Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

Siloxanes substituted with 2-methoxyethanol

Evaluation statement

30 June 2022

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AICIS evaluation statement

Subject of the evaluation

Siloxanes substituted with 2-methoxyethanol

Chemicals in this evaluation

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2,5,7,10-Tetraoxa-6-silaundecane, 6-ethenyl-6-(2-methoxyethoxy)-	1067-53-4
2,5,7,10-Tetraoxa-6-silaundecane, 6-ethenyl-6-methyl-	45117-69-9
Silicic acid (H4SiO4), tetrakis(2-methoxyethyl) ester	2157-45-1
2,5,7,10-Tetraoxa-6-silaundecane, 6-(2-methoxyethoxy)-	5700-39-0

Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health risk.

Parameters of evaluation

These chemicals are listed on the Australian Inventory of Industrial Chemicals (the Inventory). This evaluation is a human health risk assessment for all identified industrial uses of these chemicals in Australia.

These chemicals have been assessed as a group as they are structurally related siloxanes that have a common metabolite (2-methoxyethanol). These chemicals are expected to have similar use patterns, and similar toxicity and bioavailability.

Summary of assessment/evaluation

Summary of introduction, use and end use

There is currently no specific information about the introduction, use and end use of these chemicals in Australia.

Based on international use information for tris(2-methoxyethoxy)vinylsilane (CAS No. 1067-53-4) and tetra(2-methoxyethoxy)silane (CAS No. 2157-45-1), these chemicals are expected to have commercial and site limited uses in paints and coatings, adhesives and sealants, construction materials, and plastics and rubber manufacture. Although some of these commercial products may be used in domestic settings, based on available information this is not expected to be widespread.

International use information indicates that tris(2-methoxyethoxy)vinylsilane may be used in food packaging applications. However, based on available information this is not expected to be widespread.

Tris(2-methoxyethoxy)vinylsilane has a reported global use in high volumes. No specific volume data are available for the other chemicals in this group.

Human health

Summary of health hazards

The critical health effects for risk characterisation include:

- adverse systemic long-term effects (reproductive effects).

The critical health effects for chemicals in this group were assessed based on data available for tris(2-methoxyethoxy)vinylsilane. The chemical represents all the toxicologically relevant features of chemicals in this group. The risk characterisation for systemic effects was further supported by data available on the common metabolite, 2-methoxyethanol, which is classified for reproductive toxicity in the Hazardous Chemical Information System (HCIS) (SWA).

Following repeated exposure to the chemical, the male reproductive organs appear to be the target organs for systemic toxicity. Effects on the thymus and haematopoietic system were also observed. Similar effects were observed in studies with the common metabolite, 2-methoxyethanol.

In a combined repeated dose reproduction/ developmental toxicity study in rats treated with tris(2-methoxyethoxy)vinylsilane, a no observed adverse effect level (NOAEL) of 25 mg/kg bw/day was reported for male and female reproductive toxicity, and 75 mg/kg bw/day for developmental toxicity. Observed effects included:

- histopathological changes in the testes and epididymides
- impairment of the spermatogenetic cycle
- increase in precoital time
- changes in gestational length
- reduced fertility
- increased resorptions, litter losses and reduced implantations.

Based on the available data these chemicals:

- have low acute and dermal toxicity
- are slight skin and eye irritants
- are not considered to be skin sensitisers
- are not considered to have genotoxic potential.

Hazard classifications relevant for worker health and safety

These chemicals satisfy the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for worker health and safety as follows. This does not consider classification of physical and environmental hazards.

Health hazards	Hazard category	Hazard statement
Reproductive toxicity	Repr. 1B	H360FD: May damage fertility. May damage the unborn child.

Summary of health risk

Public

Australian use data are not available for these chemicals and use patterns in Australia are assumed to be similar to those overseas. Based on the available international use information, it is unlikely that the public will be exposed to these chemicals. The public could come into contact with articles or coated surfaces containing these chemicals in reacted form. It is expected that these chemicals will be bound within articles and coated surfaces, and hence will not be bioavailable. Therefore, there are no identified risks to the public that require management.

Workers

During product formulation and packaging, incidental dermal, ocular and inhalation exposure may occur, particularly where manual or open processes are used. These processes include transferring, blending, quality control, cleaning and maintaining of equipment. During end use, worker exposure to these chemicals at lower concentrations may occur while using formulated products containing these chemicals. The level and route of exposure will vary depending on the method of application, control measures and work practices. Good hygiene practices to minimise incidental oral exposure are expected to be in place.

Given the critical systemic long term health effects, these chemicals may pose a risk to workers. Control measures to minimise exposure are needed to manage the risk to workers (see **Proposed means for managing risks** section).

Proposed means for managing risks

Workers

Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the HCIS to include classifications relevant to work health and safety.

Information relating to safe introduction and use

The information in this report includes recommended hazard classifications and should be used by a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) to determine the appropriate controls under the Model Work Health and Safety Regulations.

Control measures that can be implemented to manage the risk arising from exposure to these chemicals include, but are not limited to:

- using closed systems or isolating operations

- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker
- minimising manual processes or conducting work tasks through automated processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using personal protective equipment (PPE) that is designed, constructed, and operated to ensure that workers do not come into contact with the chemical.

Measures required to eliminate or manage risk arising from storing, handling, and using a hazardous chemical depend on the physical form and the manner in which the chemical is used.

These control measures may need to be supplemented with:

- conducting health monitoring for any worker who is at significant risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health.

The PPE should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures cannot eliminate or sufficiently minimise risk. Guidance in selecting PPE can be obtained from Australian, Australian/New Zealand or other approved standards.

Model codes of practice, available from the Safe Work Australia, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Conclusions

The conclusions of this evaluation are based on the information described in this statement.

Considering the proposed means of managing risks, the Executive Director is satisfied that the identified human health risks can be managed within existing risk management frameworks. This is provided that all requirements are met under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory and the proposed means of managing the risks identified during this evaluation are implemented.

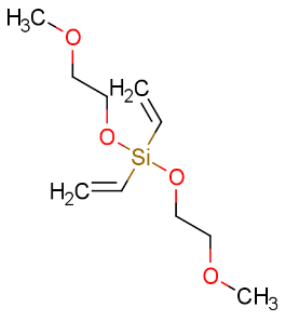
Note: Obligations to report additional information about hazards under *Section 100 of the Industrial Chemicals Act 2019* apply.

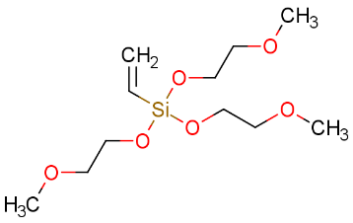
Supporting information

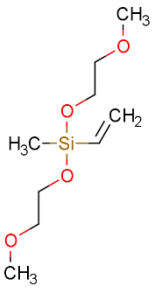
Grouping rationale / rationale

Siloxanes are saturated silicon-oxygen based substances with unbranched or branched chains of alternating silicon (Si) and oxygen (O) atoms (IUPAC). This chemical group consists of short chain linear siloxanes containing a single Si-O moiety substituted with two to four 2-methoxyethoxy groups. Chemicals in this group are expected to be metabolised in the body to 2-methoxyethanol and their corresponding silanol metabolites. Systemic toxicity in these chemicals is expected to be primarily driven by the 2-methoxyethanol moiety. While the lower molecular weight silanol metabolites have the potential to penetrate cellular membranes and bioaccumulate, there is limited evidence in literature of any systemic toxicity specifically attributed to this class of silanols (Mojsiewicz-Pieńkowska K et al. 2016). Three of these chemicals contain a reactive vinyl functional group including tris(2-methoxyethoxy)vinylsilane for which the majority of data are available. Overall data for this chemical is considered representative for all chemicals in this group.

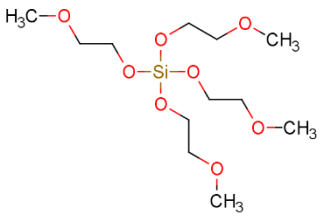
Chemical identity

Chemical name	2,5,7,10-Tetraoxa-6-silaundecane, 6,6-diethenyl-
CAS No.	17985-63-6
Synonyms	6,6-diethenyl-2,5,7,10-tetraoxa-6-silaundecane silane, bis(2-methoxyethoxy)divinyl- 6,6-divinyl-2,5,7,10-tetraoxa-6-silaundecane
Structural formula	
Molecular formula	C10H20O4Si
Molecular weight (g/mol)	232.35
SMILES	O(C)CCO[Si](OCCOC)(C=C)C=C
Chemical description	-

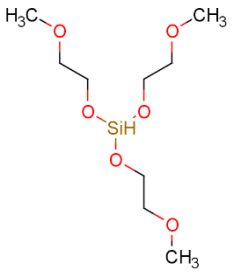
Chemical name	2,5,7,10-Tetraoxa-6-silaundecane, 6-ethenyl-6-(2-methoxyethoxy)-
CAS No.	1067-53-4
Synonyms	6-(2-methoxyethoxy)-6-vinyl-2,5,7,10-tetraoxa-6-silaundecane vinyltris(2-methoxyethoxy)silane ethenyl-tris(2-methoxyethoxy)silane tris(2-methoxyethoxy)vinylsilane Dynasylan VTMOEO
Structural formula	
Molecular formula	C11H24O6Si
Molecular weight (g/mol)	280.39
SMILES	O(C)CCO[Si](OCCOC)(OCCOC)C=C
Chemical description	Moisture-sensitive volatile liquid

Chemical name	2,5,7,10-Tetraoxa-6-silaundecane, 6-ethenyl-6-methyl-
CAS No.	45117-69-9
Synonyms	methylvinylbis(2-methoxyethoxy)silane 6-ethenyl-6-methyl-2,5,7,10-tetraoxa-6-silaundecane 6-methyl-6-vinyl-2,5,7,10-tetraoxa-6-silaundecane
Structural formula	
Molecular formula	C9H20O4Si

Molecular weight (g/mol)	220.34
SMILES	O(C)CCO[Si](OCCOC)(C=C)C
Chemical description	-

Chemical name	Silicic acid (H4SiO4), tetrakis(2-methoxyethyl) ester
CAS No.	2157-45-1
Synonyms	tetrakis(2-methoxyethoxy)silane tetra (2-methoxyethoxy) silane tetrakis(2-methoxyethyl) orthosilicate
Structural formula	
Molecular formula	C12H28O8Si
Molecular weight (g/mol)	328.43
SMILES	O(C)CCO[Si](OCCOC)(OCCOC)OCCOC
Chemical description	-

Chemical name	2,5,7,10-Tetraoxa-6-silaundecane, 6-(2-methoxyethoxy)-
CAS No.	5700-39-0
Synonyms	silane, tris(2-methoxyethoxy)- 6-(2-methoxyethoxy)-2,5,7,10-tetraoxa-6-silaundecane

Structural formula	
Molecular formula	C9H22O6Si
Molecular weight (g/mol)	254.35
SMILES	O(C)CCO[SiH](OCCOC)OCCOC
Chemical description	-

Relevant physical and chemical properties

Based on available data these chemicals are volatile liquids which hydrolyse rapidly when in contact with water or air moisture.

The following are physical and chemical properties reported for tris(2-methoxyethoxy)vinylsilane (CAS No. 1067-53-4).

Physical form	Liquid at 20°C and 1013 hPa
Melting point	-130°C
Boiling point	285°C
Vapour pressure	0.43 Pa at 25°C
Water solubility	71,000 mg/l at 20°C (QSAR)
Henry's law constant	-
Ionisable in the environment?	No
pKa	-
log K_{ow}	0.3 at 20°C (QSAR)

Introduction and use

Australia

No specific Australian information about the introduction, use and end use of these chemicals in Australia have been identified.

International

Commercial and site limited uses were reported for tris(2-methoxyethoxy)vinylsilane and tetra(2-methoxyethoxy)silane in paints and coatings, adhesives and sealants, construction materials, and plastics and rubber manufacture. The predominant reported functions are crosslinking agents and adhesion promoters (Chemwatch, OECD 2006; Pubchem; REACH; SPIN).

Some of these commercial products may also be used in domestic applications. There were no identified products containing these chemicals in North American consumer product databases (DeLima Associates). No consumer uses are registered under REACH and the Substances and Preparations in Nordic countries (SPIN) database for tris(2-methoxyethoxy)vinylsilane. Consumer preparations were identified in the SPIN database for tetra(2-methoxyethoxy)silane. However, it should be noted that SPIN does not distinguish between direct use of the chemical and use of the materials that are produced from chemical reactions involving the chemical.

Tris(2-methoxyethoxy)vinylsilane may be used in food packaging applications. Identified food contact materials include inks, silicones, and paper/board (Food Packaging Forum). However, this end use is not registered under the European Union (EU) list of authorised substances or listed on the United States Food and Drug Administration's USA FDA: Inventory of indirect additives used in food contact substances (REACH; US FDA).

Tris(2-methoxyethoxy)vinylsilane is listed on the Organisation for Economic Co-operation and Development (OECD) List of High Production Volume (HPV) Chemicals, US EPA High Production Volume Program Chemical List and it was registered under REACH with a tonnage range of > 1000 to < 10000 tonnes (Chemwatch; OECD 2006; REACH).

No use data are available for the other chemicals in this group.

Existing Australian regulatory controls

AICIS

No specific controls are currently available for these chemicals.

Public

No specific controls are currently available for these chemicals.

Workers

Chemicals in this group are not listed on the HCIS (SWA). No exposure standards are available for chemicals in this group in Australia (SWA).

International regulatory status

Exposure standards

No specific exposure standards were identified.

European Union

Tris(2-methoxyethoxy)vinylsilane is listed on the Candidate List of substances of very high concern (SVHC) for Authorisation for eventual inclusion in Annex XIV (ECHA). The reason for inclusion in the list is the chemical is considered 'toxic for reproduction (Article 57c)'. The inclusion in the Candidate List brings immediate obligations for suppliers of the substance in the EU, such as:

- supplying a safety data sheet
- communicating on safe use
- responding to consumer requests within 45 days
- notifying European Chemicals Agency (ECHA) if the article they produce contains an SVHC in quantities above one tonne per producer/importer per year and if the substance is present in in those articles above a concentration of 0.1% (w/w).

The chemical is also listed on the following (Chemwatch; ECHA; KEMI PRIO):

- ECHA's Regulatory Management Option Analysis (RMOA) – Toxic for reproduction (concluded)
- EU Cosmetic Products Regulation Annex II – List of substances prohibited in cosmetic products
- Netherlands SZW List Non-exhaustive list of reproductive toxins – Category 1B
- Swedish Chemical Agency's (KEMI) PRIO – list of phase-out substances (for meeting criteria for known or presumed human reproductive toxicants)

Health hazard information

Toxicokinetics

No in vivo data are available on toxicokinetics of these chemicals. Toxicokinetic properties of tris(2-methoxyethoxy)vinylsilane were inferred from validated predictions of physicochemical properties of the chemical and its hydrolysis products, and an in vitro guideline hydrolysis study (OECD Test Guideline (TG) 111) compliant with good laboratory practice (GLP) (REACH, ECHA 2018, OECD 2006). These data show that the chemical undergoes rapid hydrolysis at physiological pH values to form 2-methoxyethanol (CAS No. 109-86-4) and vinylsilanetriol (CAS No. 143-48-6). Methoxyethanol is expected to be subsequently oxidised to methoxyacetic acid (NICNAS 2014). Structure activity relationship analysis suggests there may also be other metabolic pathways available for this chemical (ECHA 2018).

Human exposure to these chemicals is expected to be mainly through dermal and inhalation routes. While no specific toxicokinetic studies are available for these chemicals, they are expected to be bioavailable following oral, dermal and inhalation exposure based on the molecular weights (220–330 g/mol) and predicted log K_{ow} value (0.3). Hydrolysis prior to absorption is also likely. The bioavailability is supported by observations of effects following oral exposure. Once absorbed into the body these chemicals would be hydrolysed and the

hydrolysis products would likely be widely distributed in the blood. Toxicity studies provide evidence for distribution of the metabolite, 2-methoxyethanol to the lymphoid tissue and the developing foetus (NICNAS 2014). Because of their high water solubility and low molecular weight, the chemical and its hydrolysis products are likely to be excreted by the kidneys into urine.

Acute toxicity

Oral

Available data for tris(2-methoxyethoxy)vinylsilane indicate that chemicals in this group have low oral acute toxicity (median lethal dose (LD50) >2000 mg/kg bw).

An oral LD50 of greater than 2000 mg/kg bw was determined for tris(2-methoxyethoxy)vinylsilane in rats in a GLP compliant, guideline acute oral toxicity study (OECD TG 401) (OECD 2006; REACH). Clinical signs included abnormal excretion, hypoactivity and tremors. Autopsy findings included gastrointestinal and liver abnormalities, slight congestion of the lungs and adrenals, and pale kidneys.

Dermal

Available data for tris(2-methoxyethoxy)vinylsilane indicate that chemicals in this group have low dermal acute toxicity (dermal LD50 >2000 mg/kg bw).

A dermal LD50 of greater than 2000 mg/kg bw was determined for tris(2-methoxyethoxy)vinylsilane in rats in a GLP compliant, guideline acute dermal toxicity study (OECD TG 402) (OECD 2006; REACH). The only notable adverse reaction was sporadic peeling of skin (desquamation) observed in some of the treated rats.

An older acute dermal toxicity study in rabbits reported an LD50 of 1.5mL/kg (equivalent to 1545 mg/kg) (REACH). However, since the study was not conducted according to standard guidelines it was not considered reliable for assessing acute dermal toxicity of the chemical.

Inhalation

No data are available for these chemicals.

Corrosion/Irritation

Skin irritation

Available data for tris(2-methoxyethoxy)vinylsilane indicate that chemicals in this group may be at most slightly irritating to skin.

Tris(2-methoxyethoxy)vinylsilane applied undiluted was found to be slightly irritating to rabbit skin in a GLP compliant, guideline acute dermal irritation study (OECD TG 404) (OECD 2006; REACH). The only adverse reaction observed was very slight reddening of skin (erythema) in one of the 3 test animals at 48 and 72 hours following chemical application. No oedema was noted in any animal. A primary irritation index score of 0.2 was reported in this study.

Eye irritation

Available data for tris(2-methoxyethoxy)vinylsilane indicate that chemicals in this group may be at most slightly irritating to eyes.

Tris(2-methoxyethoxy)vinylsilane applied undiluted was found to be slightly irritating to rabbit eyes in a GLP compliant, guideline acute eye irritation study (OECD TG 405) (OECD 2006; REACH). Corneal opacity and iritis were not observed in any animal. Conjunctival irritation and redness were noted in all 3 test animals. Both effects fully reversed in all animals within 48 to 72 hours. Individual mean scores following grading at 24, 48 and 72 hours were not available. Overall mean scores were 2.7, 2.0, 1.3 and 0.0 at one, 24, 48 and 72 hours respectively.

Sensitisation

Skin sensitisation

Based on limited available data for tris(2-methoxyethoxy)vinylsilane, chemicals in this group are not expected to be skin sensitisers.

In a GLP compliant, in vivo guideline study for skin sensitisation (OECD TG 406, Buehler test) with tris(2-methoxyethoxy)vinylsilane, 20 male Dunkin-Hartley guinea pigs were induced with three epidermal applications of undiluted test chemical. No adverse reactions were observed following challenge with epidermal application of 1% test chemical. The chemical was reported to be non-sensitising in this study (REACH).

Repeat dose toxicity

Oral

Based on the available data tris(2-methoxyethoxy)vinylsilane, the male reproductive organs appear to be the target organs for systemic toxicity (see **Reproductive and developmental toxicity** section). Effects on the thymus and haematopoietic system were also observed. Similar effects were observed in studies with the common metabolite 2-methoxyethanol (NICNAS 2014).

In a GLP compliant, combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test conducted similarly to OECD TG 422, tris(2-methoxyethoxy)vinylsilane was administered via oral gavage to Crl:CD(SD) rats in groups of 10/sex/dose at 0, 25, 75 or 250 mg/kg bw/day. Animals of both sexes were treated with the chemical for 14 days prior to mating and throughout mating. In females, treatment continued through to gestation and up to day 3 of lactation. No animal deaths were seen in any of the treatment groups. The following treatment-related adverse effects were reported (ECHA 2018; OECD 2006; REACH):

- Decreased body weights, body weight gains and food consumption were observed in males dosed at 250 mg/kg bw/day.
- Effects on thymus and haematopoietic system: Decreased mean red blood cell counts, haemoglobin levels, granulocyte counts, platelet counts, and increased monocyte counts were observed in both sexes dosed at 250 mg/kg bw/day. A combined assessment of the blood count data and bone marrow histopathology suggested that the decreased myeloid:erythroid ratio (ratio of bone marrow cells to red blood cells) may have resulted from a disproportionate mild suppression of both the myeloid and erythroid elements

rather than erythroid hyperplasia. However, ineffective erythropoiesis (formation of red blood cells) or an early regenerative response could not be excluded. Mean absolute and relative thymus weights were reduced in both sexes dosed at 250 mg/kg bw/day, correlating with microscopic findings of lymphoid depletion in the lymph nodes. Adhesion and/or white areas on the spleen corresponding with capsular fibrosis were observed in males dosed at 75 and 250 mg/kg bw/day, and in females dosed at 250 mg/kg bw/day. Mean absolute and relative adrenal weights were observed in males dosed at 250 mg/kg bw/day and in all toxicity phase females (but not in gestation phase), but no microscopic observations were reported to correlate with these findings.
- Effects on the male reproductive system were reported in the 75 and 250 mg/kg bw/day dose groups (see **Reproductive and developmental toxicity** section).

Based on the above effects, a NOAEL of 25 mg/kg bw/day was determined for male systemic toxicity and 75 mg/kg bw/day for female systemic toxicity.

Repeat dose oral toxicity studies with metabolite, 2-methoxyethanol reported similar adverse effects in the thymus, testes, blood and haematopoietic systems in rats, mice, rabbits, and dogs (NICNAS 2014). These studies reported a lowest observed adverse effect level (LOAEL) of 71 mg/kg bw/day for 2-methoxyethanol (NICNAS 2014).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on available in vitro data for tris(2-methoxyethoxy)vinylsilane, chemicals in this group are not considered to have any genotoxic potential.

Tris(2-methoxyethoxy)vinylsilane was reported not to be genotoxic in the following in vitro studies (ECHA 2018; OECD 2006; REACH):

- Bacterial reverse mutation assay (Ames test) (OECD TG 471, GLP compliant) – the chemical did not induce mutations in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and *Escherichia coli* strain WP2uvrA at concentrations up to 5000 µg/plate, with or without metabolic activation.
- Mammalian chromosomal aberration study (OECD TG 473, GLP compliant) – the chemical did not induce chromosomal aberrations in Chinese hamster ovary cells with or without metabolic activation up to a concentration of 2801µg/mL.
- Mammalian cell gene mutation study (OECD TG 476, GLP compliant) – the chemical did not induce gene mutations in L5178Y mouse lymphoma cells with or without metabolic activation up to a concentration of 3000 µg/mL.

The metabolite 2-methoxyethanol is considered to have, at most, weak genotoxic potential (NICNAS 2014).

Carcinogenicity

No data are available to evaluate this hazard endpoint. The metabolites 2-methoxyethanol is not expected to be carcinogenic (NICNAS 2014).

Reproductive and development toxicity

Available data for tris(2-methoxyethoxy)vinylsilane and the metabolite, 2-methoxyethanol indicate that chemicals in this group can cause significant reproductive and developmental toxicity on repeated exposure, warranting hazard classification.

In a GLP compliant, guideline study conducted similarly to OECD TG 422 with tris(2-methoxyethoxy)vinylsilane (see **Repeat dose toxicity – Oral** section), the following adverse effects on reproduction and development were reported (ECHA 2018; OECD 2006; REACH):

- Reproductive toxicity in males: Decreased male fertility rates corresponding with decreased organ weights were seen in animals dosed at 250 mg/kg bw/day. Small and/or soft testes and/or epididymides correlating with reduced mean absolute and relative organ weights, and degeneration of seminiferous tubules were observed in the 250 mg/kg bw/day group males. Secondary to the loss of spermatogenesis in the testes was hypospermia and luminal cellular debris in the epididymis, correlating with macroscopic findings. Mean absolute and relative prostate weights were reduced in the 75 and 250 mg/kg bw/day group males, correlating with microscopic findings of decreased secretion and/or atrophy. Mean absolute and relative seminal vesicle weights were reduced in the 250 mg/kg bw/day group males but these observations were not supported by microscopic findings.
- Reproductive toxicity in females: Female fertility rates and mean gestation body weight gains (attributed to resorbed litters) were reduced in females dosed at 250 mg/kg bw/day. The mean number of days between pairing and coitus was increased. Gestational length was increased in females in the 75 mg/kg bw/day dose group and in one female in the 250 mg/kg bw/day dose group. Reduced mean litter size was seen in the 75 mg/kg bw/day dose group.
- Developmental toxicity: Increased litter resorption was seen in females dosed at 75 and 250 mg/kg bw/day. Although these effects were considered chemically related in both the dose groups, this increase was found to be statistically significant only in the highest dose group. Resorbed litters may have been linked to reproductive effects in the dams or in the male parent animals or may indicate specific developmental effects.

The study clearly demonstrated that reproductive effects occurred below systemic toxicity levels. Based on the above effects, a NOAEL of 25 mg/kg bw/day was reported for male and female reproductive toxicity, and 75 mg/kg bw/day for developmental toxicity. A NOAEL for teratogenicity was reported to be ≥75 mg/kg bw/day since a role for developmental toxicity in the reduced postnatal survival at this dose could not be excluded.

The common metabolite 2-methoxyethanol is classified as a reproductive and developmental toxin (SWA). Systemic toxicity data for 2-methoxyethanol show similar effects on the male reproductive system and effects on pup viability as those seen for tris(2-methoxyethoxy)vinylsilane (ECHA 2018; NICNAS 2014).

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