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

Benzene, 1,1′-methylenebis[4-isocyanato-, homopolymer, iso-Bu alc.-blocked

Assessment statement (CA09931)

22 October 2024

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AICIS assessment (CA09931)

Chemical in this assessment

Name	CAS registry number
Benzene, 1,1′-methylenebis[4-isocyanato-, homopolymer, iso-Bu alc.-blocked	201615-11-4

Reason for the assessment

An application for an assessment certificate under section 31 of the *Industrial Chemicals Act 2019* (the Act).

Certificate application type

AICIS received the application in a Health Focus type.

Defined scope of assessment

The polymer has been assessed:

- as imported into Australia at up to 30 tonnes/year
- as imported in a formulation at up to 50% concentration
- for reformulation into adhesives at up to 20% concentration for use by professional workers only

Summary of assessment

Summary of introduction, use and end use

The assessed polymer will not be manufactured in Australia and will be imported in 205 L drums containing the assessed polymer in a formulation at up to 50% concentration. The imported formulation will be mixed with other ingredients for use as industrial adhesives containing the assessed polymer up to 20% concentration. After application, the adhesive containing the assessed polymer will be cured to form an inert solid.

There will be no consumer use of formulations containing the assessed polymer.

Human health

Summary of health hazards

Based on the analogue data provided (or available to AICIS) (see **Supporting information**), the assessed polymer is:

- of low acute oral toxicity (LD50 > 2,000 mg/kg bw in rats)
- of high acute inhalation toxicity (LC50 = 0.49 mg/L in rats)

- a skin, eye and respiratory irritant
- a skin and respiratory sensitiser
- not expected to be genotoxic

Based on the analogue data provided (or available to AICIS), the assessed polymer is expected to cause adverse effects to the respiratory system following repeated inhalation exposure, and is suspected of causing cancer through inhalation.

Hazard classifications relevant for worker health and safety

Based on the analogue data provided (or available to AICIS), the assessed polymer satisfies the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE 2017) for hazard classes relevant for worker health and safety as adopted for industrial chemicals in Australia.

Health hazards	Hazard category	Hazard statement
Acute toxicity – inhalation	Acute Tox. 2	H330: Fatal if inhaled
Skin irritation	Skin Irrit. 2	H315: Causes skin irritation
Eye irritation	Eye Irrit. 2A	H319: Causes serious eye 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
Specific target organ toxicity (single exposure)	STOT Single Exp. 3	H335: May cause respiratory irritation
Carcinogenicity	Carc. 2	H351: Suspected of causing cancer
Specific target organ toxicity (repeat exposure)	STOT Rep. Exp. 1	H372: Causes damage to organs through prolonged or repeated exposure

Summary of health risk

Public

The imported formulation or end use adhesives containing the assessed polymer will not be available for use by the public. Once the adhesive is cured, the assessed polymer is bound in an inert solid and will not be available for exposure. When introduced and used in the proposed manner, it is unlikely that the public will be exposed to the assessed polymer.

This assessment does not identify any risks to public health that require specific risk management measures.

Workers

Workers may experience dermal, inhalation and incidental ocular exposure to the assessed polymer at up to 50% concentration during reformulation of liquid formulations containing the assessed polymer. Workers may experience dermal, inhalation and incidental ocular exposure

to the assessed polymer at up to 20% concentration when handling liquid adhesive products or handling materials containing the adhesive prior to curing.

Given that risks of critical health effects of the assessed polymer through inhalation of mists or aerosols and contact with skin or eyes, control measures to minimise inhalation, dermal and ocular exposure are needed to manage the risk to workers) (see **Means for managing risk section**).

Environment

Summary of environmental hazard characteristics

According to the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals (DCCEEW, 2022) and based on the available data the assessed polymer is:

- Persistent
- Not Bioaccumulative
- Not Toxic

Environmental hazard classification

The polymer satisfies the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE, 2017) as Acute Category 2 (H401) and Chronic Category 2 (H411) based on the toxicity data for invertebrates. Considerations were also made for the rapid biodegradability of the assessed polymer.

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute / short-term)	Aquatic Acute 2	H401: Toxic to aquatic life
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 2	H411: Toxic to aquatic life with long lasting effects

Summary of environmental risk

The assessed polymer will be imported at up to 50% concentration for use as a component of industrial adhesives. No significant release of the assessed polymer is expected to occur as a result of its end use. The assessed polymer is expected to share the fate of the product it is incorporated into and be disposed of to landfill and or/collected for recycling at the end of its useful life.

The assessed polymer is not readily degradable and is persistent. The assessed polymer has no potential for bioaccumulation and is not expected to cause toxic effects in aquatic organisms according to the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals (DCCEEW, 2022).

Although the assessed polymer is persistent according to the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals (DCCEEW, 2022), it does not meet all three PBT criteria. It is hence unlikely to have unpredictable long-term effects (EPHC 2009). A Risk Quotient (PEC/PNEC) for the aquatic compartment was not calculated as the release to the environment of the assessed polymer is expected to be minimal based on its use patterns and limited bioavailability. Therefore, the risk from the assessed polymer can be managed.

Means for managing risk

Workers

Recommendation to Safe Work Australia

- It is recommended that Safe Work Australia (SWA) update the *Hazardous Chemical Information System* (HCIS) to include classifications relevant to work health and safety (see **Hazard classifications relevant for worker health and safety**).

Information relating to safe introduction and use

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

The following control measures could be implemented to manage the risk arising from exposure to the assessed polymer during reformulation or end use:

- Use of engineering controls such as
  - Enclosed and automated systems where possible
  - Adequate workplace ventilation to avoid accumulation of mists or aerosols

- Use of safe work practices to
  - Avoid contact with skin and eye
  - Avoid inhalation of mists or aerosols

- Use of personal protective equipment (PPE)
  - Impervious gloves
  - Eye protection
  - Protective clothing
  - Respiratory protection where local ventilation may be inadequate

- The storage of the assessed polymer should be in accordance with the Safe Work Australia *Code of Practice for Managing Risks of Hazardous Chemicals in the Workplace* (SWA 2023) or relevant State or Territory Code of Practice.

- Atmospheric monitoring should be conducted to measure workplace concentrations of isocyanates during use of products containing the assessed polymer. Users of the products should ensure that the exposure standard for isocyanates (SWA, 2015), listed by Safe Work Australia in the *Hazardous Chemicals Information System* (HCIS), is not exceeded for all areas where the assessed polymer is present.

- As the assessed polymer is a skin and respiratory sensitiser, the control measures may need to be supplemented with health monitoring for any worker who is at significant risk of exposure to the polymer, if valid techniques are available to monitor the effect on the worker's health.

- A copy of the Safety Data Sheet (SDS) should be easily accessible to workers.

Conclusions

The Executive Director is satisfied that the risks to human health or the environment associated with the introduction and use of the industrial chemical can be managed.

Note:

1. Obligations to report additional information about hazards under s 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

Chemical identity

CAS number	201615-11-4
CAS name	Benzene, 1,1′-methylenebis[4-isocyanato-, homopolymer, iso-Bu alc.-blocked
Molecular formula	Unspecified
Number average molecular weight (NAMW, g/mol)	1,230
Percentage of low molecular weight species (less than 1,000 g/mol)	40.5
Percentage of low molecular weight species (less than 500 g/mol)	0.8

Additional chemical identity information

The assessed polymer contains unreacted terminal isocyanate groups.

Relevant physical and chemical properties

Physical form	Yellow liquid
Melting point	< -50 °C
Boiling point	Decomposes at > 200 °C
Density	1,198 kg/m^3 at 20 °C
Vapour pressure	0.00143 Pa
Water solubility	Unstable in water
Flash Point	> 100 °C
Ionisable in the environment	No
Viscosity	800 – 1,300 mPas

* The test substance used for the properties above was the assessed polymer in the imported formulation.

Health hazard information

No toxicological data were provided for the assessed polymer. The following analogues were considered as read-across substances for the assessed polymer:

- Analogue 1: Isocyanic acid, polymethylenepolyphenylene ester, 2-ethyl-1-hexanol-blocked (CAS No.: 147993-65-5)]
- Analogue 2: Isocyanic acid, polymethylenepolyphenylene ester (CAS No.: 9016-87-9)
- A group of chemicals with free isocyanate functional groups (NICNAS 2013) that is structurally related to the assessed polymer

Acute toxicity

Oral

In an acute oral toxicity study (OECD TG 423) conducted on Analogue 1, the test substance was administered to two groups of female Wistar rats (n = 3 per group) at a single dose of 2,000 mg/kg bw via oral gavage. All animals survived during the 14-day observation period and no signs of systemic toxicity were noted. All animals showed expected body weight gains and no treatment-related gross necropsy findings were observed. The acute oral median lethal dose (LD50) of the test substance was determined to be > 2,000 mg/kg bw.

Inhalation

An Inventory Multi-tiered Assessment and Prioritisation (IMAP) report on a group of chemicals with free isocyanate functional groups concluded that the chemicals of the group are classified as hazardous with the risk phrase 'Toxic by inhalation' (NICNAS 2013). Analogue 2 is classified as acute toxicity (inhalation) Category 2 on HCIS by Safe Work Australia.

Corrosion/Irritation

Skin irritation

A skin irritation study (OECD TG 404) was conducted on Analogue 1. The test was conducted in 3 female New Zealand white rabbits using semi-occlusive patches (2.5 cm × 2.5 cm) with 0.5 mL of the test substance applied to different treated sites for 3 minutes, 1 hour and 4 hours respectively. The site was evaluated for irritation upon the patch removal at 60 minutes followed by 24, 48 and 72 hours. No signs of irritation were observed at sites exposed for 3 minutes or 1 hour. After application of the test substance for 4 hours, all animals showed very slight erythema. At the 24-hour and 48-hour observations, very slight erythema was persistent in 2 animals. All treated sites had completely recovered by 72 hours. The mean individual erythema scores from gradings at 24, 48 and 72 hours were 0.7, 0.7, 0, respectively. Based on the results, the test substance is considered to be slightly irritating to the skin and is not classified as a skin irritant according to the GHS criteria.

An IMAP report on a group of chemicals with free isocyanate functional groups concluded that the chemicals of the group are classified as hazardous with the risk phrase 'Irritating to skin' (NICNAS 2013). Analogue 2 is classified for skin irritation Category 2 on HCIS by Safe Work Australia.

Although the study data on Analogue 1 indicated that blockage of free isocyanate groups reduced irritation, the differences between Analogue 1 and the assessed polymer in molecular

weight, percentage of low molecular weight species and degree of free isocyanate blockage are unknown. Therefore, data on Analogue 1 was not used for read-across to estimate the potential for skin irritation of the assessed polymer.

Eye irritation

An eye irritation study (OECD TG 405) was conducted on Analogue 1. The test was conducted in 3 female New Zealand white rabbits, with 0.1 mL of the test substance instilled into one eye of each rabbit. The ocular irritation was evaluated after exposure at 1, 24, 48 and 72 hours. Conjunctival redness and chemosis were observed 1 hour after treatment. At the 24-hour and 48-hour observations, these effects persisted but showed some recovery. All treated sites had completely recovered by 72 hours. The mean individual conjunctivae redness scores from gradings at 24, 48 and 72 hours were 1.0, 1.0, 1.7, respectively, and the conjunctivae chemosis scores were 0.3, 0.7, 0.3, respectively. No effects on the cornea and iris were observed. Based on the results, the test substance is considered to be slightly irritating to the eyes and is not classified as an eye irritant according to the GHS criteria.

An IMAP report on a group of chemicals with free isocyanate functional groups concluded that the chemicals of the group are classified as hazardous with the risk phrase 'Irritating to eyes' (NICNAS 2013). Analogue 2 is classified for eye irritation Category 2A on HCIS by Safe Work Australia.

Although the study data on Analogue 1 indicated that blockage of free isocyanate groups reduced irritation, the differences between Analogue 1 and the assessed polymer in molecular weight, percentage of low molecular weight species and degree of free isocyanate blockage are unknown. Therefore, data on Analogue 1 was not used for read-across to estimate the potential for eye irritation of the assessed polymer.

Respiratory irritation

An IMAP report on a group of chemicals with free isocyanate functional groups concluded that the chemicals of the group are classified as hazardous with the risk phrase 'Irritating to respiratory system' (NICNAS 2013). Analogue 2 is classified as specific target organ toxicity (single exposure) Category 3 on HCIS by Safe Work Australia.

Sensitisation

Skin sensitisation

A modified local lymph node assay using the Integrated Model for Differentiation of Skin Reactions (LLNA-IMDS) (OECD TG 429) was conducted on Analogue 1, with the modification being the measurement of cell proliferation by cell counting instead of radioactive labelling. Female NMRI mice (n = 6 per group) were treated at 0%, 1%, 3% or 10% concentration of the test substance in acetone/olive oil (4:1) on both ears for 3 consecutive days. The test substance-treated animals gave lymph node cell count indexes of 2.95, 4.41 and 4.58 when compared with the negative control, which exceeded the positive index level of 1.4. The ear thickness increases were 1.17×10^{-2} mm, 2.75×10^{-2} mm and 4.67×10^{-2} mm, respectively and the values in the mid and high dose groups exceeded the positive level of 2×10^{-2} mm (Vohr et al., 2000). Differentiation index (DI) was calculated to be 5.42, 5.01 and 3.31 and a value of > 1 is considered indicative of sensitisation potential (Vohr et al., 2000). Based on the results, the test substance is considered to be a skin sensitiser, warranting a hazard classification for skin sensitisation (Category 1, H317: May cause an allergic skin reaction) according to the GHS criteria.

An IMAP report on a group of chemicals with free isocyanate functional groups concluded that the chemicals of the group are classified as hazardous with the risk phrase 'May cause sensitisation by skin contact' (NICNAS 2013). Analogue 2 is classified as skin sensitisation Category 1 on HCIS by Safe Work Australia.

Respiratory sensitisation

An IMAP report on a group of chemicals with free isocyanate functional groups concluded that the chemicals of the group are classified as hazardous with the risk phrase 'May cause sensitisation by inhalation' (AICIS 2013). Analogue 2 is classified as respiratory sensitisation Category 1 on HCIS by Safe Work Australia.

Repeat dose toxicity

Inhalation

An IMAP report on a group of chemicals with free isocyanate functional groups concluded that the chemicals of the group are classified as hazardous with the risk phrase 'Danger of serious damage to health by prolonged exposure through inhalation' (NICNAS 2013). Analogue 2 is classified as specific targeted organ toxicity (repeated exposure) Category 1 on HCIS by Safe Work Australia.

Genotoxicity

Analogue 1 was found to be non-mutagenic in a bacterial reverse mutation assay (OECD TG 471).

An IMAP report on a group of chemicals with free isocyanate functional groups reported that the genotoxicity of chemicals of the group is equivocal (NICNAS 2013). However, the report also reported that an OECD report (2003) concluded that the chemicals of this group are not genotoxic. The report also stated that potential breakdown of methylenediphenyl diisocyanate to methylenedianiline (MDA, classified as a mutagen) in the stomach could suggest potential for genotoxicity through the oral route.

Carcinogenicity

An IMAP report on a group of chemicals with free isocyanate functional groups reported that Analogue 2 was tested in a combined chronic toxicity/carcinogenicity study. Based on the lung tumours observed in this study, a No Observed Adverse Effect Concentration (NOAEC) of 1.0 mg/m^3 was derived for carcinogenicity (NICNAS 2013). Analogue 2 is classified as carcinogenicity Category 2 on HCIS by Safe Work Australia.

Environmental exposure

The assessed polymer will be used as a component of industrial adhesives. The assessed polymer will not be manufactured in Australia. It will be imported in 205 L steel drums. Reformulation will be conducted by professional workers by manually mixing the assessed polymer prior to the application process. No release to the environment is expected from these activities. Accidental spills during transport are expected to be disposed of according to local regulations.

Environmental exposures during application are expected to be minimal, as the recommended method of application will be fully enclosed and supplied with ventilation to remove any vapours and mists.

Any residues left in containers will be disposed of according to local regulations.

The majority of the assessed polymer is expected to share the fate of the substrates it's been applied to and be disposed of to landfill.

Environmental fate

Partitioning

Based on hydrolysis data on suitable analogues, the assessed polymer is expected to hydrolyse rapidly.

A hydrolysis study on a suitable analogue (4,4'-MDI) conducted according to OECD TG 111 indicates a half-life of 16.7 seconds, at pH 7 and 20°C. The same hydrolysis study reported half-lives of 17.6 seconds at pH 4 and 20°C and 11.9 seconds at pH 9 and 20°C. Based on this information, the assessed polymer is expected to be hydrolytically unstable under environmental conditions.

The assessed polymer is non-ionic and rapidly hydrolysing in water. If the assessed polymer is released to water, it is expected to stay in water only transiently, resulting in the hydrolysis products to be adsorbed strongly to soil and sediment and become immobile (US EPA, 2013).

As the assessed polymer is slightly volatile (vapour pressure = 0.00143 Pa), it is not expected to evaporate and partition to air.

Degradation

Based on its measured degradation in water, the assessed polymer is considered persistent.

The assessed polymer is not readily biodegradable based on the results of a supplied biodegradation study which showed 0% degradation of the assessed polymer (OECD 301F) over 28 days.

Bioaccumulation

Based on the results of a supplied experimental bioconcentration factors (BCF) study (OECD 305 method) for a suitable analogue (CAS RN 101-68-8) of the assessed polymer is considered to have low potential to bioaccumulate. Experimental BCF values of the suitable analogue ranged from 92-200, which are below the domestic threshold for bioaccumulation potential. Furthermore, the assessed polymer hydrolyses rapidly and is expected to only exist transiently in water and therefore, is essentially unavailable for uptake and bioaccumulation.

Predicted environmental concentration (PEC)

The predicted environmental concentration (PEC) has not been calculated as the assessed polymer is hydrolytically unstable and release of the assessed polymer to the aquatic environment is expected to be negligible based on its assessed use pattern.

Environmental effects

Effects on aquatic life

Acute toxicity

The following median lethal loading (LL50), effective loading (EC50), and inhibition concentration (IC50) values for model organisms were supplied for the assessed polymer:

Taxon	Endpoint	Method
Fish	96hr LL50 > 100 mg/L	*Danio rerio* (carp) Mortality OECD TG 203 Static Nominal loading rate (WAF)*
Invertebrate	48hr EL50 = 2.07 mg/L	*Daphnia magna* (water flea) Immobility OECD TG 202 Static Nominal loading rate (WAF)
Algae	72hr EC50 > 100 mg/L	*Desmodesmus subspicatus* (not provided) Growth rate OECD TG 201 Static Nominal concentration (WAF)
Microorganisms	3hr EC50 > 10,000 mg/L	Activated sludge from a STP Respiration inhibition OECD TG 209 Static Nominal concentration

*WAF: Water Accommodated Fractions

Predicted no-effect concentration (PNEC)

A predicted no-effect concentration (PNEC) of 20.7 µg/L was calculated for the assessed polymer in the aquatic environment. This value was derived using the most conservative endpoint value for invertebrates (2.07 mg/L). An assessment factor of 100 was applied to this endpoint as acute toxicity data were available for three trophic levels and no chronic toxicity data were available (EPHC, 2009).

Categorisation of environmental hazard

The categorisation of the environmental hazards of the assessed polymer according to the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals (DCCEEW, 2022) is presented below:

Persistence

Persistent (P). Based on measured degradation study, the assessed polymer is categorised as Persistent.

Bioaccumulation

Not Bioaccumulative (Not B). Based on low measured BCF in fish, on a suitable analogue and no evidence of biotransformation, the assessed polymer is categorised as Not Bioaccumulative.

Toxicity

Not Toxic (Not T). Based on available ecotoxicity values above 1 mg/L the assessed polymer is categorised as Not Toxic.

Environmental risk characterisation

Although the assessed polymer is persistent, it does not meet all three PBT criteria. It is hence unlikely to have unpredictable long-term effects (EPHC 2009). A Risk Quotient (PEC/PNEC) for the aquatic compartment was not calculated as the currently available information indicates the assessed polymer will have limited bioavailability and the release to the environment is expected to be minimal based on its use pattern. Therefore, the risk from the assessed polymer can be managed.

References

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