Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

Alkoxysilane ethylenediamine and polyamine derivatives

Evaluation statement

15 April 2024

Draft

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AICIS evaluation statement

Subject of the evaluation

Alkoxysilane ethylenediamine and polyamine derivatives

Chemicals in this evaluation

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1,2-Ethanediamine, N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-	23410-40-4
1,2-Ethanediamine, N-[3-(dimethoxymethylsilyl)propyl]-	3069-29-2
1,2-Ethanediamine, N-[3-(methoxydimethylsilyl)propyl]-	3069-33-8
1,2-Ethanediamine, N,N'-bis[3-(triethoxysilyl)propyl]-	30858-91-4
1,2-Ethanediamine, N-(2-aminoethyl)-N'-[3-(trimethoxysilyl)propyl]-	35141-30-1
1,2-Ethanediamine, N-(phenylmethyl)-N'-[3-(trimethoxysilyl)propyl]-, monohydrochloride	42965-91-3
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1,2-Ethanediamine, N-[2-(trimethoxysilyl)ethyl]-	7719-00-8
1,2-Ethanediamine, N-[2-methyl-3-(methyldipropoxysilyl)propyl]-	80190-61-0
1,2-Ethanediamine, N-[3-[tris(octyloxy)silyl]propyl]-	93804-22-9
1,2-Ethanediamine, N-[3-[tris(decyloxy)silyl]propyl]-	93804-23-0

Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health risk.

Parameters of evaluation

These chemicals are structurally related amino alkoxysilanes listed on the Australian Inventory of Industrial Chemicals (the Inventory). This evaluation statement is a human health risk assessment for all identified industrial uses of chemicals in this group.

Chemicals assessed in this group contain similar amine groups and have similar reactivity (hydrolysis to silanols). Unless experimental data and/or in silico results become available to indicate otherwise, they are expected to have similar toxicity. These chemicals have similar use patterns.

Summary of evaluation

Summary of introduction, use and end use

No specific information about the introduction, use and end use of these chemicals in Australia is available.

Based on international use information, chemicals in this group are expected to have mostly commercial use, commonly as sealants, paints, inks and coatings. These chemicals may also be present in such products available to consumers for domestic applications. Concentrations in consumer products up to 3% have been identified.

These chemicals also have reported site limited uses as intermediates in the manufacture of substances including silicone polymers, plastics and rubber and surface modified substrates (non-metal).

Human health

Summary of health hazards

Chemicals in this group have been placed into sub-groups for the purpose of read across of toxicological information. The 2 sub-groups consist of the 11 amino trialkoxysilanes and 5 amino mono-/dialkoxysilanes. The members of each sub-group are expected to have similar toxicity. The identified health hazards are based on available data for several chemicals which are representative of other chemicals in the 2 sub-groups. Hazard and hazard classifications have been read across to chemical subgroups as unless experimental data or physicochemical considerations indicate otherwise.

Based on the available systemic toxicity information these chemicals are expected to be absorbed following oral, dermal and inhalational exposure. No specific toxicokinetic information is available for these chemicals.

Based on the available data these chemicals:

- have low dermal toxicity
- are not expected to cause serious systemic health effects following repeated oral or dermal exposure
- are not expected to cause specific adverse effects on fertility/sexual function and foetal development
- are not expected to have genotoxic potential.

Available data indicate a difference in acute toxicities between amino trialkoxysilanes and amino di/mono alkoxysilanes. Amino mono- and dialkoxysilanes are expected to have moderate acute oral toxicity and the amino trialkoxysilanes have moderate inhalation toxicity.

Available data indicate that these chemicals are slightly to moderately irritating to skin. The observed effects in animal studies (erythema and persistent scaling) are close to the cut offs for classification (erythema score 2.3 and scaling persisting to day 14). In some studies they are above and are slightly below in other studies. Limited data indicate that amino mono- and dialkoxysilanes are potentially more irritating than the trialkoysilanes.

Based on available data these chemicals are considered to have the potential to cause serious eye damage. Similar effects (persistent corneal damage) were observed in all available studies

Based on available data, these chemicals are expected to have strong skin sensitising potential. Positive results were reported in several guinea pig maximisation tests (GPMTs). Response rates of ≥30% were observed following intradermal induction at ≤0.1%. These chemicals contain structural alerts for skin sensitisation. Two chemicals (CAS No. 93804-22-9 and 93804-23-0) have molecular weights above 500 and as such are expected to have lower dermal availability and therefore lower potency.

In the available 90 day repeated dose oral toxicity study inflammatory effects on the gastrointestinal and respiratory tract and effects on kidneys were observed at high levels of exposure (> 300 mg/kg bw/day).

Limited data are available on repeated dose inhalation toxicity with data only available for a single trialkoxysilane. In available studies (nose-only exposure to aerosols), histopathological abnormalities were observed in the nasal cavity, larynx, and lung were observed. Many of these effects persisted to the end of the recovery period although lower incidence and severity were noted for effects. The lowest observed adverse effect concentration (LOAEC) was 0.045 mg/L/6 hours/day in a 90 day study. No data are available amino mono- and dialkoxysilanes. Although effects in the respiratory tract following inhalation exposure are expected for all chemicals in this evaluation (due to irritant effects) the doses at which effects occur may be higher than for the trialkoxysilanes. Effects based on exposure to vapours has not been investigated.

Hazard classifications relevant for worker health and safety

Chemicals in this group 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 hazard. In addition, these chemicals satisfy the criteria for the following non-GHS hazard statements (SWA 2012):

- AUH071 – Corrosive to the respiratory tract.

The proposed hazard classification is based on read across principles (see **supporting information**). It should be used as a default for these chemicals as follows. If empirical data become available for a specific chemical, this data may be used to amend the default classification for that chemical.

- The acute toxicity – oral classification should apply to the amino mono- and dialkoxysilanes (CAS Nos. 23410-40-4; 3069-29-2; 3069-33-8; 66300-34-3; 80190-61-0).

- The acute toxicity–inhalation classification and specific target organ toxicity should apply to the amino trialkoxysilanes (CAS Nos.1760-24-3; 30858-91-4; 35141-30-1; 42965-91-3; 5089-72-5; 51895-55-7; 64339-13-5; 68845-16-9; 7719-00-8; 93804-22-9; 93804-23-0).
- The skin corrosion/irritation classification should apply to all chemicals except CAS No. 1760-24-3 and CAS No. 23410-40-4.
- The eye irritation classification should apply to all chemicals.
- The skin sensitisation classification should apply to all chemicals in this group although sub-categorisation does not apply to chemicals with molecular weights above 500 (CAS No. 93804-22-9 and 93804-23-0).

Health hazards	Hazard category	Hazard statement
Acute toxicity	Acute Tox. 4	H302: Harmful if swallowed.
Acute toxicity	Acute Tox. 4	H332: Harmful if inhaled.
Skin corrosion/irritation	Skin Irrit. 2	H315: Causes skin irritation.
Serious eye damage/eye irritation	Eye Damage 1	H318: Causes serious eye damage.
Skin Sensitisation	Skin Sens. 1A	H317: May cause an allergic skin reaction.
Specific target organ toxicity (repeated exposure)	STOT Rep. Exp. 2	H373: May cause damage to organs (respiratory tract) through prolonged or repeated inhalation exposure.

Summary of health risk

Public

Based on the available use information, the public may be exposed to these chemicals by incidental skin and eye contact or inhaling aerosols/vapours during use of domestic products (e.g. sealants and coatings). However, once these chemicals are added to a formulated product these chemicals are expected to react with the components of the formulation reducing concentrations to low levels (0.1–0.2%).

These chemicals are strong sensitisers and may cause adverse effects on the respiratory tract when inhaled. However, based on the low concentrations likely to be present and intermittent use of DIY home maintenance products minimal exposure is expected. Therefore, these chemicals are unlikely to pose a risk to the public.

Although the public may come into contact with articles and coated surfaces, it is expected that these chemicals will be bound within the articles and hence will not be available. Therefore, there are no identified risks to the public that require management.

Workers

During product formulation and packaging, dermal, inhalation and ocular exposure might occur, particularly where manual or open processes are used. These processes 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. Good hygiene practices to minimise incidental oral exposure are expected to be in place

Given the critical systemic and local health effects, exposure to these chemicals could pose a risk to workers. Control measures to minimise dermal, ocular and inhalation exposure are needed to manage the risk to workers (see **Proposed means for managing risks** section). Control measures implemented for identified hazards for mono- and di-alkoxysilanes are expected to be sufficient to protect workers from any potential inhalation effects following single or repeated exposure.

Proposed means for managing risk

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.

Information relating to safe introduction and use

The information in this statement should be used by a person conducting a business or undertaking at a workplace (such as an employer) to determine the appropriate control under the relevant jurisdictions and Work Health and Safety laws.

Control measures that could 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 these chemicals 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.

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.

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

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.

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 safety data sheets (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 proposes to be satisfied that the identified risks to human health from the introduction and use of the industrial chemicals can be managed.

Note:

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

Chemicals reported in this evaluation are structurally related amino alkoxysilanes. These chemicals contain multiple amine groups (primary or secondary) linked to at least one alkoxysilane group. These chemicals have been considered in the following 2 subgroups:

- amino trialkoxysilanes (11 chemicals)
- amino mono- and dialkoxysilanes (5 chemicals).

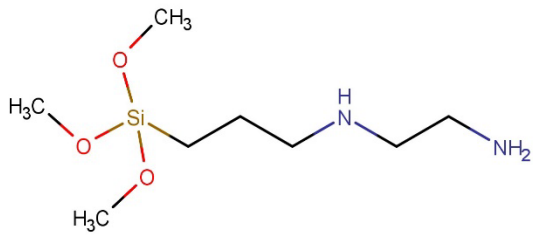
In contact with water, these chemicals rapidly hydrolyse to release corresponding alcohols and silanols.

For the purpose of this evaluation, these chemicals have been assessed as a group based on their similarities in structures, reactivity, and uses.

Chemical identity

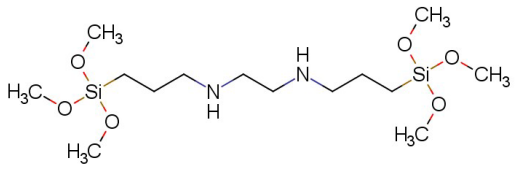
Amino trialkoxysilanes

Chemical name	1,2-Ethanediamine, N-[3-(trimethoxysilyl)propyl]-
CAS No.	1760-24-3
Synonyms	(ethylenediaminepropyl)trimethoxysilane (Trimethoxysilylpropyl)ethylenediamine N-beta-(aminoethyl)-gamma-aminopropyltrimethoxysilane (AEAPTMS) N-(3-(trimethoxysilyl)propyl)ethylenediamine
Molecular formula	C8H22N2O3Si
Molecular weight (g/mol)	222.36
SMILES (canonical)	O(C)[Si](OC)(OC)CCCNCCN
Structural formula:	



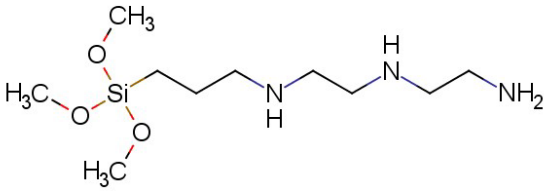
Chemical name	1,2-Ethanediamine, N,N'-bis[3-(trimethoxysilyl)propyl]-
CAS No.	68845-16-9
Synonyms	N,N'-bis[3-(trimethoxysilyl)propyl]ethylenediamine
Molecular formula	C14H36N2O6Si2
Molecular weight (g/mol)	384.62
SMILES (canonical)	O(C)[Si](OC)(OC)CCCNCCNCCC[Si](OC)(OC)OC

Structural formula:



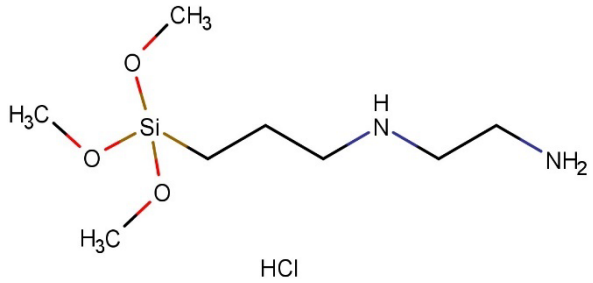
Chemical name	1,2-Ethanediamine, N-(2-aminoethyl)-N'-[3-(trimethoxysilyl)propyl]-
CAS No.	35141-30-1
Synonyms	Diethylenetriaminopropyltrimethoxysilane N-(2-aminoethyl)-N'-[3-(trimethoxysilyl)propyl]ethylenediamine
Molecular formula	C10H27N3O3Si
Molecular weight (g/mol)	265.43
SMILES (canonical)	O(C)[Si](OC)(OC)CCCNCCNCCN

Structural formula:



Chemical name	1,2-Ethanediamine, N-[3-(trimethoxysilyl)propyl]-, monohydrochloride
CAS No.	64339-13-5
Synonyms	N-(3-(trimethoxysilyl)propyl)ethylenediamine monohydrochloride
Molecular formula	C8H22N2O3Si.ClH
Molecular weight (g/mol)	258.82
SMILES (canonical)	Cl.O(C)[Si](OC)(OC)CCCNCCN

Structural formula:



Chemical name	1,2-Ethanediamine, N-(phenylmethyl)-N'-[3-(trimethoxysilyl)propyl]-, monohydrochloride
CAS No.	42965-91-3
Synonyms	N-benzyl-N'-[3-(trimethoxysilyl)propyl]ethylenediamine monohydrochloride
Molecular formula	C15H28N2O3Si.ClH
Molecular weight (g/mol)	348.94
SMILES (canonical)	Cl.O(C)[Si](OC)(OC)CCCNCCNCC=1C=CC=CC1

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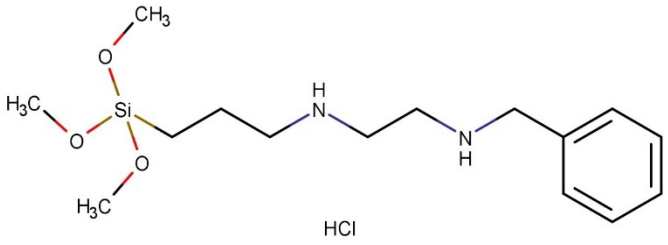
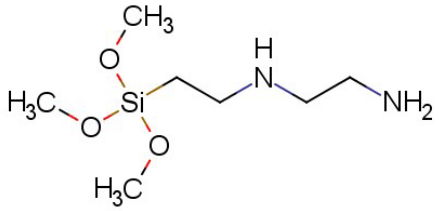


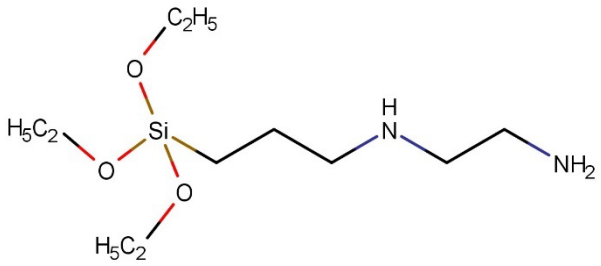
Chemical name	1,2-Ethanediamine, N-[2-(trimethoxysilyl)ethyl]-
CAS No.	7719-00-8
Synonyms	N-[2-(trimethoxysilyl)ethyl]ethylenediamine
Molecular formula	C7H20N2O3Si
Molecular weight (g/mol)	208.33
SMILES (canonical)	O(C)[Si](OC)(OC)CCNCCN

Structural formula:



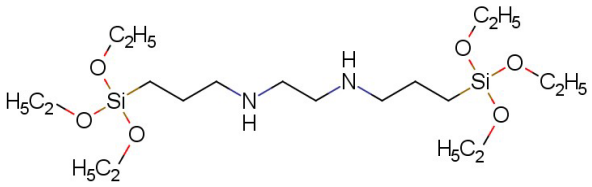
Chemical name	1,2-Ethanediamine, N-[3-(triethoxysilyl)propyl]-
CAS No.	5089-72-5
Synonyms	(Ethylenediaminepropyl)triethoxysilane
	N-[3-(triethoxysilyl)propyl]ethylenediamine
Molecular formula	C11H28N2O3Si
Molecular weight (g/mol)	264.44
SMILES (canonical)	O(CC)[Si](OCC)(OCC)CCCNCCN

Structural formula:



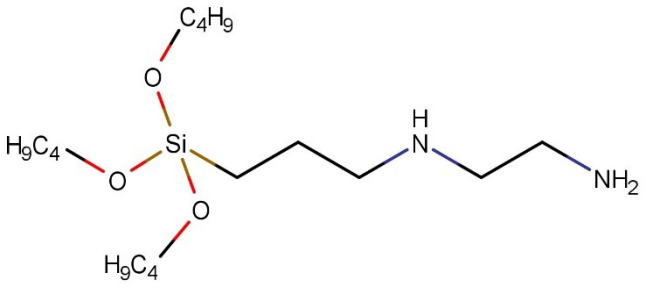
Chemical name	1,2-Ethanediamine, N,N'-bis[3-(triethoxysilyl)propyl]-
CAS No.	30858-91-4
Synonyms	N,N'-bis[3-(triethoxysilyl)propyl]ethylenediamine
Molecular formula	C20H48N2O6Si2
Molecular weight (g/mol)	468.78
SMILES (canonical)	O(CC)[Si](OCC)(OCC)CCCNCCNCCC[Si](OCC)(OCC)OCC

Structural formula:



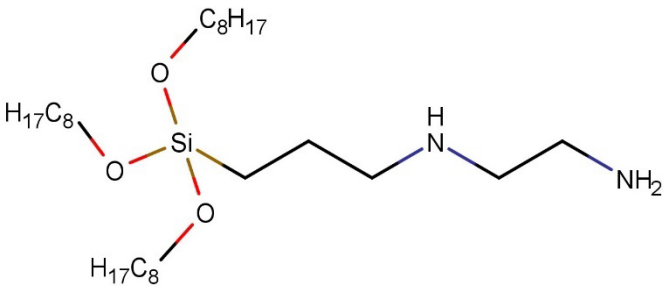
Chemical name	1,2-Ethanediamine, N-[3-(tributoxysilyl)propyl]-
CAS No.	51895-55-7
Synonyms	N-[3-(tributoxysilyl)propyl]ethylenediamine
Molecular formula	C17H40N2O3Si
Molecular weight (g/mol)	348.60
SMILES (canonical)	O(CCCC)[Si](OCCCC)(OCCCC)CCCNCCN

Structural formula:



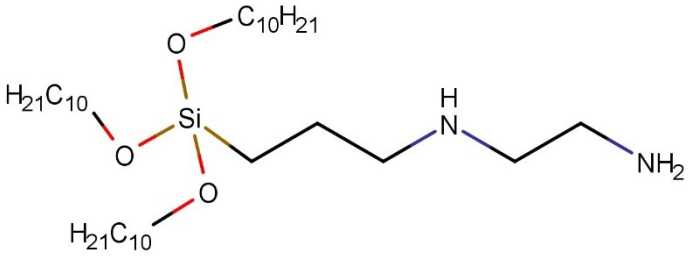
Chemical name	1,2-Ethanediamine, N-[3-[tris(octyloxy)silyl]propyl]-
CAS No.	93804-22-9
Synonyms	N-[3-[tris(octyloxy)silyl]propyl]ethylenediamine
Molecular formula	C29H64N2O3Si
Molecular weight (g/mol)	516.92
SMILES (canonical)	O(CCCCCCCC)[Si](OCCCCCCCC)(OCCCCCCCC)CCCNCCN

Structural formula:



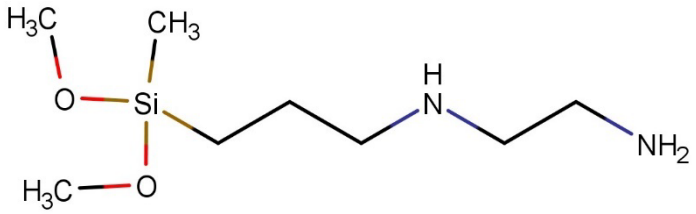
Chemical name	1,2-Ethanediamine, N-[3-[tris(decyloxy)silyl]propyl]-
CAS No.	93804-23-0
Synonyms	N-[3-[tris(decyloxy)silyl]propyl]ethylenediamine
Molecular formula	C35H76N2O3Si
Molecular weight (g/mol)	601.08
SMILES (canonical)	O(CCCCCCCCCC)[Si](OCCCCCCCCCC)(OCCCCCCCCCC)CCCNCCN

Structural formula:



Amino dialkoxysilanes

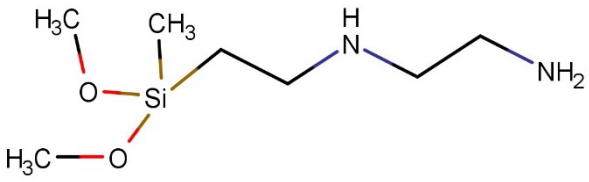
Chemical name	1,2-Ethanediamine, N-[3-(dimethoxymethylsilyl)propyl]-
CAS No.	3069-29-2
Synonyms	N-[3-(dimethoxymethylsilyl)propyl]ethylenediamine
	2-(Aminoethyl)-3-aminopropyldimethoxysilane
Molecular formula	C8H22N2O2Si
Molecular weight (g/mol)	206.36
SMILES (canonical)	O(C)[Si](OC)(C)CCCNCCN

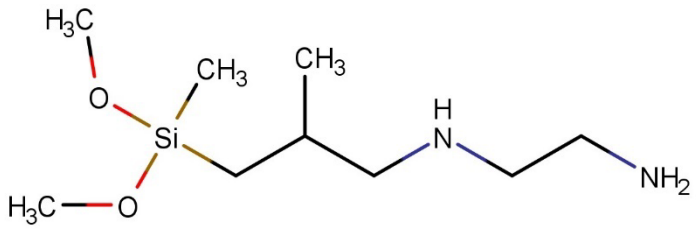


Structural formula:

Chemical name	1,2-Ethanediamine, N-[2-(dimethoxymethylsilyl)ethyl]-
CAS No.	66300-34-3
Synonyms	N-[2-(dimethoxymethylsilyl)ethyl]ethylenediamine
Molecular formula	C7H20N2O2Si
Molecular weight (g/mol)	192.33
SMILES (canonical)	O(C)[Si](OC)(C)CCNCCN

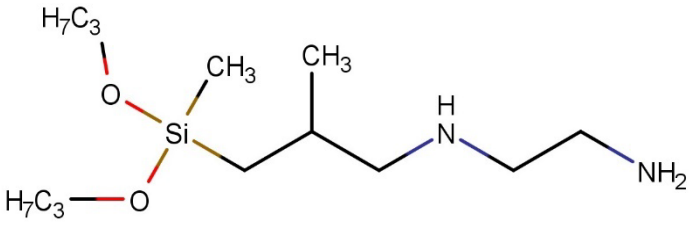
Structural formula:



Chemical name	1,2-Ethanediamine, N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-
CAS No.	23410-40-4
Synonyms	N-[3-(dimethoxymethylsilyl)-2-methylpropyl]ethylenediamine [3-(2-aminoethyl)aminoisobutyl]dimethoxysilane 3,3-dimethoxy-2-oxa-7,10-diaza-3-siladodecan-12-amine
Molecular formula	C9H24N2O2Si
Molecular weight (g/mol)	220.38
SMILES (canonical)	O(C)[Si](OC)(C)CC(C)CNCCN
Structural formula:	

Chemical name	1,2-Ethanediamine, N-[2-methyl-3-(methyldipropoxysilyl)propyl]-
CAS No.	80190-61-0
Synonyms	N-[2-methyl-3-(methyldipropoxysilyl)propyl]ethylenediamine
Molecular formula	C13H32N2O2Si
Molecular weight (g/mol)	276.49
SMILES (canonical)	O(CCC)[Si](OCCC)(C)CC(C)CNCCN

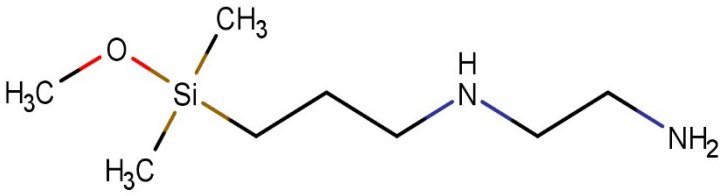
Structural formula:



Amino mono-alkoxysilanes

Chemical name	1,2-Ethanediamine, N-[3-(methoxydimethylsilyl)propyl]-
CAS No.	3069-33-8
Synonyms	N-[3-(methoxydimethylsilyl)propyl]ethylenediamine
Molecular formula	C8H22N2OSi
Molecular weight (g/mol)	190.36
SMILES (canonical)	O(C)[Si](C)(C)CCCNCCN

Structural formula:



Relevant physical and chemical properties

The majority of chemicals in this group are clear, colourless to light yellow, alkaline liquids due to the nature of the amino groups. They have molecular weights (MW) ranging from 222.36 to 468.78 g/mol, except 2 chemicals with MW > 500 g/mol due to their long carbon chain lengths of C8–C10.

Vapour pressures were estimated using the Organisation for Economic Co-operation and Development Quantitative Structure-Activity Relationship Toolbox (OECD QSAR Toolbox) version 4.5 (OECD 2021). For the majority of amino trialkoxysilanes, vapour pressures were within the range 0.0002–1.5 Pa (chemicals with MW > 500 had estimated values < 0.0001 Pa). The amino mono- and dialkoxysilanes had estimated vapour pressures in the range 0.01-6.6 Pa.

Introduction and use

Australia

No specific Australian industrial uses or introduction information have been identified for these chemicals in this evaluation.

International

The following international uses have been identified through:

- the European Union (EU) REACH dossiers (REACH n.d.-a. REACH n.d.-b, REACH n.d.-c, REACH n.d.-d, REACH n.d.-e, REACH n.d.-f)
- the Substances and Preparations in Nordic countries database (SPIN n.d.)
- industry technical data sheets
- Food Contact Chemicals database (FCCdb n.d.)
- United States Environmental Protection Agency Chemical Data Reporting (CDR) (US EPA 2016; US EPA 2020)
- USEPA Chemical and Products Database (USEPA n.d.)
- International assessments (OECD 2003).

Use information was identified for chemicals with CAS numbers 1760-24-3; 3069-29-2; 3069-33-8; 5089-72-5; 23410-40-4; 30858-91-4; 35141-30-1; 42965-91-3 and 68845-16-9. This is expected to be reflective of uses for all chemicals reported in this evaluation.

These chemicals are bifunctional organosilanes that can react with both organic polymers and inorganic surfaces to function as coupling agents or adhesion promoters for paints, inks and coatings. These chemicals have diverse uses, particularly in construction related applications and in manufacturing. Some consumer use is also expected. These chemicals are not expected to have any cosmetic uses.

These chemicals have reported commercial uses in:

- paints and coatings
- ink, toner and colourants
- adhesive and sealants
- textile and leather treatment products
- construction products such as masonry treatment.

Concentrations up to the reporting range 1–30 % were reported (USEPA CDR 2016; USEPA CDR 2020). N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) is reported to be typically used at concentrations < 1 % although some applications as a cross linker concentrations up to 5% are reported (OECD 2003).

Some of the commercial uses may also be used in domestic applications. Consumer uses in paints and coatings, inks and toners and adhesive and sealants were identified for:

- N-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-29-2)
- N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3)
- N,N'-bis[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 68845-16-9)

- N-(2-aminoethyl)-N'-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 35141-30-1).

The Consumer Product Information Database lists several adhesive and sealant products for N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) at concentrations up to 3% (DeLima Associates n.d).

These chemicals have reported site limited use as intermediates in the manufacture of chemicals including silicone polymers, plastics and rubber and surface modified substrates (non-metal). Some of these chemicals have reported use in food contact materials in plastics, coatings, paperboard, adhesives, printing inks.

Existing Australian regulatory controls

Public

No specific controls are currently available for these chemicals.

Workers

These chemicals are not listed on the Hazardous Chemical Information System and no specific exposure standards are available in Australia (SWA n.d.).

International regulatory status

Exposure standards

No exposure standards are currently available for these chemicals.

United States of America

N-[3-(trimethoxysilyl)propyl]- 1,2-Ethanediamine (CAS No. 1760-24-3) is restricted for use only in coatings at a level not exceeding 1.3% by weight of the resin when such coatings are intended for repeated use in contact with certain types of foods under some identified conditions of use (US FDA 2024).

Human exposure

Public

There is a possibility of public exposure via incidental skin or eye contact, or by inhaling aerosols/vapours through use of sealant and coating products containing these chemicals.

However, once these chemicals are added to a formulated product these chemicals are expected to react with the components of the formulation. N-[3-(trimethoxysilyl)propyl]-(CAS No. 1760-24-3)-1,2-ethanediamine is reported to be present in consumer products as the parent silane at 0.1-0.2%. After curing, these chemicals are expected to be largely bound within a matrix and are therefore, not expected to be bioavailable or mobile (OECD 2003)

Health hazard information

These chemicals contain multiple amine groups (primary or secondary) linked to an at least one alkoxysilane group. This functionality appears to be the driver of toxicity with the difference in the amine moieties in their structures considered not to significantly influence toxicity.

In contact with water, these chemicals rapidly hydrolyse to release corresponding alcohols and silanols. Therefore, any potential effect could result from exposures to both the parent compounds and their hydrolysis products (Sharma et al. 2023).

Chemicals reported in this evaluation contain various alkoxy groups: methoxy (majority), ethoxy (3 chemicals), or propoxy, butoxy, octyloxy, decyloxy (one chemical each).The alcohol hydrolysis products are linear primary aliphatic alcohols (C1–C10). Risks and hazards of the short and medium chain aliphatic alcohols have been reviewed and well documented (EFSA 2008; OECD 2017; Patocka & Kuca 2012; Sanderson et al. 2009). Based on this information variations of the alkoxy group are not expected to significantly change the systemic toxicity of these chemicals except at high concentrations. For methoxysilanes, the short term toxicity is often associated with the release of methanol. However, available toxicity data for chemicals substituted with ethoxy rather than methoxy do not indicate a significant difference in toxicity (see **acute toxicity**).

The majority of toxicity data are available for the following chemicals:

Amino trialkoxysilanes

- N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3)
- N-(2-aminoethyl)-N'-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 35141-30-1)
- N-[3-(triethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 5089-72-5; REACH n.d.-c).

Amino mono- and dialkoxysilanes

- N-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-29-2)
- N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-1,2-ethanediamine (CAS No. 23410-40-4)
- N-[3-(methoxydimethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-33-8).

Hazard classifications will be read across within the 2 identified subgroups as appropriate unless experimental data and/or in silico results or physicochemical considerations indicate otherwise.

Toxicokinetics

No in vivo toxicokinetic data are available.

The results from local and systemic toxicity studies indicate that these chemicals are absorbed from the gastrointestinal tract (GIT), respiratory tract, and the skin. Estimated vapour pressures (see **Relevant physical and chemical properties**) indicate that most of chemicals in this group are sufficiently volatile to be inhaled.

These chemicals can be distributed throughout the body. When in contact with moisture or water, these chemicals undergo hydrolysis to produce corresponding alcohols and silanols. In general, the hydrolysis rates of alkoxysilanes become slower when the leaving group is larger and branched, i.e. methoxy > ethoxy > propoxy > butoxy silanes (Issa & Luyt 2019). The rate of hydrolysis is impacted by pH. Hydrolysis studies showed increased hydrolysis rates in acidic conditions (REACH n.d.-a. REACH n.d.-b, REACH n.d.-c, REACH n.d.-d, REACH n.d.-e, REACH n.d.-f). Other factors such as temperature, humidity and solvent system affect the rate of silane hydrolysis (Indumathy et al. 2023). These chemicals are expected to be excreted by kidneys in the urine.

Acute toxicity

The available data indicate a difference in acute toxicities between amino trialkoxysilanes and amino di/mono alkoxysilanes. The available data are not sufficient to identify any further trends within the group and as such read across within the sub-groups is considered appropriate.

Oral

Amino trialkoxysilanes

Based on the available data, the amino trialkoxysilanes in this group are expected to have low acute oral toxicity. The median lethal dose (LD50) ranges between > 2000 – ≤ 5000 mg/kg bw.

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (REACH n.d. -a)

In an acute oral toxicity study in Sprague Dawley (SD) rats of both sexes (EPA 870.1100 / OECD TG 401), an oral LD50 of 2295 mg/kg body weight (bw) (ranged from 1897–2574 mg/kg bw) was reported. Sublethal effects were:

- piloerection
- hunched posture
- waddling gait
- pallid extremities
- dull eyes
- increased salvation
- abnormal respiration
- ungroomed appearance
- faecal abnormalities
- increased sensitivity
- lacrimation
- body tremor.

These clinical signs had resolved by day 6. Congestive changes in the majority of examined organs and tissues were observed in all dead animals upon necropsy.

In another study (OECD TG 401), an oral LD50 of 2413 mg/kg bw was reported in SD rats of both sexes. Clinical signs were tremors, diarrhoea and death. Necropsy of deceased animals showed congestive changes in the lungs, autolysed gastrointestinal (GIT) tract, and pale liver.

In an acute oral toxicity study in Wistar rats (reported to be similar to OECD 4012; non-GLP), an oral LD50 of was 7.46 mL/kg bw (~7609 mg/kg bw; density of 1020 kg/m^3) was reported. Observations included congestion throughout the lungs and the abdominal viscera with some haemorrhage present in the intestines.

N-[3-(triethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 5089-72-5) (REACH n.d.-c)

In an acute oral toxicity study in HanIbm:Wistar rats of both sexes (OECD TG 401), an LD50 of > 2000 mg/kg bw was reported. Sublethal clinical signs were sedation, spasm, dyspnoea, ruffled fur, and diarrhea (reversible within 1–2 days).

Amino mono- and dialkoxysilanes

Based on the available data , the amino mono- and dialkoxysilanes in this evaluation are expected to have moderate acute oral toxicity (LD50 300–2000 mg/kg bw), warranting hazard classification (see **Hazard classfications relevant for worker health and safety** section).

N-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-29-2) (REACH n.d.-d)

In an acute oral toxicity study in SD rats of both sexes, (OECD TG 423) an oral LD50 of > 200 – ≤ 2000 mg/kg bw was reported. At 2000 mg/kg bw (tested in females only), deaths were observed in 3/3 rats within 2 hours of dosing with congestion in the majority of organs and tissues (brain, heart, liver, spleen, kidneys, and stomach distension) at necropsy. At 200 mg/kg bw, all animals (3M/3F) showed piloerection; one or more animals showed:

- hunched posture
- waddling gait
- lethargy
- abnormal respiration
- partially closed eyelids
- pallid extremities
- abnormal faeces
- ungroomed appearance
- prostration.

In an acute oral toxicity study in SD rats of both sexes (OECD TG 401), an LD50 > 2000 mg/kg bw was reported. Deaths were observed in 1/5 male and 2/5 female rats at this dose. Deceased animals showed evidence of congestion in the small intestines, lungs and liver as well as haemorrhage of the rugae of the glandular stomach.

N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-1,2-ethanediamine (CAS No. 23410-40-4) (REACH n.d.-e)

In an acute oral toxicity study in SD rats of both sexes (OECD TG 401), an LD50 of 653 mg/kg bw was reported for combined male and female values (866 and436 mg/kg bw, respectively). Signs of toxicity in surviving rats included extreme lethargy, ataxia, convulsion, and coma. These signs were reported to resolve within 48 hours. Necropsy of deceased animals showed haemorrhagic GIT.

N-[3-(methoxydimethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-33-8) (REACH n.d.-f)

In an acute oral toxicity study in Crl:CD rats of both sexes (OECD TG 423), an oral LD50 of 1000 mg/kg bw was reported. At 2000 mg/kg bw (tested in males only), 2/3 male rats died within 2 days. Clinical signs were ataxia, reduced motility, reduced muscle tone and dyspnoea.

Dermal

Based on the available data, these chemicals are expected to have low acute dermal toxicity (LD50 > 2000 mg/kg bw in rats). Hazard classification is not warranted.

Amino trialkoxysilanes

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (REACH n.d.-a)

In an acute dermal toxicity study in New Zealand White (NZW) rabbits of both sexes (EPA 870.1200 / OECD TG 402), a dermal LD50 of > 2000 mg/kg bw was reported. There were no deaths or clinical signs of toxicity. At study termination (day 15), very slight erythema (grade 1) was still observed in 3/6 rabbits, desquamation of the skin on application site in 6/6 rabbits, and localised necrosis in 1/6 rabbit.

In an acute dermal toxicity study in SD rats of both sexes (OECD TG 402), a dermal LD50 of > 2009 mg/kg bw was reported. A single test dose was used. No deaths, clinical effects or abnormal macroscopic pathology were noted at this dose.

In a non-guideline dermal toxicity study conducted in NZW rabbits in 1966, a dermal LD50 > 16 mL/kg bw (~16000 mg/kg bw; density of 1000 kg/m^3). Marked erythema was observed at this level. Gross pathology investigations revealed congested lungs, liver and spleen and pale kidneys. Although this study was considered of insufficient quality for determination of a reliable LD50, the observed effects suggest dermal absorption occurred.

N-(2-aminoethyl)-N'-[3-(trimethoxysilyl)propyl]- 1,2-ethanediamine (CAS No. 35141-30-1) (REACH n.d.-b)

In an acute dermal toxicity study conducted in 1975 (non-guideline; non-GLP), LD50 (dermal, rabbit) > 16 mL/kg bw (~16320 mg/kg bw; density of 1020 kg/m3). Deaths with congested kidneys occurred in 2/7 male rats on days 9–10.

Amino mono- and dialkoxysilanes

N-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-29-2) (REACH n.d.-d)

In an acute dermal toxicity study in NZW rabbits of both sexes (OECD TG 402 equivalent; non-GLP), a dermal LD50 ≥ 16 mL/kg bw (or 16000 mg/kg bw) was reported. Erythema was present in all animals. One deceased male rat had dark red lungs and darkened liver. Male survivors had red patched trachea and discoloured lungs. Gross examination revealed scrotal swelling in 4/4 rabbits.

N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-1,2-ethanediamine CAS No. 23410-40-4 (REACH n.d.-e)

In an acute toxicity study in NZW rabbits of both sexes (OECD TG 402), a dermal LD50 of > 2000 mg/kg bw was reported. No deaths, clinical effects or abnormal macroscopic pathology were noted.

Inhalation

Amino trialkoxysilanes

Based on the available data, the amino trialkoxysilanes in this group are expected to be harmful if inhaled, warranting hazard classification (see **Hazard classifications relevant for worker health and safety** section). Similar effects were observed for the trimethoxy and triethoxy substituted silane indicating that the alcohol metabolite is not significantly impacting toxicity. Observed effects are consistent with the irritant nature of these chemicals. Reliable studies investigating effects based on exposure to vapours have not been identified.

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (REACH n.d.-a)

In an acute inhalation toxicity study (EPA 870.1300 / OECD TG 403), rats (5/sex/dose; strain unspecified) were exposed (whole body) to aerosols of the chemical at 0, 0.515, 1.06, 1.49, 2.44, 5.75 mg/L/4 hours. Mortalities with severely congested lungs were noted in 8/10 and 9/10 animals at 2.44–5.75 mg/L, respectively. The median lethal concentration (LC50) (aerosol, rat) was 1.49–2.44 mg/L/ 4 hours. Surviving female rats showed pale raised hardened areas of congestion in the lungs at 5.75 mg/L and increased lung weights at ≥ 2.44 mg/L. A dose related reduction in body weight gain was observed at 0.515–1.49 mg/L, and lower food consumption and pale raised lungs in all dosed groups.

N-[3-(triethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 5089-72-5) (REACH n.d.-c)

In an acute inhalation toxicity study (OECD TG 403), Wistar rats (5/sex/dose) were exposed to the chemical aerosol (nose only) at 0.23, 0.83, 1.78 or 5.6 mg/L/4 hours. The calculated LC50s (aerosol, rat) were 1.1–1.18 mg/L/4h (M–F). Mortality and clinical toxicity signs (panting, irregular respiration, coat bristling, uncoordinated gait, blood coloured nasal discharge) were seen in all dosed groups. A dose dependent reduction in body weight gain in the week after dosing was observed. Deceased animals showed abnormal findings at necropsy, including red coloured (congested) lungs, dark red patches, foam emission on dissection and plethoric lungs, particularly in male rats.

Amino mono- and dialkoxysilanes

Limited data are available for these chemicals. Although effects in the lungs and some mortality was observed in one study, effects are not sufficient to warrant classification. The available data indicate that the amino mono- and dialkoxy silanes have lower acute toxicity following inhalation compared with the trialkoxysilanes.

N-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-29-2) (REACH n.d.-d)

In an acute inhalation toxicity study (OECD TG 403), Wistar rats (5/sex/dose) were exposed to the chemical aerosol (via a head and nose inhalation system) at 3.7 or 5.2 mg/L/4 hours. An LC50 (aerosol, rat) of > 5.2 mg/L/4 hours was reported. Mortalities (1/10, 2/10) and abnormalities of the lungs (4/10 and 6/10) were seen in the 2 dosed groups, respectively. Animals showed impaired body weight gain, discoloured or patchy lungs with foam emission on dissection. Clinical toxicity signs included breathlessness or noisy breathing, ataxia,

prostration, narrowed eye, blood coloured nasal discharge, decreased spontaneous activity, aggressive or withdrawn behaviour, and sunken flanks.

In an acute inhalation toxicity study (OECD TG 403 equivalent), an LC50 (aerosol, rat) of > 3 mg/L/4 hours via whole body exposure was reported. No deaths or abnormal findings at necropsy were reported.

N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-1,2-ethanediamine (CAS No. 23410-40-4) (REACH n.d.-e)

In an acute inhalation toxicity study in SD rats of both sexes (OECD TG 403; non-GLP), an LC50 of > 0.6 mg/L/4 hours (> 600 mg/m³) via whole body exposure was reported. This was the highest nominal concentration tested. No information was given on the analytical verification of test concentration or the method of generating aerosol. No evidence of toxicity was observed in any of the test animals.

Corrosion/Irritation

Skin irritation

The available data indicate that these chemicals are slightly to moderately irritating to skin. The observed effects in animal studies (erythema and persistent scaling) are close to the cut offs for classification (erythema score 2.3 and scaling persisting to day 14). In some studies, they are above and others slightly below. The limited data indicate that amino mono- and dialkoxysilanes are potentially more irritating than the trialkoysilanes. Although the 2 salts of hydrochloric acid (CAS No. 42965-91-3 and CAS No. 64339-13-5) may have a lower irritation potential, no data are available to support this. The available data are not sufficient to identify any further trends within the group and as such read across is considered appropriate. Overall hazard classification is warranted unless there is specific experimental data supporting lower effects (CAS No. 1760-24-3 and CAS No. 23410-40-4) (see **Hazard classifications relevant for worker health and safety** section).

Amino trialkoxysilanes

N-[3-(triethoxysilyl)propyl]- 1,2-ethanediamine (CAS No. 5089-72-5) (REACH n.d.-c)

In a dermal irritation study (OECD TG 404; Himalayan rabbits), erythema (mean scores 1, 1, 2) was not fully reversible in 3/3 rabbits within 14 days. Very slight oedema was fully reversible in 2/3 and 1/3 rabbits within 24 hours and 72 hours, respectively. Skin induration (thickening and hardening) from day 4 and peeling of the application site from day 9 persisted to the end of the study in all animals. Laceration of skin induration was observed in 1/3 animals at day 6, 7, and 9.

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (OECD 2003; REACH n.d.-a)

In a dermal irritation study in NZW rabbits (EPA 870.2500 / OECD TG 404), well defined erythema (mean scores 1.67, 2, 2), and no oedema or very slight oedema (mean scores 0, 0, 0.67) were noted. Desquamation of the stratum corneum developed in 3/3 animals. All dermal reactions were reversible by day 13.

In a dermal irritation study in NZW rabbits (OECD TG 404; 4 hour occlusive application), slight to moderate erythema was seen in 6/6 rabbits and slight oedema in 4/6 rabbits. Total

erythema score for 6 animals at 24, 48 and 72 hours: 10, 7, 6. Total oedema score for 6 animals at 24, 48 and 72 hours: 3, 3, 2. Individual scores were not reported, Desquamation appeared on 3 animals within 3–7 days and remained on 2 animals after 10 days. No erythema or oedema was evident on day 10.

In 4 other guideline studies (OECD TG 404 or equivalent), mean scores were ≥ 1.5 and < 2.3 for either erythema or oedema in NZW rabbits (3 studies) and white Russian rabbits (one study). All dermal reactions were fully reversible within 14 days.

Amino mono- and dialkoxysilanes

N-[3-(dimethoxymethylsilyl)propyl]- 1,2-ethanediamine (CAS No. 3069-29-2) (REACH n.d.-d)

In a key dermal irritation study (OECD TG 404), the chemical was applied to the shaved skin of NZW rabbits (1 male / 2 females) under semi-occlusive conditions for 4 hours. Well defined to moderate/severe erythema (mean scores 2, 3, 3; not resolved in 2/3 animals within 14 days) and oedema (mean scores 0.7, 0.33, 1.7) were observed.

In an older study in NZW rabbits (OECD TG 404), maximum mean scores and an average of 6 readings for erythema (2 and 1.4) and for oedema (1.3 and 0.8, respectively) were reported. The reactions were fully reversible within 14 days.

N-[3-(methoxydimethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-33-8) (REACH n.d.-f)

In a dermal irritation study in Himalayan rabbits (OECD TG 404), erythema (grade 3 in 3/3 rabbits) was not fully reversible within 14 days. Very slight oedema (grade 1) was fully reversible within 24 hours. Necrosis at the application site was observed after 72 hours (2/3 animals) or 4 days (1/3 animals) after patch removal, as well as peeling after 14 days (2/3 animals).

N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-1,2-ethanediamine (CAS No. 23410-40-4) (REACH n.d.-e)

In a dermal irritation study (EPA 870.2500 / OECD TG 404; NZW rabbits), very slight erythema (grade 1; resolved within Days 9–11) and no oedema effects were observed.

Eye irritation

Based on the available data, chemicals in this group are expected to cause serious eye damage, warranting hazard classification (see **Hazard classifications relevant for worker health and safety** section). Similar effects (persistent corneal damage) were observed in all available studies. In contact with fluid in the eye, these amino alkoxysilanes hydrolyse rapidly to release alcohols and silanols. The local irritancy may be caused by the amine functionality of the chemical or hydrolysis products. Although the 2 salts of hydrochloric acid (CAS No. 42965-91-3 and CAS No. 64339-13-5) may have a lower irritation potential, no data are available to support this. The available data are not sufficient to identify any further trends within the group and as such read across is considered appropriate

Amino trialkoxysilanes

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (REACH n.d.-a)

In an eye irritation study in NZW rabbits (OECD TG 405), effects on corneal opacity, iris, conjunctivae and chemosis (mean scores 2, 1, 2–2.67, and 3, respectively). Irritation effects in 5/6 rabbits were not reversible within 21 days.

In 4 other studies (OECD TG 405 or equivalent), irreversible effects on the eyes were observed in at least one NZW rabbit (3 studies with 14 day observation period; even after washing of the eyes 4–5 seconds post instillation), or one White Russian rabbit (one study with 30-day observation period).

Two studies (OECD TG 405 or equivalent) also showed severe eye effects in a single NZW rabbit. Due to the severity of the effect, the study was terminated 2–3 days after instillation. No additional animals were tested.

N-(2-aminoethyl)-N'-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 35141-30-1) (REACH n.d.-b)

In an eye irritation study (OECD TG 405; NZW rabbits), severe effects on corneal opacity, iris, conjunctivae and chemosis (mean scores 2, 0, 2, and 2, respectively) were not fully reversed in a single rabbit within 21 days. Corneal lesions were not fully reversed by the end of the 21 day observation period.

In an in vitro eye corrosion and severe irritation study (OECD TG 437 – Bovine corneal opacity and permeability (BCOP)), the chemical at 61.5% produced an in vitro irritancy score (IVIS) of 4.2. According to the OECD TG 437 criterion, no stand-alone prediction can be made when the IVIS is > 3 and ≤ 55.

N-[3-(triethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 5089-72-5) (REACH n.d.-c)

In an eye irritation study in Himalayan rabbits (OECD TG 405), effects on cornea (grade 2) and iris (grade 1) were not fully reversible in at least 2/3 animals within the 21 day observation period.

Amino mono- and dialkoxysilanes

N-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-29-2) (REACH n.d.-d)

In an eye irritation study (OECD TG 405), severe to extremely severe effects on corneal opacity, iris, conjunctivae and chemosis (scores 3, 1, 3, and 4, respectively) were reported in a single NZW rabbit. Due to the severity of the effects, the study was terminated at 30 minutes.

In silico

The mechanistic profiling functionality of the OECD Quantitative Structure-Activity Relationship (QSAR) Application Toolbox version 4.5 (OECD 2023), or the knowledge based expert system Deductive Estimation of Risk from Existing Knowledge (DEREK) Nexus version v.6.0.1 (Lhasa Limited n.d.) did not reveal any skin irritation structural alerts for chemicals in this group.

OASIS TIMES (optimized approach based on structural indices set–tissue metabolism simulator) (OASIS LMC n.d) was utilised to estimate the skin irritation potential of these chemicals. A structural alert for skin irritation, silicon ethers, was reported for 6 chemicals

(CAS Nos. 1760-24-3; 35141-30-1; 68845-16-9; 30858-91-4; 7719-00-8; 64339-13-5). These chemicals were predicted (within applicability domain) to be irritating to skin. No structural alert was reported for the remaining chemicals in this group.

Respiratory irritation

Given the corrosive properties of these chemicals observed in eye irritation studies, inhalation could lead to irritation/corrosion of the mucous membranes of the respiratory tract. In acute inhalation studies the clinical signs and the necropsy findings (audible respiration, red coloured (congested) lungs, blood coloured nasal discharge) (see **acute toxicity** section) indicate that the mechanism of toxicity is corrosivity, warranting classification (see **Hazard classifications relevant for worker health and safety** section). Similar effects were seen for the amino trialkoxysilanes and amino mono- and dialkoxysilanes. The local irritancy may be caused by the amine functionality of the chemical or hydrolysis products. The available data are not sufficient to identify any further trends within the group and as such read across is considered appropriate.

Sensitisation

Skin sensitisation

Based on the available data, chemicals reported in this evaluation are expected to have strong skin sensitising potential. These chemicals were reported to have positive results in several guinea pig maximisation tests. Response rates ≥30% were observed following intradermal induction at ≤ 0.1%, warranting hazard classification (see **Hazard classifications relevant for worker health and safety** section).

All chemicals contain similar amino groups in their structures: majority with ethylenediamine (EDA) and one with diethylenetriamine (DETA) moiety. Both EDA and DETA are listed as skin sensitisers – Category 1 in HCIS (SWA). In addition, QSAR predictions from the Derek Nexus version 2.2 have provided structural alerts in these chemicals for skin sensitisation. Two chemicals (CAS No. 93804-22-9 and 93804-23-0) have molecular weights above 500 and as such are expected to have lower dermal availability. It is not considered appropriate to read across the sub-categorisation for these chemicals. The available data are not sufficient to identify any further trends within the group and as such read across for the remaining chemicals is considered appropriate.

Amino trialkoxysilanes

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (OECD2003, REACH n.d. -a)

Strong sensitising effects (Category 1A) were reported in 2 over 3 guideline studies. In a GPMT (OECD TG 406), Dunkin-Hartley (DH) guinea pigs of both sexes were induced via intradermal injection at 0.1% and dermal application at 10%, followed by topical challenge at 10%. A response rate of 30% (6/20 animals) was reported.

In a GPMT (OECD TG 406), DH guinea pigs of both sexes were induced via intradermal injection at 0.5% and dermal application at 100%, followed by topical challenge at 100%. A response rate of 100% (20/20 animals) was reported.

In a mouse local lymph node assay (LLNA) (OECD TG 429), stimulation indices were 1.7, 2.5, 4.7, 7.9 at concentrations of 5%, 10%, 25%, 50%, respectively. Estimated concentration needed to produce a stimulation index of 3 (EC3) was 13%.

Amino mono- and dialkoxysilanes

N-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-29-2) (REACH n.d.-d)

In a GPMT (OECD TG 406), DH guinea pigs of both sexes were induced via intradermal injection at 0.1% and topically challenge at 100%. A response rate of 95% (19/20 animals), was reported.

N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-1,2-ethanediamine (CAS No. 23410-40-4) (REACH n.d.-e)

In a GPMT (OECD TG 406 equivalent), Hartley guinea pigs were induced via intradermal injection at 5% and dermal application at 5%, followed by topical challenge at 5%. A response rate of 45% (9/20 animals) was reported. Although the result meets the criteria for subcategory 1B classification, the use of high intradermal induction concentration and low challenge concentration could not exclude classifying this chemical for subcategory 1A.

In silico

The knowledge based expert system DEREK Nexus version v.6.0.1 predicted that these chemicals had the potential for skin sensitisation (diamine) and were likely to be weak sensitisers (Lhasa Limited n.d.). The mechanistic and endpoint specific profiling functionality of the OECD QSAR Toolbox version 4.5 and OASIS TIMES predictions indicated that these chemicals were non-sensitisers. Application of skin metabolism simulator in OECD QSAR Toolbox and OASIS TIMES indicated the metabolites (aldehydes and carbonyl compounds) had skin sensitisation potentials with alerts via Schiff base formation (OASIS LMC n.d.; OECD 2023).

Repeat dose toxicity

Oral

Based on the available data, chemicals in this group could have the potential to cause irritating or inflammatory effects on the gastrointestinal tract and adverse effects on the kidneys via oral route exposure at high doses. The oral no observed adverse effect level (NOAEL) for systemic effects is 300 mg/kg bw/day, although the severity of the adverse effects and corresponding doses could vary between these chemicals. Overall classification is not warranted as the repeated dose toxicity appear related to the irritant nature of these chemicals. The available data are not sufficient to identify any further trends within the group, therefore read across is considered appropriate.

Amino trialkoxysilanes

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (OECD 2003, REACH n.d. -a)

In a combined repeated dose toxicity and reproduction/developmental toxicity screening study (OECD TG 422), SD rats (10/sex/dose) were administered the chemical at

0, 25, 125, 500 mg/kg bw/day by oral gavage for 28–68 days in male and female rats, respectively. Clear perioral soiling, laboured breathing, increased nasal sounds and/or squeaky vocalisation were seen commonly in high dose animals. These incidences were less frequent at lower doses and lasted up to day 18. These effects were not considered to be adverse by the investigators. There were no treatment related effects on body weight, organ weight, food consumption, haematology, serum chemistry, functional observational battery, motor activity, gross or histopathological examination. Therefore, the NOAEL for systemic effects was determined to be 500 mg/kg bw/day in rats (the highest dose tested).

In two 7 day dose range finding studies (non-guideline; SD rats 6F/dose or 3/sex/dose), the NOAEL was also reported at 500 mg/kg bw/day, based on either increased breathing sounds or rales at ≥750 mg/kg bw/day, or soiling and wetness around the muzzle, body weight losses and/or reduced food consumption and mortality (1M/1F) at 1000 mg/kg bw/day. Both deceased animals had gastrointestinal track distension and small, dark livers.

Amino mono- and dialkoxysilanes

N-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-29-2) (REACH n.d.-d))

In a 90 day repeated dose oral toxicity study (OECD TG 408), Wistar rats (10–15/sex/dose) were administered the chemical by gavage at 0, 100, 300 or 500 mg/kg bw/day. The NOAEL for systemic effects was determined to be 300 mg/kg bw/day, based on renal lesions correlating with increased kidney weights at 500 mg/kg bw/day. The administered high dose used in this study was reduced from 1000 to 750 (Day 24) and then to 500 mg/kg bw/day (Day 39 of treatment) due to increased mortality. Deceased animals showed necrotic and/or inflammation associated lesions in the respiratory tract and/or in the stomach and in the pleural region and/or oesophagus. These effects were considered to be due to gavage associated reflux or accidental influx causing a local tissue injury associated with the irritating nature of the chemical.

N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-1,2-ethanediamine (CAS No. 23410-40-4) (REACH n.d.-e)

In a 90 day repeated dose oral toxicity study (OECD TG 408), SD rats (10–15/sex/dose) were administered the chemical by gavage at 0, 30, 100 or 300 mg/kg bw/day. The NOAEL for systemic effects was determined to be 300 mg/kg bw/day (the highest dose tested). Six deaths occurred in both males and females of the high dose group which were considered attributable to gavage associated reflux (i.e. laryngeal and/or tracheal neutrophilic inflammation) by the study authors. Clinical observations in 5/6 animals prior to death included abnormal breathing sounds, dehydration, laboured breathing, abdominal distention, and body weight losses (5.5% in one male and 7.9–22% in all females).

Dermal

The available data are considered insufficient to evaluate repeated dose toxicity via the dermal route, although based on oral studies serious systemic effects (at doses relevant for classification) following repeated dermal exposure are not expected.

Amino trialkoxysilanes

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (REACH n.d. -a)

In an 11 day dermal repeat dose toxicity study (non-guideline), Fischer 344 rats (10–20/sex/dose) were treated with 9 applications at 0, 257.5, 772.5 or 1545 mg/kg bw/day (nominal). There were necropsy and microscopic observations as well as transient clinical signs indicative of slight to moderate skin irritation in mid and high dose males and low dose females. No clear indication of systemic toxicity was observed. The NOAEL for systemic effects was 1545 mg/kg bw/day in rats, the highest dose tested.

Amino mono- and dialkoxysilanes

No data are available.

Inhalation

Limited data are available. Based on the available guideline 90 day study, the amino trialkoxysilanes may cause damage to the respiratory tract through prolonged or repeated inhalation exposure. Effects were observed at doses 2 orders of magnitude lower than doses causing effects in the respiratory tract following acute exposures (see **acute toxicity** section), warranting hazard classification (see **Hazard classifications relevant for worker health and safety** section). Although effects in the respiratory tract following inhalation exposure is expected for all chemicals in this evaluation (due to irritant effects), the available data indicate that the amino mono- and dialkoxy silanes have lower acute toxicity following inhalation compared with the trialkoxysilanes. Therefore, the doses at which effects occur following repeated exposure may be higher than for the trialkoxysilanes. Overall, in the absence of further data read across is considered appropriate only for the trialkoxysilanes.

Amino trialkoxysilanes

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (REACH n.d. -a)

In a 90 day inhalation toxicity study (OECD TG 413), SD rats (20/sex/dose) were exposed to the chemical aerosol (via a nose only system) at approximately 0, 0.005, 0.015 or0.045 mg/L/6 hours/day for 5 days/week. The no observed adverse effect concentration (NOAEC) was 0.015 mg/L/6 hours/day, based on adverse effects at 0.045 mg/L/6 hours/day, the lowest observed adverse effect concentration (LOAEC) tested. The adverse clinical observations included lower body weights and body weight gains, gross findings in the lungs, increased lung weights, and histopathological abnormalities were observed in the nasal cavity, larynx, trachea, and lungs in both male and female rats. Many of these effects persisted to the end of the recovery period although lower incidence and severity were noted for effects on the respiratory tract in recovery high dose animals.

In a 28 day dose range finding study (non-guideline; SD rats 5/sex/dose), the NOAEC was reported at 0.01 mg/L/6 hours/day and the LOAEC was 0.05 mg/L/6h/day, based on severe microscopic findings in the nasal cavity, larynx, and lungs of both male and female rats.

Effects based on exposure to vapours has not been investigated.

Amino mono- and dialkoxysilanes

No data are available.

Genotoxicity

Based on the available data, chemicals in this group are not expected to have genotoxic potential.

Amino trialkoxysilanes:

In vitro

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (OECD 2003, REACH n.d. -a)

- Negative results were reported following:
  - Several bacterial reverse mutation assays (Ames) (EPA 870.5100 / OECD TG 471) in *Salmonella (S.) typhimurium* TA1535, TA1537, TA1538, TA97, TA98, TA100, and 2 strains of *Escherichia coli* WP2 Trp pKM101 (CM881) and WP2 Trp uvrA pKM101 (CM891), with or without metabolic activation.
  - A mammalian cell gene mutation test (OECD TG 476 equivalent) in Chinese hamster ovary (CHO) cells, using hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus, with or without metabolic activation.
  - A sister chromatid exchange test (EPA 870.5900 / OECD TG 479 equivalent) in CHO cells, with or without metabolic activation.

N-(2-aminoethyl)-N'-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine(CAS No. 35141-30-1) (REACH n.d.-b)

Negative results were reported following:

- A bacterial reverse mutation assay (OECD TG 471 equivalent) in *S. typhimurium* TA1535, TA1537, TA98, TA100, with or without metabolic activation.
- A chromosomal aberration test (OECD TG 473) in human peripheral lymphocytes, with or without metabolic activation.
- A mammalian cell gene mutation test (OECD TG 476 equivalent) in CHO cells, using Hprt locus, with or without metabolic activation.

N-[3-(triethoxysilyl)propyl]- 1,2-ethanediamine (CAS No. 5089-72-5) (REACH n.d.-c)

A negative result was reported following a bacterial reverse mutation test (OECD TG 471 equivalent) in *S. typhimurium* TA1535, TA1537, TA98, TA100, with or without metabolic activation.

Amino mono- and dialkoxysilanes

N-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine (CAS No. 3069-29-2) (REACH n.d.-d))

Negative results were reported following:

- Bacterial reverse mutation assays (EPA 870.5100 / OECD TG 471) in *S. typhimurium* TA1535, TA1537, TA98, TA100, and *E.* WP2 Trp uvrA pKM101 (CM891), with or without metabolic activation.

- A bacterial reverse mutation test (OECD TG 471) in *S. typhimurium* TA1535, TA1537, TA98, TA100, TA102, with or without metabolic activation.
- A bacterial reverse mutation test (non-guideline) in *S. typhimurium* TA97, TA98, TA100, with or without metabolic activation.

N-[3-(methoxydimethylsilyl)propyl]-1,2-ethanediamine,(CAS No. 3069-33-8) (REACH n.d.-f)

A negative result was reported following a bacterial reverse mutation test (OECD TG 471) in *S. typhimurium* TA1535, TA1537, TA98, TA100, TA102, with or without metabolic activation.

In vivo

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (OECD 2003, REACH n.d. -a)

Negative results were reported following an in vivo erythrocyte micronucleus assay (OECD TG 474 equivalent) in Swiss Webster mice (5/sex/dose) at single intraperitoneal doses of 0, 87.5, 175, or 280 mg/kg bw.

In silico

Based on the mechanistic profiling functionality of the OECD QSAR Toolbox version 4.5, structural alerts for DNA binding (Schiff base formation) and in vivo micronucleus formation (H-acceptor-path3-Hacceptor) were identified for these chemical and their metabolites (OECD 2023). No alerts for mutagenicity in vitro (no misclassified or unclassified features) and mutagenicity (Ames) in the in vivo micronucleus test were reported in DEREK Nexus version v.6.0.1 and OASIS TIMES (Lhasa Limited n.d.; OASIS LMC n.d).

Carcinogenicity

No data are available.

Reproductive and development toxicity

The available data for 2 chemicals do not indicate adverse effects on reproduction or development through repeated oral exposure.

Amino trialkoxysilanes

N-[3-(trimethoxysilyl)propyl]-1,2-ethanediamine (CAS No. 1760-24-3) (OECD 2003, REACH n.d. -a)

In a combined repeated dose toxicity and reproduction/developmental toxicity screening study (OECD TG 422), SD rats (10/sex/dose) were treated with 0, 25, 125 or 500 mg/kg bw/day by gavage for 28–68 days in male and female rats, respectively (see **Repeated Dose Toxicity**). No significant adverse effects were observed in testes weight, epididymis weight, reproductive performance, teratogenic effects or pup parameters examined at up to 500 mg/kg bw/day (the highest dose tested). The parental and developmental NOAEL was 500 mg/kg bw/day.

In a prenatal developmental toxicity study (OECD TG 414), SD rats (25F/dose) were administered the chemical by gavage at 0, 100, 500 or 750 mg/kg bw/day on gestation days 6–19. The maternal and developmental NOAEL was established at 750 mg/kg bw/day (the highest dose tested). No evidence of adverse effects on maternal and foetal survival, body weight and/or food consumption, uterine weight, macroscopic examination or foetal malformation or developmental variation at any dose levels. Chemical related effects such as increased incidences of rales, clear material around the mouth and/or salivation prior to dosing at ≥500 mg/kg bw/day were not considered adverse in the absence of maternal toxicity.

Amino mono- and dialkoxysilanes

N-[3-(dimethoxymethylsilyl)-2-methylpropyl]-1,2-ethanediamine (CAS No. 23410-40-4) (REACH n.d.-e)

In a prenatal developmental toxicity study (OECD TG 414), SD rats (25F/dose) were administered the chemical daily by gavage at 0, 50, 150 or 400 mg/kg bw/day on gestation days (GD) 6–20. Dose dependent abnormal sounds and/or laboured breathing were noted in 8/25 mid dose animals GD 7–19, and in 17/25 high dose animals GD 8–21. No significant adverse effects on maternal body weights, food consumption, intrauterine growth, fertility parameters, or foetal skeletal and visceral malformation, or anogenital distance, pup survival and body weight were noted at any dose levels. The maternal and developmental NOAEL was determined at 400 mg/kg bw/day.

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REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.-b) Dossier for *N-(2-aminoethyl)-N'-[3-(trimethoxysilyl)propyl]ethylenediamine, CAS No. 35141-30-1*, European Chemicals Agency website, assessed January 2024.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.-c) Dossier for *N-[3-(triethoxysilyl)propyl]ethylenediamine, CAS No. 5089-72-5*, European Chemicals Agency website, assessed January 2024.

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