Australian Government
Department of Health, Disability and Ageing
Australian Industrial Chemicals Introduction Scheme

2-Butanone oxime (MEKO)-releasing silanes

Evaluation statement (EVA00181)

26 June 2025

Table of contents

Contents

AICIS evaluation statement (EVA00181)

Subject of the evaluation

2-Butanone oxime (MEKO)-releasing silanes

Chemicals in this evaluation

CAS name	CAS number
2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(ethenylsilylidyne)trioxime]	2224-33-1
2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(methylsilylidyne)trioxime]	22984-54-9
2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(phenylsilylidyne)trioxime]	34036-80-1
2-Butanone, 2,2′,2″,2‴-(*O*,*O*′,*O*″,*O*‴-silanetetrayltetraoxime)	34206-40-1
2-Butanone, *O*,*O*′-(dimethylsilylene)dioxime	37843-26-8
2-Butanone, *O*,*O*′-(methylphenylsilylene)dioxime	69373-66-6
2-Butanone, 2,2′-[*O*,*O*′-(methoxymethylsilylene)dioxime]	83817-72-5
2-Butanone, 2,2′-[*O*,*O*′-(diethoxysilylene)dioxime]	93917-75-0
2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(ethoxysilylidyne)trioxime]	101371-00-0

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 of all identified industrial uses of these chemicals in Australia.

These chemicals have been assessed as a group as they all release 2-butanone, oxime (also known as methyl ethyl ketoxime (MEKO), CAS No. 96-29-7) in contact with water. The release of MEKO is expected to drive toxic effects.

The chemical, 2-butanone, 2,2′,2″-[*O*,*O*′,*O*″-(phenylsilylidyne)trioxime] (CAS No. 34036-80-1), was assessed as a new industrial chemical under section 23 of the *Industrial Chemicals (Notification and Assessment) Act 1989* (ICNA Act). This chemical is being reassessed as new hazards have been identified including for the hydrolysis product MEKO.

As a group, these chemicals can be referred to as ‘oximino silanes’ or ’oxime silanes’. In this evaluation, the group will be referred to as ‘MEKO silanes’. For clarity, specific members of the group will be referred to using the following names:

- Vinyltris(MEKO)silane for CAS No. 2224-33-1
- Methyltris(MEKO)silane for CAS No. 22984-54-9
- Phenyltris(MEKO)silane for CAS No. 34036-80-1
- Tetrakis(MEKO)silane for CAS No. 34206-40-1
- Dimethylbis(MEKO)silane for CAS No. 37843-26-8.

Summary of evaluation

Summary of introduction, use and end use

There is currently limited information about the introduction, use and end use of these chemicals in Australia. Based on Australian information, phenyltris(MEKO)silane has domestic use in adhesives and sealants at concentrations up to 10%. Available local safety data sheet (SDS) information also indicates the use of a number of these chemicals in adhesive and sealant products in Australia at concentrations up to 10%. These chemicals may be used alone or in combination with each other or MEKO in sealant products.

Based on international use information, these chemicals are primarily used in adhesive and sealant products for domestic and professional use. Typical use concentrations in sealants are less than 10% but may be as high as 30%. These chemicals also have identified use in some automotive care products including gasket makers.

Human health

Summary of health hazards

The identified health hazards are based on the available data for 4 chemicals; vinyltris(MEKO)silane, methyltris(MEKO)silane, phenyltris(MEKO)silane and dimethylbis(MEKO)silane.

Their physicochemical properties and available toxicity data indicate that these chemicals metabolise to form MEKO (CAS No. 96-29-7). In addition, MEKO is a major decomposition product of these chemicals in the presence of moisture. Moisture in the atmosphere or on the surface of the skin is sufficient to initiate this hydrolysis. Where necessary, hazard data on MEKO was used to support hazard conclusions.

Based on the available data, these chemicals:

- have low acute oral and dermal toxicity
- are at most slightly irritating to skin
- are not expected to have genotoxic potential
- are not expected to cause specific adverse effects on fertility/sexual function or foetal development.

The MEKO silanes are expected to cause narcotic effects and adverse effects on the blood system after single exposures, based on observations from acute oral toxicity studies in rats.

Observations of narcosis were characterised by decreased activity, ataxia, ptosis and prostration. These adverse effects generally cleared within 24 hours. The no-observed effect level (NOEL) for narcosis was between 100 and 300 mg/kg body weight (bw).

Dose related effects on the blood system included decreased red blood cell (RBC) counts, increased methaemoglobin and histopathological changes in the spleen. Based on these observations, these chemicals are considered to be methaemoglobin inducers, which cause regenerative anaemia (methaemoglobinaemia) after single doses including doses lower than 300 mg/kg bw. An increase in haemosiderosis in the spleen in combination with other changes indicated significant haemolytic anaemia.

Based on the available data, most chemicals in this group are expected to be irritating to eyes; however, the extent and severity of the effects differs within the group. Most available guideline studies (Organisation for Economic Cooperation and Development (OECD) Test Guideline (TG) 405) demonstrate signs of reversible effects on rabbit eyes, particularly on corneal opacity (scores greater than 1/4). Effects on corneal opacity persisted 21 days after exposure to vinyltris(MEKO)silane in some animals, suggesting that it can cause eye damage. Phenyltris(MEKO)silane was not irritating to rabbit eyes in an OECD guideline study.

These chemicals are expected to be skin sensitisers based on positive results in guideline guinea pig maximisation tests (GPMT) (OECD TG 406). Intradermal induction at concentrations of 1–5% resulted in responses in at least 40% of the animals during challenge.

Adverse effects on the blood system were observed in guideline repeated dose oral toxicity studies of these chemicals. The observed effects were similar to those observed after acute exposures. As the effects occurred at similar doses causing effects after single exposures, hazard classification for repeated dose toxicity is not warranted. Other adverse effects on the liver and kidneys were observed at high doses that do not warrant hazard classification.

There is no data on the carcinogenic potential of these chemicals. The main metabolite MEKO is considered to be carcinogenic based on the increased incidence of liver tumours in rats and mice following chronic inhalation exposures. Based on the read across to the metabolite MEKO but considering differences in physicochemical properties, chemicals in this group are suspected to have carcinogenic potential, warranting hazard classification. A harmonised GHS classification for these chemicals is under consideration in Europe. If further information supporting a different classification becomes available as part of this process, a future AICIS evaluation of the carcinogenicity classification may be required.

No inhalation data are available for these chemicals. MEKO silanes are significantly less volatile compared to MEKO. Inhalation is not expected to be a significant exposure pathway to the MEKO silanes themselves. However, MEKO is a major decomposition product of these chemicals in the presence of moisture. MEKO causes damage to the nasal epithelium after short term oral and inhalation exposures. The lowest adverse effect concentration (LOAEC) for these effects after short term exposures to MEKO was 108 mg/m^3. Although data are not sufficient to read across this classification for specific target organ toxicity (single exposure) to these chemicals, effects on the nasal epithelium would be expected if sufficient exposure to MEKO as a decomposition product occurs.

For further details of the health hazard information, see **Supporting information**.

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 evaluation does not consider classification of physical hazards and environmental hazards.

Health hazards	Hazard category	Hazard statement
Skin sensitisation	Skin Sens. 1	H317: May cause an allergic skin reaction
Serious eye damage/eye irritation	Eye Damage 1	H318: Causes serious eye damage
Serious eye damage/eye irritation	Eye Irrit. 2A	H319: Causes serious eye irritation
Specific target organ toxicity (single exposure)	STOT Single Exp. 3	H336: May cause drowsiness or dizziness
Specific target organ toxicity (single exposure)	STOT Single Exp. 1	H370: Causes damage to organs – blood system
Carcinogenicity	Carc. 2	H351: Suspected of causing cancer

For these hazard classifications, note that:

- The Eye Damage 1 classification only applies to 2-butanone, 2,2′,2″-[*O*,*O*′,*O*″-(ethenylsilylidyne)trioxime] (CAS No. 2224-33-1).
- 2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(phenylsilylidyne)trioxime] (CAS No. 34036-80-1) should not have a classification for eye damage or eye irritation.
- 2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(phenylsilylidyne)trioxime] (CAS No. 34036-80-1) is classified on the HCIS with hazard category “Specific target organ toxicity (repeat exposure)” with hazard statement “H373: May cause damage to organs through prolonged or repeated exposure” (SWA n.d.). Based on the proposed STOT-SE classification for this chemical, it is recommended that the classification for repeated exposure is removed.

Summary of health risk

Public

Based on the available use information, the public may be exposed to the MEKO silanes in sealants and adhesives. These chemicals are included at concentrations up to 10% individually. Multiple chemicals were often included in the same sealant products. Exposures are expected to be infrequent and occur by incidental skin contact during the use of domestic adhesive and sealant products that contain these chemicals. Inhalation of the decomposition product MEKO is also expected during end use of these products.

Due to infrequent domestic use of the sealants the critical health effects for the public are expected to be acute or short term effects.

The critical health risk for dermal exposure is skin sensitisation. Based on the infrequent use of these chemicals in domestic applications and incidental nature of skin contact, the risk of skin sensitisation in the public is expected to be low.

When used in silicone sealants, these chemicals are expected to decompose during the curing process and release the volatile MEKO molecule. Inhalation of released MEKO is expected to be the scenario with the highest public health risk. For inhalation exposure to volatile MEKO, the critical health effect is damage to the respiratory tract after short term exposures. Using the LOAEC for acute systemic toxicity (108 mg/m^3), the margin of exposure (MOE) levels for the use of MEKO in sealants with low and high ventilation are < 10 and 40–60, respectively.

Although there are a number of uncertainties for this type of exposure, the risk estimates indicate that there is a risk to the public that requires management. The significant difference in MOEs between low and high ventilation scenarios indicates that high ventilation rates significantly reduce the concentrations of MEKO in the air. Therefore, use of adequate ventilation would reduce exposure and; hence, minimise the risk to the public. The risk could be managed by listing these chemicals in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).

Workers

During product formulation and packaging, dermal and ocular exposure to the MEKO silanes 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 these chemicals at lower concentrations could also occur while using formulated products containing these chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic and local health effects from dermal and ocular exposure routes, these chemicals could pose a risk to workers.

In addition, when used in silicone sealants these chemicals are expected to decompose during the curing process and release the volatile MEKO molecule.

Overall control measures to minimise dermal, ocular and inhalation exposure are needed to manage the risk to workers (refer to **Proposed means of managing risk** section).

Workers who frequently use silicone sealants during construction indoors with low ventilation are at the highest risk of adverse acute effects on the nasal epithelium and blood systems. AICIS recently recommended that Safe Work Australia consider establishing a workplace exposure standard for the metabolite MEKO (AICIS 2023). The introduction of a workplace exposure standard would result in monitoring for airborne concentrations of MEKO. Therefore, this existing recommendation for workers should sufficiently protect workers from the acute health risks for these chemicals due to inhalation exposures. These measures would also be protective of long term systemic toxicity effects.

Proposed means for managing risk

Inventory listing

The specific requirement to provide information as a term of the Inventory listing for 2-butanone, 2,2′,2″-[*O*,*O*′,*O*″-(phenylsilylidyne)trioxime] (CAS No. 34036-80-1) should be varied under section 86 of the *Industrial Chemicals Act 2019* (IC Act) to align the specific information requirement with the risk identified and considered in this evaluation statement as follows:

Term of listing	Details
Specific requirements to provide information to the Executive Director under section 101 of the IC Act	Obligations to provide information apply. You must tell the Executive Director the volume of introduction, use and end use of the chemical within 20 working days if: • The end use of the chemical has changed or is likely to change from: ○ Adhesives and sealants. • The amount of the chemical being introduced has increased from 100 tonnes. • The chemical has begun to be manufactured in Australia. • Information has become available to the person as to an adverse effect of the chemical on the environment.

Public health

Recommendation to Department of Health and Aged Care

It is recommended that the delegate of the Secretary for Poisons Scheduling lists these chemicals in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).

It is recommended that to manage the potential risk associated with the use of these chemicals:

- the entry results in labelling that provides safety directions to use in a well-ventilated area
- considers concentration exemptions that align with restrictions for the main metabolite, methyl ethyl ketone oxime (MEKO).

Consideration should be given to the following:

- the likely widespread use of these chemicals in sealant and adhesive products in Australia
- these chemicals may be used alone or in combination with each other or MEKO in sealant products
- these chemicals rapidly break down and produce MEKO which is listed in the SUSMP
- exposure to these chemicals (or break down product) causes severe effects to the respiratory and blood systems after acute or short-term exposures
- these chemicals are skin sensitisers.

Workers

Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the Hazardous Chemical Information System (HCIS) to include classifications relevant to work health and safety (see **Summary of health hazards** section).

No specific recommendation regarding an exposure standard is required for these chemicals; however, release exposures to MEKO from use of these chemicals should be considered by Safe Work Australis as part of any considerations for establishing the workplace exposure standard for MEKO.

Information relating to safe introduction and use

The information in this statement including recommended hazard classifications, should be used by a person conducting a business or undertaking at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

Control measures that could be implemented to manage the risk arising from oral, dermal, ocular and inhalation exposure to these chemicals include, but are not limited to:

- using closed systems or isolating operations
- using local exhaust ventilation to prevent the decomposition product MEKO from entering the breathing zone of any worker
- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with these chemicals.

Measures required to eliminate, or manage risk arising from storing, handling and using these hazardous chemicals depend on the physical form and how these chemicals are used.

These control measures may need to be supplemented with:

- conducting health monitoring for any worker who is at significant risk of exposure to these chemicals, if valid techniques are available to monitor the effect on the worker's health
- conducting air monitoring to ensure control measures in place are working effectively and continue to do so.

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.

Model codes of practice, available from the Safe Work Australia website, 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 Executive Director is satisfied that the identified risks to human health from the introduction and use of the industrial chemicals can be managed.

The specific requirement to provide information as a term of the Inventory listing under section 101 of the IC Act assists with managing the risks from introduction of chemicals. The information currently required to be provided for 2-butanone, 2,2′,2″-[*O*,*O*′,*O*″-(phenylsilylidyne)trioxime] (CAS No. 34036-80-1) is no longer aligned with the risks identified in this evaluation statement. Therefore, a variation to the specific requirement to provide information as a term of the Inventory listing is necessary to manage the risks from introduction of the chemical (see **Proposed means of managing risk**). As this evaluation does not consider environmental risks current information requirements relevant to environmental risks have been maintained.

Note:

1. Obligations to report additional information about hazards under section 100 and to provide any information specifically required by the terms of the Inventory listing under section 101 of the IC Act apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

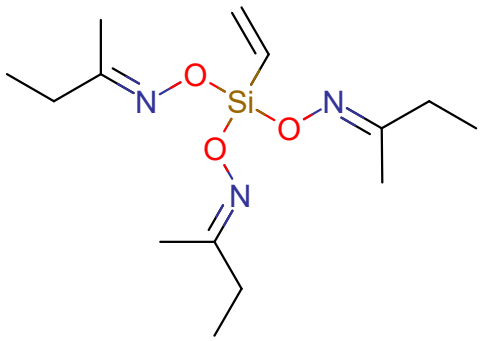
Supporting information

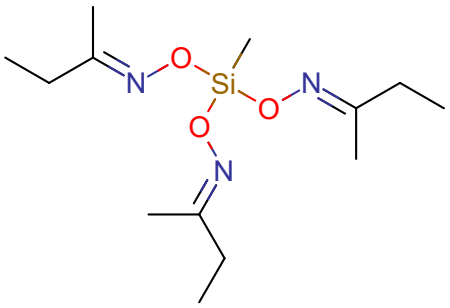
Grouping rationale

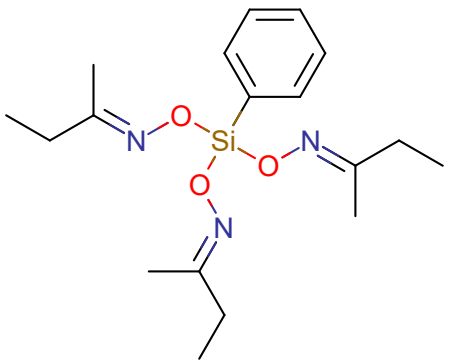
The 9 chemicals in this evaluation were grouped together as they all contain 2-butanone, oxime (also known as methyl ethyl ketoxime or MEKO). These chemicals are alkoxysilanes which have 2, 3 or 4 MEKO groups attached to the silicon atom. These chemicals may also contain a combination of vinyl, methyl, phenyl, methoxy and/or ethoxy groups attached to the silicon. The molecular weights of these chemicals range between 230 and 372 g/mol. These chemicals are expected to have similar physicochemical properties, reactivity and toxicological effects.

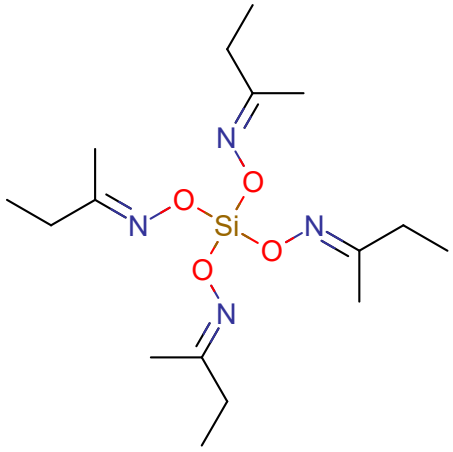
The chemical phenyltris(MEKO)silane was assessed as a new industrial chemical under section 23 of the *Industrial Chemicals (Notification and Assessment) Act 1989* (ICNA Act). This chemical is being reassessed as new hazards have been identified, including for the hydrolysis product MEKO.

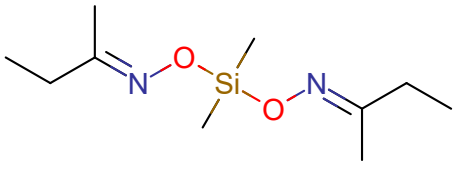
Chemical identity

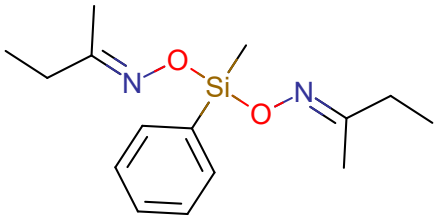
CAS number	2224-33-1
CAS name	2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(ethenylsilylidyne)trioxime]
Molecular formula	$C_{14}H_{27}N_3O_3Si$
Associated names	Butan-2-one *O*,*O*',*O*''-(vinylsilylidyne)trioxime Vinyltris(methylethylketoximino)silane Vinyl oximino silane (VOS)
Molecular weight (g/mol)	313.47
SMILES (canonical)	N(O[Si](ON=C(C)CC)(ON=C(C)CC)C=C)=C(C)CC
Structural formula	

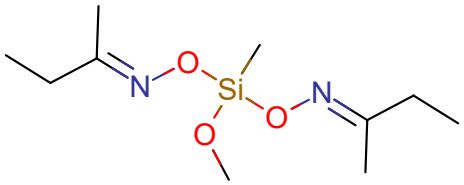
CAS number	22984-54-9
CAS name	2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(methylsilylidyne)trioxime]
Molecular formula	$C_{13}H_{27}N_3O_3Si$
Associated names	Methyltris(methylethylketoxime)silane Methyl oximino silane (MOS)
Molecular weight (g/mol)	301.46
SMILES (canonical)	N(O[Si](ON=C(C)CC)(ON=C(C)CC)C)=C(C)CC
Structural formula	

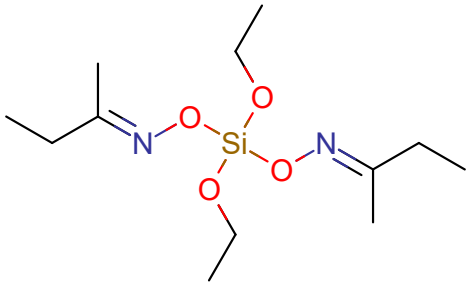
CAS number	34036-80-1
CAS name	2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(phenylsilylidyne)trioxime]
Molecular formula	$C_{18}H_{29}N_3O_3Si$
Associated names	Phenyl(methylethylketoxime)silane
Molecular weight (g/mol)	363.53
SMILES (canonical)	N(O[Si](ON=C(C)CC)(ON=C(C)CC)C=1C=CC=CC1)=C(C)CC
Structural formula	

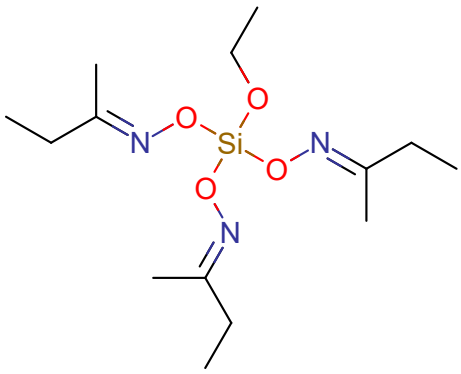
CAS number	34206-40-1
CAS name	2-Butanone, 2,2′,2″,2‴-(*O*,*O*′,*O*″,*O*‴-silanetetrayltetraoxime)
Molecular formula	$C_{16}H_{32}N_4O_4Si$
Associated names	Tetrakis(methylethylketoximino)silane
Molecular weight (g/mol)	372.54
SMILES (canonical)	N(O[Si](ON=C(C)CC)(ON=C(C)CC)ON=C(C)CC)=C(C)CC
Structural formula	

CAS number	37843-26-8
CAS name	2-Butanone, *O*,*O*′-(dimethylsilylene)dioxime
Molecular formula	$C_{10}H_{22}N_2O_2Si$
Associated names	Dimethylbis(methylethylketoxime)silane
Molecular weight (g/mol)	230.38
SMILES (canonical)	N(O[Si](ON=C(C)CC)(C)C)=C(C)CC
Structural formula	

CAS number	69373-66-6
CAS name	2-Butanone, *O*,*O*′-(methylphenylsilylene)dioxime
Molecular formula	$C_{15}H_{24}N_2O_2Si$
Associated names	Methylphenyldibutanoximesilane
Molecular weight (g/mol)	292.45
SMILES (canonical)	N(O[Si](ON=C(C)CC)(C=1C=CC=CC1)C)=C(C)CC
Structural formula	

CAS number	83817-72-5
CAS name	2-Butanone, 2,2′-[*O*,*O*′-(methoxymethylsilylene)dioxime]
Molecular formula	$C_{10}H_{22}N_2O_3Si$
Associated names	Bis(ethylmethylketoxime)methoxymethylsilane
Molecular weight (g/mol)	246.38
SMILES (canonical)	N(O[Si](ON=C(C)CC)(OC)C)=C(C)CC
Structural formula	

CAS number	93917-75-0
CAS name	2-Butanone, 2,2′-[*O*,*O*′-(diethoxysilylene)dioxime]
Molecular formula	$C_{12}H_{26}N_2O_4Si$
Associated names	Diethoxybis(ethylmethylketoximo)silane
Molecular weight (g/mol)	290.43
SMILES (canonical)	N(O[Si](ON=C(C)CC)(OCC)OCC)=C(C)CC
Structural formula	

CAS number	101371-00-0
CAS name	2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(ethoxysilylidyne)trioxime]
Molecular formula	$C_{14}H_{29}N_3O_4Si$
Associated names	Ethoxytris(ethylmethylketoximo)silane
Molecular weight (g/mol)	331.48
SMILES (canonical)	N(O[Si](ON=C(C)CC)(ON=C(C)CC)OCC)=C(C)CC
Structural formula	

Relevant physical and chemical properties

All chemicals in this group hydrolyse in contact with water and release MEKO. The hydrolysis of the MEKO silanes occurs rapidly. The half-lives of methyltris(MEKO)silane in water at 2°C and pH 4, 7 or 9 are less than 0.4, 1 and 0.8 minutes, respectively (OECD 2009). The rapid hydrolysis precludes measurement of some physical and chemical properties.

The amount of MEKO produced is proportional to the number of MEKO groups on the alkoxysilane:

- 2 equivalents of MEKO are produced for the difunctional MEKO silanes (CAS No. 37843-26-8; 69373-66-6; 83817-72-5 and 93917-75-0)
- 3 equivalents of MEKO are produced for the trifunctional MEKO silanes (CAS No. 2224-33-1; 22984-54-9; 34036-80-1 and 101371-00-0)
- 4 equivalents of MEKO are produced for the tetrafunctional MEKO silane (CAS No. 34206-40-1).

Measured vapour pressures are 0.016, 0.003 and 0.07 Pa for vinyltris(MEKO)silane at 20°C, phenyltris(MEKO)silane at 25°C and methyltris(MEKO)silane at 20°C, respectively (REACH n.d.-a; REACH n.d.-b; REACH n.d.-c). Therefore, the MEKO silanes are expected to be at least 3 orders of magnitude less volatile than the MEKO molecule, which has measured vapour pressures of 140–1070 Pa at 20°C (AICIS 2023).

Introduction and use

Australia

There is limited specific information about the introduction, use and end use of these chemicals in Australia.

Based on Australian information, phenyltris(MEKO)silane has domestic use in adhesives and sealants at concentrations up to 10%.

Based on an online survey of publicly available SDS in Australia, 5 chemicals in this group (vinyltris(MEKO)silane, methyltris(MEKO)silane, phenyltris(MEKO)silane, tetrakis(MEKO)silane and CAS No. 83817-72-5) were identified in sealant and adhesive products at concentrations between 0.14 and 10%. Multiple chemicals were often included at low concentrations in the same sealant products. Some of the products also contained MEKO at concentrations below 10%.

International

The predominant use of these chemicals is expected to be in sealants and adhesives for domestic and commercial use with typical concentrations less than 10% individually (OECD 2009). In these sealant products, the MEKO silanes function as cross linkers that form stable silicones. The curing process is initiated by moisture in the air, which causes MEKO to be released from the silane.

Based on all available information, the chemicals vinyltris(MEKO)silane, methyltris(MEKO)silane, phenyltris(MEKO)silane and tetrakis(MEKO)silane are expected to be used most frequently. There is limited or no data on specific uses and concentrations for the other chemicals in this group.

In the United States of America (USA), vinyltris(MEKO)silane, methyltris(MEKO)silane, phenyltris(MEKO)silane, dimethylbis(MEKO)silane and tetrakis(MEKO)silane have reported uses that include glues, adhesives, sealants and one-component caulks (US EPA 2020).

Vinyltris(MEKO)silane, methyltris(MEKO)silane and 2-butanone, 2,2′-[*O*,*O*′-(methoxymethylsilylene)dioxime] (CAS No. 83817-72-5) are used in domestic and professional sealants at concentrations in the range 0.1–10% (DeLima Associates n.d.).

Vinyltris(MEKO)silane and methyltris(MEKO)silane also have reported use in automotive products including gasket makers and sealants at concentrations up to 7% (DeLima Associates n.d.). These automotive products are available to the public but expected to be used professionally.

An online survey of publicly available international SDS indicated that the above chemicals are also used in sealant and adhesive products at concentrations between 0.1 and 10% in Europe, Canada and Asia. Additionally, 2 chemicals (CAS No. 93917-75-0 and CAS No. 101371-00-0) had reported use in sealants at concentrations in the range 1–5% in the USA. One SDS identified the use of phenyltris(MEKO)silane in a gasket maker product for automotive applications at concentrations 10–30%. Multiple products contained more than one identified MEKO silane.

Volume data from Scandinavian countries between 2000 and 2017 indicated that vinyltris(MEKO)silane and methyltris(MEKO)silane were produced on the largest scales with cumulative reported volumes of 42 and 257 tonnes, respectively. Tetrakis(MEKO)silane and 2-butanone, 2,2′-[*O*,*O*′-(methoxymethylsilylene)dioxime] (CAS No. 83817-72-5) had cumulative use volumes that were less than one tonne. The use functions were in adhesives, binding agents, construction materials and fillers (SPIN n.d.).

Existing Australian regulatory controls

AICIS

The chemical phenyltris(MEKO)silane (CAS No. 34036-80-1) is listed on the Australian Inventory of Industrial Chemicals (the Inventory) with a specific requirement to provide information as a term of the Inventory listing. This term is published as:

- *Specific information requirement: Obligations to provide information apply. You must tell us within 28 days if the circumstances of your importation or manufacture (introduction) are different to those in our assessment.*

Under section 75(2)(c) of the *Industrial Chemicals (Consequential Amendments and Transitional Provisions) Rules 2019* the notification obligations under Subsections 64(1) and (2) of the old law (ICNA Act) are taken to be specific information requirements to be provided to the Executive Director.

Specific obligations under section 64(1) *were not* applied to the chemical.

Under section 64(2) of the ICNA Act a person who introduces an industrial chemical that has been assessed under this Act must within 28 days of becoming aware of any of the following circumstances since the assessment, notify the Executive Director in writing:

(a) the function or use of the chemical has changed, or is likely to change, significantly;

(b) the amount of chemical being introduced has increased, or is likely to increase, significantly;
(c) in the case of a chemical not manufactured, or proposed to be manufactured, in Australia at the time of the assessment - it has begun to be manufactured in Australia;
(d) the method of manufacture of the chemical in Australia has changed, or is likely to change, in a way that may result in an increased risk of an adverse effect of the chemical on occupational health and safety, public health or the environment;
(e) additional information has become available to the person as to an adverse effect of the chemical on public health, worker health and safety or the environment.

Public

No existing controls are currently available for these chemicals.

MEKO, which is released after hydrolysis, is listed in the Poisons Standard – The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) as follows:

Schedule 6:

'METHYL ETHYL KETONE OXIME **except**:

(a) in viscous silicone adhesives or viscous silicone sealants containing 2.5% or less of methyl ethyl ketone oxime; or

(b) in other preparations containing 1% or less of methyl ethyl ketone oxime'.

Schedule 6 chemicals are labelled with 'Poison' and are described as: "Substances with a moderate potential for causing harm, the extent which can be reduced by using distinctive packaging with strong warnings and safety directions on the label" (TGA 2025a).

An amendment to the entry is currently being considered (TGA 2025b).

Workers

The chemical 2-Butanone, 2,2′,2″-[*O*,*O*′,*O*″-(phenylsilylidyne)trioxime] (CAS No. 34036-80-1) is classified on the HCIS with the following classifications (SWA n.d.):

Health hazards	Hazard category	Hazard statement
Skin sensitisation	Skin Sens. 1	H317: May cause an allergic skin reaction
Specific target organ toxicity (repeated exposure)	STOT Rep. Exp. 2	H373: May cause damage to organs through prolonged or repeated exposure

International regulatory status

Exposure standards

No exposure standards are available for these chemicals.

Human exposure

Based on the available evidence, airborne MEKO is produced during the curing of silicone sealants, particularly within the first 24 hours of curing. The available data indicates that increased ventilation and/or air exchange significantly reduces the airborne MEKO concentration during the use of silicone sealants.

Release of MEKO from silicone sealants

There are several studies which measure the amount of MEKO produced during the curing of commercial silicon sealants. These studies demonstrate that volatile MEKO is released while the sealant cures. However, these studies have some limitations for risk assessment, such as:

- limited information on the concentration of MEKO silanes in these sealants
- limited information on the composition of these sealants
- the measured values of MEKO differed by several orders of magnitude.

In a study of volatile organic compound (VOC) emissions, the emission of MEKO from a neutral silicon sealant was measured in a sealed chamber. Within the first few hours, the concentration of MEKO reached approximately 90–100 mg/m^3, and rapidly decreased thereafter, reaching values between 10–25 mg/m^3 after 24 hours. The composition of the sealant was not reported (He et. al 2019).

A study was conducted to determine the concentrations of VOCs in 20 silicone sealants that were available in China. Fourteen different VOCs were identified from these sealants and the concentration of MEKO accounted for at least 50% of the total VOC concentrations in 15 out of 20 of the sealants tested. The average MEKO concentration produced by these sealants in a chamber after 2 hours was 668 mg/m^3 with a range of 22–2221 mg/m^3 (Zhao et al. 2022).

In a study of the release rate of MEKO from silicone sealants, it was determined that the application pattern of the sealant affects the release of MEKO. Applications of sealant that maximised the surface area-to-mass ratio produced greater quantities of MEKO. Detailed information on the composition of the sealants was not provided, but “Silicone caulk T” contained 2-butanone, *O*,*O*′-(dimethoxysilylene)dioxime (CAS No. 594875-36-2) as an ingredient. For “Silicone caulk T” the concentration of MEKO released was 162 ng MEKO/mg sealant 2 hours after application. The maximum concentration was 211 ng MEKO/mg sealant at 24 hours post-application. The other silicone sealant, which was not identified as containing a MEKO silane, had a dramatically different MEKO release profile, with concentration of 171 ng MEKO/mg sealant measured 2 hours after application. After 24 hours, the emission rapidly dropped to approximately 3 ng MEKO/mg sealant. The chemical identified in “Silicone caulk T” is a suitable analogue for the difunctional MEKO silanes in this evaluation. No specific information on final concentrations in air is available (Klewicz et al. 2020).

In experiments conducted to evaluate the rate of MEKO production (or off-gassing) from adhesives and sealants it was found that airborne MEKO concentrations peaked in the first 1 to 2 hours after application and decreased steadily after. The maximum MEKO concentration was approximately 3 ppm (0.011 mg/L = 11 mg/m^3) in areas of low air exchange and non-porous wall surfaces. In areas with higher air exchange and porous wall surfaces, MEKO concentrations were 0.5–0.75 ppm (0.0018–0.0027 mg/L = 1.8–2.7 mg/m^3).

However, information on the specific chemicals used in these adhesives and sealants could not be identified (OECD 2009).

In a study of 2 commercially available sealants from Japan, the concentrations of MEKO produced were 42.6 and 38.4 mg MEKO/g sealant measured 24 hours after application. Based on these measurements, a sealant amount of 130 g and a room volume of 55.4 m^3, the indoor air concentration of MEKO at 24 hours after sealant application were approximately 4.2 mg/m^3 and 3.8 mg/m^3. Information on the specific compositions of the 2 silicone sealants is not available. The calculated air concentrations were consistent with air sampling of a newly constructed building in Japan 2015, in which the maximum measured concentration of MEKO in the air was 3.57 mg/m^3 (Tsunoda et. al 2016).

A USA study of consumer exposure to MEKO in paints indicated that air concentrations were shown to be significantly affected by the concentration in the paint (peak concentration reduced by more than 80% for paint containing 0.096% compared with paint containing 0.293%) and increasing ventilation (Chang 1998).

Workers

Specific monitoring of workers exposed to MEKO emissions from sealants containing MEKO silanes is not available. Based on the above chamber studies, it is expected that workers who frequently use silicone sealants may be exposed to volatile MEKO via inhalation.

Data on the kinetics of release of MEKO from silicone sealants over time indicates that a peak air concentration of MEKO typically occurs within the first few hours after application, meaning that workers who use sealants frequently may be exposed to greater concentrations of MEKO. In studies investigating VOC release from sealants, the peak concentration of MEKO in the first few hours was 90–100 mg/m^3 and was at least 4 times greater than the value after 24 hours (10–25 mg/m^3) (He et al. 2019).

Public

There is limited specific information on public exposures to MEKO emissions from sealants containing MEKO silanes. Based on the above studies, it is expected that the public may infrequently be exposed to MEKO via inhalation. The level of exposure will be dependent on the ventilation of the area where the sealant is applied.

Health hazard information

Health hazard data are available for 4 chemicals in this evaluation: vinyltris(MEKO)silane, methyltris(MEKO)silane, phenyltris(MEKO)silane and dimethylbis(MEKO)silane. This has been used to infer the toxicity of all chemicals in this evaluation in the absence of data.

In addition, these chemicals hydrolyse to form MEKO (CAS No. 96-29-7), and the release of MEKO is expected to be the most significant contributor to the systemic toxicity profile of MEKO silanes. As such conclusions on systemic toxicity have been supported using data from MEKO. Further information on the toxicity of MEKO is available in our previous assessments (AICIS 2023; NICNAS 2013).

Toxicokinetics

No experimental data are available.

MEKO silanes hydrolyse in the presence of water (see **Relevant physical and chemical properties** section). Moisture in the atmosphere or on the surface of the skin is sufficient to initiate this hydrolysis. After hydrolysis of the oxime and alkoxy groups, the remaining silanols will react to form polymeric siloxanes. The polymeric siloxanes are not expected to be bioavailable (OECD 2009; REACH n.d.-a). After hydrolysis, MEKO silanes will release MEKO, which is well absorbed, metabolised and excreted (AICIS 2023; OECD 2009). Based on the volatility of MEKO, dermal absorption may depend on factors such as degree of occlusion, air current and its rate of transfer across the skin. In male Fischer 344 rats, a non-occlusive dermal application of 2.7 mg/kg bw, 27 mg/kg bw and 270 mg/kg bw of ^{14}C labelled test substance led to dermal absorption of between 13–26% (NICNAS 2013).

Acute toxicity

Oral

Based on the available data, these chemicals have low acute oral toxicity.

Vinyltris(MEKO)silane

In a good laboratory practice (GLP) compliant acute oral toxicity study conducted similarly to OECD TG 425, male Sprague Dawley (SD) rats (1–3/dose) were treated with a single dose of vinyltris(MEKO)silane at 550 mg/kg bw (1 animal) or 2000 mg/kg bw (3 animals). The median lethal dose (LD50) was greater than 2000 mg/kg bw. Reported sublethal signs of toxicity of animals in the 2000 mg/kg bw group included decreased activity, partially closed eyelids, increased lacrimation, irregular respiration, red soiling of the muzzle or urogenital staining. These effects were reversible 3 days after dosing (OECD 2009; REACH n.d.-a).

In a GLP compliant acute oral toxicity study conducted similarly to OECD TG 401, Fischer F344 rats (5/sex/dose) were treated with a single dose of vinyltris(MEKO)silane in water (doses approximately 295, 990, 1980, 2960, and 3950 mg/kg bw). The LD50s were 1920 mg/kg bw in males and 2610 mg/kg bw in females. Reported clinical signs of toxicity included decreased respiration, lacrimation, decreased activity, urogenital staining and red lacrimal secretions (OECD 2009).

In a non-GLP compliant acute oral toxicity study conducted similarly to OECD TG 401, SD rats (5/sex/dose) were treated with a single dose of vinyltris(MEKO)silane. The LD50 was 4510 mg/kg bw. Clinical signs of toxicity included transient sedation, reduced muscle tone, altered breathing and cyanosis at doses from 1300 mg/kg bw (ECHA 2025).

In a non-GLP compliant acute oral toxicity study conducted similarly to OECD TG 401, Wistar rats (5/sex/dose) were treated with a single dose of vinyltris(MEKO)silane. The LD50 was 3519 mg/kg bw. Clinical signs of toxicity included sedation, piloerection, ataxia and coma (dose levels not described) (ECHA 2025).

Methyltris(MEKO)silane

In a GLP compliant acute oral toxicity study conducted in accordance with OECD TG 401, SD rats (5/sex/dose) were treated with a single dose of methyltris(MEKO)silane. The LD50

was 2463 mg/kg bw. Clinical signs of toxicity included prostration, lethargy, ptosis, ataxia and coma. These effects were reversible 3 days after dosing (REACH n.d.-b).

In a GLP compliant acute oral toxicity study, Fischer F344 rats (5/sex/dose) were treated with a single dose of methyltris(MEKO)silane. The LD50s were 2260 mg/kg bw and 2650 mg/kg bw in males and females, respectively. Transient narcosis, signs of anaemia and early hepatocyte toxicity were observed in the animals (see **Systemic target organ toxicity – single exposure**) (OECD 2009).

In a non-guideline acute oral toxicity study, CD-1 mice (20/sex/dose) were treated with a single dose of methyltris(MEKO)silane in peanut oil. The LD50 was 7000 mg/kg bw. Clinical signs of toxicity included depression (loss of righting reflex) and shortness of breath (OECD 2009).

Phenyltris(MEKO)silane

In a GLP compliant acute oral toxicity study conducted similarly to OECD TG 401, SD rats (5/sex/dose) were treated with a single dose of phenyltris(MEKO)silane (doses 100, 500, 2000 mg/kg bw). The LD50 was greater than 2000 mg/kg bw. Reported sublethal signs of toxicity included prostration, decreased activity, wobbly gait, rigidity upon handling, breathing abnormalities, urine stains, decreased defecation and partially closed eyelids with dark material around them. Gross necropsy after 14 days revealed blackish-purple spleens in rats dosed at 500 and 2000 mg/kg bw (REACH n.d.-c).

Structure-toxicity relationship studies of MEKO silanes

In a series of acute oral toxicity studies conducted similarly to OECD TG 401, rats were administered a single low, mid or high dose of three chemicals and observed for 14 days. In these studies:

- Methyltris(MEKO)silane was administered to Fischer F344 rats at doses of 295, 982 and 1964 mg/kg. The LD50 was estimated to be 2500 mg/kg bw.
- Phenyltris(MEKO)silane was administered to SD rats at doses of 100, 500 and 2000 mg/kg. The LD50 was greater than 2000 mg/kg bw.
- Dimethylbis(MEKO)silane was administered to SD rats at doses of 88, 888 and 2640 mg/kg. The LD50 was greater than 2600 mg/kg bw.

In all cases, a dose related transient narcosis and anaemia were observed in the animals (see **Specific target organ toxicity – single exposure**) (Derelanko and Rusch 2008).

Dermal

Based on the available data, these chemicals have low acute dermal toxicity.

In GLP compliant acute dermal toxicity studies conducted in accordance with OECD TG 402, SD rats (5/sex/dose) were treated with a single dose of vinyltris(MEKO)silane, methyltris(MEKO)silane or phenyltris(MEKO)silane. The LD50 was greater than 2000 mg/kg bw in all experiments. No clinical signs of toxicity were reported (REACH n.d.-a, REACH n.d.-b, REACH n.d.-c).

Specific target organ toxicity – single exposure

Narcotic effects

Based on the effects observed in acute oral toxicity studies with MEKO silanes and the metabolite MEKO, chemicals in this group are considered to cause transient narcotic effects after acute exposures, warranting hazard classification.

Signs of narcosis that were reported in acute oral toxicity studies for vinyltris(MEKO)silane, methyltris(MEKO)silane and phenyltris(MEKO)silane (see **Acute toxicity – Oral**) included:

- a significant but reversible depression of the nervous system
- decreased activity or lethargy
- wobbly gait
- decreased righting reflex
- prostration
- partially closed or droopy eyelids (ptosis)
- ataxia (loss of muscle control).

In an acute oral toxicity study with methyltris(MEKO)silane, a significant but reversible depression of the nervous system was observed in animals dosed at 980 mg/kg bw or above (OECD 2009). The no observed effect level (NOEL) for narcosis was 295 mg/kg bw.

In structure-toxicity relationship studies of the MEKO silanes (see **Acute toxicity – Oral**), rats exposed to single doses of methyltris(MEKO)silane, phenyltris(MEKO)silane or dimethylbis(MEKO)silane exhibited a dose dependent transient narcosis that typically cleared within 24 hours. Reported signs of narcosis generally were decreased activity at lower doses and prostration at higher doses. The NOEL for narcosis was between 100 and 300 mg/kg bw (Derelanko and Rusch 2008).

The main metabolite MEKO is classified on the HCIS with hazard category “Specific target organ toxicity (single exposure)” with hazard statement “H336: May cause drowsiness or dizziness” (SWA n.d.). Transient narcotic effects observed in acute oral toxicity studies with MEKO silanes are similar to those observed in acute and subchronic oral neurotoxicity studies in SD rats exposed to MEKO (NICNAS 2023).

Respiratory tract effects

Based on the low vapour pressures of these chemicals (see **Physicochemical properties**) limited exposure by inhalation is expected. However, MEKO is a major decomposition product of these chemicals in the presence of moisture, and inhalation of MEKO may occur upon exposure of these chemicals to moist air.

The main metabolite MEKO is classified on the HCIS with hazard category “Specific target organ toxicity (single exposure) – Category 1” with hazard statement “H370: Causes damage to organs – upper respiratory tract” (AICIS 2023). Classification of MEKO for these effects was based on degeneration of the nasal epithelium in short term toxicity studies in mice. The LOAEC for short term inhalation toxicity was 108 mg/m^3. Studies of radiolabelled MEKO in mice have indicated that the radiolabel accumulates rapidly in the nasal epithelium after oral exposures (AICIS 2023). Although data are not sufficient to read across this classification for specific target organ toxicity (single exposure) to these chemicals, effects on the nasal epithelium would be expected if sufficient exposure to MEKO as a decomposition product occurs.

Blood system effects

Available data from acute oral toxicity studies indicates MEKO silanes damage the blood system. Adverse effects were observed in animals exposed to MEKO silanes at doses below 300 mg/kg bw in multiple studies, warranting hazard classification as a Category 1 Specific Target Organ Toxicant (Single Exposure).

Based on the weight of evidence, chemicals in this group are considered to be methaemoglobin inducers that lead to regenerative anaemia (methaemoglobinaemia). Increased haemosiderosis in the spleen in combination with other changes indicated significant haemolytic anaemia following acute exposures to these chemicals. The acute effects are consistent with the repeat dose adverse effects on the blood for the metabolite MEKO (AICIS 2023). As the MEKO silanes hydrolyse rapidly in water, the release of MEKO is likely to be responsible for the adverse effects. The available data indicates that adverse effects on the blood system are observed after exposure to both trifunctional and difunctional MEKO silanes, indicating that all chemicals in this group may cause adverse blood effects after acute exposures.

Blood chemistry was monitored in structure-toxicity relationship studies with MEKO silanes (see **Acute toxicity – Oral**). In satellite animals given a single dose of either methyltris(MEKO)silane or dimethylbis(MEKO)silane at concentrations greater than 2500 mg/kg bw, there were increases in methaemoglobin levels that were 2 to 8 times that of the controls. Blood analysis 14 days after exposure was indicative of dose dependent anaemia exhibited by decreased RBC counts, haemoglobin and haematocrit values for all dose groups. In animals from the low dose groups, there were significant decreases compared to the control group in RBC counts after exposure to:

- methyltris(MEKO)silane at 295 mg/kg bw (15–20% in males and 20–25% in females)
- dimethylbis(MEKO)silane at 88 mg/kg bw (10–15% in males).

In the mid and high dose groups, there were significant decreases in RBC counts of equal or greater amounts than those observed in the low dose group. In the high dose groups, the mean reticulocyte values were 2–5%, a significant increase compared to the control group values of 0.3%. Histopathology of the spleen was indicative of RBC degradation (haemolysis) characterised by extramedullary haematopoiesis and deposits of haemosiderin. Blood chemistry was not reported for rats exposed to phenyltris(MEKO)silane; however, enlarged, purple coloured spleens were observed during necropsy, which are indicative of haemolysis (Derelanko and Rusch 2008). Similar effects on the spleen were observed in a guideline acute oral toxicity study with phenyltris(MEKO)silane (REACH n.d.-c).

In an acute oral toxicity study with methyltris(MEKO)silane, significant oxidative destruction of RBCs was observed at all concentrations tested (lowest dose: 295 mg/kg bw). Histopathology of the spleen was indicative of haemolysis (OECD 2009).

The effects observed in the above acute studies are similar to those observed in 28 day repeat dose studies of the MEKO silanes (see **Repeat dose toxicity – Oral**).

Corrosion/Irritation

Skin irritation

Based on the available data, these chemicals are expected to be at most, slightly irritating to skin. Mild erythema and oedema were observed in rabbits after exposure to these chemicals in guideline studies, but in all cases the signs of irritation were reversible.

Vinyltris(MEKO)silane

In a GLP compliant skin irritation study conducted in accordance with OECD TG 404, 6 New Zealand White (NZW) rabbits were treated with vinyltris(MEKO)silane for 4 hours under semi-occlusive conditions. Observations were recorded at 1, 24, 48 and 72 hours after patch removal. The following mean scores for individual animals (based on observations at 24, 48 and 72 hours) were reported: 0.0, 0.3, 1.0, 1.0, 1.0 and 1.0 for erythema. Desquamation was observed in 5 animals at 72 hours. There were no signs of oedema during the study (REACH n.d.-a). Information on the reversibility of erythema after 72 hours was not reported.

In a GLP compliant skin irritation study, 6 rabbits were treated with 96.5% vinyltris(MEKO)silane for 24 hours under semi-occlusive conditions. Observations were recorded at 24, 48 and 72 hours after patch removal. At 48 hours, necrosis was observed in 2 out of 6 animals. The necrosis was superficial and reversible. No irritation was observed in any animals 8 days after the treatment (OECD 2009). No further information on the individual animal responses is available.

Methyltris(MEKO)silane

In a GLP compliant skin irritation study conducted in accordance with OECD TG 404, 6 NZW rabbits were treated with methyltris(MEKO)silane for 4 hours under semi-occlusive conditions. Observations were recorded at 1, 24, 48 and 72 hours after patch removal. A score of 1 was reported for erythema (maximum score of 4) 1 hour after patch removal in all 6 animals. A mean score for erythema based on observations at 24, 48 and 72 hours of 0.11 was reported. Individual animal scores were not reported. Desquamation was observed in 3 out of the 6 animals at 72 hours. There were no signs of oedema during the study (REACH n.d.-b).

In a GLP compliant skin irritation study conducted similarly to OECD TG 404, 6 NZW rabbits were treated with 84.45% methyltris(MEKO)silane for 24 hours under occlusive conditions. Observations were recorded at 1, 24, 48 and 72 hours after patch removal. A score of 1 was reported for erythema and oedema (maximum score of 4) 1 hour after patch removal in 4 animals. All signs of erythema and oedema resolved fully within 24 hours, except in one animal where the erythema was resolved after 48 hours (OECD 2009; REACH n.d.-b).

Phenyltris(MEKO)silane

In a GLP compliant skin irritation study conducted in accordance with OECD TG 404, 3 male NZW rabbits were treated with phenyltris(MEKO)silane for 4 hours under semi-occlusive conditions. Observations were recorded at 24, 48 and 72 hours after patch removal. The following mean scores for individual animals (based on observations at 24, 48 and 72 hours) were reported: 1.0, 2.0 and 0.0 for erythema and 0.3, 1.3 and 0.0 for oedema. All signs of erythema and oedema had fully reversed 10 days after patch removal (REACH n.d.-c).

In a GLP compliant skin irritation study conducted similarly to OECD TG 404, 3 male NZW rabbits were treated with phenyltris(MEKO)silane for 3 minutes, 1 hour or 4 hours under occlusive conditions. Observations were recorded at 24, 48 and 72 hours after patch removal. The following mean scores for individual animals (based on observations at 24, 48 and 72 hours) were reported for 4 hour exposures: 1.3, 1.6 and 2.0 for erythema and 0.6, 0.6 and 2.0 for oedema. All signs of erythema and oedema had fully reversed 8 days after patch removal for all exposure durations (REACH n.d.-c).

Eye irritation

Based on the available data, most chemicals in this group are considered to cause eye irritation, warranting hazard classification. One study with vinyltris(MEKO)silane demonstrated effects on the cornea that persisted for 21 days, indicating possible eye damage. Other studies, including those with methyltris(MEKO)silane demonstrated mostly reversible signs of eye irritation in rabbits. No eye irritation was reported in a guideline study with phenyltris(MEKO)silane and; therefore, it should not be classified.

Vinyltris(MEKO)silane

In a GLP compliant eye irritation study conducted in accordance with OECD TG 405, vinyltris(MEKO)silane was instilled into 1 eye each of 6 NZW rabbits. The eyes were observed at 1, 24, 48 and 72 hours. Mean scores for individual animals (based on observations at 24, 48 and 72 hours) were:

- animal 1: corneal opacity 2.0/4, iritis 1.0/2, conjunctival redness 2.0/3 and chemosis 1.7/4
- animal 2: corneal opacity 2.0/4, iritis 1.0/2, conjunctival redness 2.0/3 and chemosis 2.3/4
- animal 3: corneal opacity 2.0/4, iritis 1.0/2, conjunctival redness 2.0/3 and chemosis 2.0/4
- animal 4: corneal opacity 0.7/4, iritis 1.0/2, conjunctival redness 1.0/3 and chemosis 1.3/4
- animal 5 : corneal opacity 2.0/4, iritis 1.0/2, conjunctival redness 2.0/3 and chemosis 2.7/4
- animal 6: corneal opacity 2.0/4, iritis 1.0/2, conjunctival redness 2.0/3 and chemosis 2.3/4.

Corneal ulcerations, indicative of serious eye damage, were observed in 5 animals. Congestion of the iris was observed in 2 animals and 3 animals at 48 hours and 72 hours, respectively. Pupils were constricted in 3 animals throughout the course of the test (REACH n.d.-a). No information on reversibility of effects after 72 hours was reported.

In a GLP compliant eye irritation study conducted in accordance with the United States Code of Federal Regulations 16 CFR 1500.42 - Test for eye irritants, vinyltris(MEKO)silane was instilled into 1 eye each of 6 NZW rabbits. For 3 of the animals, the eye was rinsed with water for approximately 20 seconds after instillation. The eyes were observed at 1, 24, 48, 72, 96 hours and 7, 10, 14 and 21 days post-instillation. In the animals without washing:

- Corneal opacity was observed in all animals 24 hours after exposure. This resolved in 4/6 animals by day 7, but persisted up to 21 days in the remaining 2 animals.
- Iritis was observed in 2/6 animals 24 hours after exposure but was fully resolved 48 hours after exposure. No other signs of iritis were reported.

- Conjunctival redness was observed in all animals up to 96 hours post-instillation. The intensity of redness decreased over time. The redness was fully reversed in 5/6 animals by day 14; however, it persisted in one animal up to day 21.
- Chemosis was observed in 3/6 animals 24 hours after exposure but had fully resolved by 48 hours in all animals.

The effects in animals where the test substance was washed out were similar, but all effects resolved completely by day 14 (OECD 2009). Individual animal scores were not reported.

Methyltris(MEKO)silane

In a GLP compliant eye irritation study conducted in accordance with OECD TG 405, 84.45% methyltris(MEKO)silane was instilled into 1 eye each of 6 NZW rabbits. The eyes were observed at 1, 24, 48 and 72 hours and then daily until 7 days post instillation. Mean scores for individual animals (based on observations at 24, 48 and 72 hours) were:

- animal 1: corneal opacity 1.0/4, iritis 0.0/2, conjunctival redness 0.6/3 and chemosis 0.0/4
- animal 2: corneal opacity 1.0/4, iritis 0.3/2, conjunctival redness 0.6/3 and chemosis 0.3/4
- animal 3: corneal opacity 1.6/4, iritis 0.0/2, conjunctival redness 0.6/3 and chemosis 0.0/4
- animal 4: corneal opacity 0.0/4, iritis 0.0/2, conjunctival redness 0.0/3 and chemosis 0.0/4
- animal 5: corneal opacity 1.3/4, iritis 0.6/2, conjunctival redness 0.6/3 and chemosis 0.3/4
- animal 6 : corneal opacity 1.0/4, iritis 0.6/2, conjunctival redness 1.0/3 and chemosis 0.3/4.

In 5 out of the 6 animals, signs of eye irritation 24 hours after administration included corneal opacity, iritis, conjunctival redness and chemosis. All effects were completely reversed 4 days after exposure. For 3 additional animals, the eye was rinsed with water for 1 minute, starting 20 seconds after instillation. Of these 3 animals, only 1 animal exhibited signs of eye irritation (OECD 2009; REACH n.d.-b).

In an eye irritation study, methyltris(MEKO)silane in peanut oil at concentrations of 3%, 10%, 30% or 100% were instilled into 1 eye each of 6 NZW rabbits. The eyes were observed at 6 hours and daily for 10 days post-instillation. No irritation was observed at concentrations of 3% or 10%. At 30% concentration, the animals exhibited lacrimation and slight congestion for 6 hours. At 100% concentration, the animals demonstrated lacrimation, congestion and oedema of the conjunctivae. These symptoms fully reversed within 5 days. Dullness of the cornea was initially observed in 3/6 animals but completely reversed (OECD 2009).

Phenyltris(MEKO)silane

In a GLP compliant eye irritation study conducted in accordance with OECD TG 405, phenyltris(MEKO)silane was instilled into 1 eye each of 3 female NZW rabbits. The eyes were observed at 1, 24, 48 and 72 hours. The mean scores for all animals based on observations at 24, 48 and 72 hours for corneal opacity, iritis and chemosis were 0/4, 0/2 and 0/4, respectively. For conjunctival redness, the mean scores for animals 1, 2 and 3 were 0.7/3, 0.7/3 and 1.3/3, respectively. All signs of irritation had resolved 4 days after exposure. Individual animal scores were not reported (REACH n.d.-c).

Sensitisation

Skin sensitisation

Based on the available data, these chemicals are considered to be skin sensitisers, warranting hazard classification.

Phenyltris(MEKO)silane is classified with hazard category “Skin sensitisation – Category 1” and hazard statement “H317: May cause an allergic skin reaction” (SWA n.d.). The available data supports this classification for this chemical and all chemicals in the evaluation. Based on the available data sub-categorisation is not recommended.

In a GPMT conducted similarly to OECD TG 406, intradermal induction was performed on 15 female Hartley guinea pigs using 5% methyltris(MEKO)silane in propylene glycol and topical induction with 25% of methyltris(MEKO)silane in propylene glycol. The animals were challenged with 50% methyltris(MEKO)silane in propylene glycol. Reactions were reported in 93% (14/15) of the animals at 24 hours and 48 hours after challenge (REACH n.d.-b).

In a GPMT conducted similarly to OECD TG 406, intradermal induction was performed on 10 female Hartley guinea pigs using 1% phenyltris(MEKO)silane in 5% acetone in Alembicol D and topical induction with phenyltris(MEKO)silane as supplied. The animals were challenged with 25% and 50% phenyltris(MEKO)silane in acetone. No reactions were reported in animals challenged with 25% phenyltris(MEKO)silane. At 24, 48 and 72 hours after the challenge with 50% phenyltris(MEKO)silane, there were reactions in 40% (4/10), 60% (6/10) and 60% (6/10) of the animals, respectively (REACH n.d.-c).

The metabolite MEKO is classified with hazard category “Skin sensitisation – Category 1” and hazard statement “H317: May cause an allergic skin reaction” (SWA n.d.).

In silico

For the chemicals, no structural alerts were identified for protein binding based on the endpoint specific profiling functionality of the OECD Quantitative Structure-Activity Relationship (QSAR) Application Toolbox (OECD QSAR Toolbox) version 4.5. However, all of the chemicals were predicted to share a ketone-containing metabolite (by hydrolysis). This metabolite had a structural alert for protein binding. The alert was based on the nucleophilic addition of proteins to carbonyls (OECD 2024).

The knowledge based expert system Deductive Estimation of Risk from Existing Knowledge (DEREK) Nexus version 2.2 was utilised to estimate the skin sensitisation potential of the chemicals. The chemicals had an alert for skin sensitisation based on the alkyl oxime group. Although skin sensitisation is considered equivocal, there were insufficient data to make an EC3 prediction (the predicted effective concentration for a 3 fold increase in lymphocyte proliferation in local lymph node assay) (Lhasa Limited n.d.).

Repeat dose toxicity

Based on the available data on MEKO silanes and the metabolite MEKO, these chemicals are expected to cause serious health effects on the blood system following repeated oral exposure. The effects on the blood system in studies with MEKO silanes are similar to those observed in repeat dose studies with MEKO. However, there is evidence that this toxicity arises from single or short-term exposures (see **Systemic target organ toxicity – single exposure**), at doses similar to those causing effects in repeated dose studies. Therefore,

classification for repeat dose effects is not warranted. Other adverse effects on the kidney and liver only occurred at high doses not relevant for classification.

Phenyltris(MEKO)silane is classified on the HCIS with hazard category “Specific target organ toxicity (repeat exposure)” with hazard statement “H373: May cause damage to organs through prolonged or repeated exposure” (SWA n.d.). Based on the proposed STOT-SE classification for this chemical, it is recommended that the classification for repeated exposure is removed.

Oral

Methyltris(MEKO)silane

In a combined repeated dose toxicity study with reproductive/developmental toxicity screening test conducted in accordance with OECD TG 422, Wistar rats (10/sex/dose) were administered methyltris(MEKO)silane in dried corn oil via oral gavage at 0, 10, 50 and 250 mg/kg bw/day beginning 14 days prior to mating and through gestation and lactation (OECD 2009). No significant effects on food consumption, body weights or body weight gain at any dose and no mortality were reported.

Changes in haematology were indicative of anaemia and haematopoiesis. In animals from the 50 mg/kg bw/day group, there was a significantly:

- decreased RBC count (18% in males and females)
- decreased haemoglobin concentration (10% in males and 12% in females)
- decreased haematocrit (7% in males and females)
- increased mean corpuscular volume (MCV) (14% in males and 12% in females)
- increased mean corpuscular haemoglobin (MCH) (12% in males and 7% in females)
- increased platelet concentration (24% in males only)
- increased numbers of reticulocytes (165% in males and 186% in females).

Haematology was not possible for animals in the 250 mg/kg bw/day group as significantly increased reticulocyte numbers obscured other measurements.

In animals from the 50 and 250 mg/kg bw/day groups, extramedullary haematopoiesis was noted in the spleen and liver. Haemosiderin deposits were observed in the spleen. An excess production of RBC was observed in the bone marrow.

Other statistically significant treatment related effects in animals from the 50 and/or 250 mg/kg bw/day group were:

- increases in total serum bilirubin concentration and a significantly increased albumin/globulin ratio in the 250 mg/kg bw/day group
- discoloured kidneys and enlarged spleen in the 250 mg/kg bw/day group
- increases in the absolute and relative weight of the spleen and the relative weight of the liver in the 50 mg/kg bw/day group.

The NOAEL was 10 mg/kg bw/day based on adverse effects on blood chemistry, haematology, and histopathological findings in the 50 and 250 mg/kg bw/day groups.

Phenyltris(MEKO)silane

In a GLP compliant 28 day study conducted in accordance with OECD TG 407, SD rats (5/sex/dose) were administered phenyltris(MEKO)silane in dried corn oil by gavage at 10, 150 or 300 mg/kg bw/day for 7 days/week (REACH n.d.-c). The animals were observed for the 28 days of the study and for an additional recovery period of 14 days. No significant effects on body weight, mean food consumption or neurological observations were observed for any dose group.

The haematology of animals in the 150 and 300 mg/kg bw/day groups after 28 days were indicative of a dose related regenerative anaemia characterised by:

- significant decreases in RBC count, haemoglobin concentration and haematocrit
- significant increases in MCV, MCH, platelets, nucleated RBC and leukocytes (segmented neutrophils and lymphocytes)
- abnormalities in RBC morphology that included varying degrees of polychromasia, basophilic stippling, anisocytosis and macrocytes.

At the end of the recovery period, animals in the 300 mg/kg bw/day group had normal RBC morphology and an overall reduced severity of effects on the blood system. However, significantly decreased RBCs and increased haemoglobin, haematocrit, MCV and MCH persisted. No effects on the blood system were observed in the 10 mg/kg bw/day group.

For clinical chemistry parameters in the 150 and 300 mg/kg bw/day groups, there was a significantly increased total serum bilirubin, likely a secondary effect of anaemia. There were also significant increases in phosphorus, aspartate transferase (AST), blood urea nitrogen (BUN) and albumin levels and significant decreases in potassium, globulin and cholesterol levels. These changes may have been related to anaemia, but correlation was unclear. After recovery, all clinical chemistry parameters returned to normal levels.

Histopathology of animals in the 150 and 300 mg/kg bw/day groups revealed treatment related extramedullary haematopoiesis in the spleen and liver. Significant haemosiderin deposits that resulted from RBC degradation were found in macrophages in the spleen and liver. These effects were more prevalent in the 300 mg/kg bw/day group. No histopathological effects were observed in the heart.

Other statistically significant treatment related effects in animals from the 150 and 300 mg/kg bw/day groups after the 28 day study included:

- an increase in total urine volume in males
- an increase in absolute and relative spleen weight
- increases in absolute and relative liver and heart weights in females
- darkened (blackish-purple) and enlarged spleens.

The NOAEL was 10 mg/kg bw/day based on dose related effects on the blood system in the 150 and 300 mg/kg bw/day groups (REACH n.d.-c).

Studies with MEKO

The metabolite MEKO is classified on the HCIS with hazard category “Specific target organ toxicity (repeat exposure)” with hazard statement “H373: May cause damage to organs through prolonged or repeated exposure – blood system” (SWA n.d.). Dose related adverse

effects on the blood system that were observed in guideline 28 day and 90 day oral toxicity studies on MEKO included:

- decreased RBC counts, haemoglobin concentrations and haematocrit
- increased reticulocyte counts, leukocytosis and methaemoglobin concentrations
- haematopoiesis in the spleen and outside the bone marrow
- increased haemosiderosis in the spleen and liver
- degradation of RBC by macrophages in the liver.

Based on these effects, MEKO was considered a methaemoglobin inducer that causes regenerative anaemia (AICIS 2023). These effects are similar to those observed in the above 28 day studies, indicating the systemic adverse effects caused by MEKO silanes are likely due to the release of MEKO.

Genotoxicity

Based on the available data, chemicals in this group are not expected to have genotoxic potential. Whilst vinyltris(MEKO)silane induced chromosomal aberrations *in vitro*, there were no indications of genotoxicity from *in vivo* experiments. The main metabolite MEKO is not considered to be genotoxic (NICNAS 2013).

In vitro

Negative results were reported for these chemicals in the following GLP compliant *in vitro* genotoxicity studies (ECHA 2025; OECD 2009; REACH n.d.-c):

- in bacterial reverse mutation assays (OECD TG 471) with vinyltris(MEKO)silane, methyltris(MEKO)silane and phenyltris(MEKO)silane in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537 and *Escherichia coli* WP2 *uvr*A with and without metabolic activation at concentrations up to 5000 µg/plate
- in a bacterial reverse mutation assay (conducted similarly to OECD TG 471) with methyltris(MEKO)silane in *S. typhimurium* TA 98, TA 100, TA 1535, TA 1537 and TA 1538 with and without metabolic activation at concentrations up to 500 µg/plate
- in an *in vitro* mammalian chromosome aberration assay (OECD TG 473) with methyltris(MEKO)silane in Chinese hamster ovary (CHO-K1) cells with and without metabolic activation at concentrations up to 3015 µg/mL
- in an *in vitro* mammalian chromosome aberration assay (OECD TG 473) with phenyltris(MEKO)silane in human blood lymphocytes with and without metabolic activation at concentrations up to 1600 µg/mL
- in a mammalian gene mutation assay (OECD TG 476) with methyltris(MEKO)silane in mouse lymphoma L5178Y cells with and without metabolic activation at concentrations up to 10 mM/plate.

A positive result was reported in an *in vitro* mammalian chromosome aberration assay (OECD TG 473) with vinyltris(MEKO)silane in Chinese hamster ovary cells with and without metabolic activation at concentrations up to 3140 µg/mL (OECD 2009).

In vivo

In a mammalian erythrocyte micronucleus test conducted in accordance with OECD TG 474, ICR mice (5/sex/dose) were treated with vinyltris(MEKO)silane in dried corn oil by intraperitoneal administration at single doses of 450, 900 and 1800 mg/kg bw. The incidence

of polychromatic erythrocytes did not increase in any of the treated groups, indicating a lack of clastogenicity (OECD 2009).

In a GLP compliant mammalian erythrocyte micronucleus test conducted in accordance with OECD TG 474, Swiss mice (5–10/sex/dose) were treated with phenyltris(MEKO)silane in dried corn oil by intraperitoneal administration at single doses of 500, 1000 and 2000 mg/kg bw. The incidence of polychromatic erythrocytes did not increase in any of the treated groups, indicating a lack of clastogenicity (REACH n.d.-c).

In silico

The chemicals had structural alerts for *in vivo* micronucleus formation (H-acceptor-path3-Hacceptor) based on the mechanistic profiling functionality of the OECD QSAR Toolbox version 4.5. No structural alerts for DNA binding were identified (OECD 2024).

The chemicals are not predicted to be mutagenic using the expert rule-based system, DEREK Nexus version 2.2 (Lhasa Limited n.d.).

Carcinogenicity

No data are available for chemicals in this group. Based on the read across to the metabolite MEKO, chemicals in this group are suspected to have carcinogenic potential, warranting hazard classification.

Under the GHS criteria (UNECE 2017) a substance that has not been tested for carcinogenicity may be classified based on data from an analogue. Factors such as physicochemical, toxicokinetic and toxicodynamic properties should be considered.

The metabolite MEKO is classified for carcinogenicity (Category 1B) based on the following evidence observed in 2 chronic inhalation studies (AICIS 2023, SWA n.d.):

- significantly increased incidence of liver tumours were observed in rats and mice
- clear evidence of progression to malignancy of liver tumours
- male rats and mice were more sensitive than female rats and mice
- increased incidences of benign fibroadenomas in male rats
- the relevance of the animal studies to humans cannot be ruled out.

In considering the strength of evidence, AICIS notes that:

- The available data for MEKO support a likely threshold mode of action.
- MEKO was classified for carcinogenicity based on chronic inhalation studies.
- Data are not available to rule out carcinogenic effects of MEKO by other routes of exposure. Although similar effects were observed in inhalation and oral repeated dose studies indicating similar toxicokinetic pathways, the dose at which carcinogenic effects could occur via other routes of exposure is uncertain.
- The adverse effects including effects on liver observed in 28 day repeat dose oral toxicity studies (see **Repeat dose toxicity**) with the MEKO silanes were similar to those observed in oral 28 day studies with MEKO, indicating that oral administration of MEKO silanes leads to systemically available MEKO.
- MEKO silanes are significantly less volatile compared to MEKO. Inhalation is not expected to be a significant exposure pathway to the MEKO silanes themselves although they can release MEKO during use.

- Limited data are available regarding dermal bioavailability of these chemicals. These chemicals are considered skin sensitisers which indicates dermal absorption is possible. However, narcotic effects similar to those observed following dermal absorption of MEKO were not observed in available acute dermal toxicity studies. As MEKO is volatile, the dermal absorption of any MEKO formed on the skin may depend on factors such as degree of occlusion, air current and its rate of transfer across the skin.

Overall, the strength of evidence is not considered sufficiently convincing at this stage to place the substance in Category 1 but classification in Category 2 is warranted.

A harmonised GHS classification for these chemicals is under consideration in Europe. A proposal for classification as Category 1B is proposed. If further information supporting this classification becomes available as part of this process, a future AICIS evaluation of the carcinogenicity classification may be required.

Reproductive and development toxicity

Based on the available data and the metabolite MEKO, chemicals in this group are not expected to cause adverse effects on fertility or development.

In a combined repeated dose toxicity study with reproductive/developmental toxicity screening test conducted in accordance with OECD TG 422, Wistar rats (10/sex/dose) were administered methyltris(MEKO)silane in dried corn oil via oral gavage at 0, 10, 50 and 250 mg/kg bw/day beginning 14 days prior to mating and through gestation and lactation (OECD 2009). The NOAEL for general toxicity was 10 mg/kg bw/day, based on adverse effects on the blood system (see **Repeat dose toxicity**).

There were no statistically significant changes in any of the treatment groups when compared to the controls in fertility or developmental parameters during the study. The parameters measured included:

- mean precoital time
- fertility index, conception rate, gestation index
- mean number of implantations
- number of mean post implantation loss
- mean postnatal loss
- mean litter size and weight
- litter weight gain
- pup viability
- sex ratio of pups.

The NOAEL for fertility and development was 250 mg/kg bw/day.

In structure-toxicity relationship studies on MEKO silanes (see **Acute toxicity – Oral**), there were no significant changes in testicular weights 14 days after exposure to low, mid or high doses of methyltris(MEKO)silane, phenyltris(MEKO)silane or dimethylbis(MEKO)silane. Microscopic analysis of the testes in animals exposed to dimethylbis(MEKO)silane did not reveal any significant adverse effects (Derelanko and Rusch 2008).

The metabolite MEKO is not considered to have specific reproductive or developmental toxicity based on several studies in rats and rabbits (NICNAS 2013).

Neurotoxicity

While chemicals in this group may cause transient narcotic effects following acute exposures (see **Acute toxicity**), these chemicals are not expected to be neurotoxic. The main metabolite MEKO is not considered to be neurotoxic (NICNAS 2013).

Human health risk characterisation

Critical health effects

The critical health effects for risk characterisation to workers and the public relate to the release of MEKO during end use of these chemicals. As the most likely exposure route is inhalation of released MEKO during the curing of sealants, damage to the nasal epithelium is considered to be the most significant health hazard for public risk. The LOAEC for damage to the respiratory tract was 108 mg/m^3 (AICIS 2023).

Public risk

A quantitative risk assessment using a MOE methodology was used to characterise the risk to human health associated with systemic exposure to the MEKO following end use of these chemicals. The MOE methodology is commonly used to characterise risks to human health associated with exposure to chemicals (ECB 2003).

The MOE risk estimate provides a measure of the likelihood that a particular adverse health effect will occur under the conditions of exposure. As the MOE increases, the risk of potential adverse effects decreases. To decide whether the MOE is of sufficient magnitude, expert judgment is required. Such judgments are usually made on a case-by-case basis and should consider uncertainties arising in the risk assessment process such as the completeness and quality of available data, the nature and severity of effect(s) and intra/inter species variability.

The starting points for risk characterisation are measured and estimated based on external exposure levels (see **Human exposure**). While there is limited data available, the evidence from available studies demonstrates that volatile MEKO is released from sealants after application.

The MOE values are shown in **Table 1**.

Table 1 – Margins of exposure for use of sealants containing MEKO.

Scenario	MEKO concentration (mg/m^3)	Margin of exposure
MEKO off-gassing from silicone sealant – low ventilation (OECD 2009)	11	9.8
MEKO off-gassing from silicone sealant – high ventilation (OECD 2009)	1.8–2.7	40–60
MEKO off-gassing from silicone sealant – building measurements (Tsunoda et al. 2016)	3.57	30
Peak MEKO release from sealant in first few hours – chamber study (He et al. 2019)	90–100	1.1–1.2
MEKO release from sealant after 24 hours – chamber study (He et al. 2019)	10–25	4.3–11
MEKO release from sealants after 2 hours – closed chamber (Zhao et al. 2022)	668	0.2

The low MOEs indicate that there is a public risk that requires management.

Worker risk

Workers who frequently use sealants may be exposed to greater concentrations of MEKO than the public. This is demonstrated by the dramatic difference in peak MEKO release in chamber studies in the first few hours compared to the value after 24 hours (see **Table 1**).

This exposure data indicates that worker using products containing these chemicals may be exposed to MEKO at levels higher than exposure standards established overseas. The AICIS evaluation of MEKO recommended that Safe Work Australia consider establishing a workplace exposure standard (AICIS 2023). Exposures to MEKO from use of these chemicals should be considered in establishing the workplace exposure standard.

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