Ethanol, 2,2'-(methylimino)bis-: Human health tier II assessment

22 March 2013

CAS Number: 105-59-9

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.

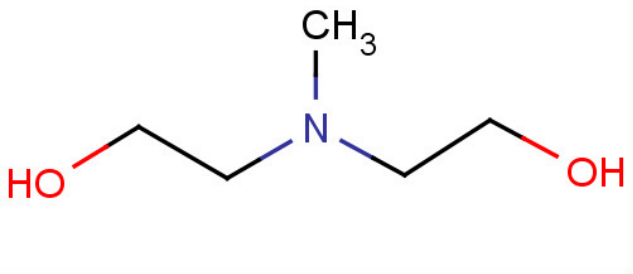
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	2,2-(Methylimino)diethanol N-Methyldiethanolamine Diethanolmethylamine Bis(2-hydroxyethyl) methyl amine MDEA
Structural Formula	
Molecular Formula	C5H13NO2
Molecular Weight (g/mol)	119.163
Appearance and Odour (where available)	A colourless liquid with an ammonia-like odour
SMILES	C(O)CN(C)CCO

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under a previous voluntary call for information.

The chemical has reported commercial use including:

- absorbents/adsorbents in the manufacture of other chemicals
- corrosion inhibitors in mining & metal extraction.

The chemical is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume between 1000 and 9999 tonnes.

International

The following international uses have been identified through the 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 & eChemPortal—OECD High Production Volume chemical program (OECD HPV), the US Environmental Protection Agency's (EPA) Aggregated Computer Toxicology Resource (ACToR), and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical was reported to have cosmetic use including:

- film formers which are used in cosmetics for various purposes such as in forming facial masks, make up films, hair holding products and nail polishes.

The chemical was reported to have domestic use including:

- cleaning/washing agents;
- colouring agents;
- paints, lacquers and varnishes; and
- adhesives, binding agents.

The chemical was reported to have commercial use including:

- solvents;
- absorption of acidic gases;
- anti-freezing, reprographic and pH-regulation agents;
- lubricants and additives, including use in the construction industry (as an additive in concrete & cement); and
- catalyst in polymerisation reactions such as polyurethane foams.

The chemical has reported site limited use including:

- as an intermediate in formulation of preparations and also as a surfactant intermediate.

Restrictions

Australian

The chemical is currently listed in the *Australian Chemical Weapons (Prohibition) Act 1994* and labelled a Schedule 3. The chemical is defined as a precursor in the manufacture of chemical weapons but also has legitimate large scale industrial use.

The chemical is also currently listed in the Australia Council of Australian Governments (COAG) Chemicals of Security Concern, due to the risk of diversion from its lawful use to other unlawful purposes, including terrorist related activity.

International

Chemical warfare:

The chemical can be a precursor in the manufacture of chemical weapons but also has legitimate large scale industrial use and is currently listed on:

Canada Chemical Weapons - Schedule 3 as a precursor;

UK - Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction, Organisation for the Prohibition of Chemical Weapons, 2005; and

US Department of Homeland Security Chemical Facility Anti-Terrorism Standards - Chemicals of Interest.

Food:

The chemical is listed in the US FDA List of "Indirect" Additives Used in Food Contact Substances.

Existing Work Health and Safety Controls

Hazard Classification

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

Xi; R36 (Irritating to eyes).

Exposure Standards

Australian

No specific exposure standards are available.

International

The following are identified (Galleria Chemica):

Temporary Emergency Exposure Limits (TEELs): TEEL-0 = 10 mg/m³, TEEL-1 = 30 mg/m³, TEEL-2 = 50 mg/m³, TEEL-3 = 250 mg/m³ by the US Department of Environment.

Health Hazard Information

Toxicokinetics

It is reported by REACH (2012) and OECD (2012) that the chemical is readily absorbed through the skin of Fisher 344 rats, and is distributed uniformly throughout the major organs, with the highest concentration being in the liver and kidneys. The major

route of excretion was urine, where the half-life was in excess of 30 hours. Based on the low molecular weight of the chemical, it is also expected to be absorbed from the gastrointestinal tract.

Acute Toxicity

Oral

The chemical was reported to have low acute toxicity via the oral route (median lethal dose (LD50) in rats is >2000 mg/kg bw).

In a modified OECD TG 401 study (REACH 2012), 10/sex/dose rats were administered 208, 1664, 3328, 4160, 5200, 6656 mg/kg bw of the chemical by oral gavage and observed for 7 days. No animals died in the 208 and 1664 mg/kg bw dose groups. Clinical signs from the higher dose groups included ruffled fur, grasping and bloody eyes and noses. Smeared snouts and urogenital tracts were observed in all rats which died during the observation period, where as the surviving rats exhibited bronchitis and bronchiectasis. A LD50 of

4680 mg/kg bw was determined.

Dermal

The chemical was reported to have low acute toxicity via the dermal route (REACH 2012). Dermal LD50 values of 10244 mg/kg bw in male and 11336 mg/kg bw in female New Zealand White rabbits were reported.

Clinical signs including sluggishness, emaciation, unsteady gait and prostration were reported after application of undiluted chemical. Surviving animals recovered during the observation period. Necropsy of animals that died revealed dark red mottled lungs and livers.

Inhalation

The chemical was reported to not have acute toxicity via the inhalation route (REACH 2012). LC50 value was not determined.

No inhalation toxicity was observed in 6 sex/dose rats exposed to saturated vapour of the chemical over 8 hours with a 7 day observation period. No mortality occurred and there was no clinical signs or gross pathology.

Corrosion / Irritation

Skin Irritation

The chemical is reported to be slightly irritating to skin in animal studies. Effects were not sufficient to warrant classification.

In a modified OECD Test Guideline (TG) 404 study (Acute Dermal Irriatation/Corrosion) (REACH 2012), the chemical was reported as a slight irritant to New Zealand White rabbits after exposure for 4 hours, under occlusive conditions. The mean erythema score was 0.2, the oedema score was 0.2 and irritation was fully reversible within 72 hours.

In another modified OECD TG 404 study, the chemical was reported as a slight irritant to Vienna White rabbits (REACH 2012) exposed for 1, 5, 15 mins or 20 hrs under occlusive conditions. The 20 hr exposure reported mean erythema score of 2.5 and oedema score of 1.3 were both fully reversible within 8 days.

Eye Irritation

The chemical is currently classified with the risk phrase 'Irritating to eyes' (Xi; R36) in Australia (Safe Work Australia - HSIS). While the available data do not support this classification, in the absence of more comprehensive information, the available data are not sufficient to recommend removal of the current HSIS classification. The available data, however, satisfy the classification criteria under the adopted Globally Harmonized System of Classification and Labelling (GHS).

In a study (REACH 2012) that was similar to OECD TG 405 (Acute Eye Irritation / Corrosion), 0.05 ml of the chemical was applied to the conjunctival sac of one eye (not washed out) of two Vienna White rabbits, and observed up to 8 days. Redness, swelling and clouding of the cornea as well as conjunctival bleeding was observed. Mean values over 24, 48 and 72 hours for cornea opacity (1), iris lesion (0), conjunctivae (1.7) and chemosis (0.7) were reported. All observed symptoms were fully reversible within 8 days.

Sensitisation

Skin Sensitisation

The chemical was reported to be not sensitising (REACH 2012).

In a modified OECD TG 406 (Skin Sensitisation) study, 10/sex/dose Dunkin-Hartley guinea pigs were intradermally injected (5%) together with Freund's Complete Adjuvant (FCA) and received topical induction (100%). They were then rechallenged with either 50% or 10% of the chemical by an occlusive patch. The chemical produced sporadic irritation, but did not produce dermal sensitisation in guinea pigs.

Repeated Dose Toxicity

Oral

No data are available.

Dermal

In a 13 week modified OECD TG 411 study in Fisher 344 rats, a NOAEL of >750 mg/kg bw/day for systemic toxicity and a NOAEL of 100 mg/kg bw/day for local effects were reported (REACH 2012).

The chemical was administered via an occlusive patch of 100, 250, 750 mg/kg bw for 6 hours/day, 5 days/week to 10 animals/sex/dose. Dose-related irritation in the mid and high dose groups was observed with major histopathological features being acanthosis, hyperkeratosis, parakeratosis, dermatitis, dermal fibrosis, eschar, and ulceration. There were no mortalities. At 750 mg/kg bw/day the chemical produced moderate to severe irritation at the site of treatment but no systemic effects.

Inhalation

No data are available.

Genotoxicity

The genotoxicity potential of the chemical is reported to be negative in several *in vitro* and *in vivo* genotoxicity studies (REACH 2012).

An *in vitro* Ames test in bacterial *S. typhimurium* with and without S9 mix, following the OECD TG 471 (Bacterial Reverse Mutation Assay) was negative. *In vitro* studies in mammalian Chinese Hamster Ovary (CHO) cells with and without S9 mix,

following the OECD TG 476 (In vitro Mammalian Cell Gene Mutation Test), and the OECD TG 479 (Genetic Toxicology: In Vitro Sister Chromatid Exchange Assay in Mammalian Cells) were both negative.

An *in vivo* study similar to the OECD TG 474 (Mammalian Erythrocyte Micronucleus Test) using 5/sex/dose of Swiss Webster mice, intraperitoneal administration of 175, 350, 560 mg/kg bw of the chemical, showed no significant increase in the incidence of micronucleated polychromatic erythrocytes.

Carcinogenicity

There are no carcinogenicity studies available (REACH 2012, OECD 2012).

Reproductive and Developmental Toxicity

Any reproductive and developmental effects were only observed secondary to maternal toxicity, so the chemical is not a specific reproductive or developmental toxin.

In an OECD TG 421 oral gavage study (REACH 2012) in Wister rats, the chemical was administered via gavage at 100, 300 and 1000 mg/kg bw/day before mating, during mating, gestation and for 4 days of lactation. A NOAEL for systemic toxicity in parental rats was derived to be 100 mg/kg bw/day based on significant weight reduction. The NOAEL for reproductive performance and fertility was 300 mg/kg bw/day based on littler loss, insufficient lactation behaviour, and increased duration of gestation. The NOAEL for developmental toxicity of the young was 300 mg/kg bw/day due to reduced viability index and reduced postnatal offspring weight gain.

In a modified OECD TG 414 study (REACH 2012) using CD rats, the chemical (0, 250, 500 or 1000 mg/kg bw/day) was administered via occluded cutaneous application for 6 hours per day to pregnant rats during gestation days 6 - 15. Maternal toxicity as indicated by skin irritation and mild anaemia was observed from 500 mg/kg bw/day onwards. No treatment related developmental effects were observed. The NOAEL for maternal toxicity was 250 mg/kg bw/day. The NOAEL for developmental toxicity was >1000 mg/kg bw/day.

Risk Characterisation

Critical Health Effects

The chemical is an eye irritant.

Public Risk Characterisation

Although use in cosmetic and domestic products in Australia has not been identified through a voluntary call for information the chemical is reported to be used in cosmetic and domestic products overseas. The only health effect of the chemical is eye irritation. It is expected that in cosmetic and domestic products the use of the chemical is likely to be well below the undiluted concentration tested in animal studies. Based on the cut-off concentration listed on HSIS, products with a concentration of the chemical under 20% are not expected to be an eye irritant. Therefore, an unreasonable risk from cosmetic and domestic products containing under 20% of the chemical is not expected.

Occupational Risk Characterisation

Occupational exposure to the chemical may occur through dermal contact at workplaces where the chemical is produced or used.

The health effect of eye irritation the risk to workers from this chemical is considered low, particularly at concentrations below 20%, or if adequate control measures to minimise occupational exposure to the chemical are implemented. The chemical should

be appropriately classified and labelled to ensure that a person conducting a business or an employee at a workplace has adequate information to determine appropriate controls. The existing hazard classification for worker health and safety is considered appropriate based on available data.

NICNAS Recommendation

The chemical is sufficiently assessed and risk managed provided the recommendation for classification and labelling is followed and the chemical is not used in cosmetic and domestic products at a concentration of 20% or over. If the chemical is used in cosmetic and domestic products at a concentration of 20%, or over, this information should be made available to NICNAS during the public comment period.

Regulatory Control

Public Health

Considering the available information and the expected low public exposure from this chemical no regulatory controls are warranted.

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted 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 eyes (Xi; R36)*	Causes serious eye irritation - Cat. 2A (H319)

[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 dermal and ocular 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 storage, handling and use of a hazardous chemical are dependent 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:

- minimisation of manual processes and work tasks through automation of processes;
- work procedures that minimise splashes and spills;
- regular cleaning of equipment and work areas; and
- use of 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 be relied upon on its own to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selection of 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 hazardous chemical are prepared; and
- management of risks arising from storage, handling and use of 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 physical hazards of the chemical has not been undertaken as part of this assessment.

References

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