Long-chain alkyl oxiranes: Human health tier II assessment

03 July 2015

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Oxirane, decyl-	2855-19-8
Oxirane, dodecyl-	3234-28-4
Oxirane, pentadecyl-	22092-38-2
Oxirane, tetradecyl-	7320-37-8
Oxirane, hexadecyl-	7390-81-0

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at

the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals in this group are composed of linear hydrocarbon molecules with carbon lengths from C12 – C18 with an a-oxirane functional group. Given the similar reactive oxirane moiety, these chemicals are expected to have similar toxicological profiles and qualify to be assessed as a group.

Import, Manufacture and Use

Australian

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

International

The following international uses have been identified through:

- the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers;
- the US EPA High Production Volume (HPV) Challenge program; and
- Ullman's Fine Chemicals.

The chemicals have reported commercial uses including:

- as reactive diluents and/or as viscosity reducers for epoxy resins, laminate, flooring and encapsulants; and
- as modifiers for epoxy resins;

The chemicals have reported site-limited uses including:

- as reactive intermediates; and
- as stabilisers for halogenated hydrocarbons.

Restrictions

Australian

These chemicals are listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP)—in Schedule 5 (SUSMP, 2015) under '*Epoxy resins, liquid*'.

Schedule 5 chemicals 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.' Schedule 5 chemicals are labelled with 'Caution' (SUSMP, 2015).

International

No international restrictions are available for the chemicals in the group.

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available for any chemicals in the group.

International

No specific exposure standards are available for any chemicals in the group.

Health Hazard Information

Toxicokinetics

There is no information available specific to the chemicals in this group. However, it was reported that orally administered aliphatic epoxides are rapidly absorbed, metabolised, and eliminated (WHO, 2006).

Acute Toxicity

Oral

A lethal median dose (LD50) value of >10000 mg/kg in rats was reported for tetradecyloxirane (CAS No 7320-37-8). No other study details were provided (REACH).

In ten Sprague Dawley rats, the LD50 value of tetradecyloxirane (CAS No 73920-37-8) was reported to be >5000 mg/kg. No deaths occurred during the study. Reported clinical signs include rough haircoat, dark material around the nose, scabs or reddened skin, hair loss, swelling in various areas, and decreased defaecation (US EPA, 2006). No other study details were provided.

No information is available for the other chemicals in this group.

Dermal

In ten Sprague Dawley (SD) rats, the LD50 value of tetradecyloxirane was reported to be >2000 mg/kg. No deaths occurred during the study. Reported clinical signs include stained urine and dark material around the facial area. Dermal irritation was noted at the site of application. In females only, weight loss which reversed by day seven of the study was also reported (US EPA, 2006). No other study details provided.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

In an experiment conducted in three Mol:Russian rabbits, undiluted decyloxirane (CAS No 2855-19-8) (dose not reported) was applied on shaved skin under semiocclusive condition for four hours. The mean erythema and oedema scores were 1.9 and 0.7, respectively (for 24, 48, and 72 hour timepoints). Although the effects were not detailed, it was reported that the effects were fully reversible after 21 days (REACH).

In a study conducted in six New Zealand White rabbits, semiocclusive application of tetradecyloxirane (CAS No 7320-37-8) produced slight oedema and blanching of the skin within one hour of application. All the effects resolved within 14 days of the study. The mean erythema and oedema scores are 3.4 and 1.4, respectively (for 24, 48, and 72 hour timepoints) (US EPA, 2006).

Although the potential for irritation was not studied for other members of this group, the oxirane moiety has been assessed cause sensitisation and irritation effects (NICNAS).

Based on the information from decyloxirane and tetradecyloxirane, there is enough evidence to classify this group of chemicals as hazardous with the risk phrase 'Irritating to skin' (Xi; R38) in the HSIS.

Eye Irritation

In an experiment conducted in three Mol:Russian rabbits, 0.1 mL of undiluted decyloxirane (CAS No 2855-19-8) was applied to the eyes for 24 hours. Minimal effects on the conjunctivae were observed, which resolved within three days of the study. The mean conjunctival score was 0.9 (REACH). No effects on the cornea and iris were reported.

In a study conducted on six New Zealand White rabbits, application of 0.1 mL of undiluted tetradecyloxirane (CAS No 7320-37-8) in the right eye produced iritis and conjunctivitis within one hour of dosing. These effects resolved by day seven of the study (US EPA, 2006).

Sensitisation

Skin Sensitisation

In a Buehler test using tetradecyloxirane conducted in 20 Hartley-derived albino guinea pigs, positive reactions were seen after three induction treatments (50% w/v in mineral oil), with two challenge applications at 5% w/v in mineral oil. Dermal irritation effects such as oedema, blanching, and eschar were also noted during the induction and challenge phases of the study (US EPA, 2006).

All the chemicals in this group have functional groups that present alerts for skin sensitisation based on their molecular structures as profiled by the OECD Quantitative Structure-Activity Relationship (QSAR) Toolbox v3.2.

Given the positive results for sensitisation with tetradecyloxirane and the sensitising potential of the oxirane group, classification for skin sensitisation is warranted.

Repeated Dose Toxicity

Oral

No data are available for any chemicals in the group.

Dermal

In a 90-day study conducted in Fischer 344 (F344) rats (10 animals/sex/dose), tetradecyloxirane was applied daily to the skin at doses of 0, 62.5, 125, 250, 500, or 1000 mg/kg bw/d for five days per week. No deaths occurred during the study. Various degrees of skin lesions and, in more severe cases, ulcerations were observed in the exposed groups. These lesions consisted of hyperkeratosis, parakeratosis, acanthosis, necrosis of cells, and necrosis with varying degrees of inflammation. Based on skin effects, the lowest observed adverse effect level (LOAEL) value was determined to be 125 mg/kg bw/d for this study (US EPA, 2006).

Inhalation

No data are available for any chemicals in the group.

Genotoxicity

Tetradecyloxirane (CAS No 7320-73-8) tested negative in reverse mutation assays in *Salmonella typhimurium* and sister chromatid exchange assays in Chinese hamster ovary (CHO) cells (US EPA, 2006).

Carcinogenicity

In a two year skin painting study conducted in mice, a high incidence of subcutaneous, mesenchymal neoplasms including malignant sarcoma, fibrosarcoma, neurofibrosarcoma, and benign fibroma was observed in both tested and control groups. The study is very limited and the carcinogenic

potential for tetradecyloxirane could not be ascertained (US EPA, 2006). No data are available for any other chemicals in this group.

Reproductive and Developmental Toxicity

No data are available for any chemicals in this group.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include local effects (skin irritation and sensitisation).

Public Risk Characterisation

Given the uses identified for the chemicals, it is unlikely that the public will be exposed. Although the public could come into contact with articles or coated surfaces containing the chemicals, it is expected that the chemicals will be bound within the article or coated surface and hence will not be bioavailable. Therefore, the chemicals are not considered to pose an unreasonable risk to public health.

Occupational Risk Characterisation

Given the critical systemic local health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise dermal exposure are implemented. The chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

NICNAS Recommendation

The assessment of these chemicals is considered to be sufficient, provided that the recommended classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

Products containing these chemicals should be labelled in accordance with state and territory legislation (SUSMP, 2015).

Work Health and Safety

The chemicals in this group are recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to skin (Xi; R38)	Causes skin irritation - Cat. 2 (H315)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for consumers

Products containing the chemicals should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from dermal exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures that could minimise the risk include, but are not limited to:

- health monitoring for any worker who is at risk of exposure to the chemical[s], if valid techniques are available to monitor the effect on the worker's health;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

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.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemicals are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of these chemicals has not been undertaken as part of this assessment.

References

Joint FAO/WHO Expert Committee on Food Additives 2006. Safety Evaluation of Certain Food Additives. WHO Food Additives Series:56. World Health Organization pp. 289-325. Accessed on June 2015 at **http://www.inchem.org/documents/jecfa/jecmono/v56je12.pdf**

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Structural alerts for permit categories. Available at **https://www.nicnas.gov.au/notify-your-chemical/types-of-assessments/permit-categories/structural-alerts-for-permit-categories**

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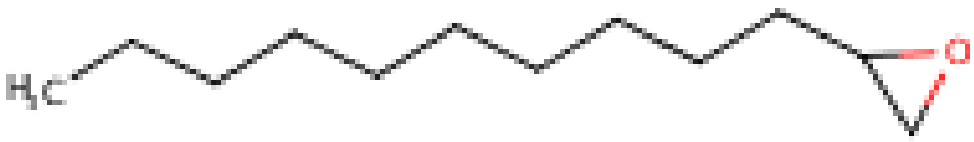
Safe Work Australia (SWA). Model Work Health and Safety Regulations. Accessed June 2015 at **http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/616/Model-WHS-Regulations-January-2014.pdf**

The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) 2015. Accessed June 2015 at **http://www.comlaw.gov.au/Details/F2015L00128**

Wiley-VCH 2013. Ullmann's Fine Chemicals. Accessed on June 2015 at **https://books.google.com.au/books?id=yZqOAgAAQBAJ&pg=RA2-PA39&lpg=RA2-PA39&dq=decyloxirane&source=bl&ots=6g2Y8mecfV&sig=QsBm5NtCITQqVDEUpDlvggqlQuw&hl=en&sa=X&ved=0CDYQ6AEwBjhGahUKEwjYqd-bkZPGAhVD5aYKHXWZAAc#v=onepage&q=decyloxirane&f=false**

Last Update 03 July 2015

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Oxirane, decyl-** 1,2-Epoxydodecane Decenoxirane 1-Dodecene oxide
CAS Number	2855-19-8
Structural Formula	
Molecular Formula	C12H24O
Molecular Weight	184.32

Chemical Name in the Inventory and Synonyms	**Oxirane, dodecyl-** 1,2-Epoxytetradecane 2-dodecyloxirane
CAS Number	3234-28-4
Structural Formula	

	
Molecular Formula	C14H28O
Molecular Weight	212.37

Chemical Name in the Inventory and Synonyms	**Oxirane, pentadecyl-** 1,2-Epoxyheptadecane 1,2-Heptadecane oxide
CAS Number	22092-38-2
Structural Formula	

	
Molecular Formula	C17H34O
Molecular Weight	254.45

Chemical Name in the Inventory and Synonyms	**Oxirane, tetradecyl-** 1,2-Hexadecane oxide 1,2-Epoxyhexadecane
CAS Number	7320-37-8
Structural Formula	

	
Molecular Formula	C16H32O
Molecular Weight	240.42

Chemical Name in the Inventory and Synonyms	**Oxirane, hexadecyl-** 1,2-Epoxyoctadecane
CAS Number	7390-81-0
Structural Formula	

	
Molecular Formula	C18H36O
Molecular Weight	268.48

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