Acetic acid, mercapto-, methyl ester: Human health tier II assessment

18 September 2014

CAS Number: 2365-48-2

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

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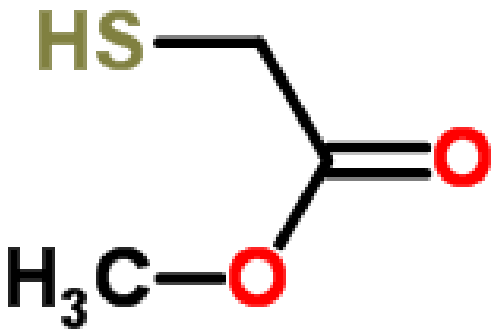
Acronyms & Abbreviations

Chemical Identity

Synonyms	Methyl thioglycolate Methyl mercaptoacetate Acetic acid, 2-mercapto-, methyl ester MTG
Structural Formula	
Molecular Formula	C3H6O2S
Molecular Weight (g/mol)	106.15
Appearance and Odour (where available)	Clear, colourless liquid with a stench
SMILES	C(=O)(CS)OC

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 European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; the Organisation for Economic Cooperation and Development Screening Information Dataset Initial 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 Computational Toxicology Resource (ACToR), and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic use with the function of hair waving or straightening (CosIng). However, no documented use of the chemical in cosmetics in the US was identified (Burnett et al., 2009; Personal Care Products Council, 2011).

No domestic uses were identified.

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

Restrictions

Australian

No known restrictions have been identified.

Mercaptoacetic acid and its salts are listed in the *Poisons Standard (Standard for the Uniform Scheduling of Medicines and Poisons*—SUSMP) in Schedules 6 and 5 (Department of Health, 2014). These entries exclude derivatives and therefore the chemicals in this group are not covered by these entries.

International

The chemical is listed on the following (Galleria Chemica):

- EU Regulation (EC) No 1223/2009 Annex III: List of substances which cosmetic ingredients must not contain except subject to the restrictions laid down (reference 2b; thioglycolic acid esters);
- New Zealand: Cosmetic Products Group Standard—Schedule 5: Components cosmetic products must not contain except subject to the restrictions and conditions laid down; and
- Association of Southeast Asian Nations (ASEAN): Cosmetic Directive Annex III, part 1: List of substances which cosmetic products must not contain except subject to restrictions and conditions.

In the above listed directives the maximum allowable concentration of the mercaptoacetate esters (measured as mercaptoacetic acid) in preparations is limited according to the type of cosmetic product:

- Hair products for waving or straightening:

(a) General use (8 %; pH 6 to 9.5);

(b) Professional use (11 %; pH 6–9.5);

Labelling requirements are specified for all these uses.

The Expert panel of the Cosmetic Ingredient review (CIR) recommended that several mercaptoacetates including MTG are safe for use in hair straighteners, permanent waves, tonic, dressings, etc., wave sets, other non-colouring hair products, and hair dyes and colours at concentrations up to 15.4% (as thioglycolic acid); but hairdressers should avoid contact and minimise consumer skin exposure (Burnett et al., 2009).

Existing Work Health and Safety Controls

Hazard Classification

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

Exposure Standards

Australian

No specific exposure standards are available for the chemical.

International

No specific exposure standards are available for the chemical.

Health Hazard Information

Limited data are available for the chemical. With the exception of developmental toxicity, data for the mercaptoacetate esters [ethylhexyl thioglycolate (CAS NO. 7659-86-1) and isooctyl thioglycolate (CAS No. 25103-09-7)] are considered representative of the toxicity of the chemical for endpoints for which there are data available. The chemical is hydrolysed in the body to form the parent alcohol (methanol) and mercaptoacetate anion. Therefore, where available, data from the parent alcohol and mercaptoacetic acid and its salts have also been considered as suitable analogues for systemic effects, particularly for longer term toxicity.

Toxicokinetics

No experimental data are available for the chemical. However, observed acute toxicity indicates that the chemical is significantly absorbed via oral route and to a certain extent by dermal route. The chemical is expected to be initially hydrolysed in several tissues by carboxylesterases to thioglycolic acid and the corresponding alcohol (methanol) (OECD, 2010).

Acute Toxicity

Oral

The chemical has moderate acute toxicity based on results from an animal test following oral exposure. A hazard classification is recommended based on the available data (refer to **Recommendation** section).

The median lethal dose (LD50) in rats administered the chemical ranged from 92-209 mg/kg bw. Observed sub-lethal effects included weakness, inactivity, prostration, tremors and rough coats (HSDB; US EPA, 1992).

Dermal

The chemical has moderate acute toxicity based on results from animal tests following oral exposure. A hazard classification is recommended based on the available data (refer **Recommendation** section).

The LD50 in guinea pigs administered the chemical was reported to be between 500 and 1000 mg/kg bw. In a separate study, covered application of the chemical (no dose specified) to the shaved skin of six guinea pigs (sex unspecified) for 24 hours resulted in death in 4/6 animals. Sub-lethal effects included necrosis, slight to moderate oedema and erythema (US EPA, 1992).

Inhalation

No data are available for the chemical.

Corrosion / Irritation

Respiratory Irritation

No data are available.

Skin Irritation

No data are available for the chemical.

Based on the available data for the other mercaptoacetate esters (NICNASc), the chemical is considered to be at most a slight skin irritant. Effects observed were not sufficient to warrant a hazard classification.

Eye Irritation

No data are available for the chemical.

Based on the available data for the other mercaptoacetate esters (NICNASc), the chemical is considered to be at most a slight eye irritant. Effects observed were not sufficient to warrant a hazard classification.

Sensitisation

Skin Sensitisation

No data are available for the chemical. Given the positive sensitisation result for the other mercaptoacetate esters and the known sensitisation potential in humans of mercaptoacetate salts, the chemical is considered to be a skin sensitiser. Classification of this chemical is warranted (refer to the **Recommendation** section).

Two other mercaptoacetate esters (CAS No. 25103-09-7 and 7659-86-1) tested positive in guinea pig maximisation tests (NICNASc).

Mercaptoacetate salts tested positive in local lymph node assay (LLNA) and guinea pig maximisation tests (NICNASa). In humans, formulations containing the salts of mercaptoacetic acid, particularly ammonium mercaptoacetate (CAS No. 5421-46-5), gave positive results for skin sensitisation in several studies (NICNASa).

Repeated Dose Toxicity

Oral

Limited data are available for the chemical. Given that the effects observed from the available study (albeit a shorter duration than a standard 28 or 90-day study) are consistent with those observed in guideline studies with sodium mercaptoacetate, classification is considered warranted under GHS (refer to the **Recommendation** section).

In a subacute oral toxicity study, rats were administered the chemical by gavage (0, 10, 100, or 300 mg/kg bw) over a 15-day period. At 300 mg/kg bw, 3/5 rats died and two were sacrificed as moribund; no deaths were seen in the other groups. Clinical signs included inactivity, weakness, prostration, dehydration, hypothermia, and tremors. At 300 mg/kg bw, histopathological changes included haemorrhagic stomachs (3/5), unilateral testicular atrophy (2/5), atrophy of adipose tissue (4/5), discoloured liver (4/5), and spleen (1/5), corneal opacity (1/5) and lymphocytic necrosis of the thymus (5/5). Effects on the blood and urine chemistry were also noted (details not available). In the liver, lipoid degeneration (5/5), hepatocyte hypertrophy (5/5) and nucleolar alterations (3/5) were seen. In the kidney, vacuolation and glomerular casts (4/5) and degeneration of the tubules (5/5) were also seen. At 100 mg/kg bw, eosinophilic cytoplasmic changes in the liver (4/5) were the only histopathological effects. No dose-related effects were seen at the lowest dose (US EPA, 1992).

Although limited study details were available, effects observed (changes in blood chemistry and histopathological changes in the kidney and liver) appear consistent with those observed for mercaptoacetate salts (NICNASa). The observations of blood biochemistry, in conjunction with microscopic histopathological changes in the liver, following exposure to sodium mercaptoacetate, are consistent with a mode of toxic action where β-oxidation of fatty acids is inhibited, leading to higher concentrations of triglycerides in the liver (NICNASa).

Although longer chain alkyl mercaptoacetate esters are not classified for repeated dose toxicity (NICNASc), given the higher acute toxicity of the chemical compared to these esters, adverse effects following repeated dose toxicity cannot be discounted. In the absence of further data, classification consistent with mercaptoacetate salts (NICNASa) is warranted for this chemical.

Dermal

No data are available for the chemical.

Inhalation

No data are available for the chemical.

Genotoxicity

No data are available for the chemical.

Based on the weight of evidence from the available studies for the rapidly produced metabolites (mercaptoacetate ion and methanol) and the other mercaptoacetate esters, the chemical is not considered to be genotoxic (NICNASa; NICNASb; NICNASc).

Carcinogenicity

No data are available for the chemical.

Data available for the rapidly produced metabolites (mercaptoacetate ion and methanol) and the other mercaptoacetate esters, indicates that the chemical is not likely to be carcinogenic (NICNASa; NICNASb, NICNASc).

Reproductive and Developmental Toxicity

No data are available for the chemical.

The data available for the rapidly produced metabolites (mercaptoacetate ion and methanol) indicate that the chemical is not likely to cause reproductive or developmental toxicity (NICNASa; NICNASb).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include local effects (skin sensitisation) and systemic acute effects (acute toxicity by the oral and dermal exposure). The chemical may also cause systemic effects following repeated exposure.

Public Risk Characterisation

International information indicates that the chemical is not likely to be widely available for domestic and cosmetic use (refer **Import, manufacture and use** section). Hence, the public risk from these chemicals is not considered to be unreasonable.

Additional regulatory controls could be required should information become available to indicate that the chemicals is used in domestic and cosmetic products in Australia.

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 health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise dermal exposure to the chemicals 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.

The data available support an amendment to the hazard classification in the HSIS (refer to the **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.

Additional regulatory controls could be required should information become available to indicate that the chemical is used in domestic and cosmetic products in Australia.

Regulatory Control

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Toxic if swallowed (T; R25) Harmful in contact with skin (Xn; R21)	Toxic if swallowed - Cat. 3 (H301) Harmful in contact with skin - Cat. 4 (H312)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)
Repeat Dose Toxicity		May cause damage to organs through prolonged or repeated exposure - Cat. 2 (H373)

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

- using closed systems or isolating operations;
- health monitoring for any worker who is at risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health;
- 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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