Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

Long-chain alkyl hydroxyethyl imidazolines

Evaluation statement

30 June 2022

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AICIS evaluation statement

Subject of evaluation

Long-chain alkyl hydroxyethyl imidazolines

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Reason for the evaluation

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

Parameters of evaluation

Chemicals in this group are all long-chain alkyl (saturated and unsaturated) hydroxyethyl imidazolines, listed on the Australian Inventory of Industrial Chemicals (the Inventory). This evaluation is a human health risk assessment for all identified industrial uses of this group of chemicals.

These chemicals have been assessed as a group as they are structurally similar, have similar use patterns and the critical health effects are not expected to vary.

Chemicals in this evaluation will be referred to by their CAS number where relevant.

Summary of evaluation

Summary of introduction, use and end use

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

Based on international use information, these chemicals predominantly have commercial and site limited uses, including in oil and gas extraction, lubricants and greases and corrosion inhibitors. Minimal incidences of domestic use (paint remover and lubricant products at up to 5%) have been reported for some of these chemicals.

The majority of chemicals in this group have identified potential use in cosmetics with anti-static and hair conditioning functions. However, available data indicates that these chemicals are not frequently used in cosmetics and any use is at low concentrations (0.3%).

Human health

Summary of health hazards

The critical health effects for risk characterisation include:

- systemic acute effects from oral exposure
- local effects (skin corrosion and eye damage).

The majority of toxicity data for the group comes from studies using CAS No. 95-38-5 and CAS No. 61791-39-7.

There is evidence of skin necrosis and irreversible eye damage in studies in rabbits. In one study necrotic effects were observed following application of CAS No. 95-38-5 at a concentration of 5% in water. In a study with CAS No. 61791-39-7, corrosive responses of the skin were seen following 1 hour and 4 hour exposures but not 3 minute exposures. Although no data are available for human health effects following inhalation exposure, respiratory irritation effects are considered likely.

Based on the available data, chemicals in this group are likely to cause moderate acute oral toxicity, with reported median lethal dose (LD50) values ranging from 1000 to 2000 mg/kg bw.

Adverse effects reported following repeated oral exposure to chemicals in this group are considered to be caused by the corrosive properties of these chemicals.

Based on the available data these chemicals:

- have low acute dermal toxicity
- are not expected to be skin sensitisers
- are not considered to be genotoxic
- are not expected to cause specific adverse effects on fertility and/or development.

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.

Some of these recommended classifications are based on read across principles (see **Supporting Information — Grouping Rationale** section). If empirical data become available for any member of the group indicating that a lower (or higher) classification is appropriate for a specific chemical, this data may be used to amend the default classification for that chemical.

Health hazards	Hazard category	Hazard statement
Acute Toxicity – oral	Acute Tox. 4	H302: Harmful if swallowed
Skin Corrosion/irritation	Skin Corr. 1B	H314: Causes severe skin burns and eye damage
Serious damage/eye irritation	Eye Damage 1	H318: Causes serious eye damage

Summary of health risk

Public

Based on the available international use information, these chemicals are not frequently used in products available to the public and any use is at low concentrations. Therefore, there are no identified risks to the public that require management. However, if information becomes available indicating that these chemicals have more widespread consumer use, further risk management may be required.

Workers

During product formulation and packaging, dermal, and ocular exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of preparation and work practices employed. Good hygiene practices to minimise oral exposure are expected to be in place.

Given the critical locals effects, these chemicals could pose a risk to workers. Control measures to minimise dermal, ocular and inhalation exposure are needed to manage the risk to workers (see **Proposed means for managing risks** section).

Control measures implemented due to the corrosivity classification are expected to be sufficient to protect workers from any potential systemic long term health effects.

Proposed means of managing risks

Workers

Recommendation to Safe Work Australia

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

Information relating to safe introduction and use

The information in this statement, including recommended hazard classifications, should be used by a person conducting a business or undertaking at the 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 exposure to these chemicals include, but are not limited to:

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

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 these chemicals are used.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk.

Model codes of practice, available from the Safe Work Australia website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare 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 conclusions of this evaluation are based on the information described in the statement.

Considering the proposed means of managing risks, 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 and the proposed means of managing the risks identified during this evaluation are implemented.

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

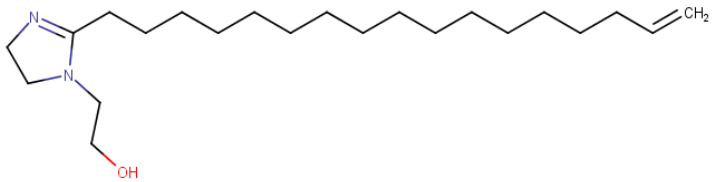
Supporting information

Grouping rationale

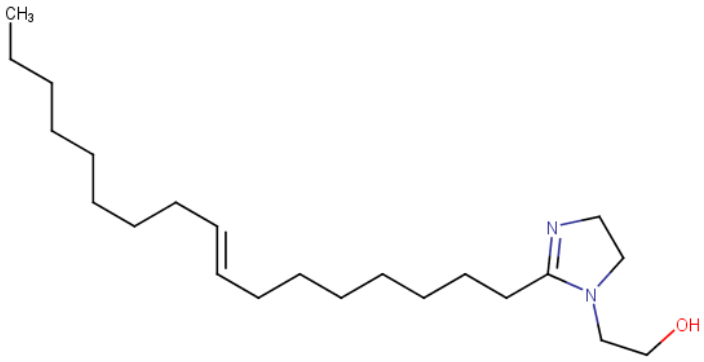
Chemicals in this group are substituted alkyl imidazolines, with each containing a hydroxyethyl group at the 1 position of the imidazoline ring, and a long chain alkyl (saturated or unsaturated) chain at the 2 positions of the imidazoline ring.

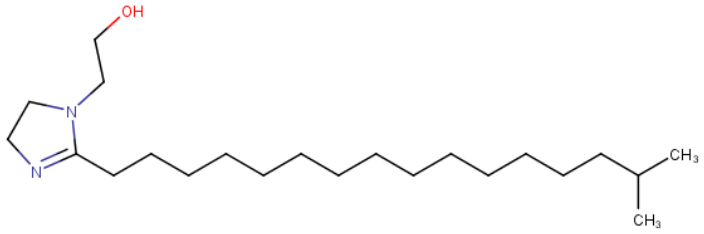
While specific toxicological information is not available for each chemical, given the close structural and physical-chemical similarities of these chemicals in this group, they are expected to have similar toxicological profiles.

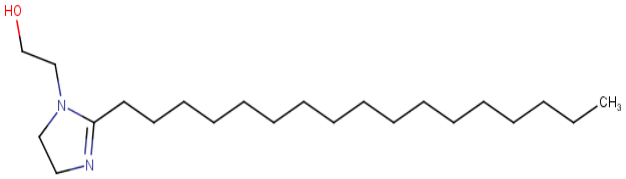
Chemical identity

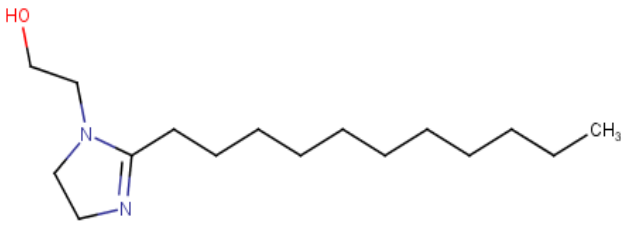
Chemical name	1H-imidazole-1-ethanol, 2-(heptadecenyl)-4,5-dihydro-
CAS No.	27136-73-8
Synonyms	imidazoline, 2-heptadecenyl-1-(2-hydroxyethyl)-4,5-dihydro- hydroxyethyl heptadecenyl glyoxalidine 2-(heptadecen-1-yl)-4,5-dihydro-1*H*-imidazole-1-ethanol 1H-imidazole-1-ethanol, 2-(heptadecen-1-yl)-4,5-dihydro- 2-(heptadecenyl)-2-imidazoline-1-ethanol oleyl hydroxyethyl imidazoline (INCI)
Structural formula	
Molecular formula	C22H42N2O
Molecular weight (g/mol)	350.59
SMILES	OCCN1CCN=C1CCCCCCCCCCCCCCCC=C

Chemical name	1H-imidazole-1-ethanol, 2-(8-heptadecenyl)-4,5-dihydro-
CAS	95-38-5

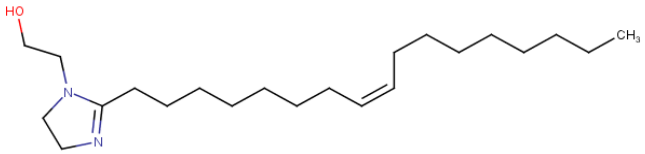
Synonyms	oleyl hydroxyethyl imidazoline (INCI) 2-(8-heptadecen-1-yl)-4,5-dihydro-1*H*-imidazole-1-ethanol 1-(2-hydroxyethyl)-2-(8-heptadecenyl)-2-imidazoline 2-(8-heptadecenyl)-2-imidazoline-1-ethanol 1-(2-hydroxyethyl)-2-heptadecenylglyoxalidine
Structural formula	
Molecular formula	C22H42N2O
Molecular weight (g/mol)	350.59
Smiles	CCCCCCCC\C=C\CCCCCCCC1=NCCN1CCO

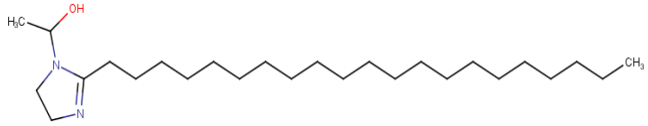
Chemical name	1H-imidazole-1-ethanol, 4,5-dihydro-2-isoheptadecyl-
CAS	68966-38-1
Synonyms	2-isoheptadecyl-4,5-dihydro-1H-imidazole-1-ethanol isostearyl hydroxyethyl imidazoline (INCI) 2-[2-(15-methylhexadecyl)-4, 5-dihydro-1H-imidazol-1-yl]ethan-1-ol 4,5-dihydro-2-isoheptadecyl-1*H*-imidazole-1-ethanol
Structural formula	
Molecular formula	C22H44N2O
Molecular weight (g/mol)	352.61
Smiles	CC(C)CCCCCCCCCCCCCCC1=NCCN1CCO

Chemical name	1H-imidazole-1-ethanol, 2-heptadecyl-4,5-dihydro-
CAS	95-19-2
Synonyms	1-(2-hydroxyethyl)-2-heptadecyl-2-imidazoline stearic acid, aminoethylethanolamine amide-imidazoline stearyl hydroxyethyl imidazoline (INCI) 2-(2-heptadecyl-4,5-dihydro-1H-imidazol-1-yl)ethan-1-ol
Structural formula	
Molecular formula	C22H44N2O
Molecular weight (g/mol)	352.61
Smiles	CCCCCCCCCCCCCCCCCC1=NCCN1CCO

Chemical name	1H-Imidazole-1-ethanol, 4,5-dihydro-2-undecyl-
CAS	136-99-2
Synonyms	1-hydroxyethyl-2-undecylimidazoline lauryl hydroxyethyl imidazoline (INCI) 1H-imidazole-1-ethanol, 4,5-dihydro-2-undecyl- 2- imidazolines-1-ethanol, 2-undecyl-
Structural formula	
Molecular formula	C16H32N2O
Molecular weight (g/mol)	268.45
Smiles	CCCCCCCCCCCC1=NCCN1CCO

Chemical name	1H-imidazole-1-ethanol, 2-(8-heptadecenyl)-4,5-dihydro-, (Z)-
CAS	21652-27-7

Synonyms	oleic acid, aminoethylethanolamine, imidazoline derivative oleyl hydroxyethyl imidazoline (INCI) 1*H*Ilmidazole-1-ethanol, 2-(8*Z*)-8-heptadecenyl-4,5-dihydro 2-(8*Z*)-8-heptadecen-1-yl-4,5-dihydro-1*H*-imidazole-1-ethanol
Structural formula	
Molecular formula	C22H42N2O
Molecular weight (g/mol)	350.59
Smiles	CCCCCCCC\C=C/CCCCCCCC1=NCCN1CCO

Chemical name	1H-imidazole-1-ethanol, 2-heneicosyl-4,5-dihydro-
CAS	39957-00-1
Synonyms	behenyl hydroxyethyl imidazoline (INCI) 1-(2-henicosyl-4,5-dihydro-1H-imidazol-1-yl)ethan-1-ol 2-henicosyl-4,5-dihydro-1H-imidazole-1-ethanol
Structural formula	
Molecular formula	C26H52N2O
Molecular weight (g/mol)	408.72
Smiles	CCCCCCCCCCCCCCCCCCCCCCC1=NCCN1C(C)O

Chemical name	1H-imidazole-1-ethanol, 4,5-dihydro-, 2-norcoco alkyl derivatives
CAS	61791-38-6
Synonyms	1-(2-hydroxyethyl)-2-coco-2-imidazoline 1-(2-hydroxyethyl)-2-nor(coconut oil alkyl)-2-imidazoline coconut fatty acid, aminoethylethanolamine imidazoline coconut oil, 1-(2-hydroxyethyl)-2-imidazolin-2-ylnor

	cocoyl hydroxyethyl imidazoline (INCI)
Structural formula	Unspecified
Molecular formula	Unspecified (UVCB). The most representative example is reported to be C16H32N2O (REACHb)
Molecular weight (g/mol)	Unspecified
Smiles	Unspecified

Chemical name	1H-imidazole-1-ethanol, 4,5-dihydro-, 2-nortall oil alkyl derivatives
CAS	61791-39-7
Synonyms	2-imidazoline, 1-(2-hydroxyethyl)-2-(tall oil alkyl)- tall oil, 1-(2-hydroxyethyl)-2-imidazolin-2-ylnor tall oil hydroxyethyl imidazoline (INCI) 1H-imidazoline-1-ethanol, 4,5-dihydro-, 2-nortall oil
Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
Smiles	Unspecified

Chemical name	1H-imidazole-1-ethanol, 4,5-dihydro-, 2-C15-17-unsaturated alkyl derivatives
CAS	68937-01-9
Synonyms	None identified
Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
Smiles	Unspecified

Chemical name	1H-imidazole-1-ethanol, 4,5-dihydro-, 2-C11-17-alkyl derivatives

CAS	103818-95-7
Synonyms	None identified
Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
Smiles	Unspecified

Chemical name	1H-imidazole-1-ethanol, 4,5-dihydro-, 2-norsoya alkyl derivatives
CAS	70024-77-0
Synonyms	soy hydroxyethyl imidazoline (INCI)
Structural formula	Unspecified
Molecular formula	Unspecified
Molecular weight (g/mol)	Unspecified
Smiles	Unspecified

Relevant physical and chemical properties

Chemicals in this group are waxy, semi-solids to liquids, with low melting points.

Introduction and use

Australia

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

International

The following international uses have been identified through the:

- European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH)
- EU Inventory of Cosmetic ingredients (CosIng)
- Substances in Preparation in Nordic Countries (SPIN) database
- United States Personal Care Products Council
- International Nomenclature of Cosmetic Ingredients (INCI) Dictionary

- Chemwatch Galleria Chemica
- United States Environmental Protection Agency (US EPA)
- Government of Canada assessment.

All chemicals except CAS No. 68937-01-9 and CAS No. 103818-95-7 have reported cosmetic uses with the reported function of anti-static and hair agents:
Limited information is available on the maximum use concentration of these chemicals in cosmetic products. However, CAS No. 68966-38-1 (isostearyl) is reported to be used in hair conditioner at up to 0.3% (Government of Canada 2020).

These chemicals were not identified as being used in cosmetic products in the United States of America (Personal Care Products Council 2011). Only CAS No. 68966-38-1(isostearyl) had identified uses in cosmetics in the EWG Skin Deep Data base. It was identified as being used in 3 shampoo and conditioner products (EWG)

Domestic uses have been identified for chemicals in this group, with the following reported use concentrations (DeLima Associates; Government of Canada 2020):

- CAS No. 95-38-5 – in paint remover at 3%
- CAS No. 71011-25-1 – in graffiti remover up to 5%
- CAS No. 27136-73-8 – in lubricant and rust blocker at 2.5%

Chemicals in this evaluation have reported commercial uses in polishes and wax blends, corrosion inhibitors, lubricants and greases, oil and gas extraction, cutting fluids, paint removers, fuel additives, anti-set off and anti-adhesive agents. These chemicals also have site limited use as intermediates.

Existing Australian regulatory controls

AICIS

No specific controls are currently available for these chemicals.

Public

No specific controls are currently available for these chemicals.

Workers

These chemicals are not listed on the HCIS, and no specific exposure standards are available in Australia (SWA).

International regulatory status

Exposure standards

No specific exposure standards are available for these chemicals.

Health hazard information

Toxicokinetics

Limited toxicokinetic data are available for these chemicals.

Absorption can occur following exposure to the skin, with dermal penetration increased due to the corrosive properties of this group of chemicals. Absorption via the gastro-intestinal tract occurs following ingestion of the chemical. On absorption these chemicals accumulate in the adipose tissues. However, these chemicals may rapidly hydrolyse and form oxidation products counteracting the potential to bioaccumulate (REACHa), with biliary excretion also identified (REACHc).

Acute toxicity

Oral

Based on the available data, chemicals in this group are likely to cause moderate acute oral toxicity, with median lethal dose (LD50) values ranging from 1000 to 2000 mg/kg bw. Data are sufficient to warrant hazard classification.

In an acute oral toxicity study conducted in accordance with OECD Test Guideline (TG) 401, rats (strain unspecified) (5/sex/dose) were treated with the chemical, CAS No. 95-38-5 at 200 mg/kg bw (females only), 500 mg/kg bw (both sexes) and 2000 mg/kg bw (males only). LD50 values of 1000 mg/kg bw for males and 1085 mg/kg bw for females were reported. Reported clinical signs of toxicity included piloerection, hunched posture, dyspnoea, reduced locomotor activity, and distended abdomen. Necropsy results showed a haemorrhagic thymus in one female at 500 mg/kg bw and dilated caecum in three animals at 2000 mg/kg bw. The calculated LD50 for both sexes was 1265 mg/kg bw (REACHa).

In an acute toxicity study conducted in accordance with OECD TG 423, rats (strain unspecified) (3/sex/dose) were treated with the chemical, CAS No. 61791-38-6 (cocoyl) at 300 mg/kg bw (females only), 1000 mg/kg bw (both sexes) and 2000 mg/kg bw (females only). The oral LD50 was reported to be between 1000 and 2000 mg/kg bw for this study. Mortality was recorded in one male and one female at 1000 mg/kg bw and three females at 2000 mg/kg. Clinical signs of toxicity included poor general state, wetness and brown staining of the mouth area, piloerection, diarrhoea, chromorhinorrhea (pigmented discharge), dyspnoea (laboured breathing), hunched posture and ptosis (sagging eyelids) (REACHb).

In another OECD TG 423 study, Sprague Dawley (SD) rats (3/sex) were treated with the chemical, CAS No. 61791-39-7 (tall oil) at 2000 mg/kg bw by gavage. Limited study details are available. Mortality was reported at 2000 mg/kg bw (numbers not reported) and one female was euthanised in extremis two days after treatment. An estimated LD50 >2500 mg/kg bw was reported. Clinical signs such as hunched posture, lethargy, piloerection, decreased respiratory rate, diarrhoea, dehydration, ptosis, gasping, laboured and noisy respiration. Necropsy results for one female showed haemorrhage and sloughing of the gastric mucosa and gastric epithelium of the stomach, and haemorrhage of the intestines. Necropsy of males showed stomach adhered to the liver and/or presence of white foci in the non-glandular epithelium of the stomach (REACHc).

Dermal

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

In an acute dermal toxicity study, New Zealand White (NZW) rabbits (5/sex) were treated with 2000 mg/kg bw/day of the chemical, CAS No. 61791-39-7 (tall oil) via an occlusive patch on the back for 24 hours, showed loss of skin elasticity and no other signs of acute dermal toxicity. A dermal LD50 of >2000 mg/kg bw was reported (REACHc).

Inhalation

No data are available.

Corrosion/Irritation

Skin corrosion

Based on the available data, chemicals in this group are considered to be corrosive, warranting hazard classification.

In an acute dermal irritation/corrosion study conducted according to OECD TG 404, male NZW rabbits (n=3) were treated with the chemical, CAS No. 95-38-5 (0.5 mL) for 4 hours under an occlusive dressing. Observations were recorded at 24 hours after patch removal. The following mean scores of 4/4 and 3/4 for erythema and oedema were reported, respectively. All treated animals were euthanised 24 hours after removal of the bandage due to severe to moderate weight loss and irreversible corrosive effects (REACHa).

In another study conducted according to OECD TG 404, NZW rabbits (3/sex) were treated with 0.5 mL of CAS No. 95-38-5 (5% in water) to shaved skin for 4 hours under occlusive dressing. After patch removal, skin reactions were assessed up to a period of 7 days. Mean scores of 3.7/4 and 3/4 for erythema and oedema were reported, respectively. Severe irritation with signs of necrosis were reported in all treated animals (REACHa).

In an in vivo skin irritation study (OECD TG 404) in NZW rabbits (n=3/dose), the chemical, CAS No. 61791-39-7 (tall oil) (0.5 mL, neat) was applied under semi-occlusive conditions for 3 minutes, 1 hour and 4 hours to intact skin. Severe erythema (score of 4/4 at 1 hour and 4 hours post treatment), severe oedema (score of 2/4 at 1 hour and 4/4 at 4 hour reading) and hardened dark brown/black scabs were observed at sites following the 1 hour and 4 hour exposure. Very slight erythema and very slight oedema was observed following the 3 minute exposure (REACHc).

In an in vitro membrane barrier skin corrosion study conducted in accordance with the OECD TG 435, the chemical, CAS No. 61791-38-6 (cocoyl) was reported as corrosive based on the mean breakthrough time of 167.89 minutes (5 replicates), required to penetrate a synthetic bio-barrier (REACHb).

Eye irritation

As these chemicals are corrosive to the skin, it is also expected that these chemicals have the potential to cause serious damage to the eyes, warranting hazard classification. This is

supported by the available experimental data, and the calculated pKa value of 12.3 at 25 °C for CAS No. 95-38-5 (REACHa).

In an eye irritation study similar to OECD TG 405, 0.1 mL of the undiluted chemical, CAS No. 95-38-5, was instilled into 1 eye each of Russian breed rabbits (3/sex). The eyes were washed out after 24 hours and observed at 1, 24, 48, 72 hours, and at 8 days. The following mean scores were reported at 24, 48 and 72 hours: corneal opacity 2.9/4, iritis 1/2, conjunctival redness 2/3, chemosis 4/4. The effects were not reversible in all animals within 8 days (REACHa).

In another reliable eye irritation study, 0.1 mL of the chemical, CAS No. 61791-39-7 (tall oil) was instilled into the eye of a NZW rabbit. Mean scores reported at 24 hours were: corneal opacity 4/4, iritis 2/2, conjunctival redness 3/3, chemosis 4/4. The study was terminated after the 24 hour reading due to severe eye irritation (REACHc).

Respiratory irritation

No data are available for effects following inhalation exposure. Given effects on skin and eyes and site of contact irritation observed in repeated dose toxicity studies, respiratory irritation effects are likely.

Sensitisation

Skin sensitisation

Based on the limited available data, these chemicals are not expected to cause skin sensitisation.

In a guinea pig maximisation test (GPMT) conducted according to OECD TG 406, male albino Dunkin-Hartley guinea pigs (n=10) were administered with chemical, CAS No. 61791-39-7 (tall oil), in PEG 300 as a 0.05% intradermal induction dose, a 3% topical induction dose and a 1% challenge dose under occlusive dressing). No local skin reactions were observed at 24 or 48 hours post treatment (REACHc).

In another skin sensitisation test (Maurer optimisation test), conducted similar to OECD TG 406 (deviations in exposure period), Pirbright-Hartley guinea pigs (10 animals/dose) were first injected intradermally with 0.1 mL of 0.1% of the chemical, CAS No. 95-38-5 (in saline). On day 7, the same area on the shoulder region was treated with a 30% topical application of the chemical. Occlusive dressing was kept in place for 48 hours. In the challenge phase, the animals were treated with 0.1 % chemical in saline epicutaneously. After 24 hours, the dressing was carefully removed, and the degree of erythema and oedema was quantified. No positive response was seen after 24 hours (REACHa).

Repeat dose toxicity

Oral

Based on the available data, adverse effects reported following repeated oral exposure to these chemicals in this group are considered to be caused by the corrosive properties of these chemicals.

In a combined repeated oral dose and reproductive/developmental toxicity study conducted according to OECD TG 422, Wistar rats (10/sex/dose) were administered the chemical, CAS

No. 95-38-5, by oral gavage at doses of 0, 5, 20, or 60 mg/kg bw/day for 31 days (males) or 51 days (females). The dose level in the highest dose group was reduced from 100 to 60 mg/kg bw/day on day 8 for females and day 9 for males. Mortality occurred in one female at 100 mg/kg bw/day within first week of treatment, while one male and one female in the 100 mg/kg bw/day and 60 mg/kg bw/day, respectively, were euthanised in week 2 due to severely reduced body weight. Mortality and the general effects were reported to be due to gastrointestinal damage caused by treatment. Severe gastro-intestinal tract dilation, mucosal atrophy, acute inflammation and erosion and intra-epithelial abscesses in the forestomach were reported. Severely reduced size of thymus was observed at necropsy and was reported to be indicative of the prolonged stress response to be caused by treatment. Changes in the absolute and relative liver and adrenal organ weights were observed at 60 mg/kg bw/day, and histopathological examination showed bilateral cortical hypertrophy of the adrenal cortex at this dose. The reported no observed adverse effect level (NOAEL) for systemic toxicity was 20 mg/kg bw/day for males and females (REACHa).

In another OECD TG 422 study, the chemical CAS No. 61791-39-7 (tall oil) in arachis oil, was administered to Wistar rats (10/sex/dose) at ingested doses of 15, 30 or 60 mg/kg bw/day for 42 days (males) or day 4 post-partum for females. Minimal to moderate squamous cell hyperplasia of the non-glandular stomach was seen in males at 30 and 60 mg/kg bw/day and all treated females. Moderate to marked submucosal inflammation was observed in males and females, respectively. Minimal focal erosion in one male and moderate focal erosion in one female at 60 mg/kg bw/day were reported. Focal slight epithelial degeneration in one female at 60 mg/kg bw/day and marked ulceration with marked submucosal inflammation and marked peritonitis in one female at 15 mg/kg bw/day were reported. The reported NOAEL for systemic toxicity was 60 mg/kg bw/day (REACHc).

Details from the 2 studies above are also presented in the **Reproductive and developmental toxicity** section.

Genotoxicity

Negative results were reported in the following in vitro assays:

- in a bacterial mutagenicity assay (OECD TG 471) with CAS No. 95-38-5 at test concentrations of up to 12.5 µg/plate in *S. typhimurium* strains TA98, TA100, TA 1537 and at test concentrations of up to 50 µg/plate in *Escherichia coli WP2*, with and without metabolic activation (REACHa)
- in a bacterial assay (OECD TG 471) with CAS No. 61791-39-7 (tall oil) and CAS No. 61791-38-6 (cocoyl) at test concentration range of 0.5 to 5000 µg/plate in *S. typhimurium* strains TA98, TA100, TA 1537 and TA1535 and *E. coli* WP2*urvA*, with and without metabolic activation (REACHb, REACHc)
- in a gene mutation (OECD TG 476) test in CHO mammalian cells at the HPRT locus at up to 48 µg/mL with CAS No. 61791-39-7 (tall oil) (REACHc)
- in a chromosome aberration (OECD TG 473) test in Chinese hamster lung fibroblasts (V79) in vitro for CAS No. 95-38-5 at up to 20 µg/mL (REACHa)
- in another OECD TG 476 (gene mutation test at HPRT locus) test in human lymphocytes with CAS No. 61791-39-7 (tall oil) at test concentrations up to 40 µg/mL (REACHc).

No in vivo study data are available for chemicals in this group.

Carcinogenicity

No data are available for this group of chemicals.

Reproductive and development toxicity

Based on the available data, these chemicals are not expected to cause specific adverse effects on fertility and/or development following oral exposure.

Details from the studies below are also presented in the **Repeat dose toxicity** section.

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test conducted in accordance with OECD TG 422, Wistar rats (10/sex/dose) were administered the chemical, CAS No. 95-38-5 by oral gavage at doses of 0, 5, 20, or 60 mg/kg bw/day from 15 days before mating for a total of 31 days (males) or from 15 days before mating to day 4 of lactation (females), during the premating, mating, gestation and lactation periods. The dose level in the highest dose group was reduced from 100 to 60 mg/kg bw/day on day 8 for females and day 9 for males due to mortality in one female at 100 mg/kg bw/day within first week of treatment. One male and one female at 100 and 60 mg/kg bw/day, respectively were euthanised in week 2. In offspring, mortality was recorded in one pup (60 mg/kg bw/day) and one pup (20 mg/kg bw/day). No treatment related effects on fertility index, mean implantation sites, gestation, litter weights or histopathology were observed. A developmental toxicity NOAEL of 60 mg/kg bw/day was reported for this study. The NOAEL for general, systemic toxicity was reported to be 20 mg/kg bw/day. (REACHa).

In a combined OECD TG 422 study using the chemical CAS No. 61791-39-7 (tall oil) in Wistar rats (10/sex/dose) administered at 15, 30 or 60 mg/kg bw/day for 42 days (males) or day 4 post-partum for females. No treatment related effects on reproductive performance were reported. No significant differences in litter size, or offspring body weights, at birth, or on days 1 and 4 post-partum were reported compared with control group animals. No clinical signs of toxicity were detected in offspring from all treatment groups. No treatment related adverse effect on surface righting reflex was detected. The NOAEL for developmental and reproductive toxicity was reported to be 60 mg/kg bw/day for this study (REACHc).

References

Chemwatch (2021) Galleria Chemica, Chemwatch website, accessed November 2021.

DeLima Associates (n.d.) *Consumer Product Information Database*, DeLima Associates website, accessed March 2022.

EC (European Commission) (n.d.) CosIng, EC website, accessed November 2021.

ECHA (European Chemicals Agency) (2016) CLH report for CAS No. 27136-73-8, ECHA, accessed November 2021.

ECHA (European Chemicals Agency) (2016) CLH report for CAS No. 68966-38-1, ECHA, accessed November 2021.

EWG (Environmental Working Group) (n.d.) *EWG's Skin Deep*, EWG website, accessed March 2022.

Government of Canada (2020). Screening Assessment Substituted Alkyl Imidazolines Group, accessed November 2021.

NLM (National Library of Medicine) (n.d.) *ChemIDplus Advanced Database*, NLM website, accessed November 2021.

REACHa (Registration, Evaluation, Authorisation and Restriction of Chemicals) (2021) Registered dossier for CAS No. 95-38-5, European Chemicals Agency website, accessed November 2021.

REACHb Registered dossier for CAS No. 61791-38-6, accessed December 2021.

REACHc Registered dossier for CAS No. 61791-39-7, accessed December 2022.

SPIN (Substances in Preparation in Nordic Countries) (2021) SPIN Database, SPIN website, accessed October 2021.

SWA (Safe Work Australia) (2021) Hazardous Chemical Information System, SWA website, accessed October 2021.

TGA (Therapeutic Goods Administration) (2014) Standard for the Uniform Scheduling of Medicines and Poisons No. 34 (Poisons Standard October 2021), TGA, accessed October 2021.

UNECE (United Nations Economic Commission for Europe) (2017), Globally Harmonized System of Classification and Labelling of Chemicals (GHS) Seventh Revised Edition, accessed October 2021.

United States Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary, accessed March 2022.