats (n = 10/sex/dose; except at the highest dose where n = 20/sex) were exposed (whole-body) vapour to the chemical at concentrations of 0, 95, 400 and 3200 ppm (equivalent to 0, 919, 3870 and 31000 mg/m^3) for 6 hours/day, 7 days/week. No treatment-related mortality, or effects on body weight, food consumption or motor activity were reported. Treatment-related effects at the two highest doses included changes to clinical parameters (increased cholesterol levels in males and females); increased liver weights (centrilobular hepatocellular hypertrophy in both sexes); and increased kidney weights (hyaline droplets and increased 2μ-globulin in males) which were considered adaptive changes that were reversible within the 28 day recovery period. The no observed adverse effect concentration (NOAEC) was reported to be 400 ppm for both sexes based on effects on the liver (accumulation of protoporphyrin pigment and associated periportal chronic inflammation, and bile duct proliferation at the highest dose) (Health Canada, 2015; REACH).

In a combined repeated dose/reproductive/developmental inhalation toxicity study (OECD TG 422) in male and female SD rats (refer to **Reproductive & Developmental Toxicity** section), no treatment-related mortality or effects on body weight, food consumption or motor activity were reported. The no observed adverse effect concentration (NOAEC) for systemic toxicity for the chemical was reported to be 7.74 mg/L (800 ppm) for females (based on increased serum cholesterol at higher concentrations and liver effects at all doses). No NOAEC could be established for males due to increased serum cholesterol and kidney effects at all doses. Histopathological findings included hyaline droplet nephropathy in the kidneys of male rats at all doses (consistent with alpha-2μ nephropathy which is not considered relevant to humans) and hepatic porphyria at the two highest doses. Adaptive changes including increased liver weights (accompanied by centrilobular hypertrophy) were reported in female rats at the 7.74 mg/L dose and in male rats exposed to the 31.0 mg/L dose (3200 ppm). Thyroid follicular hypertrophy was also reported in both sexes at the highest dose (OECD, 2010; Health Canada, 2015; REACH).

Genotoxicity

Whilst no in vivo data were available, based on the weight of evidence from in vitro studies, the chemical is not expected to be genotoxic.

In the following study summaries, several in vitro assays using the chemical gave mostly negative results (OECD, 2010; Health Canada, 2015; REACH):

- negative results in bacterial reverse mutation assays (in accordance to OECD TG 471) in *Salmonella typhimurium* strains TA 98, TA 100, TA1535 and 1537, with or without metabolic activation at concentrations up to 5000 µg/plate;
- negative results in bacterial reverse mutation assays (in accordance to OECD TG 471) in a strain of *Escherichia coli* (WP2uvrA), with or without metabolic activation, at concentrations up to 5000 µg/plate;
- negative results in chromosomal aberration assays (in accordance to OECD TG 473) in Chinese hamster ovary (CHO) cells, with or without metabolic activation, at concentrations up to 75 µg/mL; and
- mixed results in a mammalian cell gene mutation assay (study in accordance to OECD TG 476) in mouse lymphoma L5178Y (TK+/TK-) cells, with or without metabolic activation (concentrations unspecified) (Health Canada, 2015).

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

Carcinogenicity

No data are available for the chemical.

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

Reproductive and Developmental Toxicity

Based on the available data, the chemical is not expected to cause reproductive or developmental toxicity.

In a combined repeated dose/reproductive and developmental inhalation toxicity study (in accordance to OECD TG 422), SD rats (n = 10/sex/dose) were exposed (whole-body) to the chemical vapour for 6 hours/day, 7 days/week for 28 or 42 days (males treated 14 days prior to mating and 14 days after mating; females treated from 14 days prior to mating until gestation day 19). The animals were exposed to dose concentrations of 0, 7.74, 15.5 or 31.0 mg/L (0, 800, 1600 and 3200 ppm). No treatment-related adverse effects on reproductive or developmental parameters were reported up to the highest dose tested. A reproductive, maternal and developmental NOAEC of 31.0 mg/L (3200 ppm) was reported (OECD, 2010; Health Canada, 2015; REACH).

Risk Characterisation

Critical Health Effects

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

Public Risk Characterisation

In the absence of Australian use information, international uses indicate potential cosmetic and domestic uses (refer to **Import, Manufacture and Use** section). However, the chemical is most likely used as an intermediate and is not expected to be present in final consumer products, thus 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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