2-Butanone, oxime: Human health tier II assessment

17 May 2013

CAS Number: 96-29-7

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.

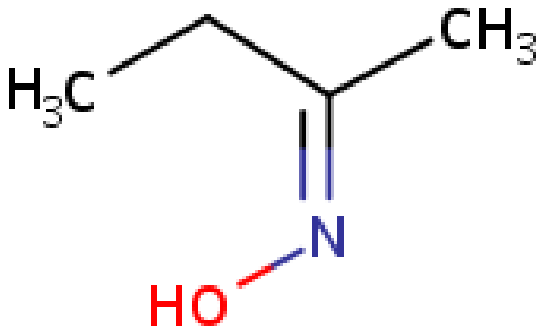
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	Methyl ethyl ketoxime MEKO Butanone Ethyl methyl ketoxime Methyl ethyl ketone oxime
Structural Formula	
Molecular Formula	C4H9NO
Molecular Weight (g/mol)	87.1204
Appearance and Odour (where available)	A clear colourless liquid with a musty odour.
SMILES	C(C)(CC)={t}NO

Import, Manufacture and Use

Australian

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

The chemical has reported domestic use including:

- Adhesives, binding agents.

International

The following International uses have been identified via 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), Galleria Chemica, Substances in Preparations in the Nordic countries (SPIN) database, eChemPortal (OECD High Production Volume chemical program (OECD HPV), and the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR).

The chemical has reported domestic use including:

- adhesives, binding agents;
- cleaning/washing agents; and
- paints, lacquers and varnishes.

The chemical has reported commercial use including:

- anti skinning agent in alkyd paints;
- blocking agent for urethane polymers;
- construction materials;
- corrosion inhibitors;
- insulating materials;
- solvents;
- viscosity adjustors; and
- fuel additives.

The chemical has reported site-limited use including:

- an intermediate in chemical processes.

Restrictions

Australian

No known restrictions have been identified.

International

Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex II Part 1: List of substances which must not form part of the composition of cosmetic products.

EU Cosmetic Directive 76/768/EEC Annex II: List of Substances which must not form part of the Composition of Cosmetic Products (English).

New Zealand Cosmetic Products Group Standard. Schedule 4: Components Cosmetic Products Must Not Contain. (Table 1).

Existing Work 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. 3; R40

Xn; R21 (acute toxicity)

Xi; R41 (irritation)

R43 (sensitisation)

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica):

An exposure limit of 10 mg/m^3 (3 ppm) TWA and 33 mg/m^3 (10 ppm) STEL in Ireland;

An exposure limit of 10 ppm TWA in USA;

US DOE Temporary Emergency Exposure Limits (TEELs) are TEEL-0:10 ppm, TEEL-1:40 ppm, TEEL-2:100 ppm and TEEL-3:100 ppm.

Health Hazard Information

Toxicokinetics

The ^{14}C labelled test substance was rapidly absorbed, and no radioactivity was retained in the stomach of pregnant mice after 20 minutes of oral gavage application. The nasal epithelium and liver had the highest concentration of radioactivity. An increased amount of radioactivity was reported in the bone marrow, spleen, seromucous and salivary glands, Harder's gland, intestinal wall, mammary ducts, and foetus, following exposure. The concentration in the pancreas peaked at 3 hours and then declined. Secretion of the test substance and/or metabolites was reported via the liver and kidney. Excretion occurred through the urine and bile (REACH).

In another toxicokinetic study, an intravenous dose of ^{14}C labelled test substance was administered to male Fischer 344 rats, at 2.7 mg/kg bw, and was primarily excreted as CO_2 (48.8 %), via urine (21.4 %), and in expired air (11.4 %). A small amount (7 %) remained in the tissues after 72 hours. The chemical was metabolised into five polar metabolites, with the major component being methyl ethyl ketone (2-butanone), produced by hydrolysis. In a second metabolic pathway, oxidation of the test substance to butane 2-nitrate by microsomal monoxygenases was reported, but at very low yields (REACH).

In male Fischer 344 rats, a non occlusive dermal application of 2.7 mg/kg bw, 27 mg/kg bw and 270 mg/kg bw of ^{14}C labelled test substance led to dermal absorption of between 13–26 % (REACH).

Acute Toxicity

Oral

The chemical is of low acute oral toxicity. The oral LD50 in rats is greater than 2000 mg/kg bw. Observed sub-lethal effects included lack of motor coordination, decreased reactivity to stimuli and decreased motor activity in one study and depression, tremors and loss of righting reflex in another study (REACH).

In an acute oral toxicity study in Sprague Dawley (SD) rats, nine males/dose were administered doses from 1500 to 4999 mg/kg bw via oral gavage (REACH). No deaths occurred at the 1500 mg/kg bw dose, although all rats died within 48 hours at a dose of 3089 mg/kg bw. An LD50 of 2326 mg/kg bw was reported. Clinical signs of toxicity included depression, tremors and loss of righting reflex.

In another acute oral toxicity study in SD rats (US EPA test guidelines), 10 animals/sex/dose were administered doses of 100, 300 and 900 mg/kg bw via oral gavage, and observed for the following 14 days. There were no mortalities during the test period, and an LD50 of > 900 mg/kg bw was reported. At the two highest doses, treatment related neurobehavioral effects were observed, although they were reversed after a few hours. Clinical sign included lack of motor coordination, decreased reactivity to stimuli and decreased motor activity (REACH).

Dermal

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

In an acute dermal toxicity study in New Zealand White rabbits (OECD TG 402), five animals/sex/dose were administered a single dermal dose of 1000 mg/kg bw via an occlusive patch for 24 hours and observed for 14 days. No mortalities were observed and an LD50 of > 1000 mg/kg bw was reported (REACH).

In another acute dermal toxicity study in New Zealand White rabbits, five animals/sex/dose were administered a single dermal dose of 18, 180 or 1800 mg/kg bw via an occlusive patch for 24 hours. All animals in the high dose group died within 48 hours of application, although no mortalities were observed in the two lower doses. The LD50 was reported to be between 180 – 1800 mg/kg bw (REACH).

Inhalation

The chemical is of low acute inhalation toxicity. In animal tests following inhalation exposure, no mortalities were observed in rats at a saturated atmospheric dose level (LC50 > 10.5 mg/L).

In an acute inhalation toxicity study in Fischer 344 rats (OECD TG 403), five animals/sex/dose were administered doses of 0, 0.19, 1.45 or 4.83 mg/L via whole body vapour inhalation for up to four hours (REACH). No mortalities were observed in any test group. There were no gross necropsy observations. A decrease in body weight gain was significant in females in all dose groups. An inhalation LC50 was reported as > 4.83 mg/L.

In another acute inhalation toxicity study, six rats/sex/dose were administered a saturated atmospheric dose of the chemical (3500 ppm or 10.5 mg/L) at 20 °C, via whole body vapour inhalation for eight hours (REACH). No mortalities were observed in male or female rats, and an LC50 > 10.5 mg/L was reported.

Corrosion / Irritation

Respiratory Irritation

The chemical showed irritation effects to the respiratory tract in a repeat dose toxicity study. The information available is not sufficient to warrant a hazard classification.

In a 13 week repeat dose inhalation study, CD-1 mice were exposed to 10, 30 and 100 ppm of the chemical for 6 hours/day 5 days/week. The incidence and severity of the degeneration found at the olfactory epithelium in the nasal cavity, were concentration dependent rather than time dependent (OECD, 2003). The effects were reversible within 4 weeks after cessation of exposure to the 10 ppm dose with complete recovery after 13 weeks at the higher concentrations.

Skin Irritation

Based on the data available, the chemical is not considered a skin irritant.

In a skin irritation study, six New Zealand White rabbits were administered undiluted test substance, via an occlusive patch to three abraded and three non abraded sites, for 24 hours and observed for 72 hours (REACH). A primary dermal irritation index for mean erythema and oedema at 72 hours was 1.5. The effects had not fully reversed after 72 hours. The test substance was reported to be slightly irritating.

In another skin irritation study (similar to OECD TG 404), New Zealand White rabbits were administered the test substance (semi occlusive patch), to a shaved skin site for four hours (REACH). The test substance was reported to be non irritating.

Eye Irritation

The chemical is classified as hazardous with the risk phrase 'Risk of serious damage to eyes' (Xi; R41) in HSIS (Safe Work Australia). The available data support this classification.

In an eye irritation study (similar to OECD TG 405), six New Zealand White rabbits were administered undiluted test substance, into one eye of each rabbit, and observed for the following 72 hours. Corneal opacity, iritis, conjunctival hyperaemia and necrosis were observed at 24, 48, and 72 hours post exposure with a mean score of > 2 (details not available). Necrosis was observed in two of six animals. Effects were non-reversible after 72 hours and the chemical was reported to be corrosive to the eyes of rabbits when applied undiluted (OECD, 2003; REACH).

Another eye irritation study indicated that the chemical was a severe eye irritant in rabbits (details not available) (OECD, 2003).

Sensitisation

Skin Sensitisation

The chemical is classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (R43) in HSIS (Safe Work Australia). The positive results reported in a guinea pig maximisation test and a Buehler test support this classification.

In a maximisation test (REACH), female Hartley guinea pigs were administered 3 % of the test substance in propylene glycol via intradermal injection. On day seven, a topical occluded patch (at concentrations of 25, 50, 75 and 100 % of the test substance) was applied for 24 hours. Animals were challenged on day 21, at 50 % via the topical occluded patch. After 48 hours of challenge, 8/10 animals in the 50 % test substance group had a positive reaction, confirming the chemical as a skin sensitiser.

In a Buehler test (REACH), 10 female Hartley guinea pigs were administered 0.3 mL of 25 % (w/v) of the test substance epicutaneously (nine applications of 24 hour exposures, with a 48 hour period between application). The animals were then challenged two weeks after the last induction application, with 0.3mL of 5 % (w/v) of the test substance and monitored at 24 and 48 hours. Five out of 10 animals were positive with erythema at 48 hours observation. The test substance was found to be a skin sensitiser.

Repeated Dose Toxicity

Oral

Haematological changes consistent with anaemia were observed in Sprague Dawley (SD) rats (≥ 40 mg/kg bw/day) and Fischer 344 rats (≥ 50 mg/kg bw/day). However, the available information is not sufficient to warrent a hazard classification, as the data do not demonstrate serious functional disturbance at these doses.

In a subchronic study, the test substance was administered to SD rats (10/sex/dose) via oral gavage at doses of 0, 40, 125 or 400 mg/kg bw/day, for five days/week over 13 weeks (REACH). Animals that received the highest dose showed a pale appearance, hypoactivity, ataxia, excessive salivation, and dark coloured urine, shortly after dosing but these signs were absent 24 hours post dose. The no observed adverse effect level (NOAEL) for transient neurobehavioural effects was reported to be 125 mg/kg bw/day for males and females based on motor activity data. The lowest observed adverse effect level (LOAEL) for systemic toxicity was reported as 40 mg/kg bw/day, based on dose dependent significant increases in methaemoglobin values, increased absolute and relative spleen weights, excessive salivation, hypoactivity and haematological changes consistent with anaemia.

In another subchronic study (equivalent to EPA OPPTS 870.3100: 90 day oral toxicity in rodents), the test substance was administered to Fischer 344 rats (10 animals/sex/dose) via drinking water for 13 weeks. The actual ingested doses were reported as 0, 25, 50, 100, 175 or 280 mg/kg bw/day for males and 0, 30, 65, 120, 215 or 335 mg/kg bw/day for females (REACH). Decreased body weight and body weight gains were observed in the two highest dose groups in males and females, and increased liver, spleen and kidney weights were observed in groups that received ≥ 100 mg/kg bw/day. Dose related increases in the incidence and severity of haematopoietic cell proliferation in the spleen was observed at concentrations of 50 mg/kg bw/day or greater, in both sexes. The NOAEL was established as 25 mg/kg bw/day in males and 30 mg/kg bw/day in females, based on decreased erythrocyte (red blood cell) count.

Dermal

No data are available.

Inhalation

Based on the available information, the chemical is considered to have low repeat dose inhalation toxicity.

In an inhalation study, the test substance was administered to Fischer 344 rats (10/sex/dose) as a vapour (whole body exposure), at doses of zero, 25, 102 or 404 ppm for 6 hours/day, five days/week over four weeks (REACH). There were no mortalities or clinical signs, changes in body weight or food consumption. Exposure to the highest dose resulted in increased methaemoglobin, a three fold increase in reticulocytes, 30 % increase in platelets, 10 % increase in the average volume of red blood cells and the average weight of haemoglobin in red blood cells and a 13 % increase in total leucocyte counts.

Haemoglobin, erythrocytes and haematocrit counts were decreased by 10 % at the highest dose. Increases were observed in the weights of the liver and spleen. A no observed adverse effect concentration (NOAEC) of 25 ppm was determined, based on increased methaemoglobin in female rats and increased absolute or relative organ weights (liver and spleen) of male and female rats.

In another study, CD-1 mice (10 males/dose) were exposed to the chemical as vapour (via whole body) at doses of 0, 3, 10, 30 or 100 ppm for six hours/day, five days/week for 1, 2, 4 or 13 weeks (REACH). Exposure to 10 ppm and above produced olfactory epithelium degeneration. However at 30 ppm, more than 50 % of mice showed no effect to the olfactory epithelium, indicating only the most sensitive animals responded at the highest exposure. The incidence and severity of degeneration were concentration dependent. The effects were reversible after four weeks at 10 ppm and after 13 weeks at the higher concentrations. The NOAEC was reported to be 3 ppm.

In a 4 week study (similar to OECD TG 412), CD 1 mice (10/sex/dose) were administered the chemical vapour via whole body exposure at doses of 0, 25 or 400 ppm for 6 hours/day, 5 days/week over 4 weeks (REACH). A NOAEC of 102 ppm was determined, based on increased levels of methaemoglobin and increased spleen and adrenal weights.

Genotoxicity

The chemical was reported to have negative results in a number of tests for genotoxicity. Based on the weight of evidence from the available in vitro and in vivo genotoxicity studies, the chemical is not considered genotoxic.

The in vitro tests showed negative results including the following tests with or without metabolic activation: bacterial reverse mutation assay (OECD TG 471) in *Salmonella typhimurium* TA 1535, TA 1537, TA 98 and TA 100; mammalian chromosome aberration test (OECD TG 473); in mammalian cell line and rat liver RL4 cell line; DNA damage and repair—unscheduled DNA synthesis in mammalian cells in vitro (OECD TG 482); and sister chromatid exchange assay in mammalian cells (OECD TG 478) (OECD, 2003; REACH).

Although a mammalian cell gene mutation assay on mouse lymphoma L5178Y cells (OECD TG 476) gave negative results with metabolic activation, positive results were shown in the absence of rat liver activating enzymes, but in the presence of cytotoxicity (OECD 2003; REACH).

Negative results were also reported for the following in vivo tests: mammalian cytogenics test—erythrocyte micronucleus assay (US EPA OTS 798.5395); mammalian cytogenetic tests—bone marrow chromosomal analysis (US EPA OPPTS 870.5385); and sex linked recessive lethal test in *Drosophila melanogaster* (US EPA OTS 798.5275) (OECD, 2003; REACH).

In another in vivo assay investigating the potential for formation of DNA and RNA modifications by the test substance in rats exposed by inhalation, no adducts or increased concentrations of metabolites were detected in the liver DNA (OECD, 2003; Government of Canada, 2010; REACH). However, there was a five times higher concentration of the 8-aminoguanosine metabolite of the test substance found in the liver RNA of male rats compared to female rats, exposed to the same concentration of the test substance. The study indicated the extent of oxidation of the test substance is dose dependent and only occurs at very high doses.

Carcinogenicity

The chemical is classified as a Category 3 carcinogen with the risk phrase ‘Limited evidence of carcinogenic effect’ (Xn; R40) in HSIS (Safe Work Australia). The available data support this classification.

In a carcinogenicity study in Fischer 344 rats and CD-1 mice (following the US EPA OTS 798.3300 guidelines), 80/sex/dose were exposed to doses of 0, 15, 75 or 374 ppm of the test substance via inhalation (whole body exposure), for 6 hours/day 5 days/week for a duration of either 3, 12, 18 or 26 months in rats and 3, 12 or 18 months in mice (OECD, 2003; REACH). There were no mortalities or clinical signs in rats and mice. The mean body weights were increased significantly in male and female rats in the 374 ppm dose group. Dose related changes in absolute and relative liver weights were observed (elevated by 33 % in the 374 ppm group of rats at three months), but tolerance or adaptation occurred and the liver weight differences decreased over time. Testes weights were 82 % increased in the 374 ppm rats, compared with the control groups, at the end of the study. The NOAEC for toxicity was 15 ppm for rats and mice, based on degenerative changes of the olfactory epithelium in the nasal turbinates at 75 ppm in male and female, rats and mice. The NOAEC for carcinogenicity in male rats and mice was 75 ppm,

based on the increased incidence of hepatocellular carcinomas reported at 374 ppm. As there were no increased tumour incidences at the highest dose in female rats and mice, a NOAEC for carcinogenicity in females was determined to be 374 ppm. As the tumour development did not affect mortality, was only present in males and was late developing, the pattern suggests the mechanism for carcinogenicity is epigenetic (alterations in the expression of genetic information without any changes to the genome) with a threshold value, rather than genotoxic and only transforms a liver cell into a tumour cell under certain circumstances (oncogene) (OECD, 2003; REACH).

Reproductive and Developmental Toxicity

Any reproductive or developmental effects were only observed secondary to maternal toxicity. Therefore, the chemical is not considered to have specific reproductive or developmental toxicity.

In a one generation oral reproductive toxicity study in rats, a lowest observed adverse effect level (LOAEL) of 100 mg/kg bw/day (highest dose) was established, based on the statistically significant decrease in the delivery index (OECD, 2003; REACH). There were no effects observed in neonates.

In a two generation oral reproductive toxicity study, CD Sprague Dawley (SD) rats (30/sex/dose for F(0) generation) were exposed to the chemical at doses of 0, 10, 100 or 200 mg/kg bw/day for a duration of five days/week for 10 weeks (OECD, 2003; REACH). Animals were randomly mated for three weeks to produce the F1 generation. The selected F1 weanlings (30 animals/sex/dose) were also administered the test substance starting at 11 weeks of age and mated randomly. There were no treatment related effects on rat reproductive activity or reproductive organ histology or on any offspring parameters assessing pre and postnatal survival and growth for two generations. The NOAEL for reproductive and developmental toxicity was determined to be ≥ 200 mg/kg bw/day. Based on histopathological evidence of extramedullary haematopoiesis and haemosiderosis in spleens and livers of F0 and F1 rats at all dose levels, a LOAEL of 10 mg/kg bw/day was reported for systemic toxicity.

In a developmental toxicity study (OECD TG 414), SD rats (25 females/dose) were exposed by oral gavage to doses of either 0, 60, 200 or 600 mg/kg bw/day of test substance from gestation day six through 15 (OECD, 2003; REACH). No developmental toxicity was observed in the juvenile rats and a NOAEL of 600 mg/kg bw/day was reported. Based on the enlarged spleens in maternal animals at the lowest dose level, a LOAEL of 60 mg/kg bw/day was reported for maternal toxicity.

In the same study above, New Zealand White rabbits (18 females/dose) were also dosed by oral gavage, with either 8, 14, 24 or 40 mg/kg bw/day from gestation day six through 18 (OECD, 2003; REACH). Clinical signs of toxicity were observed at 24 and 40 mg/kg bw/day, including maternal mortality and abortion of young at the highest dose level. A NOAEL for maternal toxicity was reported at 14 mg/kg bw/day based on dose dependent maternal toxicity at and above 24 mg/kg bw/day. Due to the high incidence of mortality and abortion in the highest dose group (40 mg/kg bw/day), no meaningful data for developmental toxicity could be obtained from the young after caesarean section removal. The NOAEL for developmental toxicity was hence reported as 24 mg/kg bw/day, based on no treatment related gestational effects, malformations or developmental variations. No developmental effects were observed, even at maternally toxic levels.

Other Health Effects

Neurotoxicity

Based on the available information, the chemical is not considered to cause neurotoxicity.

In a sub chronic neurotoxicity study (following US EPA OTS 798.6050 guidelines), Sprague Dawley rats (10 sex/dose) were administered the chemical via oral gavage with doses of 0, 40, 125 or 400 mg/kg bw/day for five days/week over 13 weeks (OECD, 2003; REACH). There were no microscopic changes in nervous tissues. Transient neurobehavioural changes recorded included motor uncoordination, decreased reactivity to general stimuli and decreased motor activity in the 400 mg/kg bw/day group, immediately after dosing, and were resolved after a few hours. A NOAEL for neurotoxicity was reported as 125 mg/kg bw/day.

In an acute neurotoxicity study (following US EPA OPPTS 870.6200 guidelines), Sprague Dawley rats (10 sex/dose) were administered the chemical at 0, 100, 300 or 900 mg/kg bw/day as a single oral gavage dose, and observed for the following 14

days (OECD, 2003; REACH). Neurobehavioural changes were recorded during cage removal, handling, posture, gait, aerial righting and motor activity following acute exposure to 300 and 900 mg/kg bw/day. A NOAEL of 100 mg/kg bw/day was reported.

Risk Characterisation

Critical Health Effects

The main critical effects to human health are severe eye irritation, skin sensitisation and harmful effects via contact with skin during short term or acute exposure. Long term exposure may cause carcinogenicity.

Public Risk Characterisation

Although use in domestic products in Australia is currently limited to binding agents in adhesives, the major application overseas of the chemical is reported to be as an anti-skinning agent in the formulation of alkyd paints, varnishes, stains and coatings for domestic use and found at concentrations up to 1 %. Overseas, the chemical is also found as minor components in some silicone sealants (up to 5 %) and adhesives, artists paint and printing materials and used for home maintenance and do-it-yourself applications (Government of Canada, 2010).

Concentrations of the chemical $\geq$ 1 % are considered to cause sensitisation (SWA HSIS, 2013) by skin contact and there is limited evidence of a carcinogenic effect from prolonged exposure.

Although exposure would be limited by the low frequency and application of the available uses of the chemical, considering the health effects, there is a concern in the use of this chemical as a ingredient in domestic products. Exposure to the general population to the chemical would be via dermal and inhalation routes during use of alkyd paints, coatings and silicone sealants. Dermal contact poses a risk of skin sensitisation, while inhalation and dermal contact may both result in systemic effects. The risk of carcinogenicity in the general public would be limited by the low frequency of use. There are no restrictions for the use of this chemical in Australia. Hence, overall there is a concern regarding the potential use of this chemical in domestic products in the absence of any regulatory controls.

Occupational Risk Characterisation

The primary occupational exposure to the chemical could occur via inhalation from its use as an anti-skinning agent in the formulation of alkyd paints, varnishes, stains and coatings. Worker exposure from use in oxime silicone sealants and adhesives, as well as a corrosion inhibitor in industrial boilers and water treatment systems, and as a blocking agent in the manufacturing process of urethane polymers would be minimal as the chemical is only a minor component (Government of Canada, 2010). Studies from professional use, such as painters using alkyd based paints in an office environment with typical ventilation, and off-gassing from silicone caulking of interior surfaces in a residential bathroom, found much lower exposure levels than occupational exposure limit restriction from Ireland and the USA (SIAM, 2003).

Given the critical health effects, the risk to workers from this chemical is considered high unless adequate control measures to minimise occupational exposure to the chemical are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business, or an employee at a workplace, has adequate information to determine appropriate controls.

NICNAS Recommendation

Further risk management is required. Sufficient information is available to recommend that the chemical be risk managed for public safety from potential use in cosmetics and/or domestic products through scheduling, and occupational health and safety through classification and labelling.

Regulatory Control

Public Health

Appropriate scheduling and labelling to be undertaken to mitigate risk from its use in domestic products.

Matters to be taken into consideration include skin sensitisation and severe eye irritation effects.

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful in contact with skin (Xn; R21)*	Harmful in contact with skin - Cat. 4 (H312)
Irritation / Corrosivity	Risk of serious eye damage (Xi; R41)*	Causes serious eye damage - Cat. 1 (H318)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)*	May cause an allergic skin reaction - Cat. 1 (H317)
Carcinogenicity	Carc. Cat 3 - Limited evidence of a carcinogenic effect (Xn; R40)*	Suspected of causing cancer - Cat. 2 (H351)

[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/ocular/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;
- 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;5
- regularly cleaning equipment and work areas;5and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical5.

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.

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