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

Cyanoacrylates

Evaluation statement

26 June 2024

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AICIS evaluation statement

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Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health risk.

Parameters of evaluation

Chemicals in this group are cyanoacrylates listed on the Australian Inventory of Industrial Chemicals (the Inventory). These chemicals have been assessed as a group as they are structurally similar and have similar use patterns.

This evaluation is a human health risk assessment of all identified industrial uses of these chemicals in Australia.

Summary of evaluation

Summary of introduction, use and end use

Chemicals in this group function as fast-setting adhesives in cosmetic, domestic, commercial and site-limited applications.

Based on international use information, cyanoacrylates are used in eyelash adhesives and nail enhancement products for professional and consumer use with reported concentrations typically 85–100%. Some of these chemicals reported in this evaluation have identified uses in cosmetic eyelash and nail glues in Australia.

In Australia, there is widespread consumer and professional use of adhesives containing cyanoacrylates (also known as 'superglue'). The concentrations in Australia can range from 60–100% in these products, which is consistent with concentrations reported internationally. According to international information, some chemicals in this evaluation are used in adhesives for specific hobby and professional use such as model building, woodworking and in archery fletching glues.

These chemicals have reported commercial uses as adhesives and have site-limited uses in polymerisation processes and manufacturing.

Some chemicals reported in this evaluation have therapeutic uses in tissue adhesives and sealants, these are considered non-industrial uses in Australia.

Human health

Summary of health hazards

The identified hazards are based on the available data for these chemicals. Most of the available data are from humans or animals that were exposed to either methyl cyanoacrylate or ethyl cyanoacrylate. Read across data from the structurally similar chemical 2-octyl cyanoacrylate (CAS No. 133978-15-1) has been used to support the hazard conclusions.

Based on the available data, these chemicals:

- have low acute, dermal and inhalation toxicity
- are not expected to cause serious systemic health effects following repeated oral, dermal or inhalation exposure
- are not considered to have genotoxic potential
- are not expected to be carcinogenic
- are not expected to cause specific adverse effects on fertility or development.

There are existing classifications for skin, eye and respiratory irritation for methyl cyanoacrylate and ethyl cyanoacrylate. There is limited available data to evaluate these classifications. However, persistent skin inflammation and eye irritation (scores >1/4 for corneal opacity and >2/3 for conjunctival redness) were reported in animal studies. There are well conducted animal studies for high molecular weight cyanoacrylates (>153 g/mol) showing, at most, slight skin irritation that did not warrant classification. The use of butyl cyanoacrylate and 2-octyl cyanoacrylate to treat eye injuries indicates that the high molecular weight cyanoacrylates are unlikely to cause serious eye irritation. No data are available to evaluate the irritation potential of isopropyl cyanoacrylate and allyl cyanoacrylate.

Based on the available animal and human data, chemicals in this group are expected to be sensory irritants. In mice, the respiratory rate was decreased by 50% after exposure to 0.6–1.4 ppm of various cyanoacrylates with different molecular weights. In humans, signs of sensory irritation such nose and throat irritation and eye pain were reported after exposure to concentrations greater than 0.3 ppm of methyl cyanoacrylate or ethyl cyanoacrylate.

Chemicals in this group have the potential to cause skin sensitisation. All animal data for this endpoint are negative (as these chemicals polymerise in water, which precludes induction and challenge experiments). Most of the available human data relates to ethyl cyanoacrylate exposure. The frequency of reactions in humans was between 0 and 9.9% in different populations. Higher frequencies of reactions were reported in workers with known exposure to (meth)acrylates or in people that had used nail products. Clinical reports from therapeutic uses indicate that the higher molecular weight cyanoacrylates also have skin sensitising potential. These chemicals all have an in silico alert for skin sensitisation. The mechanism for skin sensitisation is not known. The polymers formed from these chemicals may degrade to form formaldehyde which is a strong sensitiser.

Chemicals in this group are potential respiratory sensitisers. While there is limited data for this endpoint, the respiratory sensitisation potential of these chemicals is supported by numerous case reports of occupational asthma (OA) or rhinitis in workers. Most cases were confirmed by a positive response in a specific inhalation challenge (SIC) to individual cyanoacrylates or adhesives containing high concentrations of cyanoacrylates. Most of the available human data relate to methyl cyanoacrylate or ethyl cyanoacrylate exposure, although some human case reports often refer to cyanoacrylates as a class rather than by the specific chemical. These chemicals all have an in silico alert for respiratory sensitisation.

For further details on 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) for hazard classes relevant for work health and safety as follows. This does not consider classification of physical hazards and environmental hazards.

Note that the classifications for skin irritation, eye irritation and specific target organ toxicity (single exposure) only apply to methyl cyanoacrylate (CAS No. 137-05-3) and ethyl cyanoacrylate (CAS No. 7085-85-0).

Health hazards	Hazard category	Hazard statement
Skin Irritation	Skin Irrit. 2	H315: Causes skin irritation
Eye Irritation	Eye Irrit. 2	H319: Causes serious eye irritation
Specific target organ toxicity (single exposure)	STOT Single Exp. 3	H335: May cause respiratory irritation
Respiratory Sensitisation	Resp. Sens. 1	H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled
Skin Sensitisation	Skin Sens. 1	H317: May cause an allergic skin reaction

Summary of health risk

Public

Based on the available use information, the public may be exposed to these chemicals:

- at concentrations up to 100%
- by direct application of the chemical to the skin (eyelash adhesives)
- by incidental skin and eye contact with chemicals in this group during use of eyelash and nail glues and domestic adhesive products (superglue)
- by inhaling vapours during use.

The critical health effects for this group are:
- skin, eye and respiratory irritation
- sensory irritation
- skin and respiratory sensitisation.

The risk of potential adverse effects associated with the use of these chemicals for the public depends on the likely exposure scenarios. These chemicals are currently listed on Schedule 5 of the *Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons)* (SUSMP) under "Cyanoacrylate esters" unless they are labelled with instructions to avoid contact with skin and eyes and to avoid breathing vapours. Provided that normal precautions are taken to avoid skin and eye contact and to use products in a well-ventilated area, the risk of adverse effects where the public is infrequently using adhesives (superglue) is considered low. The current risk management is considered adequate for this use scenario.

The current labelling does not indicate that these chemicals may cause an allergy. There is a risk of sensitisation in users that are frequently exposed to these chemicals (cosmetic applications of nail or eyelash glues and hobbyist applications where there is frequent use of adhesives). The risk of sensitisation is considered greatest for exposures due to eyelash glues where intentional prolonged contact of skin around the eye with the adhesive is expected and there is a high frequency of reapplication. There are several reported incidences of allergic contact dermatitis (ACD) in individuals with direct exposure to cosmetic products containing ethyl cyanoacrylate. There are increasing trends in the consumer application of false eyelashes and in the consumer use of nail products in particular fast setting acrylate-based polishes. Overall, there is a risk to the public that requires management (see **Proposed means for managing risk**). This risk could be managed by reviewing the entry in the *Poisons Standard (SUSMP)*.

Workers

Given the critical systemic acute and local health effects, these chemicals could pose a risk to workers.

Workers who frequently use cyanoacrylate-based adhesives in the beauty industry or in manufacturing are at greatest risk of developing adverse effects. Frequent dermal exposure to cyanoacrylate-based adhesives is a direct risk factor for potential ACD. Reports of asthma or rhinitis caused by cyanoacrylates are almost exclusively in workers who were regularly exposed to a cyanoacrylate-based adhesive. However, the actual exposure to cyanoacrylate monomers is dependent on the volatility of the chemical, the products that the worker uses, as well as humidity and ventilation of the work environment.

Control measures to minimise dermal, ocular and inhalation exposure are needed to manage the risk to workers (refer to **Recommendation** section).

Safe Work Australia has published the *Workplace exposure limits for airborne contaminants* (WEL list). A combined WEL for cyanoacrylates (methyl cyanoacrylate (CAS No. 137-05-3) and ethyl cyanoacrylate (CAS No. 7085-85-0)) will be introduced in Australia from 1 December 2026, following implementation in the Commonwealth, state and territory work

health and safety legislation. There are no workplace exposure limits for the other cyanoacrylates. The other cyanoacrylates have similar hazardous properties (sensory irritation and potential respiratory sensitisation) following inhalation. Based on estimated vapour pressures the chemicals are volatile with potential for workplace inhalation exposure. A broadening of the workplace exposure limits for cyanoacrylates to the other chemicals in this evaluation may be beneficial to mitigate the risk of adverse effects.

Proposed means for managing risk

Public

Recommendation to Department of Health and Aged Care

It is recommended that the delegate of the Secretary for Poisons Scheduling reviews the entry for cyanoacrylate esters in the *Poisons Standard (SUSMP).*

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

- results in labelling requirements that provide warning statements and safety directions relating to skin sensitisation for consumer uses including cosmetic applications
- the delegate should also review the appropriateness of the entry for eyelash glues given the intentional and prolonged contact with skin.

Consideration should be given to the following:

- these chemicals are skin sensitisers and can cause eye irritation
- there are several reported incidences of allergic contact dermatitis in individuals with direct exposure to cosmetic products containing ethyl cyanoacrylate
- there is an increasing trend in the consumer use of nail products, in particular, fast setting cyanoacrylate-based polishes and application of false eyelashes
- Canada has restricted use of cyanoacrylate-based eyelash glues to professional settings
- polymerised cyanoacrylates may release formaldehyde (a strong sensitiser) by degradation.

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.

It is recommended that Safe Work Australia consider establishing a workplace exposure limit (WEL) for all cyanoacrylates in this evaluation.

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 (PCBU) 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 and inhalation 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 the chemical.

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 the chemical, 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 these industrial chemicals can be managed.

Note:

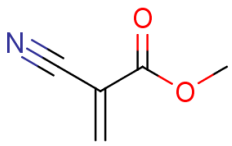
1. Obligations to report additional information about hazards under *Section 100 of the Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Grouping rationale

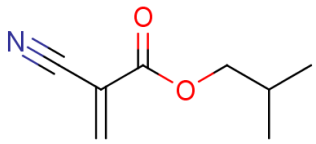
The 9 chemicals in this evaluation have been evaluated as a group as they are all esters of cyanoacrylic acid. Esters within this group have either linear alkyl, branched alkyl, linear alkenyl or alkoxylated side chains. As they all contain a cyanoacrylate group, these chemicals are expected to have similar reactivity and similar toxicological effects.

Chemical identity

Chemical name	2-Propenoic acid, 2-cyano-, methyl ester
CAS No.	137-05-3
Synonyms	methyl cyanoacrylate methyl 2-cyanoacrylate mecrilate MCA
Molecular formula	C5H5NO2
Molecular weight (g/mol)	111.10
SMILES (canonical)	N#CC(=C)C(=O)OC
Chemical description	-
Structural formula:	

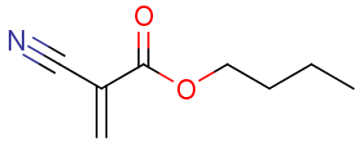
Chemical name	2-Propenoic acid, 2-cyano-, 2-methylpropyl ester
CAS No.	1069-55-2
Synonyms	isobutyl cyanoacrylate bucrilate
Molecular formula	C8H11NO2
Molecular weight (g/mol)	153.18
SMILES (canonical)	N#CC(=C)C(=O)OCC(C)C
Chemical description	-

Structural formula:



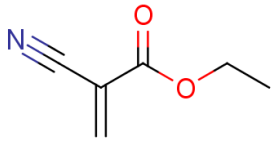
Chemical name	2-Propenoic acid, 2-cyano-, butyl ester
CAS No.	6606-65-1
Synonyms	butyl cyanoacrylate n-butyl cyanoacrylate enbucrilate butyl 2-cyano-2-propenoate
Molecular formula	C8H11NO2
Molecular weight (g/mol)	153.18
SMILES (canonical)	N#CC(=C)C(=O)OCCCC
Chemical description	-

Structural formula:



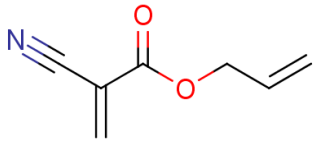
Chemical name	2-Propenoic acid, 2-cyano-, ethyl ester
CAS No.	7085-85-0
Synonyms	ethyl cyanoacrylate (INCI) ethyl 2-cyanoacrylate 2-cyanoacrylic acid ethyl ester acrylic acid, 2-cyano-, ethyl ester ECA
Molecular formula	C6H7NO2
Molecular weight (g/mol)	125.13
SMILES (canonical)	N#CC(=C)C(=O)OCC
Chemical description	-

Structural formula:



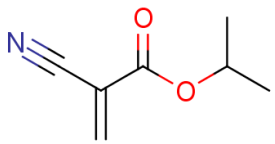
Chemical name	2-Propenoic acid, 2-cyano-, 2-propenyl ester
CAS No.	7324-02-9
Synonyms	allyl cyanoacrylate allyl 2-cyanoacrylate
Molecular formula	C7H7NO2
Molecular weight (g/mol)	137.14
SMILES (canonical)	N#CC(=C)C(=O)OCC=C
Chemical description	-

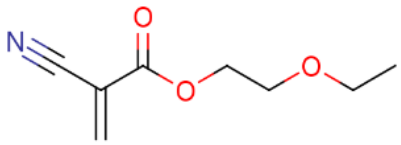
Structural formula:

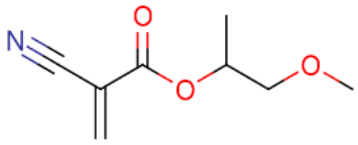


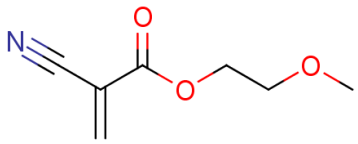
Chemical name	2-Propenoic acid, 2-cyano-, 1-methylethyl ester
CAS No.	10586-17-1
Synonyms	isopropyl cyanoacrylate (INCI) isopropyl 2-cyanoacrylate acrylic acid, 2-cyano-, isopropyl ester
Molecular formula	C7H9NO2
Molecular weight (g/mol)	139.15
SMILES (canonical)	N#CC(=C)C(=O)OC(C)C
Chemical description	-

Structural formula:



Chemical name	2-Propenoic acid, 2-cyano-, 2-ethoxyethyl ester
CAS No.	21982-43-4
Synonyms	ethoxyethyl cyanoacrylate (INCI) 2-ethoxyethyl 2-cyanoacrylate
Molecular formula	C8H11NO3
Molecular weight (g/mol)	169.18
SMILES (canonical)	N#CC(=C)C(=O)OCCOCC
Chemical description	-
Structural formula:	

Chemical name	2-Propenoic acid, 2-cyano-, 2-methoxy-1-methylethyl ester
CAS No.	27279-62-5
Synonyms	methoxyisopropyl cyanoacrylate acrylic acid, 2-cyano-, 2-methoxy-1-methylethyl ester 1-methoxypropan-2-yl 2-cyanoacrylate
Molecular formula	C8H11NO3
Molecular weight (g/mol)	169.18
SMILES (canonical)	N#CC(=C)C(=O)OC(C)COC
Chemical description	-
Structural formula:	

Chemical name	2-Propenoic acid, 2-cyano-, 2-methoxyethyl ester
CAS No.	27816-23-5
Synonyms	methoxyethyl cyanoacrylate (INCI) acrylic acid, 2-cyano-, 2-methoxyethyl ester 2-methoxyethyl 2-cyanoacrylate
Molecular formula	C7H9NO3
Molecular weight (g/mol)	155.15
SMILES (canonical)	N#CC(=C)C(=O)OCCOC
Chemical description	-
Structural formula:	

Relevant physical and chemical properties

Chemicals in this group are colourless liquids at room temperature that rapidly polymerise (within seconds) in the presence of water to form a solid. Humidity in the air, or moisture on skin or other membranes is sufficient to initiate polymerisation. The rate of polymerisation is expected to be similar for all members of the group. The length of the alkyl substituents on the ester affects the adhesive strength and flexibility of the resultant polymer (Duffy et al. 2018; Nam and Mooney 2021; REACH n.d.-b). Therefore, there is limited physical and chemical data available for the cyanoacrylates in their monomer form.

There is limited data on the vapour pressures of chemicals in this group, with some reported as wide ranges. The typical reported vapour pressures for methyl cyanoacrylate and ethyl cyanoacrylate are 24 Pa at 25 °C and 41 Pa at 20 °C, respectively (ACGIH 2018). The saturated vapour concentration for both methyl cyanoacrylate and ethyl cyanoacrylate was reported to be less than 2700 ppm (WHO 2001).

It has been reported that ethyl cyanoacrylate and butyl cyanoacrylate are less volatile than methyl cyanoacrylate (Lozewicz 1985). Methoxyethyl cyanoacrylate and ethoxyethyl cyanoacrylate have lower vapour pressures than cyanoacrylates with lower molecular weights (Duffy et al. 2018). The humidity of the environment affects the vapour pressure of these chemicals, as more humid environments contain more water, which increases polymerisation and results in less of the volatile monomeric form (Lozewicz et al. 1985).

To support risk characterisation for the intermediate and higher molecular weight cyanoacrylates, 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). The ranges of estimated vapour pressures are presented in **Table 1**. A trend of decreasing vapour pressure with increasing molecular weight was observed, consistent with the above qualitative reports. The measured vapour

pressure for ethyl cyanoacrylate falls within the estimated range of vapour pressures. However, the estimation for methyl cyanoacrylate is much greater than the reported vapour pressure.

Table 1 – Ranges of predicted vapour pressures of cyanoacrylates using OECD QSAR Toolbox version 4.5

CAS No.	Name	Molecular weight (g/mol)	Estimated vapour pressures (Pa)
137-05-3	methyl cyanoacrylate	111.10	96.5–152.0
7085-85-0	ethyl cyanoacrylate	125.13	35.9–59
7324-02-9	allyl cyanoacrylate	137.74	15–25
10586-17-1	isopropyl cyanoacrylate	139.15	24–40
1069-55-2	isobutyl cyanoacrylate	153.18	9.4–16
6606-65-1	butyl cyanoacrylate	153.18	5.4–9.4
27816-23-5	methoxyethyl cyanoacrylate	155.15	5.2–9.1
27279-62-5	methoxyisopropyl cyanoacrylate	169.18	3.6–6.4
21982-43-4	ethoxyethyl cyanoacrylate	169.18	1.9–3.5

Introduction and use

Australia

Chemicals in this group are expected to have widespread use in cyanoacrylate-based glues and adhesives for cosmetic, domestic and professional use in Australia. The domestic and professional adhesives are commonly referred to as ‘superglue’. These uses are consistent with those identified internationally.

An online product search and review of online retailers in Australia indicates that products containing cyanoacrylates are available for public use. From this online search, the following chemicals were identified as having specific industrial end uses in Australian products:

- Nail glues: ethyl cyanoacrylate, isopropyl cyanoacrylate
- Eyelash glues: ethyl cyanoacrylate, methoxyethyl cyanoacrylate, ethoxyethyl cyanoacrylate
- Domestic adhesives: methyl cyanoacrylate, ethyl cyanoacrylate, methoxyethyl cyanoacrylate
- Professional or specialist adhesives: ethyl cyanoacrylate, allyl cyanoacrylate.

For products where concentration information was available, chemicals in this group were reported to be used at concentrations between 60–100%. Note that this list is not exhaustive as all chemicals in this evaluation can function as adhesives.

From the online product searches, ethyl cyanoacrylate and butyl cyanoacrylate were identified as having non-industrial uses in Australia as components of spray on wound adhesives or coverings available for consumer or professional use.

International

The following international uses have been identified through the:

- European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH n.d.) dossiers
- European Commission Cosmetic Ingredients and Substances (CosIng) database (EC n.d.)
- United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary (Personal Care Products Council n.d.)
- US Environmental Protection Agency Chemical Data Reporting (CDR) (US EPA n.d.)
- publicly available information including Safety Data Sheets (SDSs).

Cyanoacrylates are used in cosmetic products including eyelash adhesives and nail products that are readily available for at home use. Ethyl cyanoacrylate, methyl cyanoacrylate, ethoxyethyl cyanoacrylate, methoxyethyl cyanoacrylate and butyl cyanoacrylate have reported cosmetic use in in eyelash adhesives. Of these, ethyl cyanoacrylate is the most commonly reported and is used at concentrations ranging from 85–90%. Typically, the adhesive is applied to the back of the hand and the false eyelash is dipped in the adhesive or the adhesive is directly applied to the false eyelash (Symanzik et al. 2022). The false eyelash is then bonded to the eyelid resulting in direct skin contact. False eyelashes may be replaced every 2–3 weeks. There is an increasing trend in the consumer use of eyelash extension glues worldwide (Lindstrom et al. 2013). Methyl cyanoacrylate, ethyl cyanoacrylate, isopropyl cyanoacrylate, methoxyethyl cyanoacrylate and ethoxyethyl cyanoacrylate have reported cosmetic use in artificial nail adhesives including polymer “dip” powders and artificial nail builders for professional and consumer use (Lipman and Tosti 2021). On the Environmental Working Group (EWG) Skin Deep database, there are 101 nail products which contain ethyl cyanoacrylate (EWG n.d.). While specific concentration data is not reported, online searches for SDSs of available nail glue products indicate that ethyl cyanoacrylate can be used in these products at concentrations around 90%. There is an increasing trend in the consumer use of nail products, in particular, fast setting acrylate based polishes (Atwater and Reeder 2019; Brambilla et al. 2020; Chou et al. 2017).

Chemicals in this group have reported widespread use in cyanoacrylate-based glues and adhesives for both professional and domestic use. The reported concentrations of methyl cyanoacrylate, ethyl cyanoacrylate, butyl cyanoacrylate and methoxyethyl cyanoacrylate in adhesives were typically 60–100% (DeLima Associates n.d.). Online product searches indicate cyanoacrylate adhesives are available for specific hobby use such as model building, woodworking and in archery fletching glues. Ethyl cyanoacrylate has reported professional use as part of a fingerprint detection method in forensics (Casault et al. 2017).

Cyanoacrylates have site-limited uses in polymerisation processes and manufacturing including in:

- machinery and vehicles
- paints and coatings
- electronics
- textiles and furniture
- wood and paper products
- thermoplastic manufacture.

Once polymerised, these chemicals are expected to be largely bound within a polymer matrix and are therefore, not expected to be bioavailable or mobile.

Butyl cyanoacrylate, isopropyl cyanoacrylate and isobutyl cyanoacrylate have non-industrial uses in medical and surgical settings as tissue adhesives and sealants (Nam and Mooney 2021; Sanders and Nagatomi 2014). Cyanoacrylate wound adhesives are also available to the public for use as a superficial wound sealant.

There was no identified use data for methoxyisopropyl cyanoacrylate.

Existing Australian regulatory controls

Public

Chemicals in this group are listed under a group entry in the *Poisons Standard* (SUSMP) as follows (TGA 2024):

Schedule 5:

CYANOACRYLATE ESTERS in contact adhesives **except**:

(a) when labelled with the warning:

KEEP OUT OF REACH OF CHILDREN. Avoid contact with skin and eyes and avoid breathing vapour. Bonds on contact. Should fingers stick together apply a solvent such as acetone to contact areas then wash off with water. Do not use solvents near eyes or open wounds. In case of eye contact immediately flush with water; or

(b) when packed in sealed measure packs each containing 0.5 g or less of cyanoacrylate esters:

(i) labelled with the approved name or trade name of the poison, the quantity and the warning:

Can cause eye injury. Instantly bonds skin; and

enclosed in a primary pack labelled with the warning:

KEEP OUT OF REACH OF CHILDREN. Avoid contact with skin and eyes and avoid breathing vapour. Bonds on contact. Should fingers stick together apply a solvent such as acetone to contact areas then wash off with water. Do not use solvents near eyes or open wounds. In case of eye contact immediately flush with water."

Schedule 5 chemicals are labelled with 'Caution' and are described as: "Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label" (TGA 2024).

Workers

Methyl cyanoacrylate (CAS No. 137-05-3) and ethyl cyanoacrylate (CAS No. 7085-85-0) are listed on the HCIS with the following hazard categories and statements for human health (SWA n.d.-a).

Health hazards	Hazard category	Hazard statement
Skin Irritation	Skin Irrit. 2	H315: Causes skin irritation
Eye Irritation	Eye Irrit. 2	H319: Causes serious eye irritation
Specific Target Organ Toxicity (single exposure)	STOT Single Exp. 3	H335: May cause respiratory irritation

Methyl cyanoacrylate (CAS No. 137-05-3) is listed on the HCIS (SWA 2024) with the following exposure standards:

- Time Weighted Average (TWA): 2 ppm (9.1 mg/m^3)
- Short Term Exposure Limit (STEL): 4 ppm (18 mg/m^3).

Safe Work Australia has published the *Workplace exposure limits for airborne contaminants* (WEL list). A combined workplace exposure limit (WEL) for cyanoacrylates (methyl cyanoacrylate (CAS 137-05-3) and ethyl cyanoacrylate (CAS No. 7085-85-0)) will be introduced in Australia on 1 December 2026, following implementation into Commonwealth, state and territory work health and safety legislation. Further information about the WEL is available on the SWA website (SWA n.d.-b).

International regulatory status

Exposure standards

Methyl cyanoacrylate

The following exposure standards were identified (Chemwatch n.d.):

- TWA: 0.2 ppm (0.9 mg/m^3) — Belgium, Canada, China, Columbia, Finland, Indonesia, Peru, Portugal, Spain, Uruguay and Venezuela.
- TWA: 2 ppm (8–9.2 mg/m^3) — Argentina, Canada, Denmark, Estonia, France, Germany, Greece, Iceland, Mexico, New Zealand, Nicaragua, Norway, Poland, Singapore, South Africa, South Korea, Sweden, Switzerland, Taiwan, United Arab Emirates and United States of America.
- STEL: 4 ppm (16–18 mg/m^3) — Argentina, Canada, Denmark, Estonia, France, Greece, South Korea, Mexico, New Zealand, Singapore, South Africa, Sweden, United Arab Emirates, United States of America and Venezuela.
- STEL: 1 ppm — Colombia and Nicaragua.
- STEL: 0.3 ppm (1.4 mg/m^3) — Croatia and United Kingdom.
- The National Institute for Occupational Safety and Health (NIOSH) has a recommended exposure limit (REL) of 2 ppm (as a TWA for up to 8 hours/day or 40 hours/week) and a STEL of 4 ppm (CDC n.d.).

The following temporary emergency exposure limits (TEELs) have been recommended by the United States Department of Energy (US DOE n.d.):

- 5.1 ppm (TEEL-3)
- 0.85 ppm (TEEL-2)
- 0.6 ppm (TEEL-1).

As stated by the US DOE, TEELs are intended for use until Acute Exposure Guideline Levels (AEGLs) or Emergency Response Planning Guidelines (ERPGs) are adopted for these chemicals.

Ethyl cyanoacrylate

The following exposure standards were identified (Chemwatch n.d.):

- TWA: 0.2 ppm (1 mg/m^3) — Belgium, Canada, China, Colombia, Finland, Nicaragua, Poland, Portugal, Spain, Uruguay and United States of America.
- TWA: 2 ppm (9–10 mg/m^3) — Austria, Denmark, Estonia, Iceland, Sweden and Switzerland.
- STEL: 0.3 ppm (1.5 mg/m^3) — Croatia and United Kingdom.
- STEL: 4 ppm (20 mg/m^3) — Denmark and Estonia.

Canada

Methyl cyanoacrylate, ethyl cyanoacrylate and isopropyl cyanoacrylate are included on the Health Canada Cosmetic Ingredient Hotlist—List of Ingredients that are Restricted for Use in Cosmetic Products (Government of Canada 2022).

They are listed under the entry for “Cyanoacrylate-based adhesives” with the following conditions of use and required warning and cautionary statements:

a) “Cyanoacrylate adhesives for eyelash extensions must be sold for professional use only (i.e., not for direct sale to consumers)” must have labels which indicate "For application by trained professionals only" and "Ensure the eye is protected and immobilized during application." and "WARNING. BONDS SKIN INSTANTLY. AVOID CONTACT WITH EYES, MOUTH AND SKIN. KEEP AWAY FROM CHILDREN. Eyelid bonding: consult a physician. Skin bonding: soak and ease apart gently."
b) Other cosmetics must be labelled with "WARNING. BONDS SKIN INSTANTLY. AVOID CONTACT WITH EYES, MOUTH AND SKIN. KEEP AWAY FROM CHILDREN. Eyelid bonding: consult a physician. Skin bonding: soak and ease apart gently. Not for use in the area of the eye."

Health hazard information

Most of the available data are from humans or animals that were exposed to either methyl cyanoacrylate or ethyl cyanoacrylate.

The molecular weights of this group range from 111–169 g/mol. For hazard characterisation in this evaluation, the following groupings are used:

- lower molecular weight (<126 g/mol): methyl cyanoacrylate and ethyl cyanoacrylate
- intermediate molecular weight (137–139 g/mol): isopropyl cyanoacrylate and allyl cyanoacrylate
- higher molecular weight (>153 g/mol): isobutyl cyanoacrylate, butyl cyanoacrylate, methoxyethyl cyanoacrylate, ethoxyethyl cyanoacrylate and methoxyisopropyl cyanoacrylate.

Read across data from the structurally similar chemical 2-octyl cyanoacrylate (CAS No. 133978-15-1) has been used to support the hazard conclusions for the higher molecular weight cyanoacrylates.

Toxicokinetics

The cyanoacrylates in this group are not expected to be absorbed extensively based on their rapid polymerisation (see **Relevant physical and chemical properties**). There is only a small window in which oral or dermal absorption of the liquid monomer is possible. After polymerisation, it is not expected that significant amounts of the polymer will be absorbed bioaccumulated by the oral or dermal routes. As such there are limited, meaningful well conducted studies investigating the toxicokinetics or metabolism of these chemicals. The data are largely conflicting and may relate to absorption of degradation products from the polymer that forms at the site of administration (REACH n.d.-b).

In an oral absorption study, radiolabelled methyl cyanoacrylate (mixed monomer and polymer) was administered orally to rats. Approximately 2% of the radioactivity was recovered in urine over a 48 hour period and 18% of the radioactivity was detected in the faeces after 4 days (WHO 2001). This may indicate some absorption; however, in acute oral toxicity studies with methyl cyanoacrylate, solid masses were found in animals dosed orally with the liquid chemical, indicating that the chemical may aggregate as a polymer rather than be absorbed or metabolised (see **Acute Toxicity – Oral**).

The limited available data indicates that the dermal availability decreases with molecular weight. In a percutaneous absorption study, where various radiolabelled cyanoacrylates were administered dermal to rats, the total amounts of radioactivity in urine samples decreased in the order methyl cyanoacrylate > butyl cyanoacrylate > heptyl cyanoacrylate. For methyl cyanoacrylate, 4% of the total radioactivity was detected in the urine over 6 days. The radioactivity increased 3 fold when the chemical was applied on skin where the epidermis was removed (MAK 2012; WHO 2001). This suggests that the epidermis reduces absorption of methyl cyanoacrylate. In humans, direct exposure of a cyanoacrylate to the skin will typically form a hard polymer film.

Polymers formed by these chemicals may be hydrolysed to yield formaldehyde and alkyl cyanoacetate (Nam and Mooney 2021). Formaldehyde production was demonstrated in radioactive labelling experiments with methyl cyanoacrylate (MAK 2012). Polymers of the lower homologues are reported to be more rapidly metabolised. One study investigating the release of formaldehyde from various cyanoacrylates in vitro concluded that formaldehyde release was lower as the molecular weight of the monomer increased (Pascual et. al 2016).

There is no information available on absorption of cyanoacrylate vapours by the inhalation route. Estimated vapour pressures (see **Relevant physical and chemical properties**) indicate that it is likely that all chemicals in the group are sufficiently volatile to be inhaled.

Acute toxicity

Oral

Based on available data, chemicals in this group are expected to have low acute oral toxicity.

In a good laboratory practice (GLP) compliant acute oral toxicity study conducted according to the Organisation for Economic Cooperation and Development Test Guideline (OECD TG) 423, female Wistar rats received a single dose of allyl 2-cyanoacrylate in saline

or cottonseed oil by oral gavage. Slight piloerection was observed 3–4 hours after administration but was reversible. Body weight gain was normal in control and dosed animals. The LD50 was greater than 2000 mg/kg bw (REACH n.d.-a).

In a non-GLP compliant acute oral toxicity study conducted similarly to OECD TG 423, male albino rats received a single dose of neat ethyl cyanoacrylate by oral gavage. One animal died during the study; however, no clinical signs of toxicity were reported. A solid mass was found in the stomach of this animal. Investigators reported that this mass was almost certainly the polymerised adhesive, as opposed to an organic mass or lesion. The LD50 was greater than 5000 mg/kg bw (REACH n.d.-b; WHO 2001).

In a non-GLP compliant acute oral toxicity study conducted similarly to OECD TG 423, male albino rats received a single dose of methyl cyanoacrylate (purity 88.8%, vehicle not specified) at 5000 mg/kg bw by oral gavage. Clinical signs of toxicity included pilo-erection and lethargy that were reversible within 5–6 days. During autopsy, a large, hardened mass of test material was found in the stomach of each animal sacrificed. The LD50 was greater than 4400 mg/kg bw. (REACH n.d.-b; WHO 2001).

Dermal

Based on the available data, chemicals in this group are expected to have low acute dermal toxicity.

In an acute dermal toxicity study conducted similarly to OECD TG 402, New Zealand White (NZW) rabbits received a single topical application of neat ethyl cyanoacrylate at 2000 mg/kg bw for 24 hours under occlusive conditions. No clinical signs of toxicity were reported. Large open sores were observed after patch removal, likely due to bandages being adhered to the skin. The LD50 was greater than 2000 mg/kg bw (REACH n.d.-b; WHO 2001).

In a non-guideline acute dermal toxicity study, no adverse effects were reported when an adhesive containing mostly methyl cyanoacrylate was applied directly to guinea pig skin at 10 mL/kg bw (MAK 2012).

Inhalation

There are insufficient data to make a determination about the acute inhalation toxicity of these chemicals.

In a non-guideline acute inhalation toxicity study, 10 rats were exposed to ethyl cyanoacrylate aerosol at 21.1 mg/L for 1 hour. A 70% mortality rate was observed in the 4 days post exposure; however, the concentration was excessive and did not permit an assessment of acute inhalation toxicity. During the exposure, the rats were irritable and had clear signs of respiratory, skin and eye irritation (REACH n.d.-c; WHO 2001).

Corrosion/Irritation

Skin irritation

Methyl cyanoacrylate and ethyl cyanoacrylate are classified with hazard category “Skin - irritation - Category 2” with hazard statement “H315: Causes skin irritation” (see **Existing Australian Regulatory Controls**). There is limited animal and human data to evaluate this classification. Persistent inflammation was observed in a study in rabbits following 4 hour exposure to methyl cyanoacrylate. Irritant dermatitis has been reported in humans exposed

to cyanoacrylates (see **Corrosion/Irritation** - **Observations in Humans**). Based on data for butyl cyanoacrylate and methoxyisopropyl cyanoacrylate, higher molecular weight cyanoacrylates are expected to be at most, slightly irritating. No data are available to evaluate the irritation potential of the intermediate molecular weight cyanoacrylates.

In a skin irritation study conducted similarly to OECD TG 404, 3 albino NZW rabbits were treated with methyl cyanoacrylate for 4 hours under semi-occlusive conditions. Observations were recorded at 1, 24, 48 and 72 hours, and at 7 and 14 days. The mean scores for erythema and oedema were 3 and 1.5, respectively. The erythema and oedema were not reversible in 2/3 animals after 14 days (REACH n.d.-c).

In a skin irritation study conducted similarly to OECD TG 404, 6 albino NZW rabbits were treated with methyl cyanoacrylate (purity 88.8%) for 24 hours under occlusive conditions. Observations were recorded at 24 and 72 hours. The following mean scores were reported: 1.5, 0.5, 1, 0.5, 0.5, 0.5 for erythema. No oedema was observed in the study. It was noted that the test patches were bonded to skin after 24 hours, preventing removal without further skin damage. At 72 hours, the skin surrounding the test patch was hard and irritated with signs of eschar formation (REACH n.d.-c).

In a skin irritation study conducted similarly to OECD TG 404, 6 male albino NZW rabbits were treated with ethyl cyanoacrylate for 24 hours under occlusive conditions. Observations were recorded at 24 and 72 hours. The following mean scores were reported: 1, 1, 0.5, 0.5, 0.5 and 1.5 for erythema and 1, 1, 0.5, 0.5, 0.5 and 1.5 for oedema. Reversibility of effects was not reported (REACH n.d.-b).

Well conducted studies of the higher molecular weight cyanoacrylates indicate that they are, at most, slightly irritating.

In a GLP compliant skin irritation study conducted according to OECD TG 404, 3 albino NZW rabbits were treated with butyl cyanoacrylate for 4 hours under semi-occlusive conditions. Observations were recorded at 1, 24, 48 and 72 hours and at 6, 9, 12 and 15 days after patch removal. A hard film of test material was noted on all animals for the first 72 hours of observations. The mean scores for individual animals at 24, 48 and 72 hours were 1, 1 and 1.33 for erythema and 0, 0 and 0.33 for oedema. Other observations of erythema and oedema at the edges of test sites were considered to be a result of the cracking of the hard film and/or grooming. Signs of erythema had fully reversed by day 12 in 2/3 animals, and no signs of oedema were present after day 6 in all animals. (REACH n.d.-d).

In a GLP compliant skin irritation study conducted similarly to OECD TG 404, 3 NZW rabbits were treated with methoxyisopropyl cyanoacrylate for 4 hours under occlusive conditions. Observations were recorded at 1, 24, 48 and 72 hours and 6, 9 and 15 days after patch removal. The chemical formed a hard film under the patch, so all scores were from the edge of the test site. The mean scores over 24, 48 and 72 hours were: 1, 1 and 1 for erythema and 1, 0 and 0 for oedema. All signs of irritation resolved by day 12 (REACH n.d.-e).

The structurally similar chemical 2-octyl cyanoacrylate is not considered irritating to the skin based on well conducted animal studies using intracutaneous injection of the chemical or subcutaneous implantation of the chemical adhesive strip (REACH n.d.-f).

In silico

The knowledge based expert system Deductive Estimation of Risk from Existing Knowledge (DEREK) Nexus version 6.01 was used to estimate the skin irritation potential of these

chemicals. Irritation (of the skin) was predicted based on the alert “alpha,beta-Unsaturated ester”. The alert was rated plausible for all group members (Lhasa Limited n.d.).

No alerts for skin irritation were found with OECD QSAR Toolbox version 4.5 (OECD 2021).

Eye irritation

Methyl cyanoacrylate and ethyl cyanoacrylate are classified with hazard category “Eye irritation - Category 2” with hazard statement “H319: Causes serious eye irritation” (see **Existing Australian Regulatory Controls**). This classification is supported by the limited available animal data and human observations. Limited data are available for the other chemicals in this group. The use of butyl cyanoacrylate, isopropyl cyanoacrylate and isobutyl cyanoacrylate to treat eye injuries indicate that the intermediate and higher molecular weight cyanoacrylates are unlikely to cause serious eye irritation. No data are available to evaluate the irritation potential of intermediate molecular weight cyanoacrylates.

The animal data and human data suggest that chemicals in this group are sensory irritants (see **Respiratory irritation**) and vapours may cause a burning sensation in the eyes. In addition, eye contact with adhesives containing these chemicals may cause eye damage through physical abrasion (see **Observation in humans**).

In an eye irritation study conducted according to OECD TG 405, ethyl cyanoacrylate was instilled in to 1 eye each of 9 male NZW Rabbits. The eyes were observed at 24, 48 and 72 hours. The mean scores based on observations at 24, 48 and 72 hours were: ≥ 1 for corneal opacity in 4 out of 9 animals, ≥ 1 for iritis in 3 out of 9 animals, ≥2 for conjunctival redness in 2 out of 9 animals and ≥2 for chemosis in one animal. Conjunctival discharge was noted in all rabbits at 24 and 48 hours and in 4/9 rabbits after 72 hours. Irritation scores generally decreased over the 72 hour period. Reversibility was not assessed (REACH n.d.-b).

In an eye irritation study conducted similarly to OECD TG 405, methyl cyanoacrylate (purity 88.8%) was instilled into 1 eye each of 6 NZW Rabbits. Each eye was washed in 3 animals, and each eye of the remaining 3 animals was not washed. Observations were made at 24, 48 and 72 hours and at 7 days post treatment. In all cases, the eyelids were bonded shut, and were gently pried open to make observations. In the washed group, the eyelids of 2 animals could not be opened at 24 or 48 hours post exposure. In the unwashed group, the eyelids of animal 1 could be opened at 24 hours post exposure. For animal 2 from the unwashed group, the mean scores at 24, 48 and 72 hours were: corneal opacity 0/4, iritis 0/2, conjunctival redness 1.67/3 and chemosis 0.33/4. For animal 3 from the unwashed group, the mean scores at 24, 48 and 72 hours were: corneal opacity 1/4, iritis 1.33/2, conjunctival redness 2/3 and chemosis 0.67/4. For the animal in the washed group, the mean scores at 24, 48 and 72 hours were: corneal opacity 1/4, iritis 0.67/2, conjunctival redness 2.67/3 and chemosis 1.33/4. Four of the 6 animals had no signs of irritation 7 days after treatment (REACH n.d.-c; WHO 2001).

There are 3 further reports of non-guideline studies in rabbit eyes exposed to different adhesives containing either methyl cyanoacrylate or ethyl cyanoacrylate. Whilst full study details are not available, the adverse effects reported included mechanical irritation, adhesion of the eyelids, iritis, corneal opacity, irritation of the conjunctivae and staining of the cornea. In one study, the effects were completely reversed within 14 days (MAK 2012).

There are limited studies available on the other cyanoacrylates. In an in vitro Hen’s Egg Test – Chorioallantoic Membrane (HET-CAM), the total haemorrhage irritation score for 6 eggs treated with methoxyethyl cyanoacrylate was 8. Based on the test score, methoxyethyl cyanoacrylate has a moderate irritation potential to eyes (REACH n.d.-e).

In silico

The knowledge based expert system DEREK Nexus version 6.01 was used to estimate the eye irritation potential of these chemicals. Irritation (of the eye) was predicted based on the alert “alpha,beta-Unsaturated ester”. The alert was rated plausible for all group members (Lhasa Limited n.d.).

No alerts for eye irritation were found with OECD QSAR Toolbox version 4.5 (OECD 2021).

Respiratory irritation

Methyl cyanoacrylate and ethyl cyanoacrylate are classified with hazard category “Specific target organ toxicity (single exposure) - Category 3” with hazard statement “H335: May cause respiratory irritation” (see **Existing Australian Regulatory Controls**). Limited data are available to evaluate these classifications.

The animal data and human data suggest that chemicals in this group are sensory irritants. In mice the respiratory rate was decreased by 50% after exposure to 0.6–1.4 ppm cyanoacrylates. In humans, signs of sensory irritation such nose and throat irritation and eye pain were reported after exposure to concentrations >0.3 ppm of methyl cyanoacrylate or ethyl cyanoacrylate (see **Corrosion/Irritation** - **Observations in humans**). While there is clear evidence of irritation, sensory irritation is not considered to be classified as specific target organ toxicity (STOT) under GHS.

In the acute inhalation study above (see **Acute Toxicity - Inhalation**) high concentrations of ethyl cyanoacrylate caused signs of severe respiratory distress (WHO 2001).

In an investigation of the sensory irritation effects of alkyl cyanoacrylates, 4 chemicals in this group (methyl cyanoacrylate, ethyl cyanoacrylate, isopropyl cyanoacrylate and methoxyethyl cyanoacrylate) were administered directly to the nose of mice for 60 minutes. The concentration that causes a 50% respiratory rate decrease (RD50) values of methyl cyanoacrylate, ethyl cyanoacrylate, isopropyl cyanoacrylate and methoxyethyl cyanoacrylate were 1.4, 0.7, 0.6 and 1.0 ppm, respectively. This study suggests that the cyanoacrylates are strong sensory irritants (Gagnaire et al. 2003). Sensory irritation is the result of the chemical stimulating the trigeminal nerve endings in the cornea and nasal mucosa, which evokes a stinging or burning sensation in the eyes and upper respiratory tract (nose and throat). This is a receptor mediated mode of action and occurs at relatively low concentrations. Sensory irritation is different to eye and skin irritation used for hazard classification and also different from the irritation leading to cytotoxicity. This latter example is a result of physical damage to the cells, whereas sensory irritation is a nerve response (NICNAS 2006).

Observation in humans

Human data demonstrates that a single exposure of methyl cyanoacrylate or ethyl cyanoacrylate in liquid form does not cause serious skin irritation. Repeated exposure to these chemicals may cause skin irritation. Skin irritation may also occur from mechanical abrasion of the polymerised adhesive on the skin, rather than the chemical itself (WHO 2001). There are some case reports of irritant dermatitis in workers exposed to adhesives containing methyl cyanoacrylate or ethyl cyanoacrylate (ACGIH 2018). However, these reports are limited in detail.

There are approximately 10 clinical reports of skin burns from cyanoacrylate adhesives (including nail glues), mostly in children. However, they are not considered a chemical burn, but a thermal burn from the exothermic reaction of the cyanoacrylate with cotton or other

material (Alhumsi and Shah Mardan 2021). As the skin burns derive from a specific chemical reaction with materials, this does not warrant classification of these chemicals as corrosive.

Case reports of accidental spillage of cyanoacrylate-based adhesives into the eye have indicated that subjects experience pain in the eye, lacrimation and corneal defects. However, in all cases, the eye damage was reversible and there were no reports of permanent injury (WHO 2001). Reported cases of ocular cyanoacrylate injury typically involve conjunctival and corneal abrasion due to physical scratching (Wetarini 2020). Butyl cyanoacrylate, isopropyl cyanoacrylate and isobutyl cyanoacrylate have reported clinical use for treating eye injuries. This indicates that they not expected to cause serious eye irritation. There are some case reports of reversible eye irritation from 2-octyl cyanoacrylate, but the overall weight of evidence suggests that it is not irritating to eyes (REACH n.d.-f).

Human respiratory and eye irritation studies

In an irritation study, 14 subjects were exposed to 1–60 ppm methyl cyanoacrylate by applying adhesive containing methyl cyanoacrylate to glass slides in a controlled environment, to simulate occupational exposure. The subjects reported “irritation of the nose and throat” at 3 ppm and “burning irritation of the eyes” at approximately 5 ppm. At 50–60 ppm, painful eye irritation and blurred vision for 2 hours was reported.
The no observed adverse effect level (NOAEL) for eye and respiratory irritation was 1 ppm (WHO 2001; MAK 2012). It should be noted that this study was based on subjective responses from the participants and detailed information about the frequency and types of responses is not available.

The medical and health records of 450 workers who worked in monomer manufacture and repackaging of methyl cyanoacrylate and ethyl cyanoacrylate-based adhesives for 17 years were studied. The mean airborne ethyl cyanoacrylate concentration was 0.2 ppm (1.0 mg/m^3). It was found that workers who reported rhinitis, sinusitis or conjunctivitis were more likely to have been exposed to cyanoacrylates. Workers who were exposed to “peak” ethyl cyanoacrylate concentrations of 1.5 ppm were most likely to report these symptoms. No airborne concentrations were reported for methyl cyanoacrylate (WHO 2001).

In a study of 73 factory workers, those who used ethyl cyanoacrylate-based adhesives had significantly higher self-reporting of symptoms of respiratory and eye irritation compared to workers who were not exposed to the adhesives. The airborne ethyl cyanoacrylate concentrations were less than 0.35 ppm (0–1.8 mg/m^3) (WHO 2001).

In a survey of workers exposed to ethyl cyanoacrylate-based adhesives, 10/16 subjects reported eye irritation and 8/16 subjects reported tearing of the eyes as symptoms of exposure. Irritated nose (14/16 subjects) and irritated or sore throats (11/16) were also reported indicating some respiratory irritation. The average 8 hour airborne ethyl cyanoacrylate concentration was 0.90 ppm (4.6 mg/m^3) (NIOSH 1985).

In a 5 year study of factory workers who frequently used methyl cyanoacrylate-based adhesives, irritation and inflammatory changes in the conjunctivae, nose and throat were observed with exposure to 0.4 ppm methyl cyanoacrylate vapours. Installation of an air purification system removed all symptoms of irritation (NIWL 1997).

Sensitisation

Skin sensitisation

Based on the weight of evidence of the available data, the cyanoacrylates have sensitising potential. Hazard classification is warranted.

All animal data for this endpoint are negative (as these chemicals polymerise in water, which precludes induction and challenge experiments). Most of the available human data relates to ethyl cyanoacrylate exposure. The frequency of reactions in humans to ethyl cyanoacrylate was between 0 and 9.9% in different populations. Higher frequencies of reactions were reported in workers with known exposure to (meth)acrylates or in people that had used nail products. Clinical reports from therapeutic uses indicate that the higher molecular weight cyanoacrylates also have skin sensitising potential. No data are available to evaluate the sensitisation potential of intermediate molecular weight cyanoacrylates. These chemicals all have an in silico alert for skin sensitisation. Overall hazard classification is warranted with data not sufficient for sub-classification.

In a non-GLP guinea pig maximisation test (GPMT) (Polak method), intradermal induction was performed on Hartley guinea pigs (number of animals and sex not specified) using 0.2% methyl cyanoacrylate or butyl cyanoacrylate in ethanol:saline (1:4), in Freund's complete adjuvant (FCA). The animals were challenged with 5% methyl cyanoacrylate or butyl cyanoacrylate in acetone:olive oil (4:1) using an open skin test on day 7, and then weekly for 12 weeks. No reactions were reported in the animals (Parker and Turk 1983).

In a GLP compliant GPMT conducted according to OECD TG 406, intradermal induction was performed on 10 Hartley guinea pigs using saline or cottonseed oil extracts of a commercial formulation of 2-octyl cyanoacrylate (exact concentrations unknown). The animals were challenged with the same extracts. No reactions were reported in any of the animals (REACH n.d.-f).

A suspension of polymerised butyl cyanoacrylate did not elicit sensitisation in a GPMT (REACH n.d.-d).

In silico

The knowledge based expert system DEREK Nexus version 6.01 was used to estimate the skin sensitisation potential of these chemicals. An alert for skin sensitisation was reported based on the cyanoacrylate functional group. The alert was rated equivocal in all cases except ethyl cyanoacrylate which was probable. No EC3 value could be predicted for any chemicals in the group (Lhasa Limited n.d.).

Allyl cyanoacrylate has a structural alert for protein-binding based on the mechanistic (and endpoint-specific) profiling functionality of the OECD QSAR Toolbox. The alert is based on "activated alkyl esters" which are electrophilic and can react with nucleophilic skin proteins. No alerts were found for other members of the group (OECD 2021).

Other

The mechanism for skin sensitisation is not known. The polymers formed from these chemicals may degrade to form formaldehyde (see **Toxicokinetics**) which is a strong sensitiser. Polymers of the lower homologue cyanoacrylates are reported to be more rapidly degraded.

Respiratory sensitisation

Based on the weight of evidence, the cyanoacrylates may be respiratory sensitisers. Hazard classification is warranted.

There are no animal data on respiratory sensitisation. Extensive clinical diagnoses of respiratory sensitisation caused by cyanoacrylates are not available. However, numerous individual case reports indicate that OA can be caused by exposure to cyanoacrylates in the workplace (see **Sensitisation - Observation in humans**). Most of the available human data relates to methyl cyanoacrylate or ethyl cyanoacrylate exposure, although some human case reports often refer to cyanoacrylates as a class rather than by the specific chemical. Chemicals in this group all have a common chemical functional group and a corresponding in silico alert for respiratory sensitisation. Overall hazard classification is warranted with data not sufficient for sub-classification.

The exact mechanisms for respiratory sensitisation by cyanoacrylates are unknown. Sensitisation has been characterised by a mixture of early phase, late phase and dual (a combination of early and late phase) asthmatic reactions. These responses are not affected by existing atopy or prior skin sensitisation to cyanoacrylates. These modes of asthma like reactions are not typically mediated by immunoglobulin E (IgE) (classical allergic type IV hypersensitivity reactions) (Walters et al. 2017). It is likely that the skin and respiratory sensitisation mechanisms for these chemicals are distinct. The difference between an irritating mechanism and sensitisation can be difficult to define with respect to clinical symptoms. However, generally a latency between the first exposure and the occurrence of the symptoms indicates more in favour of sensitisation.

In silico

All chemicals in this group have a structural alert for respiratory sensitisation based on the mechanistic (and endpoint-specific) profiling functionality of the OECD QSAR Toolbox. The alert is based on a Michael Addition mechanism, where nucleophilic skin proteins can react with electrophilic cyanoacrylates (OECD 2021).

Observation in humans

Cyanoacrylates were previously considered unlikely to cause skin or respiratory sensitisation as their rapid polymerisation means that minimal amounts of the free monomer are bioavailable via dermal and inhalational routes. However, retrospective studies conducted between 2004 and 2014 demonstrated that there is a significant increase in both consumer and occupational cases of ACD due to nail cosmetics (Chou et al. 2017). In addition, studies have shown that populations exposed to cyanoacrylates may have increased risks of asthma (Suojalehto et al. 2020). These increasing trends suggest that cyanoacrylates have sensitising potential. While one person can be sensitised to multiple (meth)acrylates due to cross-sensitivity, these types of reactions are mutually exclusive with cyanoacrylate allergy (Chou et al. 2017). Direct exposure to cyanoacrylate containing products is the main risk factor for inducing sensitisation.

Patch testing with ethyl cyanoacrylate

Table 2 summarises the available patch testing data for ethyl cyanoacrylate. No information on patch tests with other cyanoacrylates was found. The incidence of positive reactions to ethyl cyanoacrylate ranges from 0 to 9.9%. The incidences in populations with dermatitis indicate a high frequency of skin sensitisation after exposure to ethyl cyanoacrylate.

Table 2 – Summary of human patch tests with ethyl cyanoacrylate

No. of subjects	Subject details	Concentration and vehicle	Positive reactions (%) (no. of cases)	Reference
111	Dermatitis patients that had ACD caused by nail acrylates	10% in petrolatum	9.9% (11)	Goncalo et al. 2017
55	Patients with suspected acrylate allergy from their occupation	10%	7.3% (4)	Aalto-Korte and Suuronen 2020
175	Dermatitis patients patch tested that had used nail products	Not specified	6.9% (12)	Warshaw et al. 2020
230	Patients with ACD that used or worked with nail products	10% in petrolatum	5.7% (13)	Raposo et al. 2017
871	Patients with ACD that had reacted to personal care products	10%	1.1% (10)	Wetter et al. 2010
4230	Unselected dermatitis patients	10% in petrolatum	0.3% (13)	Warshaw et al. 2015
87	Patients with a history of exposure to acrylates	2% in petrolatum	0	Kanerva et al. 1997
122	Patients with suspected acrylate allergy due to exposure to medical devices (69), acrylic nail exposure (35) and other industrial activities (18)	Not specified	0	Ramos et al. 2014
10	Dermatitis patients sensitised from glue	10% in petrolatum	0	Aalto-Korte et al. 2008

There are several case reports of ACD in individuals with direct exposure to cosmetic products containing ethyl cyanoacrylate (ACGIH 2018; WHO 2001):

- A hairstylist reported ACD on the fingertips and around the eyes due to occupational exposure to ethyl cyanoacrylate-based adhesives. The individual reacted to ethyl cyanoacrylate-based adhesives in a series of patch tests.
- A consumer who used eyelash adhesives containing ethyl cyanoacrylate, ethoxyethyl cyanoacrylate and an alkoxy-2-cyanoacrylate developed ACD. They had a positive reaction to 10% ethyl cyanoacrylate in petrolatum.
- A nail technician with a history of atopic dermatitis developed ACD from use of cyanoacrylate-based adhesives. In patch tests, they had a positive response to the adhesive and a weak positive response to ethyl cyanoacrylate.
- Three cases of ACD were reported from a nail salon in a worker and two clients after exposure to ethyl cyanoacrylate containing adhesives. All cases had positive responses to a patch test using 25% ethyl cyanoacrylate in olive oil.
- A consumer who applied artificial nails using an ethyl cyanoacrylate-based adhesive developed ACD on the fingers had a positive patch test result to the adhesive.
- A consumer who applied false eyelashes using ethyl cyanoacrylate-based adhesives developed ACD. They had positive patch tests to 10% ethyl cyanoacrylate in

petrolatum, as well as positive results to other (meth)acrylates used in cosmetics (Shanmugam and Wilkinson 2012).

A worker who regularly affixed microchips to phone cards using an ethyl cyanoacrylate containing adhesive developed hyperkeratotic lesions on their right hand. Patch testing with the adhesive at 1, 5 or 10% concentrations gave positive responses (ACGIH 2018).

A worker with significant exposure to adhesives containing 90% ethyl cyanoacrylate developed ACD. The worker had a positive patch test to ethyl cyanoacrylate and was negative for other allergens. No reactions were observed in 20 control subjects who were patch tested with the adhesive (WHO 2001).

Clinical reports (skin sensitisation)

A review of patients who had skin closure treatments after foot or ankle surgery between 2017 and 2021 in Korea with cyanoacrylate-based adhesives was conducted to identify reports of ACD (Park et al. 2021). The incidence of ACD in 1145 patients was 2.7% for 2-octyl cyanoacrylate-based adhesives and 2.2% for butyl cyanoacrylate-based adhesives. Existing risk factors including age, sex, diabetes, smoking status, asthma or histories of dermatitis or allergies did not significantly increase the incidence of ACD in these patients. The review also noted that previous studies of patients who had been treated with 2-octyl cyanoacrylate-based adhesives revealed the following incidences of ACD:

- 0.5% (29 of 6088) of patients who underwent elective orthopaedic surgery
- 1.8% (5 of 281) patients who underwent joint arthroplasty surgery
- 1.7% (of 912) of patients who underwent joint arthroplasty surgery
- 7.0% (7 of 100) of patients who underwent breast reconstruction surgery.

No other studies relating to incidences of ACD from butyl cyanoacrylate skin adhesives was available. This is likely due to their less frequent use. Whilst patch testing was not conducted on these patients, the incidences in these unselected groups of patients directly exposed to the cyanoacrylates indicated a high frequency of sensitisation.

The sensitising potential for 2-octyl cyanoacrylate and butyl cyanoacrylate in adhesives used in wound care may be exaggerated given that these chemicals are applied to non-intact skin (Alavi et al. 2016). Exposure of a chemical to non-intact skin increases the potential for dermal absorption. When the barrier function of the skin is impaired, greater interaction between the chemical and the cellular and molecular components of the skin involved in the initial phases of the induction of skin sensitisation is expected (hapten-carrier interactions and subsequent processing by epidermal and dermal dendritic cells) (OECD 2012).

There is limited specific information on sensitisation to other cyanoacrylates after exposure to clinical cyanoacrylate-based wound adhesives. In a study of patients with contact dermatitis after exposure to 2-octyl cyanoacrylate post-surgery, 29% of 38 patients had a positive patch test to 10% ethyl cyanoacrylate in petrolatum (Cook et al. 2019). There is also one case report of a patient who was exposed to 2-octyl cyanoacrylate post-surgery and had later skin reactions to butyl cyanoacrylate- and ethyl cyanoacrylate-based adhesives. The patient had a positive patch test to both the adhesives and 10% ethyl cyanoacrylate in petroleum (Sato et al. 2017). These reports indicate that sensitisation from a cyanoacrylate chemical may induce allergy to a different cyanoacrylate chemical.

Respiratory sensitisation and occupational asthma

In a retrospective study of patients with a diagnosis of OA in the European network for the PHenotyping of OCcupational ASthma (E-PHOCAS) that were diagnosed between 2006 and 2015, 446 patients had OA induced by low molecular weight compounds (Suojalehto et al. 2020). Of these, 29 patients had been exposed to products containing cyanoacrylates. Workers who were exposed to cyanoacrylates were beauticians (specifically eyelash and nail glue users), manufacturing workers, mechanics, maintenance workers or painters. While the study combined (meth)acrylates and cyanoacrylates for statistical analysis, 29/446 = 6.5% of OA cases in this study were attributable to cyanoacrylates. Diagnoses in this cohort were confirmed by a SIC, indicative of respiratory sensitivity.

Respiratory sensitivity was diagnosed in beauty professionals who had frequently applied eyelash adhesives (containing ethyl cyanoacrylate concentrations >95%) to customers in Finland (Lindstrom et al. 2013). One case also exhibited ACD from exposure to adhesive. The patients initially showed no response to the SIC with the glue; however, upon retesting, one patient experienced a late asthmatic reaction indicative of OA and the other a rhinitis reaction. The level of volatile organic compounds (VOC) during the SIC was assessed using gas chromatography-mass spectrometry (GC-MS) for one of the cases. The VOC levels were below irritant levels, and the levels of ethyl cyanoacrylate were about 0.4 mg/m^3. No other (meth)acrylates were detected.

In a surveillance study of the United Kingdom's Midland Thoracic Society's voluntary surveillance scheme (SHIELD) reports between 1989 and 2014, there were 1790 reports of OA with 20 of these due to cyanoacrylates or (meth)acrylates (Walters et al. 2017). 10 of these patients were exposed to cyanoacrylates and worked as beauticians, dentists, manufacturers or in education. It should be noted that the cases from the education industry resulted from exposure to a cyanoacrylate adhesive used on flooring in renovations. 7 of the 10 patients had existing atopy. A limitation of this study is that all 10 patients were diagnosed by changes in peak exploratory flow (PEF) measurements without a SIC. However, all patients reported a pre-symptomatic latent period of exposure to the suspected sensitising agents, which suggests respiratory sensitisation.

There are other case reports of OA confirmed through SIC testing after exposure to cyanoacrylates. The studies do not present sufficient information or controls to confirm that the responses to challenges are below sub-irritant concentrations:

- 5 cases due to methyl cyanoacrylate (1), ethyl cyanoacrylate (3) and an unspecified cyanoacrylate (not specified) in adhesives. 3 patients had existing atopy. The asthmatic reactions were characterised as late or dual phase in 3 and 2 patients respectively. In three of these cases placebo-controls (non-cyanoacrylate glue) produced no asthmatic reaction (Lozewicz et al. 1985).
- 10 cases due to cyanoacrylates in adhesives identified from 880 hospital admissions. The asthmatic reactions were characterised as immediate, late or dual phase in 1, 6 and 3 patients respectively. The sources of cyanoacrylate exposure were not identified (WHO 2001).
- 2 cases due to cyanoacrylates in adhesives in patients with no existing atopy. One of the asthmatic reactions was characterised as late phase (Walters et al. 2017).
- 2 cases due to cyanoacrylates in adhesives. Both asthmatic reactions were characterised as late phase (Walters et al. 2017).
- 3 cases of possible asthma and rhinitis were reported in workers exposed to ethyl cyanoacrylate-based adhesives (WHO 2001).
- One case exhibited respiratory tract symptoms 4 months after exposure to an ethyl cyanoacrylate-based adhesive. In the first SIC there was a delayed asthmatic

response and a second SIC with a reported immediate asthmatic response (WHO 2001).

In some cohort studies of the irritation potential of cyanoacrylates (see **Irritation/Corrosion – Observation in humans**), OA was reported. However, it was not possible to determine whether cyanoacrylates directly caused asthma symptoms (ACGIH 2018; NIOSH 1985; WHO 2001;):

- In a study of 450 workers who handled cyanoacrylates with a mean airborne concentration of 0.2 ppm (1.0 mg/m^3), there was no increased risk of pulmonary obstruction disease in workers who were exposed to cyanoacrylates compared to workers who were not exposed.
- In a factory of 73 workers where the measured airborne ethyl cyanoacrylate at concentrations were up to 0.31 ppm (1.6 mg/m^3), OA was diagnosed in 13 of the 23 symptomatic workers based on PEF measurements only. It could not be determined if ethyl cyanoacrylate was the causative agent.
- In a factory of 16 workers where the average 8 hour airborne ethyl cyanoacrylate concentration was 0.90 ppm (4.6 mg/m^3), there was some evidence of pulmonary sensitisation. However, there was insufficient evidence that ethyl cyanoacrylate exposure caused sensitisation.

There are limited case reports of reactions in the public. However, there is a case report of a hobbyist who developed asthma after frequent use of cyanoacrylate adhesives (Yacoub et al. 2005). Therefore, respiratory sensitisation to cyanoacrylates is possible in frequent users of cyanoacrylates.

Repeat dose toxicity

No data are available for repeat dose toxicity by any exposure route. As the cyanoacrylates rapidly polymerise in presence of water, these chemicals are not expected to cause serious systemic health effects following repeated exposure.

In a 90 day oral repeat dose study in rats and dogs that were exposed to polymerised methyl cyanoacrylate in diet, no adverse effects were reported at doses up to 200 mg/kg bw/day (REACH n.d.-c).

Genotoxicity

Based on the weight of evidence of the in vitro, in vivo and in silico data, chemicals in this group are not expected to have genotoxic potential. Mostly negative results were reported for in vitro genotoxicity tests for 6 chemicals in this group. There are multiple positive in vitro genotoxicity tests in a single strain of *Salmonella (S.) typhimurium* and positive in silico alerts for methyl cyanoacrylate only. However, there was no evidence of genotoxicity in in vivo studies, which suggests that methyl cyanoacrylate is not expected to have genotoxic potential in vivo.

In vitro

Four cyanoacrylates were tested in a bacterial reverse mutation assay (Ames test) (OECD TG 471) in *S. typhimurium* TA 98, 1538, 1535 and 100 with and without metabolic activation at concentrations up to 20,000 µg/plate. A positive result was observed for methyl cyanoacrylate in TA 100. Negative results were observed for ethyl cyanoacrylate, butyl cyanoacrylate and allyl cyanoacrylate (REACH n.d.-a; REACH n.d.-b).

For methyl cyanoacrylate, mixed results were reported in the following in vitro genotoxicity studies (REACH n.d.-c):

- A positive result was reported in a bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA 1535, 1537, 98 and 100 with and without metabolic activation at concentrations up to 1666 µg/plate. The positive result was in strain TA 100.
- A positive result was reported in a bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA 1537, 98, 1538, 1535 and 100 with and without metabolic activation at concentrations up to 4000 µg/plate. The positive result was in strain TA 100.
- A negative result was reported in a bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA 100, 1535 and 1537 without metabolic activation at concentrations up to 1620 µg/plate.

For ethyl cyanoacrylate, negative results were reported in the following in vitro genotoxicity studies (REACH n.d.-b):

- A bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA 1535, 1537, 1538, 98 and 100 with and without metabolic activation at concentrations up to 4000 µg/plate.
- A mammalian chromosome aberration test (OECD TG 473) in human lymphoblastoid cells (TK6) with and without metabolic activation at concentrations up to 1280 µg/mL.

A positive result was reported for ethyl cyanoacrylate in an in vitro a mammalian gene mutation assay (OECD TG 476) in mouse lymphoma L5178Y cells with and without metabolic activation up to 1280 µg/mL. However, the test material contained 0.1% hydroquinone which was shown to induce a positive result in this test in the absence of ethyl cyanoacrylate (REACH n.d.-b).

For butyl cyanoacrylate, negative results were reported in the following in vitro genotoxicity studies (REACH n.d.-d):

- A bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA 1535, 1537, 98 and 100 with and without metabolic activation at concentrations up to 2500 µg/plate.
- A bacterial reverse mutation assay in *S. typhimurium* TA 100 and 1535 at concentrations up to 1620 µg/plate.
- A bacterial reverse mutation assay in *S. typhimurium* TA 1537 without metabolic activation at concentrations up to 1620 µg/plate.
- A mammalian chromosome aberration test (OECD TG 473) in human lymphocytes with and without metabolic activation at concentrations up to 5.5 mg/mL.

A negative result was reported for allyl cyanoacrylate in a bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA 98, 100, 1535 and 1537 and Escherichia coli WP2 uvrA with and without metabolic activation at concentrations up to 5.0 µL/plate (REACH n.d.-a).

A negative result was reported for methoxyethyl cyanoacrylate in a bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA 1535, 1537, 98 and 100 with and without metabolic activation at concentrations up to 5000 µg/plate (REACH n.d.-e).

In vivo

In a GLP compliant sex linked recessive lethal (SLRL) test in *Drosophila melanogaster* conducted in accordance with OECD TG 477, methyl cyanoacrylate was administered orally at 0.03, 0.045 or 0.06 mL. No evidence of sex linked lethal mutations was observed (REACH n.d.-c).

In a mammalian erythrocyte micronucleus test conducted similarly to OECD TG 474, mice (5/sex/dose) were treated with the methyl cyanoacrylate by intraperitoneal injection at a dose of 600 mg/kg bw. The incidence of micronuclei in bone marrow polychromatic erythrocytes did not increase in any of the treated groups, indicating a lack of clastogenicity (WHO 2001).

In silico

All chemicals in the group have a structural alert for protein binding for chromosomal aberration, based on the mechanistic (and endpoint-specific) profiling functionality of the OECD QSAR Toolbox. The alert is based on “Michael addition to alpha-beta unsaturated acids and esters”, where nucleophilic proteins can react with electrophilic cyanoacrylates. In addition, methyl cyanoacrylate had an DNA alert for Ames test, chromosomal aberration and mouse nucleus tests based on a “Michael-type conjugate addition to activated alkene derivatives” (OECD 2021).

The knowledge based expert system DEREK Nexus version 6.01 was used to estimate the genotoxic potential of these chemicals. An alert for “mutagenicity in vitro bacterium” was reported based on the alert “alpha-beta-unsaturated compound”. The alert was rated plausible in all cases except methyl cyanoacrylate which was probable (Lhasa Limited n.d.).

Carcinogenicity

No data are available. As the cyanoacrylates rapidly polymerise in the presence of water, these chemicals are not expected to cause carcinogenicity. Although the polymers produced from these chemicals may degrade to form formaldehyde, the carcinogenicity concerns for formaldehyde relate to inhaled formaldehyde at high concentrations (NICNAS 2006).

Reproductive and development toxicity

Limited data are available to evaluate this endpoint. As the cyanoacrylates rapidly polymerise in presence of water, these chemicals are not expected to cause effects on reproduction and development.

In a non-guideline reproductive and developmental toxicity study, there were no reported effects on the second generation of rats where the parent’s livers were sprayed with either butyl or isobutyl cyanoacrylate (NIWL 1997). No further details are available.

Two members of the higher molecular weight group are esters of known human reproductive toxicants:

- 2-methoxyethyl cyanoacrylate is the ester of cyanoacrylic acid with 2-methoxyethanol (CAS No. 109-86-4)
- 2-ethoxyethyl cyanoacrylate is the ester of cyanoacrylic acid with 2-ethoxyethanol (CAS No. 110-80-5).

However, the hydrolysis by esterases would require absorption and distribution in the bloodstream. As the polymerisation of cyanoacrylates happens quickly and there is limited expected systemic absorption (see **Toxicokinetics**), these chemicals are not expected to cause adverse effects on reproduction or development.

References

Aalto-Korte K, Alanko K, Kuuliala O and Jolanki R (2008) 'Occupational methacrylate and acrylate allergy from glues', *Contact Dermatitis*, 58, 340-346, doi: 10.1111/j.1600-0536.2008.01333.x.

Aalto-Korte K and Suuronen K (2020) 'Ten years of contact allergy from acrylic compounds in an occupation dermatology clinic', *Contact Dermatitis*, 2021, 84, 240-246, doi: 10.1111/cod.13739.

ACGIH (American Conference of Governmental Industrial Hygienists) (2018) *Cyanoacrylates*, ACGIH, accessed 08 March 2024.

Alavi A, Sibbald RG, Ladizinski B, Saraiya A, Lee KC, Skotnicki-Grant S and Maibach H (2016) 'Wound-related allergic/irritant contact dermatitis', *Advances in Skin & Wound Care*, 29(6), 278-286, doi: 10.1097/01.ASW.0000482834.94375.1e.

Alhumsi TR and Shah Mardan QN (2021) 'Burn Injury Due to Cyanoacrylate-Based Nail Glue: A Case Report and Literature Review', *Cureus*, 13(3), e13878, doi: 10.7759/cureus.13878.

Atwater AR and Reeder M (2019) 'Trends in Nail Services May Cause Dermatitis: Not Your Mother's Nail Polish', *Cutis*, 103(6) 315-317.

Brambilla E, Crevani M, Petrolini VM, Scaravaggi G, Di Primo M, Roda E and Locatelli C (2020) 'Exposure to Nail and False Eyelash Glue: A Case Series Study', *International Journal of Environmental Research and Public Health*, 17, 4283, doi: doi:10.3390/ijerph17124283.

Casault P, Gilbert N and Daoust B (2017) 'Comparison of various alkyl cyanoacrylates for fingerprint development', *Canadian Society of Forensic Science Journal*, 50(1), 1-22, doi: 10.1080/00085030.2016.1223438.

CDC (Centers for Disease Control and Prevention) (n.d.) National Institute for Occupational Safety and Health (NIOSH), Pocket Guide to Chemical Hazards. CDC website, accessed 22 January 2024.

Chemwatch (n.d.) *Galleria Chemica*, Chemwatch website, accessed 07 February 2024.

Chou M, Dhingra N and Strugar TL (2017) 'Contact Sensitization to Allergens in Nail Cosmetics', *Dermatitis*, 28(4), 231-240, doi: 10.1097/DER.0000000000000301.

Cook KA, White AA and Shaw DW (2019) 'Patch Testing Ingredients of Dermabond and Other Cyanoacrylate-Containing Adhesives' *Dermatitis,* 30(5)- 314-322, doi: 10.1097/DER.0000000000000514.

DeLima Associates (n.d.) *Consumer Product Information Database*, DeLima Associates website, accessed 16 February 2024.

Duffy C, Zetterlund PB and Aldababagh F (2018) 'Radical Polymerization of Alkyl 2-Cyanoacrylates', *Molecules*, 23(2), 465, doi: 10.3390/molecules23020465.

EC (European Commission) (n.d.) *CosIng*, EC website, accessed 19 February 2024.

EWG (Environmental Working Group) (n.d.) *EWG's Skin Deep*, EWG website, accessed 22 February 2024.

Gagnaire F, Marignac B, Morel G, Nunge H and Grossman S (2003) 'Sensory Irritation due to Methyl-2-cyanoacrylate, Ethyl-2-cyanoacrylate, Isopropyl-2-cyanoacrylate, 2-Methoxyethyl-2-cyanoacrylate in Mice', *The Annals of Occupational Hygiene,* 47(4), 297-304, doi: 10.1093/annhyg/meg038.

Goncalo M, Pinho A, Agner T, Andersen KE, Bruze M, Diepgen T, Foti C, Gimenez-Arnau A, Gooseens A, Johanseen JD, Paulsen E, Svedman C, Wilkinson M and Aalto-Korte K (2017) 'Allergic contact dermatitis caused by nail acrylates in Europe. An EECDRG study', *Contact Dermatitis*, 78, 254-260, doi: 10.1111/cod.12942.

Government of Canada (2022) *Cosmetic Ingredient Hotlist - List of Ingredients that are Restricted for Use in Cosmetic Products*, Government of Canada, accessed 21 November 2023.

Kanerva L, Jolanki R and Estlander T (1997) '10 years of patch testing with the (meth)acrylate series', *Contact Dermatitis*, 37, 255-258, doi: 10.1111/j.1600-0536.1997.tb02460.x.

Lhasa Limited (n.d.) Deductive Estimation of Risk from Existing Knowledge (DEREK) Nexus(Version 6.0.1), [Computer software], Lhasa Limited website, accessed 18 January 2024.

Lindstrom I, Suojalehto H, Henriks-Eckerman ML and Suuronen K (2013) 'Occupational asthma and rhinitis caused by cyanoacrylate-based eyelash extension glues', *Occupational Medicine*, 63, 294-297, doi: 10.1093/occmed/kqt020.

Lipman ZM and Tosti A (2021) 'Contact Dermatitis in Nail Cosmetics', *Allergies*, 1, 225–232, doi: 10.3390/allergies1040021.

Lozewicz S, Davison AG, Hopkirk A, Burge PS, Boldy DAR, Riordan JF, McGivern DV, Platts BW, Davies D and Newman Taylor AJ (1985) 'Occupational asthma due to methyl methacrylate and cyanoacrylates', *Thorax*, 40, 836-839, doi: 10.1136/thx.40.11.836.

MAK (The German MAK-Commission) (2012) *Methyl 2-cyanoacrylate and ethyl 2-cyanoacrylate*, MAK, accessed 5 January 2023.

Nam S and Mooney D (2021) 'Polymeric Tissue Adhesives', *Chemical Reviews*, 121, 11336-11384, doi: 10.1021/acs.chemrev.0c00798.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2006) *Priority Existing Chemical Assessment Report No. 28 Formaldehyde*, NICNAS, accessed 15 March 2024.

NIOSH (The National Institute for Occupational Safety and Health) (1985) *KP Industries, Delphos, Ohio - Health Hazard Evaluation Report No. 84-011*, NIOSH, accessed 24 January 2024.

NIWL (National Institute for Working Life) (1995) *The Nordic Expert group for Criteria Documentation of Health Risks from Chemicals 118. Cyanoacrylates*, NIWL, accessed 24 January 2024.

OECD (Organisation for Economic Co-operation and Development) (2012), *The Adverse Outcome Pathway for Skin Sensitisation Initiated by Covalent Binding to Proteins, Part 1: Scientific Evidence*, OECD, accessed 13 February 2024.

OECD (Organisation for Economic Co-operation and Development) (2021) Quantitative Structure-Activity Relationship (QSAR) Toolbox (Version 4.5), [Computer software], OECD website, accessed 18 January 2024.

Park YH, Choi JS, Cho JW and Kim HJ (2021) 'Incidence and risk factor of allergic contact dermatitis to 2-octyl cyanoacrylate and n-butyl cyanoacrylate topical skin adhesives', *Scientific Reports*, 11, 23762, doi: 10.1038/s41598-021-03319-3.

Parker D and Turk JL (1983) 'Contact sensitivity to acrylate compounds in guinea pigs', *Contact Dermatitis*, 9, 55-60, doi: 10.1111/j.1600-0536.1983.tb04626.x.

Pascual G, Sotomayor S, Rodriguez M, Perez-Kohler B, Kuhnhardt A, Fernandez-Gutierrez M, Roman JS and Bellon JM (2016) 'Cytotoxicity of Cyanoacrylate-Based Tissue Adhesives and Short-Term Preclinical In Vivo Biocompatibility in Abdominal Hernia Repair', *PLOS One*, doi: 10.1371/journal.pone.0157920.

Personal Care Products Council (n.d.) *Cosmetic Ingredient Identification Database*, Personal Care Products Council website, accessed 22 February 2024.

Ramos L, Cabral R and Goncalo M (2014) 'Allergic contact dermatitis caused by acrylates and methacrylates – a 7-year study', *Contact Dermatitis*, 71, 102-107, doi: 10.1111/cod.12266.

Raposo I, Lobo I, Amaro C, de Lurdes Lobo M, Melo H, Parente J, Pereira T, Rocha J, Cunha AP, Baptista A, Serrano P, Correia T, Travassos AR, Dias M, Pereira F and Goncalo M (2017) 'Allergic contact dermatitis caused by (meth)acrylates in nail cosmetic products in users and nail technicians – a 5-year study', *Contact Dermatitis*, 77, 356-359, doi: 10.1111/cod.12817.

REACH-a (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.) *Registered dossier for allyl 2-cyanoacrylate, CAS No. 7324-02-9*, European Chemicals Agency website, accessed 18 January 2024.

REACH-b (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.) *Registered dossier for ethyl 2-cyanoacrylate, CAS No. 7085-85-0*, European Chemicals Agency website, accessed 18 January 2024.

REACH-c (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.) *Registered dossier for mecrilate, CAS No. 137-05-3*, European Chemicals Agency website, accessed 18 January 2024.

REACH-d (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.) *Registered dossier for enbucrilate, CAS No. 6606-65-1*, European Chemicals Agency website, accessed 18 January 2024.

REACH-e (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.) *Registered dossier for 2-methoxyethyl 2-cyanoacrylate, CAS No. 27816-23-5*, European Chemicals Agency website, accessed 18 January 2024.

REACH-f (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.) *Registered dossier for 2-Propenoic acid, 2-cyano-, 1-methylheptyl ester, CAS No. 133978-15-1*, European Chemicals Agency website, accessed 18 January 2024.

Sanders L and Nagatomi J (2014) 'Clinical applications of surgical adhesives and sealants', *Critical reviews in biomedical engineering*, 42(3-4), 271–292, doi: 10.1615/critrevbiomedeng.2014011676.

Sato M, Inomata N and Aihara M (2017) 'A case of contact dermatitis syndrome caused by Dermabond®, followed by contact dermatitis caused by false eyelash glue and Aron Alpha® glue: possibility of cross-reactions among cyanoacrylates', *Contact Dermatitis*, 77, 414-415, doi: 10.1111/cod.12823.

Shanmugam S and Wilkson M (2012) 'Allergic contact dermatitis caused by a cyanoacrylate-containing false eyelash glue', *Contact Dermatitis*, 67, 306-320, doi: 10.1111/cod.12000.

Suojalehto H, Suuronen K, Cullinan P, Lindstrom I, Sastre J, Walusiak-Skorupa J, Munoz X, Talini D, Klusackova P, Moore V, Merget R, Svanes C, Mason P, dell'Omo M, Moscato G, Quirce S, Hoyle J, Sherson, D, Preisser A, Seed M, Rifflart C, Godet J, de Blay F and Vandenplas O (2020) 'Phenotypical Occupational Asthma Caused by Acrylates in a Multicenter Cohort Study', *The Journal of Allergy and Clinical Immunology: In Practice*, 8(3), 971-979, doi: 0.1016/j.jaip.2019.10.017.

SWA-a (Safe Work Australia) (n.d.) *Hazardous Chemical Information System*, SWA website, accessed 21 November 2023.

SWA-b (Safe Work Australia) (n.d.) *Workplace Exposure Limits – airborne contaminants*, SWA website, accessed 12 June 2024.

SWA (Safe Work Australia) (2024) *Workplace exposure standards for airborne contaminants*, SWA website, accessed 12 June 2024.

Symanzik C, Weinert P, Babić Ž, Hallmann S, Havmose MS, Johansen J, Kezic S, Macan M, Macan J, Strahwald J, Turk R, van der Molen HF, Jogn SM and Uter W (2022) 'Allergic contact dermatitis caused by 2-hydroxyethyl methacrylate and ethyl cyanoacrylate contained in cosmetic glues among hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications: A systematic review', *Contact Dermatitis*, 86(6), 480-492, doi:10.1111/cod.14056.

TGA (Therapeutic Goods Administration) (2024) *Standard for the Uniform Scheduling of Medicines and Poisons (Poisons Standard—February 2024)*, TGA, accessed 6 February 2024.

US DOE (United States Department of Energy) (n.d.) *Protective Action Criteria (PAC): chemicals with AEGLs, ERPGs, & TEELs*, US DOE website, accessed 22 January 2024.

US EPA (United States Environmental Protection Agency) (n.d.) *2020 CDR Data*, US EPA website, accessed 22 February 2024.

Walters GI, Robertson AS, Moore VC and Burge PS (2017) 'Occupational asthma caused by acrylic compounds from SHIELD surveillance (1989-2014)', *Occupational Medicine*, 67, 282-289, doi: 10.1093/occmed/kqx036.

Warshaw EM, Maibach HI, Taylor JS, Sasseville D, DeKoven JD, Zirwas MJ, Fransway AF, Mathias CGT, Zug KA, DeLeo VA, Fowler Jr JF, Marks JG, Pratt MD, Storrs FJ and Belsito DV (2015) 'North American Contact Dermatitis Group Patch Test Results: 2011-2012', *Dermatitis*, 26(1), 49-59, doi: 10.1097/DER.0000000000000097.

Warshaw EM, Voller LM, Silverberg JI, DeKoven JG, Atwater AR, Maibach HI, Reeder MJ, Sasseville D, Belsito DV, DeLeo VA, Fransway AF, Folwer Jr JF, Taylor JS, Pratt MD, Mathias T, Marks Jr JG, Zug KA and Zirwas MJ (2020) 'Contact Dermatitis Associated With Nail Care Products: Retrospective Analysis of North American Contact Dermatitis Group Data, 2001-2016', *Dermatitis*, 31(3), 191-201, doi: 10.1097/DER.0000000000000583.

Wetarini, K, (2020) 'Ocular superglue injury: a case report and review of literature', *Bali Journal of Ophthalmology* 4(1), 18-23, doi: 10.15562/bjo.v4i1.52.

Wetter DA, Yiannas JA, Prakash AV, Davis MDP, Farmer BA and el-Azhary RA (2010) 'Results of patch testing to personal care product allergens in a standard series and a supplemental cosmetic series: An analysis of 945 patients from the Mayo Clinic Contact Dermatitis Group, 2000-2007', *Journal of the American Academy of Dermatology*, 63(5), 789-798, doi: 10.1016/j.jaad.2009.11.033.

WHO (World Health Organisation) (2001) *Methyl cyanoacrylate and ethyl cyanoacrylate*, WHO, accessed 22 November 2023.

Yacoub M, Lemiere C and Malo J (2005) 'Asthma caused by cyanoacrylate used in a leisure activity', *The Journal of Allergy and Clinical Immunology*, 116(2), 462, doi: 10.1016/j.jaci.2005.04.015.