Methyloxirane (R-, S- and (R,S)-): Human health tier II assessment

22 November 2013

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Oxirane, methyl-	75-56-9
Oxirane, methyl-, (R)-	15448-47-2
Oxirane, methyl-, (S)-	16088-62-3

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

This group consists of the racemic mixture of methyloxirane and its two individual enantiomers (non-superimposable mirror images of a chemical structure). A racemic mixture is composed of equal amounts of two enantiomers.

The toxicity of methyloxirane is based on the high reactivity of the oxirane functional group. Effects due to the enantio-specific reaction of the optical isomers are considered to be less significant. The chemicals in this group are therefore considered to be toxicologically equivalent.

The information contained in this report pertains to the racemic mixture of methyl oxirane (CAS No. 75-56-9) and these data are considered to also represent the individual enantiomers.

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information.

The racemic methyloxirane has reported site-limited use including:

- in manufacturing other chemicals.

The chemical is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume between 10000 and 99999 tonnes.

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers, the Organisation for Economic Cooperation and Development Screening information data set International Assessment Report (OECD SIAR), Canadian Assessments (Challenge List Batch 1), Galleria Chemica, the Substances and Preparations in the Nordic countries (SPIN) database, the European Commission Cosmetic Ingredients and Substances (CosIng) database, the Personal Care Council Website (INCI Dictionary), the US National Library of Medicine's Household Products Database, and via eChemPortal sources including the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

Reported domestic use including:

- in adhesives and binding agents; and
- in cleaning agents.

Reported commercial use including:

- in process regulators, synthetic lubricants, and fuel additives;
- as a stabiliser for dichloromethane and other chlorinated hydrocarbon solvents;
- in paint, lacquer and varnish production;
- as an anti-corrosion additive; and
- in construction material production.

Reported site-limited use including:

- as an intermediate in manufacturing laboratory chemicals such as propylene glycol (used in producing unsaturated polyester resin in textile and plastics industries) and butanediol;
- as a monomer in polymer production of polyether polyols, which are used in the production of polyurethane foams for furniture and automotive industries; and
- as a dehydrohalination stabiliser for vinyl resin solutions.

Restrictions

Australian

This chemical is listed in the Poisons Standard (Standard for the Uniform Scheduling of Medicines and Poisons—SUSMP, 2012) in Schedule 7.

Schedule 7 chemicals are labelled with 'Dangerous Poison'. These are substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely. Special regulations restricting their availability, possession, storage or use may apply.

International

The following international restrictions have been identified:

- ASEAN Cosmetic Directive Annex II Part 1—List of substances which must not form part of the composition of cosmetic products;
- Canada's list of prohibited and restricted cosmetic ingredients;

- EU Cosmetic Directive 76/768/EEC Annex II: List of substances which must not form part of the composition of cosmetic products; and
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain.

Existing Worker Health and Safety Controls

Hazard Classification

The chemical is classified as hazardous with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

Carc. Cat. 2; R45: May cause cancer

Muta. Cat. 2; R46: May cause heritable genetic damage

Xn; R20/21/22: Harmful by inhalation, in contact with skin and if swallowed.

Xi; R36/37/38: Irritating to eyes, respiratory system and skin

Exposure Standards

Australian

The chemical has an exposure standard of 48 mg/m^3 (20 ppm) time weighted average (TWA).

The chemical is also listed to have a threshold quantity of 50 tonnes at major hazard facilities under the Australian Work Health and Safety Regulations, 2011.

International

The following exposure standards are identified (Galleria Chemica):

An exposure limit (TWA) of 2–20 ppm in different countries such as USA (Hawaii, Minnesota, and Vermont), Canada (Quebec and Alberta), Singapore, Spain, United Kingdom, Sweden and Switzerland.

Health Hazard Information

All of the toxicology data discussed below are for racemic methyloxirane, which is referred to as "the chemical".

Toxicokinetics

Studies have shown that the chemical and its metabolites are readily absorbed through the gastrointestinal and respiratory tracts (EU RAR, 2002). The chemical is metabolised through conjugation with glutathione, or hydrolysis via epoxide hydrolase. Excretion of the chemical and its metabolites from the body occurs via urine and expired air.

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in HSIS (Safe Work Australia). The available data support this classification.

The median lethal dose (LD50) values in rat, mouse and guinea pig were reported to be 520, 630, and 660 mg/kg bw, respectively (EU RAR, 2002; EHC, 1985). Reported signs of toxicity at lethal doses included necrosis of the stomach mucosa, oedema, fatty changes in liver cells, and disturbed kidney function.

Dermal

The chemical is classified as hazardous with the risk phrase ‘Harmful in contact with skin’ (Xn; R21) in HSIS (Safe Work Australia). The data available support this classification.

In two separate dermal studies conducted in rabbits, LD50 values of 1250 and 950 mg/kg bw were reported (EU RAR, 2002).

Inhalation

The chemical is classified as hazardous with the risk phrase ‘Harmful by inhalation’ (Xn; R20) in HSIS (Safe Work Australia). The data available support this classification.

Median lethal concentration (LC50) values of 1740 ppm (4.12 mg/L) and >4000 ppm (>9.48 mg/L) were reported for mice and rats, respectively (EU RAR, 2002).

Based on studies carried out by the National Toxicology Program (NTP, 1985), Fischer 344/N (F344/N) rats (five animals/sex/dose) were given a single four-hour exposure to the chemical at doses of 1277, 2970, 3794, or 3900 ppm (3.03, 7.05, 9.01, or 9.20 mg/L). Mortalities were observed at ≥2970 ppm for both sexes. Clinical observations at the three highest concentrations included dyspnoea and red nasal discharge. For the same experimental duration, B6C3F1 mice (5 animals/sex/dose) were exposed to 387, 859, 1102, 1277, and 2970 ppm (0.92, 2.04, 2.61, 3.03, and 7.05 mg/L). Mortalities were observed at ≥1102 ppm (for males) and ≥387 ppm (for females). It was reported that all groups showed dyspnoea, while lachrymation (secretion of tears) was only observed at the highest dose (NTP, 1985; EU RAR, 2002).

In another study conducted in rats (10 animals/dose) and guinea pigs (five animals/dose), mortalities were observed in animals that were exposed to 4000 ppm (9.48 mg/L) of the chemical for four hours (4/10 rats; 1/5 guinea pigs). The animals exhibited ocular and nasal irritation, breathing difficulty, drowsiness, weakness, and occasional incoordination (EU RAR, 2002).

Corrosion / Irritation

Corrosivity

Based on experimental data from skin and eye irritation studies in animals (particularly scar formation and corneal necrosis) and observations in humans, as described in the following sections, there is sufficient evidence to classify the chemical as corrosive.

Respiratory Irritation

The chemical is classified as hazardous with the risk phrase 'Irritating to respiratory system' (Xi; R37) in HSIS (Safe Work Australia). The available data support this classification.

In an inhalation study conducted in rats (10 animals/dose) and guinea pigs (five animals/dose), effects reported following exposure to the chemical included nasal irritation and breathing difficulty. It was also reported that the severity of the response

was proportional to the concentration and duration of exposure (EU RAR, 2002). This result was consistent with the experiments conducted in rats by the NTP, where irritation of the nasal mucosa occurred following exposure to the chemical (NTP, 1985).

Skin Irritation

The chemical is classified as hazardous with the risk phrase 'Irritating to skin' (Xi; R38) in HSIS (Safe Work Australia). The available data support an amendment to this classification (refer to Recommendation section) to reflect the findings reported below.

In a study conducted in rabbits, the chemical was applied under occlusive conditions to intact skin at 100 or 200 g/L, resulting in hyperaemia, oedema, and scar formation after six minutes or more of exposure (EHC, 1985).

Other studies have reported no skin effects when the chemical was applied under a semi-occlusive dressing (EU RAR, 2002; REACH). However, due to the very high volatility of the chemical, it was recognised that a semi-occlusive application to intact skin may be an inappropriate method of applying the chemical. Evaporation of the chemical from the test patch during the exposure period cannot be excluded as a possible reason for the lack of skin effects.

Eye Irritation

The chemical is classified as hazardous with the risk phrase 'Irritating to eyes' (Xi; R36) in HSIS (Safe Work Australia). The available data support an amendment to this classification (refer to Recommendation section) to reflect the findings reported below.

In a study conducted in rabbits, application of 5 µL of the undiluted chemical to the cornea resulted in severe burns with necrosis (EHC, 1985).

In an inhalation study conducted in rats and guinea pigs, it was observed that ocular and nasal irritation occurred, along with breathing difficulty, drowsiness, weakness, and occasional incoordination (EU RAR, 2002).

Observation in humans

Alterations in the cornea and conjunctiva were reported in individuals who experienced accidental eye exposure to the chemical (EU RAR, 2002). In one case study, where a man was exposed to vapours of the chemical for 10 minutes, signs of respiratory and eye irritation were observed. Other individuals exposed to the chemical developed eczema, contact dermatitis, or corneal burns (IARC, 1994; HSDB).

Sensitisation

Skin Sensitisation

While the chemical did not induce dermal sensitisation in an experiment conducted in guinea pigs (EU RAR, 2002), there is evidence from observations in humans to indicate that the chemical is a potential skin sensitiser.

In a study conducted in male Hartley guinea pigs (10 animals/dose), the chemical (10 % solution in a Dowanol DPM/Tween 80 (9:1) vehicle) was applied occlusively on a gauze patch to the clipped backs of the animals four times over 10 days. Signs of irritation were not observed during the induction period. Two weeks later, the animals were challenged with the chemical. No sensitisation effects were observed at 24 or 48 hours post-application (EU RAR, 2002).

Observation in humans

This chemical has the potential to cause skin sensitisation in humans based on case studies (EU RAR, 2002). A laboratory technician, who had previous daily contact with the chemical, reported eczema on her hands for eight months; a standard patch test gave a positive reaction to the chemical (EU RAR, 2002).

In another case, a 52-year old woman developed erythema and oedema on her hands upon exposure to the chemical at work. A standard patch test using the chemical (diluted to 1:10,000, 1:3,000, 1:1,000) gave positive results while disinfectants and rubber constituents gave negative results (EU RAR, 2002).

Another report also described signs of contact dermatitis in two individuals who used a commercial disinfecting swab containing the chemical (1 %) and isopropanol (70 %). Although a patch test with the International Contact Dermatitis Research Group (ICDRG) standard series gave negative results, both individuals responded to 0.5 % or 1 % solution of the chemical with an allergic-type reaction. Skin biopsy revealed spongiosis in the epidermis, oedema in the corium/cutis, and dense perivascular infiltrates in mononuclear cells (EU RAR, 2002; EHC, 1985).

Repeated Dose Toxicity

Oral

In an experiment conducted in female Sprague Dawley rats (50 animals/dose), the chemical was administered by gavage twice weekly at doses of 0, 15 or 60 mg/kg bw for 150 weeks. Survival rates of the treated animals were comparable with the control. The main findings were reactive changes in the epithelium and associated neoplasms in the forestomach. A no observed adverse effect level (NOAEL) was not determined. Due to the combined incidence of hyperkeratosis, hyperplasia, and papilloma, the lowest observed adverse effect level (LOAEL) was determined to be 15 mg/kg bw (EU RAR, 2002; IARC, 1994). Details on the neoplastic findings can be found under the Carcinogenicity section of this report.

Dermal

No data are available.

Inhalation

In a study conducted in F344/N rats and B6C3F1 mice (10 animals/sex/dose), the chemical was administered by inhalation at doses of 0, 31, 63, 125, 250, or 500 ppm for six hours a day, five days a week, for 13 weeks. No deaths were observed in rats. One death was recorded in mice (at 125 ppm), which was not considered related to chemical exposure. Aside from chronic pneumonia in all rat groups (including controls), no other gross or histopathological effects were observed in any animals at any dose (EU RAR, 2002; NTP, 1985).

In a two-year study conducted in F344/N rats and B6C3F1 mice (50 animals/sex/dose), the chemical was administered by inhalation at doses of 0, 200, or 400 ppm for six hours a day, five days a week, throughout the duration of the study (EU RAR, 2002; NTP, 1985). During the second year, reductions in mean body weights, compared with controls, were noted for mice and rats in the highest dose groups. However, the mean terminal body weight in rats was within 10 % of controls and no effect was seen on survival. In mice, only 29/50 males and 10/50 females in the highest dose group survived to the end of the study period, compared with 34/50 males and 29/50 females in the 200 ppm dose group, and 42/50 males and 38/50 females in the control group. Suppurative rhinitis was observed in rats (12 % of controls, 26 % of the 200 ppm dose group and 61 % in the 400 ppm dose group) along with dose-related increase of squamous metaplasia (non-cancerous changes to cells) and hyperplasia (cell proliferation) of the respiratory epithelium, the nasal mucosa, and the epithelial cells of the mucosal gland. Epithelial lesions were localised in the nasal cavity around the nasal or maxillary turbinates. A no observed adverse effect concentration (NOAEC) was not determined. Due to changes in the nasal cavity, the lowest observed adverse effect concentration (LOAEC) for both mice and guinea pigs was determined to be 200 ppm (EU RAR, 2002; NTP, 1985).

In another study, Wistar Cpb:WU rats were exposed to the chemical at 0, 75, 150, 300, and 600 ppm for six hours a day, five days a week for 13 weeks. Along with reduced body weight gain in the 300 and 600 ppm dose group, degenerative and

hyperplastic epithelial changes in the nasal passages in the 600 ppm dose groups were observed. The NOAEC for this study was determined to be 150 ppm (EU RAR, 2002; NTP, 1985).

In an additional study, Wistar Cpb:WU rats (100 animals/sex/dose) were exposed to the chemical at concentrations of 0, 30, 100, or 300 ppm for six hours per day, five days per week for 124 weeks (males) or 123 weeks (females) (EU RAR, 2002; NTP, 1985). Reduction in body weight gain was observed in the 300 ppm dose groups during the first year, but the animals recovered during the second year. An increase in mortality was observed by week 115 in the 300 ppm dose groups (both sexes), and by week 119 in the 100 ppm dose groups (females only). There was also increased degenerative change in the nasal mucosa in all exposed groups. In particular, hyperplasia of the nasal epithelium was observed in the 300 pm dose group. The LOAEC for this study was determined to be 300 ppm (EU RAR, 2002; NTP, 1985). Details on the neoplastic findings can be found under Carcinogenicity section of this report.

Observation in humans

An evaluation of 279 employees in eight plants in Germany exposed to the chemical found no adverse effects that could be attributed to the chemical. The workers were employed for an average of 10.8 years and were exposed to other substances apart from the chemical. Exposure to the chemical was measured using personal samplers up to 10 hours. The average exposure to the chemical was below the maximum allowable concentration (MAK) of 100 ppm. No abnormalities were observed (EU RAR, 2002).

Genotoxicity

The chemical is classified as hazardous, as a Category 2 mutagenic substance, with the risk phrase ‘May cause heritable genetic damage’ (T; R46) in HSIS (Safe Work Australia). The available data support this classification.

In vitro

The chemical was found to cause mutations in *Salmonella typhimurium* bacterial strains TA100 and TA1535 with or without metabolic activation (EU RAR, 2002). It was also mutagenic in spot tests in *Escherichia coli* strains WP2, CM891, CM871, and in *Klebsiella pneumoniae*. The chemical also caused mutations in *Schizosaccharomyces pombe* with or without metabolic activation, as well as in *Neurospora crassa* (EU RAR, 2002).

In mammalian cells, the chemical caused chromosomal aberrations in human lymphocytes, Chinese hamster ovary (CHO) cells, and epithelial-type cell line (RL1) from rat liver. The chemical also induced sister chromatid exchanges in human peripheral lymphocytes and Chinese hamster V79 cells, increased the frequency of micronuclei in human lymphocytes, caused hprt locus gene mutations in CHO cells, and was mutagenic in a L5178Y mouse lymphoma assay modified for gases and volatile liquids (EU RAR, 2002).

In vivo

The chemical increased the incidence of sex-linked recessive lethal mutations in exposed *Drosophila melanogaster* flies (4.28 %) compared with controls (0.25 %) (EU RAR, 2002).

Carcinogenicity

The chemical is classified as hazardous, as a Category 2 carcinogenic substance, with the risk phrase ‘May cause cancer’ (T; R45) in HSIS (Safe Work Australia). The available data support this classification.

The International Agency for Research on Cancer (IARC) has classified the chemical as ‘Possibly carcinogenic to humans’ (Group 2B), based on inadequate evidence for carcinogenicity in humans, but sufficient evidence for carcinogenicity based on animal testing.

In an experiment conducted on female Sprague Dawley rats (50 animals/dose), the chemical was administered by gavage twice weekly at doses of 0, 15 or 60 mg/kg bw for 150 weeks. Dose-related increases in the incidence of epithelial hyperplasia, papilloma, and squamous cell carcinoma of the forestomach were observed. In the groups that received 0, 15, or 60 mg/kg bw,

the combined prevalence of hyperkeratosis (thickening of the stratum corneum associated with keratin abnormality), hyperplasia, and papilloma was 0/50, 7/50, and 17/50, respectively, while the incidence of squamous cell carcinoma was 0/100, 2/50, and 19/50, respectively. Incidence of tumours at other sites in treated animals were comparable with the control group (EU RAR, 2002; IARC, 1994).

In an inhalation experiment, Wistar Cpb:WU rats (100 animals/sex/dose) were exposed to the chemical at concentrations of 0, 30, 100, or 300 ppm for six hours a day, five days a week for 124 weeks (male) or 123 weeks (female) (EU RAR, 2002; NTP, 1985). A malignant nasal tumour (ameloblastic fibrosarcoma) was observed in one low-dose male (1/61) as well as squamous cell carcinoma in one low-dose male (1/61) and in one high-dose male (1/63). Historical control data indicate 0–3 % observed nasal squamous-cell carcinoma in Wistar rats. Squamous cell metaplasia and tumours in the nasal turbinates were not observed. There was a dose-related increase in benign liver tumours (focal nodular hyperplasia). Carcinoma in the larynx/pharynx was also observed in males (4/63) in the 300 ppm dose group. Since carcinoma in this part of the respiratory tract is rare in Wistar rats, it is justifiable to associate these tumours with chemical exposure. The number of females in the 300 ppm dose group with a benign mammary gland tumour was significantly increased, compared with controls. The mean number of mammary fibrosarcoma in tumour-bearing animals showed a dose-related increase in all exposed groups (1.3 at 0 ppm group; 2.1 at 30 ppm; 2.2 at 100 ppm; 2.4 at 300 ppm). Although the incidence of malignant tumours was reported to be within the range of historical controls (0–15 %), there was an increased incidence of malignant tumours (tubulo-papillary carcinoma) in females in all exposed groups (6/71 at 30 ppm; 5/69 at 100 ppm; 8/70 at 300 ppm) compared with the controls (3/69) (EU RAR, 2002; NTP, 1985).

Reproductive and Developmental Toxicity

The chemical does not show specific reproductive or developmental toxicity. Any reproductive or developmental effects were only observed secondary to maternal toxicity.

In a two-generation reproduction study on F344 rats (30 animals/sex/dose), the chemical was administered by inhalation at doses of 0, 30, 100, or 300 ppm for six hours a day, five days a week, for 14 weeks before mating. Exposure periods were increased to seven days a week during mating, gestation, and lactation. After weaning, resulting pups (F_1) were exposed to the chemical (30 sex/group) for 17 weeks and then mated to produce second generation pups (F_2). Reduced body weight gain was observed in parents (8 %) and F_1 (16 %) at 300 ppm. No mortality or treatment-related effects were observed in any animals during the pre-mating period. There were no observable treatment-related effects on fertility, mating, or conception in parents or in F_1 matings. Litter size and pathological examination in adults and weanlings revealed no changes that could be attributed to chemical exposure. The results indicate that this chemical does not have an effect on reproductive function (EU RAR, 2002; IARC, 1994).

In a developmental study conducted in New Zealand White rabbits, the chemical was administered by inhalation at 0 ppm (17 animals) or 500 ppm for seven hours a day on gestation days 7–19 (11 animals), or 1–19 (19 animals). Foetuses were examined at day 30 of gestation. A decrease in food consumption was observed in the treated groups during the exposure period. Although the fertility was low in all groups, the resorption rate was not increased. No adverse effects in the foetuses were observed in the treated groups. In the same study, Sprague Dawley rats were exposed to the chemical at 0 ppm (46 animals) or 500 ppm for seven hours a day either from three weeks before gestation to day 16 of gestation (43 animals), or on days 1–16 (41 animals) or 7–16 of gestation (44 animals). Food consumption was reduced in females exposed to the chemical pre-gestation. Maternal weight gain and foetal growth were lower in all treated groups compared with controls. The incidence of rib dysmorphology ('wavy ribs') increased in all treated groups. However, this effect was attributed to be an indirect consequence of maternal toxicity from exposure to the chemical (EU RAR, 2002; IARC, 1994).

An additional study conducted on 25 female F344 rats exposed at to up to 500 ppm of the chemical for six hours a day on gestation days 6–15 inclusive, did not show evidence of developmental toxicity (EU RAR, 2002; IARC, 1994).

Other Health Effects

Neurotoxicity

In an experiment conducted on male cynomolgus monkeys (two animals/dose), the chemical was administered by inhalation at 0, 100, or 300 ppm for six hours a day, five days a week, for 24 months. The only treatment-related neuropathy was

degeneration of the nerve fibres in the brain (neuroaxonal dystrophy in the nucleus gracilis of the medulla oblongata). This effect did not have an apparent dose-response relationship and the same lesions were observed in the control animals (1/2). Furthermore, neuronal dystrophy is a non-specific finding which increases with age and is associated with a variety of human and animal conditions. No conclusions for the potential neurotoxicity of this chemical were drawn from this study (EU RAR, 2002).

In a two-generation reproduction study conducted on F344 rats (10 males/dose), the chemical was administered by inhalation at doses of 0, 100, or 300 ppm for six hours a day, five days a week, for 24 weeks. No treatment related changes were observed in functional and behavioural tests on all groups. Equivalent incidences of very slight axonal degeneration in the cervical spinal cord and mild neuronal dystrophy were observed in the control group and the 300 ppm dose group. Similar to the experiment conducted on cynomolgus monkeys, potential neurotoxicity of this chemical cannot be inferred (EU RAR, 2002).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (carcinogenicity and mutagenicity) and local effects (corrosivity and potential skin sensitisation). The chemical may also cause harmful systemic effects following a single exposure through oral, dermal, and inhalation exposure, and respiratory irritation.

Public Risk Characterisation

The chemical is currently listed on Schedule 7 of the SUSMP. A number of warning statements, first aid instructions and safety directions relating to the chemical apply. The chemical is not expected to be used in domestic and/or cosmetic products in Australia. The current controls are considered adequate to minimise the risk to the public, therefore, the chemical is not considered to pose an unreasonable risk to public health.

Occupational Risk Characterisation

Given the critical systemic long-term health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise dermal and inhalation exposure to the chemical are implemented. The chemical 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 appropriate controls.

While the chemical is a potential skin sensitiser, it has a boiling point of 35 °C, which is lower than normal human body temperature. Therefore, the chemical is expected to be highly volatile on dermal exposure, which significantly reduces the likelihood of repeated dermal exposure to the chemical in liquid form, hence reducing the potential for skin sensitisation.

NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended amendment to the 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 the chemical should be labelled in accordance with state and territory legislation (SUSMP).

Work Health and Safety

The chemical is recommended for classification and labelling under the current Approved Criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

The classifications below apply to all chemicals in this group (refer to Grouping Rationale section). If empirical data become available for any member of the group indicating that a lower (or higher) classification is appropriate for the specific chemical, this may be used to amend the default classification for that chemical.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)* Harmful in contact with skin (Xn; R21)* Harmful by inhalation (Xn; R20)*	Harmful if swallowed - Cat. 4 (H302) Harmful in contact with skin - Cat. 4 (H312) Harmful if inhaled - Cat. 4 (H332)
Irritation / Corrosivity	Irritating to respiratory system (Xi; R37)* Causes burns (C; R34)	May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335) Causes severe skin burns and eye damage - Cat. 1B (H314)
Genotoxicity	Muta. Cat 2 - May cause heritable genetic damage (T; R46)*	May cause genetic defects - Cat. 1B (H340)
Carcinogenicity	Carc. Cat 2 - May cause cancer (T; R45)*	May cause cancer - Cat. 1B (H350)

[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 chemical should be used according to label instructions.

Advice for industry

Control measures

Control measures to minimise the risk from dermal and inhalation exposure to the chemical 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 chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;

- health monitoring for any worker who is at risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- 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 chemical.

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 assist with meeting 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 chemical 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 the chemical has not been undertaken as part of this assessment.

References

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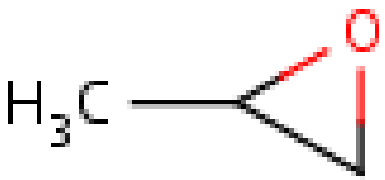
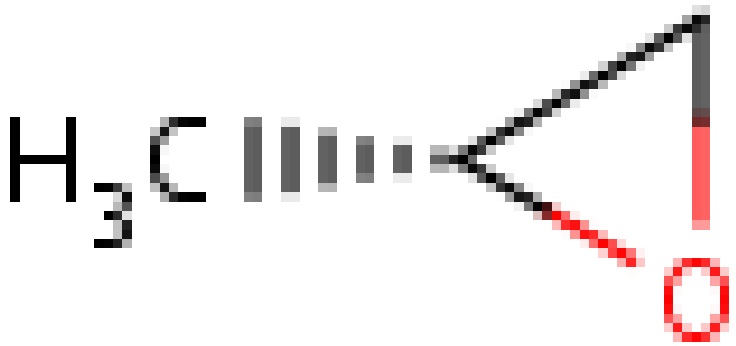
Last Update 22 November 2013

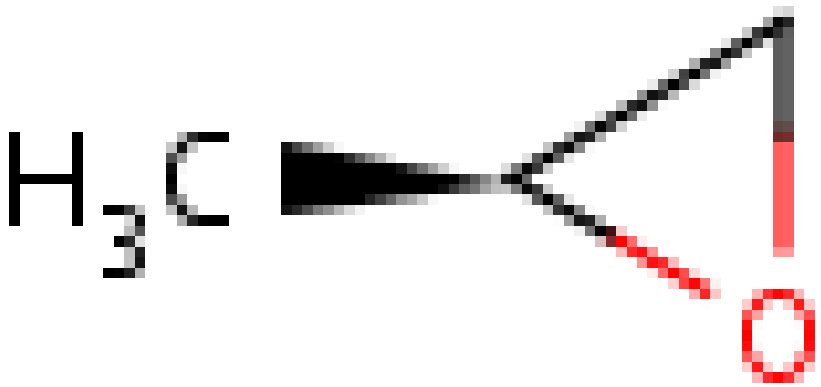
Chemical Identities

Chemical Name in the Inventory and Synonyms	**Oxirane, methyl-** 1,2-Epoxypropane Methyloxirane Propylene oxide methyloxacyclopropane propene oxide
CAS Number	75-56-9
Structural Formula	

Molecular Formula	C3H6O
Molecular Weight	58.0791

Chemical Name in the Inventory and Synonyms	**Oxirane, methyl-, (R)-** Propylene oxide, (+)- (+)-methyl oxirane (R)-epoxypropane (R)-Propylene oxide
CAS Number	15448-47-2
Structural Formula	
Molecular Formula	C3H6O
Molecular Weight	58.0791

Chemical Name in the Inventory and Synonyms	**Oxirane, methyl-, (S)-** (-)-methyl oxirane (-)-propylene oxide (S)-methyl oxirane (S)-propylene oxide
CAS Number	16088-62-3
Structural Formula	

	
Molecular Formula	C3H6O
Molecular Weight	58.0791

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