2-Propenamide, N-(hydroxymethyl)-2-methyl-: Human health tier II assessment

12 December 2019

CAS Number: 923-02-4

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.

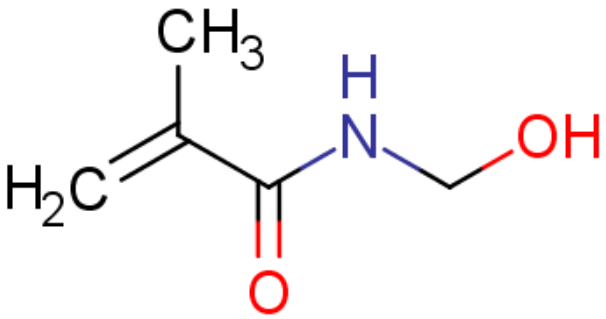
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	methylolmethacrylamide N-methylolmethacrylamide N-(hydroxymethyl)methacrylamide acrylamide, N-(hydroxymethyl)-2-methyl-
Structural Formula	
Molecular Formula	C5H9NO2
Molecular Weight (g/mol)	115.13
Appearance and Odour (where available)	clear, colourless to yellowish liquid with a faintly ester-like odour
SMILES	C(=O)(C(=C)C)NCO

Import, Manufacture and Use

Australian

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

International

The following international uses have been identified through European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; United States (US) Environmental Protection Agency (EPA) ChemView database; US EPA Chemical and Product Categories (CPCat).

The chemical has reported domestic uses in paints, lacquers and varnishes in the SPIN database. However, it should be noted that SPIN does not distinguish between direct use of the chemical, or use of the materials that are produced from chemical reactions involving the chemical.

The chemical has reported commercial uses as a component in food contact materials and articles such as adhesives, coatings, paper and cardboard components.

The chemical has reported site-limited uses as a reactant in the manufacture of polymers for:

- bulk, large scale chemicals (including petroleum products);
- paint and coating;
- plastic material and resin; and
- textiles, leather and fur.

Restrictions

Australian

No known restrictions have been identified; however, the chemical is formaldehyde donor.

Formaldehyde (CAS No. 50-00-0) is listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP, 2019) in Schedule 6 and Schedule 10:

Schedule 6:

'FORMALDEHYDE (excluding its derivatives) in preparations containing 0.05 per cent or more of free formaldehyde **except**:

(a) for human therapeutic use;

(b) in oral hygiene preparations;

(c) in nail hardener cosmetic preparations containing 5 per cent or more of free formaldehyde;

(d) in nail hardener cosmetic preparations containing 0.2 per cent or less of free formaldehyde when labelled with the statement: PROTECT CUTICLES WITH GREASE OR OIL;

(e) in all other cosmetic preparations; or

(f) in other preparations containing 0.2 per cent or less of free formaldehyde when labelled with the warning statement: CONTAINS FORMALDEHYDE.'

Schedule 6 chemicals are labelled with 'Poison' and are 'substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label'.

Schedule 10:

'FORMALDEHYDE (excluding its derivatives):

(a) in oral hygiene preparations containing more than 0.1 per cent of free formaldehyde;

(b) in aerosol sprays for cosmetic use containing 0.005 per cent or more of free formaldehyde;

(c) in nail hardener cosmetic preparations containing 5 per cent or more of free formaldehyde; or

(d) in all other cosmetic preparations containing 0.05 per cent or more of free formaldehyde except in preparations containing 0.2 per cent or less of free formaldehyde when labelled with the warning statement: CONTAINS FORMALDEHYDE.'

Schedule 10 chemicals are 'substances, other than those included in Schedule 9, of such danger to health as to warrant prohibition of sale, supply and use'.

Formaldehyde donors are mentioned in the definition of free formaldehyde in Part I of the Poisons Standard (SUSMP) as follows:

"Free formaldehyde" includes all hydrated and non-hydrated formaldehyde present in aqueous solution, including methylene glycol and formaldehyde released from formaldehyde donors.

International

The chemical is regulated for use as a component of food contact substances under the US FDA - List of Indirect Additives Used in Food Contact Substances (US FDA, 2018) with the following limitation:

- plastic articles intended for single-use food contact: the polymers used in these plastics must not contain more than 5 % w/w of total polymer units derived from the chemical.

The chemical is also regulated for use as a component of food contact substances under the EU – Commission Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food (EC, 2011) with the following limitations:

- authorised to be used as monomer or other starting substance but not as an additive or polymer production aid; and
- the specific migration limit (SML) 0.05 mg substance per kg of food applies.

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

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

The structure of the chemical, also referred to as N-methylolmethacrylamide in this assessment, includes structural alerts for several toxicological endpoints. Limited data are available for the chemical. Where appropriate, data on a structurally similar chemical, N-methylol acrylamide (CAS No. 924-42-5), and the hydrolysis products, methacrylamide (2-propenamide, 2-methyl; CAS No. 79-39-0) and formaldehyde (CAS No. 50-00-0), are read across to fill data gaps in the assessment. The risks of N-methylol acrylamide and formaldehyde have previously been assessed by NICNAS (NICNAS; NICNAS, 2006).

Toxicokinetics

There are limited data available on the toxicokinetics of the chemical.

Hydrolysis of the chemical was observed in simulated saliva (pH 9.0), with the concentration of the chemical decreasing to 94 % within 4 hours and the amount of the hydrolysis product, methacrylamide increasing by almost the same amount. The chemical was hydrolysed to a minor extent in simulated gastric fluid (pH 1.2) and simulated intestinal fluid (pH 7.5) within 4 hours (REACHa).

Based on N-methylol acrylamide, the chemical is expected to be well absorbed and widely distributed throughout the body, metabolised via glutathione conjugation and excreted primarily in the urine and faeces following oral administration (NICNAS).

Dermal absorption of the chemical was predicted to be low by QSAR modelling for skin permeability established by Potts and Guy (1992), where a penetration rate of 0.768 μg/cm^2/hr in human skin is obtained (REACHa). However, considering the evidence of skin permeability for methacrylamide (Hashimoto, 1985), the chemical may have the potential to be absorbed through the skin.

Acute Toxicity

Oral

The chemical has moderate acute toxicity based on results from animal tests following oral exposure. Hazard classification is warranted (see **Recommendation** section).

In a study conducted in accordance with the Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 401 (Acute Oral Toxicity), the median lethal dose (LD50) in Wistar rats is 1153 mg/kg bodyweight (bw) for males and 853 mg/kg bw for females. Observed clinical signs included sedation, dyspnoea, lacrimation, ataxia, curved body position, diarrhoea, spasms and ruffled fur (REACHa).

In an oral administration study (OECD TG 401), the LD50 was reported as 940 mg/kg bw in Sprague Dawley (SD) rats administered 60 % aqueous solution of the chemical with carboxymethyl cellulose at a single dose of 500, 1077, 2321 or 5000 mg/kg bw. Sub-lethal effects observed in this study were similar to those in the previously described study (REACHa).

In a non-guideline study, the approximate lethal dose (ALD) in male albino rats was reported as 670 mg/kg bw. Observed clinical signs included discomfort, ruffled fur, convulsions, salivation, diarrhoea, unsteady or hunched posture, weakness and/or irregular respiration (US EPA, 2009).

Dermal

No data are available for the chemical. Based on studies on N-methylol acrylamide and methacrylamide, the chemical is expected to have low dermal acute toxicity. Following dermal treatment with N-methylol acrylamide in rabbits, irritant effects were observed as well as sub-lethal effects including tremors and hind leg impairment. The lowest dermal lethal dose (LDLo) published is >16000 mg/kg bw (NICNAS, 2016). For rats dermally treated with 10 % or 20 % methacrylamide for 4 hours, no mortality was observed and the LDLo was determined to be >1600 mg/kg bw (OECD, 2002; REACHb).

Inhalation

Based on a non-guideline study, the chemical has low acute inhalation toxicity. No mortality was observed after male and female Wistar rats were exposed to a saturated atmosphere containing up to 15 % chemical concentration for 7 hours. Wiping of the snouts and watery nasal secretions were observed during exposure, while blood was observed in the nasal secretions, lasting for a day after exposure. No adverse effects were noted during the subsequent 14-day observation period (REACHa).

Corrosion / Irritation

Respiratory Irritation

Based on the available data, the chemical may cause respiratory irritation. Hazard classification is warranted (see **Recommendation** section).

Signs of respiratory irritation was observed in the acute inhalation toxicity study with the chemical, where wiping of the snouts and watery nasal secretions were observed during exposure. Blood was also observed in the nasal secretions after exposure, lasting for 1 day (REACHa). This is supported by the potential for formaldehyde—a known respiratory irritant (NICNAS, 2006)—to be released upon contact with mucous membranes.

Skin Irritation

Based on the limited data available, the chemical is a slight skin irritant.

In a non-guideline acute dermal irritation study with New Zealand White (NZW) rabbits, the chemical (60 % in aqueous solution) was applied to 6 animals under occlusive conditions and removed after 24 hours. The skin was observed for 72 hours following dose administration. Evidence of erythema and oedema was observed after 24 hours but these were fully reversed after 72 hours. The chemical was concluded to be slightly irritating (REACHa). These effects may be due to the release of low levels of formaldehyde—a known skin irritant (NICNAS, 2006)—which is expected to occur in aqueous solutions of the chemical.

Eye Irritation

Based on the limited data available, the chemical is a slight eye irritant.

In a non-guideline study, the chemical (60 % in aqueous solution) was administered to 1 eye of 6 NZW rabbits. The eyes remained unwashed, and were observed over a 7-day period. Slight to moderate redness and chemosis were observed after 24 hours following application. Three of the animals had mean scores between 1.33 and 1.66 following grading at 24, 48 and 72 hours after administration. The effects decreased after 3 days and were fully reversed after 7 days (REACHa). These effects may be due to the release of low levels of formaldehyde—a known eye irritant (NICNAS, 2006)—which is expected to occur in aqueous solutions of the chemical.

Sensitisation

Skin Sensitisation

Based on the available data, the chemical is a skin sensitiser. Hazard classification is warranted (see **Recommendation** section).

In a guinea pig maximisation test (OECD TG 406), animals were intradermally induced with the chemical at 5 % in aqueous solution. This was followed by topical induction at 60 %. Following a 2-week rest period, challenge at 60 % resulted in positive reactions in 5/10 animals (50 %) after 24 hours. Therefore, the chemical is a skin sensitiser (REACHa). This is supported by

available data on the similar chemical, N-methylol acrylamide, which is considered to be a weak to moderate skin sensitiser based on animal and human studies (NICNAS), and the hydrolysis product, formaldehyde, which is a known skin sensitiser (NICNAS, 2006).

Repeated Dose Toxicity

Oral

No data are available for the chemical. Based on the available studies on N-methylol acrylamide and methacrylamide, the chemical is considered to cause serious damage to health (neurotoxicity) from repeated oral exposure, warranting hazard classification (see **Recommendation** section).

Available animal studies on N-methylol acrylamide reported neurotoxic effects from repeated oral exposure, including ataxia, neuropathy and nerve degeneration (NICNAS). In studies using methacrylamide, clinical signs and histopathological changes related to neurotoxicity were observed in many cases in rodents (OECD, 2002).

In a 28-day study, methacrylamide was administered to rats at doses of 0, 30, 100 or 300 mg/kg bw/day. Non-lethal, treatment-related clinical signs in the 100 and 300 mg/kg bw/day groups included ataxia, decrease in muscle tone and grip strength and decreased bodyweights. Decreased locomotor activity was observed in males at 100 mg/kg bw/day and higher and in females at 30 mg/kg bw/day and higher. At 300 mg/kg bw/day, degeneration of the sciatic nerve fibres and axonal swelling in the cerebellar peduncle were noted; also decreases in haematocrit, haemoglobin, urea nitrogen, creatinine, alpha1- globulin, alpha2-globulin and alkaline phosphatase, and increases in albumin and triglyceride. Increases in absolute and relative testes weights were found at the end of the recovery period. No observed adverse effect levels (NOAELs) of 30 mg/kg bw/day for males and less than 30 mg/kg bw/day for females were determined (OECD, 2002).

In a non-guideline, 12 month study, methacrylamide was administered to mice and rats in drinking water (200, 400, 800 and 1200 ppm corresponding to ca. 4.6, 9.1, 19.5 and 31.6 mg/kg bw/day for rats, and ca. 24.3, 49.6, 120 and 220.6 mg/kg bw/day for mice). In rats and mice, reduction in the rotarod performance, distension of the urinary bladder, atrophy of gastrocnemius muscle, decrease in grip strength and abnormal gait (symptoms of peripheral neuropathy) were observed at 800 ppm (ca. 19.5 mg/kg bw/day) and higher. Shrinkage and loss of sciatic nerve fibres were observed in rats at 800 ppm (ca. 19.5 mg/kg bw/day) and higher, while in mice it was observed at 400 ppm (ca. 49.6 mg/kg bw/day) and higher along with paralysis of hindlimb. At the highest dose, significant increases in serum total cholesterol and phospholipid content were also noted in rats. NOAELs of 9.1 mg/kg bw/day (400 ppm) in rats and ca. 24.3 mg/kg bw/day (200 ppm) in mice were determined (OECD, 2002; REACHb).

Dermal

No data are available for the chemical. Based on the available studies on N-methylol acrylamide and methacrylamide, the chemical is considered to cause serious damage to health (neurotoxicity) from repeated dermal exposure, warranting hazard classification (see **Recommendation** section).

While the chemical is expected to have low acute dermal toxicity based on studies with N-methylol acrylamide in rabbits, the observed sub-lethal effects including tremors and hind leg impairment in this study indicate that there may be some concerns for adverse health effects, particularly neurotoxicity.

In a non-guideline dermal repeated dose study, NZW rabbits were treated with methacrylamide at doses of 0, 5, 50 (12 weeks) or 500 mg/kg/ bw/day (5 weeks) (24 animals per dose group). The incidence and severity of clinical signs of neurotoxicity including splaying and forward extension of hindlimbs steadily increased over time in 15/23 animals at 500 mg/kg bw/day. However, these effects were reversible within 20 days after the last administration (OECD, 2002; REACHb).

Inhalation

No data are available for the chemical. Based on the available studies on methacrylamide, there is limited evidence that the chemical is considered to cause toxicity from repeated inhalation exposure.

In a guideline (OECD TG 413: Subchronic inhalation toxicity) 90-day study, Wistar rats (40 males and 40 females) were exposed to methacrylamide at doses of 0, 10, 25 or 62.5 mg/m^3 for 6 hours once daily, 5 days per week for a total of 13 consecutive weeks. There was no mortality throughout the 13-week treatment period. Body weight gain was significantly reduced at the mid and high dose level in males but not in females. Degeneration, squamous metaplasia and respiratory metaplasia of olfactory mucosa in level IV of the nasal cavities were observed at the mid and high dose groups. Therefore, the NOAEL for local effects was set at 10 mg/m^3. As there were no changes observed in organs, tissues or other parameters investigated which were attributed to systemic toxicity, the NOAEL for systemic effects were set at 62.5 mg/m^3 (REACHb).

In a non-guideline 16-week inhalation study, 6 rats per dose group were exposed to methacrylamide at doses of 0, 3.2, 12 or 34.5 mg/m^3. At the mid and high doses after 16 weeks, clinical signs such as reduced activity, increased startle reaction, increased aggressiveness were observed. Increased tryptophan, serotonin, 5-hydroxyindoleacetic acid and histidine levels in the brain were observed. Autopsy findings included slightly smaller testes and tendency for reduced mobility of spermatozoa. However, the details of this study were not well documented and the reliability of this study was found to be limited (OECD, 2002).

Observation in humans

The potential adverse health effects of the chemical from repeated dermal exposure are supported by evidence of harmful health effects in humans following occupational exposure to the N-methylol acrylamide. Several case studies have reported adverse effects on the peripheral nervous system, the visual system, local effects and possible genotoxic effects on workers exposed to grout containing N-methylol acrylamide (NICNAS).

Genotoxicity

The chemical may have genotoxic potential but available data are not sufficient to determine this. The structurally-similar chemical N-methylol acylamide is a classified mutagen.

In vitro

In a guideline bacterial reverse mutation test (OECD TG 471), the chemical (15 % aqueous solution) was tested for point mutations in *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98 and TA 100 at test concentrations of 0, 100, 500, 2500, 5000 and 7500 µg/plate (all 4 strains) and at 2500, 5000, 7500 and 10,000 µg/plate (TA 100 only) with or without metabolic activation. Investigators of the study concluded that the chemical is weakly mutagenic in the strain TA 100, but a re-evaluation by the European Scientific Committee on Food (SCF) determined the result to be negative (REACHa).

In a guideline in vitro mammalian chromosome aberration test (OECD TG 473), CHO cells were exposed to the chemical at test concentrations of 0, 2.54, 5.08, 10.2, 20.3, 40.6, 81.3, 163, 325, 650, 1300 and 2600 µg/mL. A dose-related increase in chromosomal aberrations was observed both with and without metabolic activation (RTC, 2000).

In vivo

In a guideline mouse micronucleus test (OECD TG 474), mice were administered with the chemical via oral gavage at 0, 83.9, 251.7 and 839 mg/kg bw/day in aqueous carboxymethylcellulose. No significant increase in frequency of micronucleated polychromatic erythrocytes was observed following administration (REACHa).

Carcinogenicity

No data are available for the chemical. Based on the reported carcinogenic potential of N-methylol acrylamide and formaldehyde, the chemical may have the potential to cause cancer. However, in the absence of any toxicokinetic and mechanistic information, there is insufficient evidence to classify the chemical.

Reproductive and Developmental Toxicity

No data are available for the chemical. Based on the testicular effects of the chemical in 1 repeat dose toxicity study (refer to **Repeat dose toxicity: Oral**) and available studies on N-methylol acrylamide and methacrylamide, the chemical is suspected to cause reproductive and developmental toxicity, warranting hazard classification (see **Recommendation** section).

Testicular effects were observed in male mice in the absence of significant neurotoxicity or other systemic toxicity in some reproductive toxicity studies with the similar chemical, N-methylol acrylamide. It is classified as a Category 2 reproductive toxicant. No evidence of developmental toxicity was observed (NICNAS).

The studies on the hydrolysis product, methacrylamide, showed variable results for toxic effects on reproduction and development.

In an oral acute toxicity study, changes in testes and epididymis such as decrease of spermatozoa were observed at a high dose of 1512 mg/kg and above, while a tendency for reduced mobility of spermatozoa were noted in the 16 week repeated dose inhalation study in rats (OECD, 2002).

In a reproduction/developmental toxicity screening test, male and female SD rats (13 animals/group) were administered methacrylamide at doses of 0, 12.5, 50 or 200 mg/kg bw/day. Males were dosed for 42 days and females were dosed for 14 days before mating, throughout pregnancy to day 3 of lactation. At 200 mg/kg bw/day, the copulation rate was decreased, delayed parturition and abnormal nursing were observed. Low body weights and decreased viability of the pups were observed at 200 mg/kg bw/day, however, these changes may be related to severe maternal systemic toxicity. The NOAEL for reproductive and developmental toxicity was considered to be 50 mg/kg bw/day (OECD, 2002).

In a non-guideline 1-generation reproduction study (modified reproductive assessment continuous breeding protocol), male (18 or 19 animals/group) and female CD-1 mice (18 or 19 animals/group) received 0, 24, 80 or 240 ppm (0, 4.5, 15.4, 49 mg/kg bw/day) of methacrylamide in drinking water for 27 weeks. During the study period, the F1 generation were also assessed and maintained on the same dose of methacrylamide as their parents (0, 24, 80 or 240 ppm). Clinical signs such as bodyweight, food and water consumption were unaffected in all animals. Normal fertility with no evidence of dominant lethality was observed. A temporary slight diminished grip strength in juvenile mice was noted but these effects became insignificant when the animals grew older at 24 ppm (6.8 mg/kg bw/day) and 80 ppm (23.8 mg/kg bw/day). However, the recovery from the neurotoxic effect was not completed in the highest dose group. For F0 the NOAEL for reproductive toxicity is >240 ppm (49 mg/kg bw/day), and for F1 the NOAEL is >240 ppm (71.3 mg/kg bw/day in males, 69 mg/kg bw/day in females). The NOAEL for developmental toxicity in this study was considered to be less than 24 ppm (6.8 mg/kg bw/day) (OECD, 2002; REACHb).

In a developmental study, pregnant female CD-1 mice were dosed daily (gestational days 6 to 17) with methacrylamide at doses of 0, 60, 120 or 180 mg/kg bw/day). A decrease in maternal weight gain and gravid uterine weight was observed at 180 mg/kg bw/day. Relative maternal liver weight increased at 120 mg/kg bw/day and higher. At 120 mg/kg bw/day, the observed decrease in mean foetal body weight was considered to result from specific developmental toxicity as only a little increase in maternal relative liver weight was noted at this dose. At 180 mg/kg bw/day, increased post-implantation death per litter and decrease in mean foetal body weight were observed. The maternal NOAEL for developmental toxicity was considered to be 60 mg/kg bw/day (OECD, 2002).

Other Health Effects

Neurotoxicity

Based on acute and repeated dose toxicity studies in animals for the chemical (refer to **Acute toxicity** and **Repeated dose toxicity**), the similar chemical, N-methylol acrylamide and the metabolite, methacrylamide (NICNAS; NICNAS, 2006), the observed neurotoxic effects have been considered in the hazard classification of the chemical for acute and repeated dose toxicity endpoints. The effects observed in an animal study following single oral exposures to high concentrations of the chemical included ataxia, spasms and convulsions. Repeated exposures to low concentrations of the similar chemicals, N-methylol acrylamide and methacrylamide have caused signs of severe neurotoxicity in mice.

Risk Characterisation

Critical Health Effects

The critical health effect for risk characterisation is neurotoxicity following acute and chronic exposure to the chemical. Other potential health effects include systemic long term effects (reproductive and developmental toxicity) and local effect (respiratory irritation). The chemical may also cause skin sensitisation.

Public Risk Characterisation

Although use in consumer products in Australia is not known, the chemical has reported domestic use overseas as a component in paints, lacquers and varnishes. However, it is not clear whether the use is for the chemical alone or for the polymer containing the chemical. In these instances, the general public could be exposed to the chemical or the polymer through dermal or inhalation routes.

The public could come into contact with food contact articles and coated surfaces containing the chemical, although it is expected that the chemical will be bound within the article or coated surfaces and not expected to be released.

The chemical falls within the scope of the listing of ‘formaldehyde’ in Schedule 6 and Schedule 10 of the SUSMP (see **Restrictions: Australian**). The current controls are considered adequate to minimise the risk to public health posed by domestic products containing the chemical. Therefore, the chemical is not considered to pose an unreasonable risk to public health provided the concentrations of the free formaldehyde present in products meet the SUSMP limit.

Occupational Risk Characterisation

During product formulation, oral, dermal 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 long-term, systemic acute and local health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal 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.

Occupational risks to free formaldehyde exposures can be mitigated by ensuring effective ventilation when products containing the chemical are used in indoor environments. If symptoms of burning, stinging or itching of the eyes and/or nose, sore throat, watery eyes, blocked sinuses, runny nose or sneezing occurs, the worker is advised to move to an area with fresh air.

The data available support an amendment to the hazard classification in the Hazardous Chemical Information System (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.

Companies using or marketing products containing this chemical should seek sufficient information to determine whether the product contains free formaldehyde or releases formaldehyde, and take appropriate risk management measures to control the hazards stipulated in the HCIS, and the advice and controls in the SUSMP.

It is recommended that occupational and public health controls for the formaldehyde vapours released from products containing the chemical be implemented in line with the recommendation of the NICNAS PEC assessment report on formaldehyde (NICNAS 2006).

Regulatory Control

Public Health

The chemical falls within the scope of the listing of ‘formaldehyde’ in Schedule 6 and Schedule 10 of the SUSMP. Therefore, any products containing the chemical as a formaldehyde donor should be labelled in accordance with state and territory legislation (SUSMP, 2019).

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 swallowed - Cat. 4 (H302)
Irritation / Corrosivity	Not Applicable	May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)
Sensitisation	Not Applicable	May cause an allergic skin reaction - Cat. 1B (H317)
Repeat Dose Toxicity	Not Applicable	May cause damage to nervous system through prolonged or repeated exposure - Cat. 2 (H373)
Reproductive and Developmental Toxicity	Not Applicable	Suspected of damaging fertility or the unborn child - Cat. 2 (H361)

[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 the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, 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 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;
- 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.

References

European Commission (EC) 2011. Commission Regulation No 10/2011 on plastic materials and articles intended to come into contact with food, Official Journal of the European Union, L 12/1. Accessed July 2019 at https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32011R0010&from=EN#d1e889-1-1

Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Accessed at http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

Hashimoto K, Tanii H (1985). Percutaneous absorption of [14C]methacrylamide in animals. Arch Toxicol 57(2):94-98.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS), 2006. Formaldehyde (CAS No. 50-00-0). Priority Existing Chemical Secondary Notification Assessment Report No. 28. Accessed July 2019 at https://www.nicnas.gov.au

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). 2-Propenamide, N-(hydroxymethyl)-: Human health tier II assessment. Accessed July 2019 at https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessment-details?assessment_id=2038

Organisation for Economic Co-operation and Development (OECD) 2002. Methacrylamide, CAS No. 79-39-0, Screening Information DataSet (SIDS) Initial Assessment Report For Screening Infomation Assessment Meeting (SIAM) 15. Accessed July 2019 at https://hpvchemicals.oecd.org/UI/handler.axd?id=0c32cacd-95df-4ec9-b74c-

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACHa) Dossier on N-(hydroxymethyl)methacrylamide (CAS No. 923-02-4). Accessed July 2019 at https://echa.europa.eu

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACHb) Dossier on methacrylamide (CAS No. 79-39-0). Accessed July 2019 at https://echa.europa.eu

Research Toxicology Centre (RTC) 2000 S.p.A., Pomezia, Italy, Report no.: 7386-M-04499.N-methylol methacrylamide chromosome aberrations in chinese hamster ovary cells in vitro.

Safe Work Australia (SWA). Hazardous Chemical Information System (HCIS). Accessed July 2019 at http://hcis.safeworkaustralia.gov.au/

The Poisons Standard October 2019. The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) No. 25. Accessed November 2019 at https://www.tga.gov.au/publication/poisons-standard-susmp

US Environmental Protection Agency (US EPA, 2009). Substantial Risk Report Submission: 8EHQ-09-17704A. Accessed July 2019 at https://chemview.epa.gov/chemview/chemicaldata.do?sourceId=5&chemicalDataId=38162386&chemicalId=4764443

US Food&Drug Administration (US FDA, 2018). Code of Federal Regulations, Title 21, Volume 3. Revised April 1, 2018. Accessed July 2019 at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=177.1010

Last update 12 December 2019

Share this page