2-Hydroxypropyl methacrylate: Human health tier II assessment

22 November 2013

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
2-Propenoic acid, 2-methyl-, 2-hydroxypropyl ester	923-26-2
2-Propenoic acid, 2-methyl-, monoester with 1,2-propanediol	27813-02-1

Preface

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

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

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

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

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to

human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

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

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

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

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

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemical 2-propenoic acid, 2-methyl-, monoester with 1,2-propanediol (CAS No. 27813-02-1) consists of two isomers. This occurs due to the method of industrial production, which is usually either the reaction between methacrylic acid and propylene oxide, or methacrylic acid esterification of 1,2-propanediol.

The predominant isomer is the secondary alcohol 2-propenoic acid, 2-methyl, 2-hydroxypropyl ester, which is assigned the CAS No. 923-26-2, the other chemical in this group.

Therefore toxicity information for both CAS No. 923-26-2 and CAS No. 27813-02-1 is considered to be applicable to both chemicals.

Import, Manufacture and Use

Australian

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

- HPMA (CAS No. 27813-02-1) has reported domestic use as a surfactant.
- 2-HPMA (CAS No. 923-26-2) has reported domestic use as an adhesive and binding agent.
- HPMA (CAS No. 27813-02-1) has identified use as a cosmetic from Australian (M)SDS.

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; the Organisation for Economic Cooperation and Development Screening information data set International Assessment Report (OECD SIAR); Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; and eChemPortal: OECD High Production Volume chemical program—OECD HPV, the US Environmental Protection Agency's Aggregated Computer Toxicology Resource—ACToR, and the US National Library of Medicine's Hazardous Substances Data Bank—HSDB.

HPMA (CAS No. 27813-02-1) has reported cosmetic use in film forming. A maximum use concentration of 25 % in nail enhancement products has been reported (CIR, 2005).

The chemicals have reported domestic use including as:

- adhesives and binding agents;
- a surface treatment;
- paints, lacquers and varnishes; and
- fillers.

The chemicals have reported commercial use including:

- in construction materials;
- as friction agents;
- as process regulators;
- in lubricants and additives; and
- in food contact material manufacture.

The chemicals have reported site-limited use including:

- as an intermediate in polymer manufacture; and
- in laboratory chemicals.

Restrictions

Australian

No known restrictions have been identified.

International

No known restrictions have been identified.

Existing Worker Health and Safety Controls

Hazard Classification

2-HPMA (CAS No. 923-26-2) is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

Xi; R36 (Irritating to eyes)

R43 (May cause sensitisation by skin contact).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Toxicokinetics

Based on the calculated water solubility (2.09 x 10^4 mg/L at 25 °C), calculated partition coefficient (log Pow = 1.21) and the low molecular weight (<500 Da) of the chemicals, passive diffusion across the gastrointestinal tract and dermal absorption may occur. The expected irritant effects of the chemicals may increase the dermal absorption potential. The chemicals may also be absorbed through the respiratory tract.

The chemicals are absorbed from the skin. In an eight-hour radiolabelled dermal absorption study in rats, 29 % of the HPMA (CAS No. 27813-02-1) was absorbed, while 56 % of the chemical evaporated (OECD 2008).

Methacrylates are detoxified predominantly by conjugation with glutathione by the Michael addition reaction or glutathione-*S*-transferase. The ester functionality is also likely to be hydrolysed by carboxylesterases. HPMA (CAS No. 27813-02-1) is hydrolysed to methacrylic acid and 1, 2-propanediol at pH 6.5 and 37 °C catalysed by an non-specific esterase (porcine liver esterase) in vitro (OECD 2008; REACH). Methacrylates of lower molecular weight are rapidly metabolised and eliminated and are not likely to cause cumulative toxicity (Patty's Toxicology, 2012).

Acute Toxicity

Oral

The chemicals are of low acute toxicity in animal tests following oral exposure performed to a test equivalent to OECD Test Guideline (TG) 401. The median lethal dose (LD50) in rats is greater than 2000 mg/kg bw (REACH).

Dermal

HPMA (CAS No. 27813-02-1) was of low acute toxicity in animal tests following dermal exposure. The LD50 in New Zealand White rabbits is greater than 5000 mg/kg bw (REACH).

Inhalation

No data for the chemicals are available.

The results of studies conducted on a variety of methacrylates indicate that they are of low acute inhalation toxicity (Patty's Toxicology, 2012).

Corrosion / Irritation

Respiratory Irritation

Respiratory irritation has been observed in both test animals and in humans following exposure to vapours of other methacrylates (CIR, 2005). Respiratory irritation from inhaling other methacrylates is ascribed to methacrylic acid formation due to carboxylesterase hydrolysis of the methacrylate esters in the nasal tissue.

Although the mechanism of action for respiratory irritation may be relevant for the chemicals, the low volatilty of the chemicals (estimated 0.01 kPa) will limit inhalation exposure to vapours.

Skin Irritation

HPMA (CAS No. 27813-02-1) was reported to be slightly irritating to the skin in four reliable studies conducted using the Draize method in rabbits (OECD 2008; REACH). Therefore, based on the available information, the chemicals are considered to be slightly irritating to the skin.

Eye Irritation

2-HPMA (CAS No. 923-26-2) is classified as hazardous with the risk phrase 'Irritating to eyes' (Xi; R36) in HSIS (Safe Work Australia). While the available data do not directly support this classification, in the absence of more comprehensive information, there is insufficient evidence to support a recommendation to amend this classification.

In a reliable study conducted using the Draize method on HPMA (CAS No. 27813-02-1), observations at 24 hours post application included slight to moderate conjunctival redness (5 out of 6 animals) and slight opaqueness of the cornea (5 out of 6 animals). All effects were reversible after four days. Iris lesions were observed in another study but the purity of the test material (94.8 %) may have affected the result (OECD 2008; REACH).

Sensitisation

Skin Sensitisation

2-HPMA (CAS No. 923-26-2) is classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (R43) in HSIS (Safe Work Australia). The results from animal tests for HPMA (CAS No. 27813-02-1) (four guinea pig maximisation tests (GPMT) and one local lymph node assay (LLNA)) do not meet the classification criteria for a positive result. However, a weak sensitisation response was observed in two GMPT (1/10 and 3/12 animals sensitised) and in the LLNA, and cross sensitisation with other methacrylates has been observed in animals and humans (described below) (CIR 2005; OECD 2008; REACH). Overall, an amendment to this classification is not recommended.

Exposure to one methacrylate may induce sensitisation to other structurally related methacrylates, also known as skin sensitisation cross-reactivity. This has been observed with the chemical 2-HPMA (CAS No. not stated) (Rustemeyer et al, 1998). Skin sensitisation cross-reactivity by the chemicals cannot be ruled out.

Observation in humans

Patients previously exposed to methacrylates elicited positive reactions to patch tests at concentrations of the chemical as low as 0.02 % (CIR 2005; OECD 2008). While it is not clear from these results whether induction of sensitisation has resulted from the chemical alone, cross-sensitisation was indicated in individuals with prior exposure to other acrylates or methacrylates.

The human data support the classification of the chemicals for sensitisation.

Repeated Dose Toxicity

Oral

Considering the no observed-effect level (NOEL) of 300 mg/kg bw/day (both sexes) available from a combined oral repeated dose toxicity study with the reproductive/developmental toxicity screening test (OECD TG 422) using Sprague Dawley (SD) rats (CAS No. 27813-02-1), the chemicals are not considered to cause serious damage to health from repeated oral exposure (OECD 2008). Observed effects at the highest dose tested (1000 mg/kg bw/day) included salivation, decreases in locomotor activity, ptosis (drooping eyelid), changes to haematological parameters (decreased haematocrit and decrease in erythrocyte (RBC) and haemoglobin) and increased liver weights.

Dermal

No data are available.

Inhalation

No data for the chemicals are available.

Following subchronic exposures to atmospheres of excessive concentrations of acrylates and/or methacrylates, pulmonary congestion or haemorrhage and cloudy swelling and organ weight changes of the liver and kidney have been reported (Patty's Toxicology, 2012). Repeated dose inhalation toxicity from the chemicals cannot be ruled out, although the low volatilty of the chemicals (estimated 0.01 kPa) will limit inhalation exposure to vapours.

Genotoxicity

Based on the weight of evidence from the available genotoxicity studies, the chemicals are not considered to be genotoxic. While some positive test results have been reported in vitro, based on the available information the chemicals are not expected to be genotoxic in vivo.

HPMA (CAS No. 27813-02-1) tested negative in an Ames test in *Salmonella typhimurium* (strains TA 98, 100, 1535, and 1537) and *Escherichia coli* (WP2 uvrA) with and without metabolic activation at all doses (313–5000 µg/plate). In vitro studies in mammalian Chinese hamster ovary cells with and without metabolic activation reported clastogenicity and polyploidy. Clastogenicity was reported without metabolic activation at 0.35 mg/mL (continuous treatment) and 1.4 mg/mL (short-term treatment) and with metabolic activation at 0.35 mg/mL (short-term treatment). Polyploidy was reported without metabolic activation at 0.18 mg/mL (continuous treatment) and with metabolic activation at 0.35 mg/mL (short-term treatment) (CIR 2005; OECD 2008).

HPMA (CAS No. 27813-02-1) was negative in an in vivo micronucleus assay (OECD TG 474) to the maximum tolerated dose (OECD 2008; REACH). This chemical was also reported to be negative in combined in vivo micronucleus and Comet assays in liver and at the site of first contact (stomach) (EFSA 2012). The bioavailability of the chemical was demonstrated in vivo.

The results of mutagenicity studies on various methacrylates have been evaluated (Johannsen et al., 2008). In general, it was found that methacrylates were negative in bacterial reverse mutation assays (and other in vitro mammalian point mutation assays) and while positive results were noted in in vitro mammalian clastogenicity assays, the results of in vivo assays were negative.

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Based on the information available, the chemicals are not expected to show specific reproductive or developmental toxicity.

In the above-mentioned combined oral repeated dose toxicity study (OECD 2008) with the reproductive/developmental toxicity screening test (OECD TG 422) using SD rats, no adverse effects were observed; HPMA (CAS No. 27813-02-1) is not considered to cause serious damage to reproduction and development.

Based on the results of a study reported in CIR (2005), a reported NOAEL of 1000 mg/kg bw/day was determined for reproductive and developmental toxicity. No adverse effects on the reproductive parameters of the parental males or developmental parameters of the offspring were reported.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include local effects (skin sensitisation). The chemicals may also cause skin and eye irritation. Skin sensitisation cross reactivity may occur following exposure to other structurally related methacrylates.

The low volatility of the chemicals limit the potential for respiratory irritation.

Public Risk Characterisation

Use of HPMA (CAS No. 27813-02-1) in cosmetic products in Australia at concentrations up to 10 % has been identified. HPMA (CAS No. 27813-02-1) is reported to be used in cosmetic/domestic products overseas at concentrations up to 25 %.

The main route of public exposure is expected to be through the skin, although the rate of polymerisation would be expected to limit the extent of the exposure (CIR, 2005). When used in nail enhancement products, short-term small volume skin contact in the immediate vicinity of the fingernail may occur. Exposure is considered more probable for home use of the chemicals than in salon use by trained personnel. Dermal exposure to other parts of the body may occur during domestic use. The low volatility of the chemicals limit the potential for exposure through vapour inhalation.

The Cosmetic Ingredient Review concluded that the chemicals ‘are safe to use in nail enhancement products when skin contact is avoided. Products containing these ingredients should be accompanied with directions to avoid skin contact, because of the sensitising potential of methacrylates’ (CIR, 2005).

There are currently no labelling requirements for products containing the chemicals. Therefore, in the absence of any regulatory controls, the characterised critical health effects (sensitisation) have the potential to pose an unreasonable risk under the domestic and cosmetic uses identified.

The EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids concluded that there is no safety concern for the consumer if HPMA (CAS No. 27813-02-1) is used as monomer in acrylic resin coatings for food cans, and cured at a temperature of at least 200 °C (EFSA 2012). The use of the chemicals in food contact material is not considered to pose an unreasonable risk to the public.

Occupational Risk Characterisation

During product formulation, dermal and ocular exposure of workers to the chemical may occur, particularly where manual or open processes are used. These may include transfer and blending activities, quality control analysis, and cleaning and maintenance of equipment. Worker exposure to the chemical at lower concentrations may 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 local health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise dermal exposure to the chemical are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine appropriate controls.

Based on the available data, the hazard classification in HSIS for CAS No. 923-26-2 is considered appropriate. However, the data available support including the hazard classification in HSIS for CAS No. 27813-02-1 (refer to **Recommendation section**).

The chemical is stable in the presence of an inhibitor. High temperatures, inhibitor depletion, accidental impurities, or exposure to radiation or oxidising agents may cause spontaneous polymerisation reactions generating heat/pressure. Closed containers may rupture or explode during runaway polymerisation.

NICNAS Recommendation

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

Assessment of the chemical is considered to be sufficient provided that risk management recommendations are implemented and all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

Appropriate scheduling and labelling should be undertaken to mitigate risk for the chemicals use in both domestic and cosmetic products. Due to the toxicity profile at concentrations reported to be in use, this chemical should be considered for listing in Schedule 5 of the SUSMP, consistent with the Scheduling Policy Framework guidelines. Matters to be taken into consideration include:

- skin sensitisation which may occur following exposure to other structurally related methacrylates;
- the respiratory irritation effects observed with other methacrylates is limited by the low volatility of the chemicals; and
- the Cosmetic Ingredient Review recommendation that products containing the chemicals should be accompanied with directions to avoid skin contact.

Work Health and Safety

The chemicals are recommended for classification and labelling under the current approved criteria and adopted GHS as below (this is the existing classification for CAS No. 923-26-2, which should also be applied to CAS No. 27813-02-1). This assessment does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to eyes (Xi; R36)	Causes serious eye irritation - Cat. 2A (H319)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)

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

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

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

Advice for consumers

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

Advice for industry

Control measures

Control measures to minimise the risk from dermal and ocular exposure to the chemical(s) 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:

- 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 assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and

- managing risks arising from storing, handling and using a hazardous chemical.

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

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

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

References

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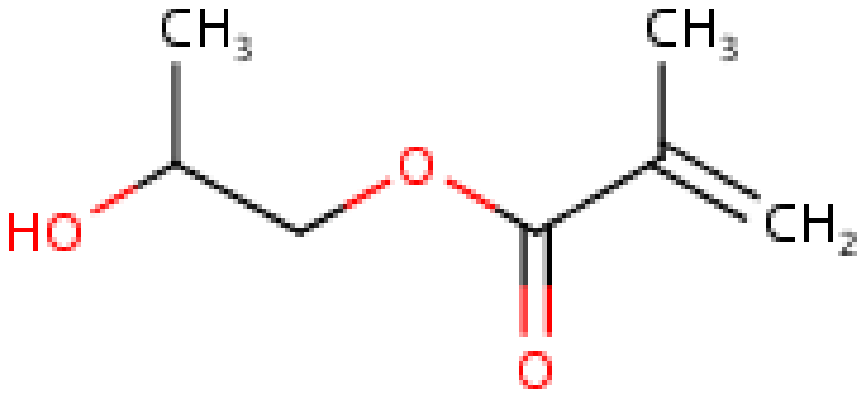
Rustemeyer T, de Groot J, von Blomberg E, Frosch PJ& Scheper RJ 1998. Cross-reactivity patterns of contact-sensitizing methacrylates. Toxicol. Appl. Pharm. 148: 83-90.

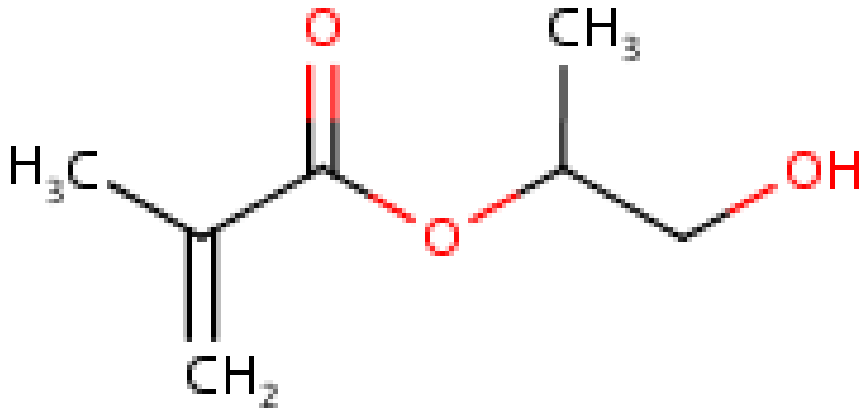
Last Update 22 November 2013

Chemical Identities

Chemical Name in the Inventory and Synonyms	**2-Propenoic acid, 2-methyl-, 2-hydroxypropyl ester** 2-Hydroxypropyl methacrylate Methacrylic acid, 2-hydroxypropyl ester 1,2-Propanediol, 1-methacrylate 2-HPMA
CAS Number	923-26-2
Structural Formula	

	
Molecular Formula	C7H12O3
Molecular Weight	144.17

Chemical Name in the Inventory and Synonyms	**2-Propenoic acid, 2-methyl-, monoester with 1,2-propanediol** Hydroxypropyl methacrylate Methacrylic acid, monoester with 1,2-propanediol 2-Methyl-2-propenoic acid monoester with 1,2-propanediol 1,2-Propylene glycol methacrylate HPMA
CAS Number	27813-02-1
Structural Formula	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