3(2H)-Isothiazolone, 5-chloro-2-methyl-, hydrochloride: Human health tier II assessment

08 March 2019

CAS Number: 26530-03-0

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.

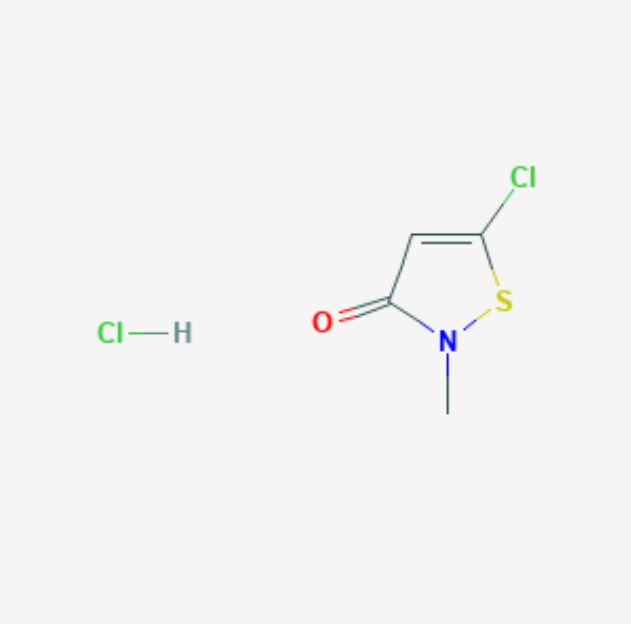
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	5-chloro-2-methyl-4-isothiazolin-3-one hydrochloride 5-chloro-2-methylisothiazolin-3-one hydrochloride 3(2H)-isothiazolone, 5-chloro-2-methyl-, hydrochloride (1:1) 5-chloro-2-methylisothiazol-3(2H)-one hydrochloride
Structural Formula	
Molecular Formula	C4H4ClNOS.ClH
Molecular Weight (g/mol)	186.1
Appearance and Odour (where available)	yellow liquid

SMILES	C1(=O)C=C(Cl)SN1C_Cl

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information was reported for the chemical under previous voluntary and/or mandatory calls for information. - The chemical is the salt of methylchloroisothiazolinone (MCI, CAS No. 26172-55-4), which is widely used in Australia as a preservative in cosmetic, personal care (including baby products), cleaning and laundry products (NICNAS). The parent chemical, MCI is generally used as a 3:1 mixture of methylchloroisothiazolinone

and methylisothiazolinone (MCI/MI, CAS No. 55965-84-9). It is expected that the chemical may be used in similar products. However, the chemical has now been reported to have domestic use as a preservative in paint formulations.

International

No specific use information is available on the chemical other than its listing by several chemical supply companies as a preservative. The CAS No. is not listed in the US Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) directory (Personal Care Products Council), the European Commission Cosmetic Substances and Ingredients (CosIng) database, or in the United States Household Products Database (US HPD).

However, uses identified for the parent chemical (CAS No. 26530-03-0) are considered relevant to the chemical. The parent chemical, MCI, has reported use in a range of rinse-off and leave-on cosmetic products and in home maintenance and cleaning products. The chemical also has reported commercial, site-limited and non-industrial uses (NICNAS).

Restrictions

Australian

The chemical is not individually listed in *the Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP). However, it is covered under the entry for the parent chemical methylchloroisothiazolinone (MCI) in Schedule 6, as its salt.

METHYLISOTHIAZOLINONE except:

a) in rinse off cosmetic preparations or therapeutic goods intended for topical rinse–off application containing 0.0015 per cent or less of methylchloroisothiazolinone and methylisothiazolinone in total; or

b) in other preparations that are not intended for direct application to the skin containing 0.1 per cent or less of methylchloroisothiazolinone and methylisothiazolinone in total.

Schedule 6 chemicals are described as 'Poison – 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' (SUSMP, 2019).

International

No restrictions were identified for the chemical.

The use of the parent chemical, MCI is currently restricted:

- in the EU with a maximum authorised mixture concentration of 0.0015 %;

- in Canada it is only permitted in combination with methylisothiazolinone (MI, CAS No. 2682-20-4) in rinse-off products only at 0.0015% (15 µg/mL or 15 ppm) and is not permitted in leave-on products; and

- in United States of America at a concentration of 15 ppm MCI/MI (76.7 % MCI and 23.3 % MI) for cosmetic rinse-off products and =7.5 ppm in cosmetic leave-on products (NICNAS).

Existing Work Health and Safety Controls

Hazard Classification

The chemical, 3(2H)-isothiazolone, 5-chloro-2-methyl-, hydrochloride is classified as hazardous with the following hazard categories and hazard statement for human health in the Hazardous Chemicals Information System (HCIS) (Safe Work Australia). This classification is based on the recommended amendment to the hazard classification in the HCIS from the IMAP assessment published in Tranche 20.

Acute toxicity – Category 3; H301 (Toxic if swallowed)

Acute toxicity – Category 3; H311 (Toxic in contact with skin)

Acute toxicity – Category 2; H330 (Fatal if inhaled)

Skin sensitisation – Category 1; H317 (May cause an allergic skin reaction)

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available for the chemical.

The following exposure standards were identified for MCI (NICNAS):

- an exposure limit—TWA of 0.2 mg/m^3 and STEL of 0.4 mg/m^3 was identified in Switzerland.

Health Hazard Information

No specific toxicity data were available for the chemical. The chemical is the salt of methylchloroisothiazolinone (MCI, CAS No. 26172-55-4). Using read-across principles (OECD, 2007) data from the parent chemical was used for the toxicity assessment. This report should be read in conjunction with the Tier II assessment of the parent chemical- MCI, which can be accessed at https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessment-details?assessment_id=1066

The critical health effect for the parent chemical is sensitisation. Positive results were reported in several animal tests (guinea pig maximisation tests, Buehler test and local lymph node assays). The chemical and a 3:1 mixture of methylchloroisothiazolinone and methylisothiazolinone (MCI/MI, CAS No. 55965-84-9) are reported to be sensitisers at low concentrations in both cosmetic and occupational settings with a strong potential to cause skin sensitisation in human patch tests (NICNAS). Airborne allergic contact dermatitis following non-occupational exposures to isothiazolinones in water-based paints has been reported (Lundov et al., 2014; Aerts et al., 2017; Amsler et al., 2017). Based on the available information, the chemical is recommended for classification as a sensitiser.

The parent chemical was classified as hazardous for systemic acute toxicity (toxic by all routes of exposure) based on animal test data for the analogue chemical (MCI/MI, CAS No. 55965-84-9) (NICNAS). Based on this, the chemical is acutely toxic (by all route of exposure) and warrants classification.

Whilst the parent chemical was also classified for skin corrosion and possibly serious eye damage, these severe irritant effects cannot be read across to the salt.

The key issue driving the need to regulate the parent chemical (MCI) by scheduling was its sensitisation potential. Following the recommendation from the Tier II IMAP assessment report for MCI, this chemical was added to Schedule 6 of *Poisons Standard —the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) (SUSMP, 2019).

Risk Characterisation

Critical Health Effects

Based on information for the parent chemical, the critical health effect for risk characterisation is skin sensitisation. The chemical may also cause systemic acute toxicity (by all routes of exposure).

Public Risk Characterisation

The chemical is currently listed (as a derivative of methylchloroisothiazolinone) on Schedule 6 of the Poisons Standard (SUSMP, 2019).

Direct exposure to paint formulations containing the chemical and several other isothiazolinones have resulted in allergic reactions (see **Skin sensitisation: Observation in humans** section). Currently, there are no restrictions in Australia on using the chemical and several other isothiazolinones in paint formulations. Further characterisation of the risks from the use of the chemical and other isothiazolinones as a preservative in water-based paint formulations should be examined. In the absence of any regulatory controls, the characterised critical health effect of skin sensitisation has the potential to pose an unreasonable risk when used as a preservative in paint formulations.

Occupational Risk Characterisation

During product formulation, dermal, ocular and 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 of equipment. Worker exposure to the chemical at lower concentrations can also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

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

NICNAS Recommendation

The chemical is recommended for Tier III assessment to further characterise the risks from its use in domestic products. The Tier III assessment would consider the risks and appropriate concentration limits to manage the risks from the use of the chemical and other isothiazolinones as preservatives in paint formulations.

Regulatory Control

Public Health

At present, the chemical falls within the scope of the listing of methylchloroisothiazolinone (MCI, CAS No. 26172-55-4) on Schedule 6 of the Poisons Standard. Therefore, products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2019).

The need for further regulatory control for public health will be determined as part of the Tier III assessment.

Work Health and Safety

The chemical is classified as hazardous for human health in the Hazardous Chemicals Information System (HCIS) (Safe Work Australia).

Note that the classification below was based on the recommended amendment to the hazard classification in the HCIS from the IMAP assessment published in Tranche 20, as discussed in the **Health Hazard Information** section of this report.

This updated assessment report does not change the recommended classifications (see Existing Work Health and Safety Controls). 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	Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) Fatal if inhaled - Cat. 2 (H330)
Sensitisation	Not Applicable	May cause an allergic skin reaction - Cat. 1 (H317)

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

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

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

Advice for 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, ocular, and inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend

on the physical form and the manner in which the chemicals are used. Examples of control measures which may minimise the risk include, but are not limited to:

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

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

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

Obligations under workplace health and safety legislation

Information in this report should be taken into account to 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 chemicals are prepared; and
- managing risks arising from storing, handling and using hazardous chemicals.

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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