Pentanal: Human health tier II assessment

30 June 2017

CAS Number: 110-62-3

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.

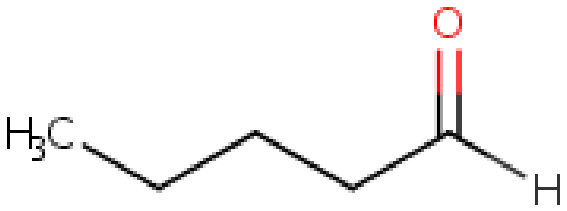
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	n-valeraldehyde valeric aldehyde amyl aldehyde n-pentanal valeral
Structural Formula	
Molecular Formula	C5H10O
Molecular Weight (g/mol)	86.13
Appearance and Odour (where available)	Clear liquid, with a strong, acrid/pungent odour.
SMILES	C(=O)CCCC

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 Organisation for Economic Co-operation and Development Screening information data set International Assessment Report (OECD SIAR); Galleria Chemica; the European Commission Cosmetic Ingredients and Substances (CosIng) database; the International Fragrance Association (IFRA) Survey 2011; and the United States National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic use in perfuming.

The chemical has reported site-limited use as an intermediate.

The chemical has reported non-industrial uses as a flavouring agent.

Restrictions

Australian

No known restrictions have been identified.

International

No known international restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

The chemical has an exposure standard of 176 mg/m^3 (50 ppm) time weighted average (TWA) (Safe Work Australia).

International

The following exposure standards are identified (Galleria Chemica).

An exposure limit of 90–179 mg/m^3 (25–50 ppm) TWA and 262–350 mg/m^3 (60–100 ppm) short-term exposure limit (STEL)/MAK/ occupational exposure limit (OEL) in different countries such as Austria, Belgium, Canada (Alberta, British Columbia, Manitoba, North West territories, Nova Scotia, Prince Edward Island, Quebec, Saskatchewan, Yukon), Colombia, Croatia, Denmark, Finland, France, Iceland, Indonesia, Ireland, Italy, Korea, Malaysia, Mexico, Nicaragua, Norway, Peru, Poland, Portugal, Singapore, Spain, Switzerland, Taiwan, the United Arab Emirates, the United States of America (Alaska, California, Hawaii, Idaho, Michigan, Vermont, Washington, Tennessee) and Venezuela.

Health Hazard Information

When data for the chemical being assessed (pentanal, also known as valeraldehyde) are not available, health hazard information for 3-methylbutanal (CAS No. 590-86-3), n-butyraldehyde (CAS No. 123-72-8), isobutyraldehyde (CAS No. 78-84-2) and propionaldehyde (CAS No. 123-38-6) has been included in this report. Pentanal, 3-methylbutanal, n-butyraldehyde, isobutyraldehyde and propionaldehyde have similar uses, structural similarities, undergo similar metabolic processess, and are expected to have similar systemic effects based on the properties of the reactive aldehyde group, to the chemical (SIAR, 2005). Therefore, they are considered to be a suitable analogues for the chemical.

Acute Toxicity

Oral

Based on the available data, the chemical has low acute oral toxicity.

The following oral median lethal dose (LD50) values were reported for the chemical (NTP, 1997; REACH; RTECS):

- 3200–6400 mg/kg bw in rats;
- >4582 mg/kg bw in male Wistar rats;
- 6490 mg/kg bw (8 mL/kg bw) in male and female Sprague Dawley (SD) rats; and
- 6400–12800 mg/kg bw in mice.

Observed sub-lethal effects included dyspnoea, apathy, staggering, narcosis-like state with loss of pain and corneal reflex, spastic movement, exsiccosis (dehydration due to lack of fluid intake) and exophthalmos (protrusion of the eyeballs).

Dermal

Based on the available data, the chemical has low acute dermal toxicity.

The following dermal LD50 values were reported for the chemical (NTP, 1997; SIAR, 2005; REACH; RTECS):

- 4857 mg/kg bw in rabbits; and
- 20000 mg/kg bw in guinea pig.

Observed sub-lethal effects included necrosis at the application site.

Inhalation

Based on the available data, the chemical has moderate acute inhalation toxicity warranting hazard classification (see **Recommendation** section).

The median lethal concentration (LC50) was reported to be 14.3 mg/L (4000 ppm) following a four hour exposure in albino rats (NTP, 1997; REACH; RTECS).

Corrosion / Irritation

Respiratory Irritation

Based on data from the **Repeat Dose Toxicity: Inhalation** and **Carcinogenicity** sections using the more volatile analogue isobutyraldehyde, and on respiratory rate depression in mice caused by the volatile 3-methylbutanal (chemical analogue), the chemical is considered to be a respiratory irritant, warranting hazard classification (see **Recommendation** section).

Effects reported include mild epithelial hyperplasia of the mucosa of the nasal cavity and nasopharynx along with increased incidences of squamous metaplasia and inflammation. At high doses necrosis of the olfactory epithelium has been reported (SIAR, 2005; REACH).

The chemical, 3-methylbutanal, an isomer of pentanal having similar volatility, caused reduced respiratory rates in mice, indicative of respiratory irritation (REACH).

Skin Irritation

Based on the available data in rabbits, the chemical is considered to be slightly irritating to skin. Observations in humans (see below) indicate that hazard classification is required.

In a skin irritation study (OECD TG 404), New Zealand White (NZW) rabbits (n = 3 males) were dermally exposed to 0.5 mL of the chemical (occlusive) for four hours. Erythema was noted one hour after removal of the patch on all three animals (erythema grade 2), and lasted up to seven days in two of the animals, and 14 days in one of the animals. Mean scores (21–72 h) for erythema and oedma were 1.9 and 0.4 respectively (REACH).

Eye Irritation

Based on the available data, the chemical is considered to be an eye irritant warranting hazard classification (see **Recommendation** section).

In an eye irritation study (similar to OECD TG 405—using half the recommended volume of the chemical), Vienna White rabbits (n = 2) were exposed to 0.05 mL of the chemical in one eye each and observed up to eight days. Irritation of the cornea and conjunctivae developed within an hour after application and persisted up to 8 days after administration, after which all irritation effects subsided. Iritis was not reported. In the first rabbit, the mean cornea and conjunctivae scores were 0.5 and 1.5, respectively. In the second rabbit, the mean cornea and conjunctivae scores were 1.5 and 2, respectively. The authors note that by doubling the volume of the chemical used, the reversibility of the eye damage is expected to be maintained but the cornea and conjunctivae scores will be elevated (REACH).

Observation in humans

In humans, three subjects were dermally exposed to 25 µL of the chemical (75 % v/v, occlusive) for five minutes. All three subjects displayed intense positive responses to the chemical. Other aldehydes tested such as propionaldehyde and buturaldehyde had similar effects (HSDB).

Sensitisation

Skin Sensitisation

Based on the weight of evidence from Quantitative Structure-Activity Relationship (QSAR) modelling using the chemical and sensitisation studies using structural analogues of the chemical, the chemical is considered to cause sensitisation reactions warranting hazard classification (see **Recommendation** section).

The chemical has structural alerts for protein binding based on the mechanistic profiling functionality of the Organisation for Economic Co-operation and development (OECD) QSAR Application Toolbox (OECD QSAR Toolbox v3.4). Results from standard sensitisation tests on a variety of structurally different aldehydes were taken into consideration and indicate that the chemical is likely to be a weak skin sensitiser.

In a guinea pig maximisation test (GPMT), female Himalayan spotted guinea pigs (n = 10) were induced intradermally with a 5 % concentration of the structural analogue propionaldehyde. An occlusive topical induction with a 30 % aqueous solution of the analogue was then performed. The first challenge was performed two weeks later under occlusive conditions with a 30 % solution of the analogue. A positive response was observed, with 80 % of animals having a reaction (erythema reaction grade 1–2) after 24 hours. After 48 hours, 60 % of the animals still had a reaction (erythema reaction grade 1–2) to the analogue. Negative controls yielded no responses. A second challenge was conducted two weeks after the first and mirrored the results in the first challenge, but with lower incidence and intensity, as 40 % of the animals had a reaction after 48 hours (erythema reaction grade 1) (REACH).

In a LLNA study using the structural analogue propionaldehyde, female CBA/CaOlaHsd mice (n = 6/dose) were tested using concentrations of 1, 3 and 10 % w/w of the test substance in acetone. No statistical increase in the SI scores was noted in the 1 and 3 % doses; however, at the 10 % dose a small but significant increase was observed. In a mouse ear swelling test (MEST), all three doses resulted in statistically significant increase in ear weight compared to the control group. No signs of systemic toxicity were noted at the tested concentrations (REACH).

In another MEST study using the structural analogue isobutyraldehyde, female B6C3F1 mice (n = 4/dose) were treated with the 20 µL of test chemical by direct dermal application on the left ear, for five days at concentrations of 3, 10 and 30 %. The animals were rested for seven days, during which they were observed for any signs of toxicity. After seven days the animals were challenged with 20 µL of the test substance at a concentration of 30 % on the left ear. The thickness of the treated left ear and untreated right ear was compared to the controls. After two days the mice were euthanised and the ears biopsied to determine the hypersensitivity and irritancy indexes. Results indicated that application of the analogue produced no statistically significant dose-dependent response in mice (REACH).

In a Buehler test (OECD TG 406), the structural analogue butyraldehyde was administered (occlusive) to the skin of Hartley guinea pigs (n = 10/sex). Induction was performed with a 50 % solution of the test chemical in acetone for six hours per day, three days per week within three weeks. The animals were challenged 14 days later with a 25 % solution for six hours. Five animals had a slight positive reaction 24 hours after the challenge and three had a reaction 48 hours after the challenge. A re-challenge was conducted eight days after the initial challenge with a 40 % solution of the analogue. After 24 hours one animal had a positive response (erythema reaction grade 1) and eight had an equivocal response. After 48 hours, one animal had a positive reaction while seven had an equivocal response (REACH).

In a second Buehler test (OECD TG 406), the structural analogue butyraldehyde was administered (occlusive) to the skin of Hartley guinea pigs (n = 10/sex). Induction was performed with a 50 % solution of the analogue in acetone for six hours/day, three days/week for three weeks. The animals were challenged 16 days later with a 10 % solution of the analogue epicutaneously and again seven days later with a 25 % solution. There were no reactions at the 10 % challenge while only 2/20 animals exhibited mild reactions to the 25 % challenge (REACH).

Repeated Dose Toxicity

Oral

Based on the available data, the chemical is not considered to cause serious health effects following repeated oral exposure.

In a repeat dose oral toxicity study (OECD TG 407), Wistar rats (n = 5/sex/dose) were administered the chemical at 300 or 1000 mg/kg via gavage for a period of 28 days. The plasma metabolomes of the animals were examined and compared to control animals on days seven, 14 and 28. Results indicated that the chemical did not match pre-existing metabolite profiles for specific toxicity in the male and female test groups. A no observed effect level (NOEL) of 1000 mg/kg bw/day was reported (REACH).

Dermal

No data are available.

Inhalation

No data are available for the chemical. Based on the available data for the analogue isobutyraldehyde, the chemical is not considered to cause systemic toxicity following repeated inhalation exposure. Localised lesions and animal mortality at high concentrations was related to respiratory irritation effects.

In repeated dose inhalation toxicity studies, B6C3F1 mice and F334/N rats (n = 10/sex/dose) were exposed to the analogue, isobutyraldehyde, at concentrations of 0, 500, 1000, 2000, 4000 and 8000 ppm (0, 1475, 2949, 5899, 11797 and 23594 mg/m^3) for six hours a day, five days a week for 13 weeks. All mice in the 8000 ppm group, except for one male in the 4000 ppm group, and one male in the 1000 ppm dose group were deceased before the end of the study. The mean body weight of the surviving male mice was similar to the controls; however, females in the 1000 ppm dose group had body weights which were significantly lower than controls. At necropsy, no gross lesions attributed to the exposure were observed. Significant increases in the absolute and relative kidney weight were observed in the 1000 and 2000 ppm male dose groups. The absolute liver and thymus weight of females in the 1000 and 2000 ppm dose groups respectively, were less than the controls. In the 1000 and 2000 ppm dose groups there was an increase in the incidence of non-neoplastic lesions of the naval cavity which included inflammation, hyperplasia, squamous metaplasia of the epithelium and necrosis. In the F344/N rats, all animals in the 8000 ppm dose group, three males and six females in the 4000 ppm dose group, and one female in the 500 ppm dose group were deceased before the end of the study. Clinical observations of the two highest dose groups noted abnormal breathing sounds, lethargy, nasal discharge and prostration. Necropsy of the animals showed no visible gross lesions associated with exposure. There was no change in the organ weight of treated animals compared to the control groups. In the 8000 ppm dose group, necropsy revealed necrosis of the larynx and trachea. In rats administered 4000 ppm, mild epithelial hyperplasia of the mucosa of the nasal cavity and nasopharynx along with increased incidences of squamous metaplasia and inflammation were recorded (SIAR, 2005).

In carcinogenicity studies (see **Carcinogenicity** section) using the analogue isobutyraldehyde at concentrations of 0, 500, 1000 and 2000 ppm (0, 1475, 2949 and 5899 mg/m^3), an increase in mortality at the highest concentration was seen in male mice compared with controls. Female B6C3F1 mice in the two highest dose groups were observed to have lower mean body weights than controls in the second half of the study. In all other dose groups, the mean body weight of the treated males was similar to that of the controls throughout the study. In the 1000 and 2000 ppm dose groups there was an increase in the incidence of olfactory epithelial deterioration—two animals in each of these groups were observed to have necrosis of the olfactory epithelium. The no observed adverse effect concentration (NOAEC) for systemic effects in males and females in this study was 1475 mg/m^3. In F344/N rats, mortalities observed in treated groups were similar to that of the control groups. There were no clinical findings associated with treatment. At the higher concentrations there were increases in the incidences of inflammation, mild squamous metaplasia and deterioration of the olfactory epithelium (SIAR, 2005).

Genotoxicity

Based on the weight of evidence of the available data using the chemical and its analogues in the in vitro and in vivo genotoxicity studies below, the chemical is not considered to be genotoxic.

In vitro studies yielded mostly negative results (NTP, 1997; SIAR, 2005; REACH):

- A bacterial reverse mutation assay (OECD TG 471) yielded negative results when 4 strains of *Salmonella typhimurium* (TA97, TA98, TA100 and TA1535) were tested with the chemical at 0, 10, 33, 100, 333, 1000, 2000 µg/plate, with and without metabolic activation. Cytotoxic effects were noted at the two highest concentrations.
- Five gene mutation studies in bacteria (OECD TG 471 or Ames) yielded negative results when strains of *S. typhimurium* (TA97, TA98, TA100, TA102, TA104, TA1535, TA1537 and TA1538) were tested with pentanal, n-butyraldehyde, isobutyraldehyde or propionaldehyde at a concentrations up to 10000 µg/plate, with and without metabolic activation.

- A gene mutation study in mammalian cells (OECD TG 476) of Chinese hamster lung fibroblasts tested with the chemical (0, 0.26, 0.86 and 2.58 mg/mL) was positive without activation. A concentration related positive response was noted.
- A DNA damage and repair study (OECD TG 482) was conducted in hepatocytes from the livers of SD rats. The liver cells were exposed to the chemical at concentrations of 0, 0.26, 0.86 and 2.58 mg/mL for 20 hours. A positive response was noted.
- A second DNA damage and repair study (OECD TG 482) was conducted in hepatocytes from the livers of two human volunteers. The liver cells were exposed to the chemical at concentrations of 0, 0.26, 0.86 and 2.58 mg/mL for 20 hours. A negative response was noted.
- Two gene mutation studies in mammalian cells (OECD TG 476) in Chinese hamster fibroblast cells were conducted with the analogue, isobutyraldehyde. In the first experiment the cells were treated with 0, 50, 100, 200, 400 and 800 µg/mL. In the second experiment the cells were treated with 0, 200, 400, 600 and 800 µg/mL. Both experiments yielded negative results, with and without metabolic activation.
- A DNA damage and repair study was conducted in Chinese hamster ovary (CHO) cells. The cells were exposed to the chemical at concentrations of 0, 0.043, 0.13 and 0.39 mg/mL for 90 minutes, without metabolic activation. The results indicated that the chemical was genotoxic to CHO cells without activation, causing dose dependent damage to DNA, and single strand breaks. No cross linking was observed.
- A Mouse Lymphoma Assay was conducted using L5178Y mouse lymphoma cells. The study gave negative results with exposure to the chemical over a range of concentrations from 15 to 150 µg/mL without activation, and between 50 to 500 µg/mL with activation.

In vivo tests gave negative results (SIAR, 2005; REACH)

- A mammalian somatic cell study was conducted in male B6C3F1 mice (n = 10/group) administered 0.4 mL of the analogue isobutyraldehyde at concentrations of 39, 78, 156, 312.5, 625, 1250 mg/kg bw/day by intraperitoneal (i.p.) injection for three days. The animals were euthanised after 24 hours and samples of the bone marrow were collected. Blood smears were prepared and investigated for an increase in the micronucleated PCEs for all doses compared to the corresponding controls. It was determined that the results from the experiments using the isobutyraldehyde were negative.
- A mammalian somatic cell micronucleus study was conducted in male F344/N rats (n = 5/group) administered 0.4 mL of the analogue isobutyraldehyde at concentrations of 312.5, 625 and 1250 mg/kg bw/day by i.p. injection for three days. Animals were euthanised 24 hours after the last dose and the bone marrow was collected. Subsequent blood smears indicated that the results from the experiments using isobutyraldehyde were negative.
- A study of sex linked lethal mutations in *Drosophila melanogaster* was negative when administered the analogue (isobutyraldehyde) by injection (50000 ppm) or by feed (80000 ppm) to one day old male flies.

Carcinogenicity

No data are available for the chemical. Based on the available inhalation data for the analogue, isobutyraldehyde, the chemical is not considered likely to be carcinogenic.

Groups of B6C3F1 mice and F-344/N rats (n = 50/sex/dose) were exposed to the analogue, isobutyraldehyde, at concentrations of 0, 500, 1000 and 2000 ppm (0, 1475, 2949 and 5899 mg/m^3) for six hours a day, five days a week for 103 (rats) or 104 (mice) weeks. In B6C3F1 mice, there were no increases in the incidence of neoplasms in either sex that could be attributed to exposure to the analogue. The only treatment related effects observed were non-neoplastic nasal lesions. In F334/N rats, mortalities observed in treated groups were similar to that of the control groups. There were no clinical findings associated with the administration of the analogue. At the higher concentrations there was an increase in the incidences of inflammation, mild squamous metaplasia and deterioration of the olfactory epithelium. No increase in the incidence of neoplasms in the animals could be attributed to exposure to the analogue (SIAR, 2005).

Reproductive and Developmental Toxicity

No data are available for the chemical. Based on the data available for the analogues, isobutyraldehyde and propionaldehyde, the chemical is not considered likely to cause specific reproductive or developmental toxicity.

Groups of CD rats (n = 15/sex/dose) were administered the analogue propionaldehyde at concentrations of 0, 150, 750 and 1500 ppm (0, 356, 1782 and 3563 mg/m^3) for six hours/day, seven days/week for two weeks. The animals were exposed during a premating interval of 14 days, and a mating interval of up to 14 days. The males were exposed up until they were euthanised (after 52 exposures) and did not show any signs of toxicity throughout the study. The females were exposed until gestation day (GD) 20 and were allowed to deliver and raise their pups until day four of lactation, after which the F0 females and F1 pups were euthanised. Analysis of the sacrificed animals indicated that there were no significant effects on any of the reproductive parameters assessed. The litter size and variability were similar among the exposed and control groups. Pup weights were not affected by exposure to the analogue; however, the authors reported that the pup body weight gains between lactation days zero to four were slightly depressed in the high concentration group. The NOAEC for reproductive toxicity was 3563 mg/m^3 and the NOAEC for pup toxicity was 1782 mg/m^3 (SIAR, 2005).

Groups of pregnant Wistar rats (n = 25) were administered the analogue isobutyraldehyde at concentrations of 0, 1000, 2500 and 4000 ppm (0, 2949, 7373 and 11797 mg/m^3) for six hours/day, for 10 consecutive days (GD 6–15). The animals were euthanised on GD 20 and foetuses were removed from the uterus. Exposure to the analogue results in a dose related increase in maternal toxicity based on a significant decrease in female body weight gain when exposed to ≥ 2500 ppm. Exposure to the analogue had no effect on gestational or litter parameters and did not induce embryo foetal toxicity. There was no increase in foetal deformity up to 4000 ppm. The NOEL for developmental toxicity of the analogue is 11797 mg/m^3 (SIAR, 2005).

Groups of pregnant SD rats (number not specified) were administered the analogue chemical, propionaldehyde via intra-amniotic injection at concentrations of 10, 100 and 1000 µg/embryo. The rats were euthanised on GD 20, the foetuses were removed, and the number of dead or resorbed foetuses were determined. Intra-amniotic treatment with the analogue chemical resulted in a significant dose related increase in embryo lethality compared to controls. The analogue chemical did not result in an increase in foetal deformities at any dose (SIAR, 2005).

In repeated dose toxicity studies in B6C3F1 mice and F334/N rats exposed to isobutyraldehyde (see **Repeated Dose Toxicity: Inhalation** section), there were no changes in spem motility, density, morphology or reproductive organ weight between the exposed and control groups in male B6C3F1 mice. Among female mice, there were no effects on vaginal cytology. In male F334/N rats, there was a decrease in the absolute weight of the right cauda epididymis and right epididymis recorded in rats exposed to the highest dose. In groups of rats exposed to ≥2000 ppm there were no changes in sperm motility, density or morphology between the exposed and control groups. Sperm motility decreased in rats exposed to 500 and 1000 ppm. In female rats there was significant mortality in the highest dose group and only four female rats were evaluated further. In this group the length of the oestrous cycle was slightly increased compared to the controls. In the 2000 ppm groups there was no significant difference in the time spent in the cycle between exposed animals and the controls (SIAR, 2005).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic acute effects (acute toxicity from inhalation exposure) and local effects (skin sensitisation). The chemical can also cause skin, eye and respiratory irritation.

Public Risk Characterisation

Although use in cosmetic products in Australia is not known, the chemical is reported to be used in cosmetic products overseas as a fragrance compound. In such cosmetic formulations, the chemical is expected to be used at the lowest necessary concentrations. Hence, the public risk from this chemical is not considered to be unreasonable.

Occupational Risk Characterisation

During product formulation, dermal, ocular and inhalation exposure may 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 application and work practices employed.

Given the critical systemic acute and local health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure 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 the appropriate controls.

The data available support an amendment to the hazard classification in the HCIS (Safe Work Australia) (see **Recommendation** section).

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

Work Health and Safety

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

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Not Applicable	Harmful if inhaled - Cat. 4 (H332)
Irritation / Corrosivity	Not Applicable	Causes serious eye irritation - Cat. 2A (H319) Causes skin irritation - Cat. 2 (H315) May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)
Sensitisation	Not Applicable	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 industry

Control measures

Control measures to minimise the risk from dermal, ocular 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 that could 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 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 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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