2-Propenoic acid, 2-methyl-, methyl ester: Human health tier II assessment

11 April 2014

CAS Number: 80-62-6

Preface

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

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

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

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

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

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

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted

and published separately, using information available at the time, and may be undertaken at different tiers.

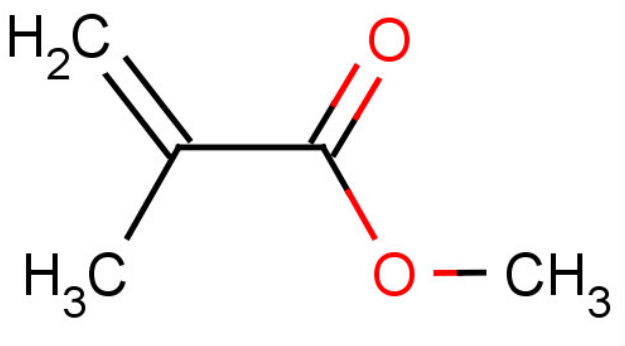
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	methyl methacrylate monomer methacrylic acid, methyl ester 2-methylacrylic acid methyl ester methyl 2-methyl-2-propenoate MMA
Structural Formula	
Molecular Formula	C5H8O2
Molecular Weight (g/mol)	100.12
Appearance and Odour (where available)	Colourless volatile liquid with a characteristic odour described as fragrant, fruity, acrid and pungent, or onion-like.
SMILES	C(=O)(C(=C)C)OC

Import, Manufacture and Use

Australian

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

The chemical has reported cosmetic use:

- in fingernail enhancement products such as nail polish and acrylic gel.

Reported domestic use including:

- in adhesives, caulks and sealants; and
- in floor polishes.

Reported commercial use including:

- in formulating polyester gelcoats and flowcoats used in manufacturing fibreglass.

Reported site-limited use including:

- in producing acrylic copolymer emulsions for paints, resins, textiles and non-woven fabrics.

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

International

The following international uses have been identified through the Organisation for Economic Cooperation and Development Screening information data set International Assessment Report (OECD 2001), the European Commission Cosmetic Substances and Ingredients (CosIng) database, United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) directory and other data sources via eChemPortal including the Aggregated Computer Toxicology Resource (ACToR), and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

Reported cosmetic use as:

- anticaking and opacifying agents;
- artificial nail builders; and
- dispersing agents (non-surfactant).

Reported domestic use including in:

- adhesives and binding agents;
- cleaning/washing agents;
- fillers;
- colouring agents;
- paints, lacquers and varnishes;
- surface−active agents; and
- surface treatment.

The chemical has reported domestic uses in the Substances and Preparations in the Nordic countries (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.

Reported commercial use including:

- as corrosion inhibitors;
- in insulating materials;
- in producing polymers, acrylics and resins;
- as absorbents and adsorbents;
- in lubricants and additives;
- as photographic and reprographic chemicals;
- in process regulators; and
- in solvents and viscosity adjustors.

Reported site-limited use including:

- as an intermediate; and
- as a laboratory chemical.

Restrictions

Australian

The chemical is listed in The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons—SUSMP (SUSMP, 2013) under the following Schedules:

Appendix C

'For cosmetic use **except** in preparations containing ≤1 % of the chemical as residual monomer in a polymer.' (SUSMP, 2013)

'Appendix C substances are poisons prohibited from sale, supply or use because of their known potential for harm to human and/or animal health.' (SUSMP, 2013)

Schedule 6

'The chemical (excluding its derivatives) **except**:

(a) for cosmetic use; or

(b) in preparations containing ≤1 % of the chemical as residual monomer in a polymer.' (SUSMP, 2013)

'Schedule 6 substances are considered to be poisons 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.' (SUSMP, 2013)

International

Cosmetics

- Canada list of prohibited and restricted cosmetic ingredients ("Hotlist").
- International Fragrance Association (IFRA) Standards—Prohibited substance.

- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain.

Food packaging

Europe Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food—Annex I: Substances: specific migration limit (SML) of 6 mg/kg.

Existing Work Health and Safety Controls

Hazard Classification

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

Xi; R37/38 (irritating to respiratory system and skin)

Xi; R43 (may cause sensitisation by skin contact)

Exposure Standards

Australian

The chemical has an exposure standard of 50 ppm (208 mg/m³) time weighted average (TWA) and 100 ppm (416 mg/m³) short-term exposure limit (STEL) (Safe Work Australia).

International

The following exposure standards are identified (Galleria Chemica):

TWA: 50 ppm (210 mg/m³) [Austria, Belgium, United Kingdom, Switzerland, South Africa, New Zealand, Canada (Alberta)]

TWA: 100 ppm (410 mg/m³) [Argentina, Singapore, USA (Michigan, Vermont, Washington)]

STEL: 100 ppm (420 mg/m³) [Austria, Belgium, UK, Switzerland, South Africa, New Zealand, Canada (Alberta)]

STEL: 125 ppm (510 mg/m³) [Argentina]

STEL: 150 ppm [USA (Washington)]

Health Hazard Information

Toxicokinetics

The chemical is readily absorbed into the blood following oral, dermal and inhalation exposure and it is rapidly metabolised to methacrylic acid and eventually to carbon dioxide via the body's tricarboxylic acid (TCA) cycle (US EPA, 1998; OECD, 2001; HSDB).

Acute Toxicity

Oral

The chemical had low oral acute toxicity in animal tests. The oral median lethal dose (LD50) values in rats, mice and rabbits were reported to be >5000 mg/kg bw (OECD, 2001).

Dermal

The chemical had low dermal acute toxicity in animal tests. The dermal LD50 in rabbits was reported to be >5000 mg/kg bw (OECD, 2001).

Inhalation

The chemical had low acute inhalation toxicity in animal tests. The median lethal concentration (LC50) in rats was reported to be >25 mg/L following four hours of exposure. No mortalities or toxic effects were observed (OECD, 2001).

Corrosion / Irritation

Respiratory Irritation

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

In an acute inhalation study in rats exposed to 100 ppm (410 mg/m³) for two or more hours, irritating effects in the respiratory tract were reported (ECB, 2002). Inflammatory degeneration of the nasal epithelium was also observed in rats exposed to the chemical at 410 mg/m³ for two years (OECD, 2001; HSDB).

Skin Irritation

The chemical is classified as hazardous with the risk phrase 'Irritating to skin' (Xi; R38) in HSIS (Safe Work Australia). The available data from animal studies and observations in humans support this classification.

The chemical is reported to be a severe irritant when applied undiluted to rabbit skin (OECD, 2001; ECB, 2002). In a range-finding study conducted in rabbits, the chemical was applied dermally under occluded conditions for 24 hours at doses of 200, 2000, or 5000 mg/kg. Erythema and some oedema within 72 hours were observed along with dessication, blanching, and eschar formation. In the 2000 and 5000 mg/kg group, well-defined to severe erythema with blanching and moderate to severe oedema, which developed at 24 hours, were still present in the animals until day 14 (Rohm & Haas, 1982). A single dose of 10 mL/kg of the chemical applied to the clipped abdomen of rabbits was reported to produce temporary local irritation and the animals recovered within an hour. Another study reported slight reaction in rabbit skin following the topical application of the chemical for 15 days to shaved skin (US EPA, 1998). However, two other studies of the chemical applied to rabbit skin report no irritation (REACH).

Eye Irritation

The chemical was reported to slightly irritate the eyes of rabbits when tested according to OECD Test Guideline (TG) 405 (OECD, 2001). The effects were not sufficient to warrant hazard classification.

Observation in humans

Workers exposed to the chemical have reported cases of skin and respiratory irritation including asthmatic reactions, local neurological symptoms, irritations and local dermatological reactions, with respiratory irritation occurring at concentrations lower than 112 ppm (US EPA, 1998; OECD, 2001; HSDB).

Topical treatment with 5 % of the chemical caused erythema and eczematous dermatitis in 18/20 volunteers (Nyquist, 1958). In another study, after a 48-hour skin exposure to cotton pellets saturated with the chemical, mild erythema was observed in one third of the volunteers (Spealman et al., 1945).

Sensitisation

Respiratory Sensitisation

Available data from observations in humans (below) indicate that the chemical is unlikely to cause respiratory sensitisation.

Skin Sensitisation

The chemical is classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (Xi; R43) in HSIS (Safe Work Australia). The available data from animal studies and observations in humans support this classification.

The positive sensitisation results reported when tested in guinea pigs according to OECD TG 406 support this classification. An intradermal induction concentration of 5 % of the chemical, topical induction with 100 % and challenge with 1 % and 5 % of the chemical, showed a 10 % and 50 % positive sensitisation rate, respectively (US EPA, 1998; OECD, 2001; HSDB).

Observation in humans

There are numerous human clinical reports of skin sensitisation and local dermatological reactions following exposure to the chemical (HSDB).

In a 48-hour occlusive human patch test in 20 volunteers followed by a challenge test on day 19, two positive skin reactions were observed after 48 hours followed by a third positive reaction after 10 days, showing lymphocyte infiltration (Cavelier et al., 1981). After exhibiting mild skin irritation following cotton pellets saturated with the chemical, 10/21 affected individuals showed skin erythema four days after exposure to the chemical at another site (Spealman et al., 1945).

Human exposure during acrylic cast sheet production of up to 50 ppm of the chemical with a mean exposure time of 9.6 years showed no association with respiratory symptoms or olfactory dysfunction (ECB, 2002; US EPA, 1998). In another study to determine if occupational asthma is associated with exposure to the chemical in an acrylic factory, no significant dose-response correlation could be determined (US EPA, 1998).

Repeated Dose Toxicity

Oral

The chemical is not considered to cause serious damage to health following repeated oral exposure.

In a two-year study in rats exposed to the chemical through drinking water, a no observed effect level (NOEL) of 146 mg/kg bw/day was established. Body weight depression and reduction in fluid consumption were observed. However, these effects did not persist throughout the study and were considered as temporary non-adverse effects. Significantly increased kidney weight ratios were observed in female rats only. However, no substance-related effects were reported in histopathological examinations. Therefore the effect was not considered to be biologically relevant (OECD, 2001; REACH). Several other studies in rats reported lowest observed adverse effect level (LOAEL) values of 500 mg/kg bw/day following oral administration. Effects that were observed included impaired learning and locomotor activity as well as aggressive behaviour (REACH).

Dermal

No data are available.

Inhalation

In inhalation studies, respiratory tract effects were seen from 100 ppm, while systemic effects such as changes in body weight were seen from 500 ppm. At doses >500 ppm, effects were seen in the liver, kidneys, spleen, bone marrow and central nervous system (US EPA, 1998; REACH).

Genotoxicity

The chemical is not considered to be a mutagen.

The chemical did not cause mutagenic effects in in vitro studies using a bacterial system (*Salmonella typhimurium* strains TA 1535, TA 98 and TA 100 reverse mutation assay, with or without metabolic activation), but did cause mutagenic and clastogenic effects in in vitro studies using mammalian cells. However, no mutagenic effects were induced in in vivo studies using mice (micronucleus assay and dominant lethal assay) (HSDB; REACH).

Carcinogenicity

The International Agency for Research on Cancer (IARC) has classified the chemical as 'Unclassifiable as to carcinogenicity in humans' (Group 3)**.** There is no evidence at present that it causes cancer in humans (IARC, 1994). The evidence from the literature, including studies in rats and mice using the OECD TG 451, which resulted in no treatment related tumours, support this IARC classification (US EPA, 1998; REACH; HSDB; OECD, 2001).

Reproductive and Developmental Toxicity

Based on the information available, the chemical is not likely to be a reproductive or developmental toxicant. The no observed adverse effect level (NOAEL) for developmental toxicity in rats is reported to be 400 mg/kg bw/day (the highest dose tested) (REACH). There was no reduction in fertility reported in a dominant lethal assay in mice exposed to the chemical at concentrations up to 36,900 mg/m³ and no adverse effects on reproductive organs in repeated dose studies (HSDB).

Additionally, no teratogenicity, embryotoxicity or foetotoxicity was observed at exposure levels up to and including 2000 ppm (8425 mg/m³) in an inhalation study of rats conducted according to OECD Guideline 414 (OECD, 2001).

Other Health Effects

Neurotoxicity

Available data on the neurotoxicity of the chemical are limited, although, in one study, impaired locomotor activity and learning and behavioural effects on the brain were observed in rats exposed orally to 500 mg/kg bw/day for 21 days (HSDB). There have been several reported cases of reactions in individuals exposed to the chemical for short periods during mixing of the monomer and polymer. Typical nervous system symptoms included headache, lethargy, lightheadedness, and a sensation of heaviness in the arms and legs (US EPA , 1998).

Risk Characterisation

Critical Health Effects

The critical health effect for risk characterisation is the local effect of skin sensitisation. The chemical may also cause respiratory tract irritation, skin irritation and slight eye irritation.

Public Risk Characterisation

The chemical is currently listed on Schedule 6 (except for cosmetic use or in preparations containing ≤1% of the chemical as a residual monomer in a polymer) and Appendix C for cosmetic use (except in preparations containing ≤1% of the chemical as a residual monomer in a polymer).

Provided that normal precautions are taken to avoid prolonged skin contact, the risk to the public posed by domestic products containing the chemical is not considered to be unreasonable at concentrations below 1 %. At higher concentrations, potential harm is reduced by using strong warnings and safety directions on the label, including: '(Over) (Repeated) exposure may cause sensitisation'; and 'Use only in well ventilated area' (SUSMP, 2012).

The current controls are considered adequate to minimise the risk to public health posed by domestic and cosmetic products containing this chemical. Therefore the risk to public health is not considered unreasonable.

Occupational Risk Characterisation

During product formulation, inhalation 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 maintaining 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 worker practices employed.

Given the critical health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise 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 is considered appropriate.

NICNAS Recommendation

Current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

Regulatory Control

Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2013).

Work Health and Safety

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

physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to skin (Xi; R38)* Irritating to respiratory system (Xi; R37)*	Causes skin irritation - Cat. 2 (H315) May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)
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 label instructions.

Advice for industry

Control measures

Control measures to minimise the risk from exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

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

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

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

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