Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

1H-Imidazole, 1-ethenyl-

Evaluation statement

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AICIS evaluation statement

Subject of the evaluation

1H-Imidazole, 1-ethenyl- (N-vinyl imidazole)

Chemical in this evaluation

Name	CAS registry number
1H-Imidazole, 1-ethenyl-	1072-63-5

Reason for the evaluation

The Evaluation Selection Analysis of the chemical indicated a potential risk to human health.

Parameters of evaluation

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

Summary of evaluation

Summary of introduction, use and end use

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

The chemical has a high reactivity for radical polymerisation (ECHA 2016) and is generally used worldwide as a monomer for further polymerisation. The following use patterns for the chemical are identified internationally:

- The chemical or its polymerised product has reported commercial uses in trade and repair of motor vehicles, construction and surface treatment (REACH; SPIN; ECHA 2016).
- The chemical has reported site-limited uses in the manufacture of other chemicals and chemical products (REACH; SPIN).

The chemical is listed on the Personal Care Products Council database as a reference for the definition of other INCI names and the database indicates that it might not be a marketed cosmetic ingredient (Personal Care Products Council).

The chemical has reported domestic use (e.g. paints) in the Substances and Preparations in Nordic countries (SPIN) database. However, it should be noted that SPIN does not distinguish between direct use of the chemical, and use of the materials that are produced

from chemical reactions involving the chemical. There is no evidence from available consumer product databases for use of this chemical in consumer industrial products.

Human health

Summary of health hazards

The critical health effects for risk characterisation include:

- local effects (skin irritation and serious eye damage)
- adverse systemic long term effects including reproductive effects.

Based on the available data, the chemical is considered harmful if swallowed with a median lethal dose (LD50) of 1040 mg/kg body weight (bw) in rats. Acute dermal toxicity of the chemical is considered low with a LD50 >2000 mg/kg bw in rats.

The chemical is considered to be a skin irritant based on a dermal irritation study that showed skin redness and scaling in rabbits for 1–3 weeks at 50% or 100% concentration.

The chemical is considered to be corrosive to the eyes based on an eye irritation study in rabbits. Exposure of eyes to the chemical resulted in severe redness or bleeding of conjunctivae, secretion of pus, ciliary injection and severe oedema. Cloudiness of the cornea was also observed.

The chemical is expected to cause serious systemic health effects following repeated or prolonged exposure. In a repeated oral toxicity study, rats were administered the chemical at doses of 0, 90 or 180 mg/kg bw/day for 3 months. Mortalities occurred at 180 mg/kg bw/day. The affected animals showed poor general state, lack of appetite and reduced body weight gain combined with reduced food consumption and increased water consumption. Gamma-glutamyl transferase (GGT) activity in the liver was also increased. A no observed adverse effect level (NOAEL) for the chemical could not be established for the study. The lowest observed adverse effect level (LOAEL) was the lowest dose tested (90 mg/kg bw/day) (REACH).

The chemical also has the potential to damage the unborn child. In a combined repeated dose toxicity with reproduction/developmental toxicity study, rats were administered the chemical at doses of 0, 5, 15 or 35 mg/kg bw/day for 30 days in males and 50 days in females. Parental animals treated at 15 mg/kg bw/day or above had significantly reduced food consumption and body weight gain, increased liver weight with centrilobular hypertrophy, and increased kidney weight. Numbers of stillborn, deceased and cannibalised pups were significantly increased in the group treated at 35 mg/kg bw/day, and hence the pup viability index was significantly reduced. Affected live pups had significantly reduced body weight. Macroscopic examination of the pups showed dilated aneurysms in the blood vessels including aorta, arteries and ductus arteriosus. Based on the observations, a NOAEL was established at 5 mg/kg bw/day for systemic toxicity in the parental animals and for developmental toxicity in the F1 pups. The NOAEL for adult fertility was established at 35 mg/kg bw/day (REACH).

Health hazard classification

The chemical 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 follows. This does not consider classification of physical and environmental hazards.

Health hazards	Hazard category	Hazard statement
Acute toxicity – oral	Acute Tox. 4	H302: Harmful if swallowed
Skin irritation	Skin Irrit. 2	H315: Causes skin irritation
Serious eye damage	Eye damage 1	H318: Causes serious eye damage
Specific target organ toxicity – repeated exposure	STOT Rep. Exp. 2	H373: My cause damage to organs through prolonged or repeated exposure
Reproductive toxicity	Repr. 1B	H360D: May damage the unborn child

Summary of health risk

Public

Australian use data are not available for the chemical and use patterns in Australia are assumed to be similar to those overseas.

Based on the available international use information, it is unlikely that the public will be exposed to the chemical. Therefore, there are no identified risks to the public that require management.

Workers

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

Given the critical local and systemic long term health effects, the chemical may pose a risk to workers. Control measures to minimise dermal and ocular and inhalation exposure are needed to manage the risk to workers (refer to **Recommendations** section).

Conclusions

The conclusions of this evaluation are based on the information described in this statement. Obligations to report additional information about hazards under section 100 of the Industrial Chemicals Act 2019 apply.

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

Recommendations

Workers

Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the Hazardous Chemical Information System (HCIS) to include new classifications relevant to work health and safety as listed above.

Information on managing identified risks

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

Control measures that can be implemented to manage the risk arising from dermal, ocular or oral exposure to the chemical include, but are not limited to:

- using closed systems or isolating operations
- minimising manual processes or conducting work tasks through automated processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using personal protective equipment (PPE) that is designed, constructed and operated to ensure that workers do not come into contact with the chemical.

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

These control measures may need to be supplemented with:

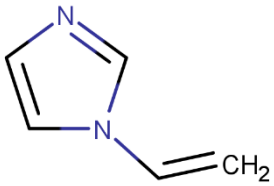
- conducting health monitoring for any worker who is at significant risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker's health.

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

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

Supporting information

Chemical identity

Synonyms	N-Vinyl imidazole Imidazole, 1-vinyl- 1-ethenylimidazole 1-vinyl-1*H*-imidazole 1-vinylimidazole
Structural formula	
Molecular formula	$C_5H_6N_2$
Molecular weight (g/mol)	94.11
SMILES	N=1C=CN(C1)C=C
Chemical description	-

Relevant physical and chemical properties

Physical form	Liquid at 20 °C and 1013 hPa
Melting point	<-100 °C
Boiling point	100 – 113 °C
Vapour pressure	0.38 hPa at 20 °C
Water solubility	Completely miscible in water at 20°C
pKa	6.07 ± 0.10
Log Kow	0.54 at 25°C

Introduction and use

Australia

No specific Australian use, import, or manufacturing information have been identified.

International

The chemical is listed on the Personal Care Products Council database without a function. The database indicated that the chemical might not be a marketed cosmetic ingredient and is listed as a reference for the definition of other INCI names (Personal Care Products Council). No function is listed in the CosIng database (EC).

The chemical has been found as an impurity/non-reacted monomer in raw material for different consumer mixtures at concentrations ranging 0.6% to 4.5%. The concentrations are likely to be lower in consumer mixtures as a result of dilution (ECHA 2020).

According to the US Environmental Protection Agency's (EPA) Chemical Data Reporting (CDR) (US EPA 2016), the chemical is reported to be used as an emulsifier in the manufacture of petroleum lubricating oils and greases, as well as plastics and resins.

In addition, the following uses of the chemical or its polymerised products are also reported internationally:

Domestic uses in (SPIN; ECHA 2016):

- paints, lacquers and varnishes
- coating additives
- lubricants
- home care applications (dye transfer inhibition)
- cleaning and washing products.

Commercial uses in (REACH; SPIN; ECHA 2016):

- trade and repair of motor vehicles and motorcycles in wholesale and retail
- construction
- polymer for metal ion filtration
- surface treatment.

Site limited uses in the manufacture of other chemicals and chemical products (REACH; SPIN).

The chemical is widely used as a monomer for further polymerisation and SPIN does not distinguish between direct use of the chemical and use of its polymerise products. The above listed domestic and commercial uses identified are likely to be related to the polymerised products which are not included in this evaluation. There is no evidence from available consumer product databases for use of this chemical in consumer products.

Existing Australian regulatory controls

AICIS

No specific controls are currently available for the chemical.

Public

No specific controls are currently available for the chemical.

Workers

The chemical is classified as hazardous with the following risk phrases for human health in the HCIS (SWA):

- Reproductive toxicity – Category 1B: H360D (May damage the unborn child).

No exposure standards are available for this chemical in Australia (SWA).

International regulatory status

European Union

The chemical is listed in Regulation (European Commission (EC)) 1223/2009 on cosmetic products, Annex II – List of substances prohibited in cosmetic products.

The chemical is listed on the candidate list of substances of very high concern (SVHC) for eventual inclusion in Annex XIV (ECHA 2020). The reason for inclusion in the list is the chemical is considered to be 'toxic for reproduction (Article 57c)'. In the European Union (EU), companies have legal obligations to protect the public if the chemical that they produce, supply, or use is included on the candidate list whether on its own, in mixtures, or in articles.

Health hazard information

Toxicokinetics

The chemical has a log Kow value between -1 and 4, which favours absorption by passive diffusion. Furthermore, the molecular weight below 200 makes the chemical also favourable for absorption. This suggests that the chemical may be readily absorbed by the gastrointestinal and respiratory tract (ECHA 2016).

Acute toxicity

Oral

Based on the available data, the chemical has moderate acute oral toxicity, which warrants hazard classification (refer to **Health hazard classification** section).

In an acute oral toxicity study conducted similarly to the Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 401, not compliant with good laboratory practice (GLP), the chemical was administered to rats (sex and strain unspecified) in groups of 5 per dose by oral gavage at doses equivalent to 520, 1040 and 2080 mg/kg bw. At 1040 mg/kg bw, 2 out of 5 animals died. At 2080 mg/kg bw, all animals died within 2–5 days. The reported LD50 for acute oral toxicity was approximately 1040 mg/kg bw in rats (REACH).

Dermal

Based on the available data, the chemical has low acute dermal toxicity and does not warrant hazard classification.

In an acute dermal toxicity study conducted according to OECD TG 402, the chemical was applied to the skin of Wistar rats (5/sex/dose) under occlusion at a dose of 2000 mg/kg bw for 24 hours. No mortalities occurred during the 14 day observation period. Clinical signs observed in both sexes included impaired general state, dyspnoea and lacrimation. Chromodacryorrhoea (blood in tears) was observed from days 1–2 after administration. Red clammy snout and eyelids were observed in males, while smeared fur was observed in females. In 3 females, skin effects observed at the application site were very slight and well defined erythema, scaling and superficial scabbing from days 3–10. The reported LD50 for acute dermal toxicity was determined to be >2000 mg/kg bw in Wistar rats (REACH).

In a non-guideline skin absorption study, 15–20 mL/kg bw of the chemical was applied dermally to rats (sex and strain unspecified) in groups of 3 per exposure period for 15, 30 or 60 minutes without occlusion. Clinical signs observed included apathy, accelerated breathing, slight convulsions, staggering gait, atony, face down position, reddening and brownish colouration of the skin. Mortalities were reported to be 2/3, 3/3 and 3/3 when exposed for 15, 30 and 60 minutes, respectively (REACH).

Inhalation

Limited data is available for this chemical. Based on the available data, the chemical is likely to have low acute inhalation toxicity.

In a non-GLP compliant acute inhalation toxicity study conducted similarly to OECD TG 403, rats (strain unspecified) in groups of 4/sex/dose were exposed to the chemical as a vapour at concentration 0.6–2.3 mg/L for 6–7 hours, 5 times a week. No clinical signs or mortalities were reported (REACH).

Corrosion/Irritation

Skin irritation

Based on the weight of evidence, the chemical is considered to be a skin irritant, which warrants hazard classification (refer to **Health hazard classification** section).

In a dermal irritation study conducted according to OECD TG 404, 0.5 mL of the chemical was applied to the skin of 3 New Zealand White rabbits for 4 hours under occlusion. Oedema was not observed. Slight erythema was observed in all animals with mean scores ranging from 0.3 to 1.3. The erythema effects were fully reversible within 7 days. The chemical was not considered to be a skin irritant under the conditions of the study (REACH).

In a non-guideline dermal irritation study, the chemical was applied to the skin of rabbits (sex and strain unspecified) in groups of 2 per dose at concentrations of 0, 5%, 10%, 50% or 100% for 20 hours under occlusion. Treated animals were observed for 22 days. No irritation was observed after treatment with the chemical at 5%. At 10%, slight redness was observed on days 1–3. The chemical at 50% and 100% concentration resulted in slight redness and scaling lasting for 1–3 weeks. The chemical was considered to be a skin irritant under the conditions of the study (REACH).

In an in vitro skin corrosion study conducted similarly to OECD TG 431, the chemical was applied to a reconstructed human epidermis (EpiDerm, n = 2) for 3 minutes or 1 hour. The tissue viability was 56% and 12% after 3 minutes and 1 hour exposure, respectively. The chemical was considered to be corrosive under the conditions of the study (REACH).

The in vivo dermal irritation studies above are considered sufficient for classification of the chemical as a skin irritant.

Eye irritation

Based on the available data, the chemical is considered to be corrosive to the eyes, which warrants hazard classification (refer to **Health hazard classification** section).

In an eye irritation study conducted similarly to OECD TG 405, the chemical was applied to the conjunctival sac of one eye of rabbits (strain unspecified) at concentrations of 0.1%, 1%, 5%, 10% or 100% (undiluted) in the volume of 50 µL. Two animals were used for the undiluted chemical and one animal per concentration was administered at lower concentrations. The treated animals were observed for 24 days. Slight redness of the conjunctivae was observed after treatment with the chemical at 0.1% and 1%, and was reversible within 1 day. Redness and swelling of the conjunctivae were reversible in 2–3 days after exposure to the chemical at 5% and 10%. Exposure to undiluted chemical resulted in severe redness or bleeding of the conjunctivae, secretion of pus, ciliary injection and severe oedema. Cloudiness of the cornea was observed to the end of the 24 day observation period. The chemical was considered to be corrosive to the eyes under the conditions of the study (REACH).

In a hen's egg test – chorioallantoic membrane (HET-CAM) in vitro corrosion test, water solutions of the chemical at 0, 10% or 100% (undiluted) concentration were applied to the chorionallantoic membrane of 3 chicken eggs (white leghorn) in the volume of 0.3 mL for 3.5 minutes. At 10%, moderate intravascular coagulation and haemorrhage were observed. The mean time to coagulation was 30–62 seconds, and the mean time to haemorrhage was 25 – 30 seconds. At 100%, the mean time to coagulation was 6–11 seconds, and the mean time to haemorrhage was 3–6 seconds. The chemical was considered to cause severe eye damage under the conditions of the study (REACH).

Sensitisation

Based on the available data, the chemical is not considered to be a skin sensitiser up to 5% concentration.

In a local lymph node assay (LLNA) conducted according to OECD TG 429, the chemical in acetone:olive oil (4:1) was applied topically to the dorsum of each ear of CBA female mice in groups of 5 per dose at concentrations of 0, 1, 2.5 or 5% by weight. The reported stimulation indexes for all tested concentrations were below 3. The chemical was not considered a skin sensitiser under the conditions of the study (REACH).

Repeat dose toxicity

Based on the available data, the chemical is expected to cause serious systemic health effects following repeated oral exposure, which warrants hazard classification (refer to **Health hazard classification** section).

Oral study 1

In a repeated oral toxicity study conducted similarly to OECD TG 408, Wistar rats in groups of 10/sex/dose were administered the chemical by oral gavage at doses of 0, 90 or 180 mg/kg bw/day, 5 days/week for 3 months with a total of 66 administrations per animal.

Administration of 180 mg/kg bw/day was discontinued after 14 days for males and 21 days for females. A total of 5 mortalities occurred at this dose level, and the rest of the animals showed poor general state, lack of appetite and reduced body weight gain and were euthanised during the study.

In the 90 mg/kg bw/day dose group, excessive salivation was observed after 10 minutes in 8 males and 9 females on the 37th and 34th administration, respectively. Food consumption was reduced and water consumption was increased. The males had significantly decreased body weight during the study. The absolute liver weight of males was decreased due to poor general state, and the absolute and relative liver weights of females were increased.

A dose dependent increase in GGT activity in the liver was observed after necropsy of animals treated at 90 and 180 mg/kg bw/day; however, no significant histopathological changes in the liver were noted. The histopathological examination of the liver of both sexes showed less fat compared with the controls, and some males had centrilobular fatty infiltration. The decreased fatty infiltration in the liver was due to the decreased body weight. No histopathological correlation with the increased liver weight were observed in females. The LOAEL was 90 mg/kg bw/day in both sexes based on the adverse effects observed at the lowest dose tested (REACH).

Oral study 2

In a combined repeated dose toxicity with reproduction/developmental toxicity study conducted according to OECD TG 422, Wistar rats in groups of 10/sex/dose were administered the chemical by oral gavage at doses of 0, 5, 15 or 35 mg/kg bw/day. The duration of treatment covered a 2 week pre-mating and a mating period for both sexes. In males, treatment lasted 30 days. Females were continually treated during the entire gestation period through to approximately 2 weeks of the lactation period and were sacrificed 50 days after the beginning of administration.

There were no reported mortalities in any of the male and female animals in any of the dose groups.

Semi-closed eyelids and piloerection were observed in males and females treated at 15 and 35 mg/kg bw/day. Food consumption was significantly reduced in conjunction with significant body weight reduction in the affected animals. Males had higher urea levels. Absolute and relative liver weight increase was observed and correlated with centrilobular hypertrophy in both sexes. Increased absolute and relative kidney weights were also observed.

In all animals treated with the chemical, including the dose group of 5 mg/kg bw/day, urine pH values were higher compared to controls. Crystals were observed in the urine sediment in

some of the treated animals; however, that was not considered by the study authors as an adverse effect in the absence of alterations in other urine parameters.

The NOAEL was considered at 5 mg/kg bw/day for both sexes based on clinical signs, body weight effects, reduced food consumption, and liver and kidney effects observed at higher doses (REACH).

Genotoxicity

Based on the available data, the chemical is not expected to have genotoxic potential.

In a bacterial reverse mutation test conducted according to OECD TG 471, the chemical was not mutagenic in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537 and *Escherichia coli* WP2 at concentrations up to 5000 µg/plate with or without metabolic activation (REACH).

In an in vitro mammalian chromosome aberration test conducted in Chinese hamster lung fibroblasts (V79) according to OECD TG 473, the chemical was not clastogenic up to 5000 µg/mL with or without metabolic activation (REACH).

In a mammalian cell gene mutation test using hypoxanthine-guanine phosphoribosyl transferase (HPRT) locus conducted in Chinese hamster ovary (CHO) cells according to OECD TG 476, the chemical was not mutagenic up to 10 mg/mL with or without metabolic activation (REACH).

Carcinogenicity

No data are available to evaluate this hazard endpoint.

Reproductive and development toxicity

Based on the available data, the chemical is expected to cause specific adverse effects on development following repeated or prolonged exposure. The available data support the current classification on the HCIS (Safe Work Australia) (refer to **Health hazard classification** section).

In the above combined repeated dose toxicity with reproduction/developmental toxicity study conducted according to OECD TG 422, the numbers of stillborn, deceased and cannibalised pups were significantly increased in the dose group of 35 mg/kg bw/day. The pup viability index (an indicator of mortality) was significantly reduced and live pups had reduced mean body weights during the lactation period. Macroscopic examination of the affected pups showed dilated aneurysms in the vessels including aorta, arteries and ductus arteriosus.

The NOAEL for developmental effects was considered at 5 mg/kg bw/day based on pup viability, body weight effects and aneurysm observed at higher doses in the F1 pups. The NOAEL for adult fertility was considered at 35 mg/kg bw/day based on the absence of adverse effects related to fertility (REACH).

References

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