Alkoxyethanols (C1-C2) and their acetates: Human health tier II assessment

04 July 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Ethanol, 2-methoxy-	109-86-4
Ethanol, 2-methoxy-, acetate	110-49-6
Ethanol, 2-ethoxy-	110-80-5
Ethanol, 2-ethoxy-, acetate	111-15-9

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

Grouping Rationale

The acetate chemicals in this group, CAS Nos 110-49-6 (EGMEA) and 111-15-9 (EGEEA), are rapidly hydrolysed by esterases to the glycol ethers, CAS Nos 109-86-4 (EGME) and 110-80-5 (EGEE), respectively.

EGME and EGEE differ only by a single carbon chain length in the ether terminus. The metabolic pathways (see **Toxicokinetics**) and toxicological profile for all chemicals in this group are similar.

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; 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; the US National Library of Medicine's Hazardous

Substances Data Bank (HSDB); and various international assessments (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b)

The predominant use of the chemicals is reported to be site-limited use, as chemical intermediates.

The second main use of the chemicals is commercial use as industrial solvents including in:

- lacquers, varnishes and paints;
- printing inks;
- cleaning agents for food and non-food surfaces;
- photographic processes;
- in manufacturing coatings and adhesives for food packaging; and
- the semi-conductor industry.

Whilst some of the commercial uses identified might be relevant in a domestic setting, domestic use of the chemicals is restricted internationally (see **International: restrictions**). The chemicals are not listed in international domestic products databases except EGEEA, which reported the chemicals as being present in one discontinued varnish product (CPID; Household Products Database).

The chemicals are included in the CosIng database and US Personal Care Products Council INCI directory with the identified functions of solvents and viscosity-decreasing agents. Identified previous cosmetic uses include in shampoos, eye make-up products, moisturisers and nail polish. However, cosmetic use of the chemicals is restricted internationally (see **International: restrictions**) and no reported uses were identified in the compilation of ingredients used in cosmetics in the United States (Personal Care Products Council, 2011).

Restrictions

Australian

The chemicals fall within the scope of ethylene glycol monoalkyl ethers and their acetates, which are listed in the *Poisons Standard*—the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) in Schedule 6 (SUSMP, 2013).

Schedule 6:

'ETHYLENE GLYCOL MONOALKYL ETHERS and their ACETATES, except:

(a) when separately specified in these Schedules; or

(b) in preparations containing 10 per cent or less of such substances.'

The chemicals are not separately specified in the Schedules.

Schedule 6 chemicals are described as '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.' Schedule 6 chemicals are labelled with 'Poison' (SUSMP, 2013).

International

The chemicals are listed on the following (Galleria Chemica):

- EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products;

- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain;
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient "Hotlist").

In 2005, the United States (US) Environmental Protection Agency (EPA) issued a significant new use rule (SNUR) under section 5(a)(2) of the *Toxic Substances Control Act* (TSCA) for all the chemicals in this group. This requires persons to notify the EPA at least 90 days before commencing the manufacture, import, or processing of the chemicals for domestic use in a consumer product or the manufacture or import of EGMEA at levels greater than 10,000 pounds per year (US EPA, 2005).

The chemicals are restricted by Annex XVII to REACH Regulations. The chemicals cannot be used in substances and preparations placed on the market for sale to the general public in individual concentrations ≥0.5 % (European Parliament & Council 1999; European Parliament & Council 2006; European Parliament & Council 2008).

The chemicals, except EGMEA, are listed on the candidate list of Substances of Very High Concern (SVHC) for eventual inclusion in Annex XIV (ECHA, 2013). In the EU, companies could have legal obligations if the chemical that they produce, supply, or use is included on the candidate list whether on its own, in mixtures, or present in articles.

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals, except EGEE, are classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- Repr. Cat. 2; R60-61 (reproductive and developmental toxicity);
- Xn; R20/21/22 (acute toxicity)

The chemical, EGEE, is classified as hazardous, with the following risk phrases for human health in the HSIS (Safe Work Australia):

- Repr. Cat. 2; R60-61 (reproductive and developmental toxicity);
- Xn; R20/22 (acute toxicity)

The classifications for all the chemicals are subject to Note E.

"**Note E**: For substances ascribed Note E, the Risk Phrases R20, R21, R22, R23, R24, R25, R26, R27, R28 R39, R68 (harmful), R48 and R65 and all combinations of these Risk Phrases should be preceded by the word ‘also’.

Examples:

R23: ‘also toxic by inhalation’.

R27/28: ‘also very toxic in contact with skin and if swallowed’"

Exposure Standards

Australian

The chemicals have an exposure standard of 5 ppm (16–27 mg/m^3) time weighted average (TWA). The notice Sk (absorption through the skin may be a significant source of exposure) applies (Safe Work Australia).

International

The following exposure standards are identified for EGME and EGMEA (Galleria Chemica).

An exposure limit (TWA) of 0.1–5 ppm (0.3–24 mg/m³) in different countries such as Belgium, Finland, France, Germany, Hong Kong, Japan, New Zealand, Canada (Quebec and British Columbia), United Kingdom and the US (National Institute for Occupational Safety and Health—NIOSH).

The following exposure standards are identified for EGEE and EGEEA (Galleria Chemica):

An exposure limit (TWA) of 0.5–5 ppm (1.8–27 mg/m³ in different countries such as Belgium, Finland, France, Germany, Hong Kong, Japan, New Zealand, Canada (Quebec and British Columbia), United Kingdom and the US (National Institute for Occupational Safety and Health—NIOSH).

The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a threshold limit value (TLV) TWA of 5 ppm (18–27 mg/m³ (TWA) for EGEE, EGEEA and 0.1 ppm (0.3 mg/m³) for EGME and EGMEA (ACGIH, 2011).

The European Scientific Committee on Occupational Exposure Limits (SCOEL) recommended an 8 hr TWA of 1 ppm for EGME and EGMEA and 2 ppm for EGEE and EGEEA (SCOEL, 2006; SCOEL, 2007).

Health Hazard Information

Given the rapid metabolism of EGEEA to EGEE and EGMEA to EGME, data for the parent glycols (EGEE and EGME) are considered representative of the toxicity of the related acetate. Data for another ethyleneglycol ether, 2-butoxyethanol, have also been provided as supporting data.

Toxicokinetics

The chemicals are well absorbed by all routes of exposure. Uptake through the skin is considered to be a significant source of exposure in humans exposed to vapours (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b; NIOSH, 2011).

Once absorbed, the chemicals are widely distributed throughout the body, including the developing foetus. This can result in levels of metabolites in the foetus greater than in the mother. The chemicals are extensively metabolised, with the majority excreted in the urine. EGMEA and EGEEA are rapidly hydrolysed by esterases to their respective glycol ethers. The glycol ethers are substrates for alcohol dehydrogenase isoenzyme ADH-3, which catalyses the conversion of the terminal alcohol to an aldehyde (which is a transient metabolite). Further rapid conversion of the aldehyde by dehydrogenase produces the alkoxyacetic acid, which is the main metabolite. The systemic toxicity of the chemicals is considered attributable to this metabolite. The alkoxyacetic acid metabolite has been shown to be excreted more slowly in humans than in rats (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b). Other metabolites include ethylene glycol (humans and animals) and alkoxyacetic acid conjugates (animals only).

Acute Toxicity

Oral

The chemicals are classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in HSIS (Safe Work Australia). The available data support this classification. Whilst the reported median lethal dose (LD50) values are generally greater than 2000 mg/kg bw/day, LD50 values in guinea pigs and rabbits are reported to be in the range of 1000–1500 mg/kg bw/day. Reported signs of toxicity include haematuria, sluggishness, unsteady gait, slow breathing, mottled and red lungs, liquid-filled stomachs, dark red and yellow intestines, and bladders filled with dark red liquid (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b, ECHA 2011).

Dermal

The chemicals, except EGEE, are classified as hazardous with the risk phrase 'Harmful in contact with skin' (Xn; R21) in HSIS (Safe Work Australia). The available data (LD50 = 860–1290 mg/kg bw) for EGME support this classification (NIOSH, 2011). However the reported LD50 values for EGEEA and EGMEA (3720–10300 mg/kg bw/day) support the removal of the classification for these chemicals (refer to **Recommendation** section) (Government of Canada 2009a; Government of Canada 2009b). The classification for acute dermal toxicity was recently removed from EGEE based on available data (LD50 = 3720–4576 mg/kg bw (ECHA, 2011).

Inhalation

The chemical is classified as hazardous with the risk phrase 'Harmful by inhalation' (Xn; R20) in HSIS (Safe Work Australia). The available data support this classification. The lowest reported median lethal dose concentration (LC50) values are:

- approximately 17.8 mg/L for a 4-hour exposure for EGME (REACH);
- 7.36 mg/L for an 8-hour exposure (corresponding to 10.4 mg/L/4h) for EGEE; and
- 8.25 mg/L for EGEEA (exposure period not specified) (Government of Canada, 2009b).

An LC50 value for EGMEA has not been established (Government of Canada, 2009a).

Corrosion / Irritation

Skin Irritation

The chemicals are reported to be at most slightly irritating to skin in animal studies and are considered to have low potential for skin irritation effects (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b, REACH).

Eye Irritation

Whilst the chemicals, in particular EGEE, caused eye irritant effects in animal studies, effects were generally reversible (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b, REACH). The severity of effects observed are not sufficient to warrant a hazard classification.

Sensitisation

Skin Sensitisation

Based on the reported negative results in various guinea pig studies, the chemicals are not considered to be skin sensitisers (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b).

Repeated Dose Toxicity

Oral

A number of repeated dose oral toxicity studies on EGME and EGEE are available, with investigations performed in rats, mice, rabbits, and dogs. Limited data are available for the acetates. Adverse effects have been observed in the thymus, testes, blood and hematopoietic systems including:

- reduced weight and histopathological changes in the thymus;
- reduced weight and histopathological changes in the testes (see **Reproductive and developmental toxicity**);
- haemosiderin accumulation and isolated haematopoietic foci in the spleen;
- decreased haemoglobin level and haematocrit values; and
- reduced white blood cell and platelet counts.

Effects are observed even following short exposure periods (3–10 days). Rats were more sensitive to the chemicals than mice.

The reported lowest observed adverse effect level (LOAEL) for EGME was 71 mg/kg bw/day. The reported no observed adverse effect level (NOAEL) for EGEE was 93 mg/kg bw/day (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b).

Dermal

Limited data are available. In a 28-day study in rats with the chemical EGME, effects in the testes and haematological parameters were observed at dose levels of 1000 mg/kg bw/day. A NOAEL of 100 mg/kg bw/day was reported (REACH). Similar effects were observed in a 13-week dermal study in guinea pigs at doses of 1000 mg/kg bw/day (Government of Canada, 2002a).

Inhalation

A number of repeated dose inhalation toxicity studies on EGME and EGEE are available, with investigations performed in rats, rabbits, and dogs. Limited data are available for the acetates. Adverse effects similar to those observed in oral toxicity studies have been observed in the thymus, testes, blood and haematopoietic systems. Rabbits were more sensitive to the chemicals than mice.

The reported no observed adverse effect concentration (NOAEC), not including reproductive or developmental effects, for EGME was 93 mg/m³ in rabbits. The lowest reported NOAEC for EGEE was 390 mg/m³ in rabbits (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b).

Observation in humans

Effects on blood, bone marrow and sperm have been observed in workers exposed to the chemicals. These include increased prevalence of anaemia, increased incidence of leukopaenia, hypoplasia of the bone marrow, and reduced sperm production.

In a cross-sectional study, effects on the blood were observed in a group of painters exposed to solvents containing EGEEA. Effects on the white blood cell count and mean corpuscular volume were significant in the high exposure group (mean concentration 3 ppm (16 mg/m³)) but less so in the low exposure group (mean concentration 1.8 ppm (9.7 mg/m³)). Anaemic effects were noted in workers exposed to mean airborne concentrations of 35.7 ppm (113 mg/m³) EGME. These effects were resolved when concentrations were reduced to 0.55 ppm (1.7 mg/m³) (WHO, 2009; ACGIH, 2011).

An increased prevalence of oligospermia and azoospermia was noted in shipyard workers using paint containing EGME and EGEE. Mean work place concentrations were 0.8 ppm (2.6 mg/m³) EGME and 2.6 ppm (9.6 mg/m³) EGEE with TWA concentrations reported to be up to 5.6 ppm (17.7 mg/m³) and 21.5 ppm (79 mg/m³), respectively. No effects on sperm were noted in 15 manufacturing and packing workers exposed to 5 (15.6 mg/m³) to 10 ppm (31.1 mg/m³) EGME (ACGIH, 2011).

Whilst confounding factors such as exposure to other chemicals could not completely be ruled out with some of these observations, the observations are consistent with those in animals (Government of Canada, 2002a; EU RAR, 2008;

Government of Canada 2009a; Government of Canada 2009b).

Genotoxicity

Based on the available data, the chemicals could have, at most, weak genotoxic potential. The chemicals were negative in bacterial gene mutation tests and in a gene mutation test with mammalian cells, but induced in vitro clastogenicity in mammallian cells. In vivo, the chemicals did not induce chromosomal aberrations or micronuclei in the bone marrow in the animals tested. In a comet assay, transient DNA damage was observed in the bone marrow and testicular cells in rats exposed orally to 500 mg/kg bw of EGME (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b).

The chemical 2-methoxyacetaldehyde (a metabolite of EGME and EGMEA) induced gene mutations in *Salmonella typhimurium* and was a more potent inducer of chromosomal aberrations in mammalian cells than EGME or the main metabolite methoxyacetic acid (Government of Canada 2002a).

No induction of micronuclei or sister chromatid exchange were observed in workers exposed to glycol ethers, including EGEE, at levels up to 20 mg/m³ (Government of Canada, 2009b).

Carcinogenicity

Limited data are available. There is no evidence of carcinogenicity in the available long-term studies with the chemical EGEE in rats and mice, although the studies had limitations compared with guideline studies (EU RAR, 2008).

Two carcinogenicity studies in rats and mice (2-year, via inhalation) are available for 2-butoxyethanol (CAS No. 111-76-2). A significant increase in the incidence of liver haemangiosarcomas was seen in male mice, and forestomach tumours were observed in female mice. However, several international reviews of this data (OECD, United States and the European Union) have concluded that the results of these studies are not relevant to humans and that 2-butoxyethanol is not considered a human carcinogen (OECD, 2006; SCHER, 2008).

Based on the proposed mode of action for the observed tumours (haematotoxicity) (OECD, 2006; SCHER, 2008) and the similar effects observed with the chemicals in acute and chronic toxicity studies (NICNAS, 1996), 2-butoxyethanol is considered a suitable analogue for the chemicals being assessed for this endpoint.

Reproductive and Developmental Toxicity

The chemicals are classified as hazardous—Category 2 substance toxic to reproduction—with the risk phrase ‘May impair fertility’ (T; R60) and Category 2 substance toxic to reproduction—with the risk phrase ‘May cause harm to the unborn child’ (T; R61) in HSIS (Safe Work Australia). The available data support this classification.

The chemicals have been shown to cause adverse effects to the male reproductive system in a number of species following exposure by all routes (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b). Effects observed included:

- decreased testes weight;
- atrophy of the testes;
- decreased sperm motility; and
- changes in sperm morphology.

Although not as extensively investigated, the effects on the female reproductive system have also been reported. Decreased female fertility was observed in a cross-over breeding study with EGEE. Changes in the oestrus cycle and hormone levels, together with histopathological changes in the ovaries, were observed in rats exposed to EGME (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b).

The chemicals have also been shown to cause adverse developmental effects, in the absence of maternal toxicity, in a number of species following exposure by all routes (Government of Canada, 2002a; Government of Canada, 2002b; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b). Effects observed included:

- decreased number of litters;
- reduced foetal body weight;
- reduced pup viability;
- neurochemical and behavioural changes; and
- increased incidence of foetal malformations

Developmental effects were generally observed at lower doses than both reproductive effects and haematological effects. Effects were often observed for EGME at the lowest doses tested. The lowest observed effect concentration (LOEC) for delayed ossification following exposure to EGME is 10 ppm (32 mg/m³) in rabbits (NOAEC 3 ppm (9 mg/m³)) and 25 ppm (78 mg/m³) in rats. Major congenital malformations occurred in rabbits following exposure to 50 ppm (156 mg/m³). An oral NOAEL was not established (Government of Canada, 2002a; ACGIH, 2011). For EGEE the critical NOAEL is considered to be 23 mg/kg bw (rats—oral) and NOAEC 10 ppm (37 mg/m³) (rats—inhalation) (EU RAR, 2008).

In humans, data are available that indicate an association between exposures to the chemicals and adverse reproductive or developmental effects, including decreased sperm production, changes in sperm morphology, spontaneous abortion and congenital malformations (also refer to **Repeated dose toxicity: observation in humans**).

Whilst confounding factors such as exposure to other chemicals could not completely be ruled out with some of these observations, the observations are consistent with those in animals (Government of Canada, 2002a; EU RAR, 2008; Government of Canada 2009a; Government of Canada 2009b).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (reproductive toxicity and developmental toxicity) and systemic acute effects (acute toxicity from oral/dermal/inhalation exposure). The chemical may also cause long-term effects on the blood and bone marrow.

Physiologically-based pharmacokinetic (PBPK) modelling suggests that humans could experience toxic effects at levels lower than those observed in animals (Sweeney et al., 2001; SCOEL 2006; SCOEL, 2007; ACGIH, 2011).

Public Risk Characterisation

The chemicals are currently listed on Schedule 6 of the SUSMP for preparations containing more than 10 %. At concentrations greater than 10 %, a number of first aid instructions and safety directions relating to skin and eye contact apply.

Based on information on use of the chemicals internationally, the chemicals are not likely to be widely available for domestic use. Hence, the public risk from these chemicals is not considered to be unreasonable and further risk management is not considered necessary for public safety. However, a modification to the entry in the SUSMP may be appropriate (refer to **Recommendation** section).

Occupational Risk Characterisation

During product formulation, dermal, ocular and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could 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. Skin absorption is considered a significant source of exposure for workers exposed to vapours.

Given the critical systemic long-term health effects, these chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure to the chemicals are implemented. The chemicals 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 current exposure standard might not be adequate to mitigate the risk of adverse effects. Current use of the chemicals is not known in Australia. However, a risk assessment conducted internationally for the chemicals (EU RAR, 2008) concluded that for the occupational exposure scenario, production and further processing in the large-scale industry, 'there is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account' (EU RAR, 2008). Adverse effects have been observed in humans and animals at levels that are the same order of magnitude as the current exposure standards. PBPK modelling indicates that occupational exposure limits (OELs) (eight-hour time-weighted average) that should protect workers from the most sensitive adverse effects of these chemicals are 2 ppm EGEEA and EGEE (11 mg/m³ EGEEA, 7 mg/m³ EGEE) and 0.9 ppm (3 mg/m³) EGME. These recommendations assume that dermal exposure will be minimal or non-existent (Sweeney et al., 2001).

Based on the available data, the hazard classification in HSIS is considered appropriate, although removing the acute dermal toxicity classification for EGEEA and EGMEA is considered appropriate.

NICNAS Recommendation

It is recommended that Safe Work Australia consider whether current controls adequately minimise the risk to workers. A Tier III assessment may be necessary to provide further information to determine whether the current exposure controls offer adequate protection to workers.

Based on the available data, the hazard classification in HSIS is considered appropriate, although removing the acute dermal toxicity classification for EGEEA and EGMEA is considered appropriate.

Current risk management measures are considered adequate for the protection of public health. However, a modified entry in the SUSMP for these chemicals may be appropriate, as explained below.

Regulatory Control

Public Health

Further risk management is not considered necessary for public safety. However, a modification to the entry in the SUSMP might be appropriate. Consideration should be given to the following:

- At present, the chemicals fall within the scope of the listing of ethylene glycol monoalkyl ethers in Schedule 6 of the SUSMP for preparations containing more than 10 % glycol ether. However, the health effects of the members of this class of chemicals vary significantly and a separate listing for the chemicals in this group might be more appropriate.
- Whilst the chemicals meet the criteria for Schedule 6, given the critical health effects identified, a lower concentration cut off (than the current 10 %) might be appropriate.
- Physiologically based pharmacokinetic (PBPK) modelling suggests that humans could experience toxic effects at levels lower than those observed in animals.
- Any review of the entry in the SUSMP should form part of a review of the entries for all ethylene glycol monoalkyl ethers and their acetates.

Work Health and Safety

The chemicals are 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.

Please note:

The acute toxicity classification, 'Harmful in contact with skin', applies only to 2-methoxyethanol (CAS No. 109-86-4).

Based on the lowest reported LC50 values for EGEE and EGEEA (refer **Acute toxicity: inhalation**), the GHS classification Acute Tox. 3—H331 is considered more appropriate than the current (translated) classification as Acute Tox. 4*—H332 for EGEE and EGEEA.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)* Harmful in contact with skin (Xn; R21)* Harmful by inhalation (Xn; R20)*	Harmful if swallowed - Cat. 4 (H302) Harmful in contact with skin - Cat. 4 (H312) Harmful if inhaled - Cat. 4 (H332)
Reproductive and Developmental Toxicity	Repro. Cat 2 - May impair fertility (T; R60)* Repro. Cat 2 - May cause harm to the unborn child (T; R61)*	May damage fertility or the unborn child - Cat. 1B (H360FD)

[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/inhalation 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 could 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 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 chemicals has not been undertaken as part of this assessment.

References

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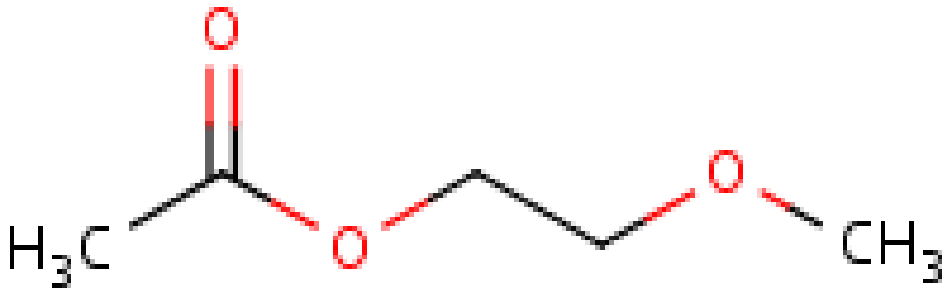
Last Update 04 July 2014

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Ethanol, 2-methoxy-** beta.-Methoxyethanol Ethylene glycol, monomethyl ether EGME 2-ME Methyl Cellosolve
CAS Number	109-86-4
Structural Formula	
Molecular Formula	C3H8O2
Molecular Weight	76.1

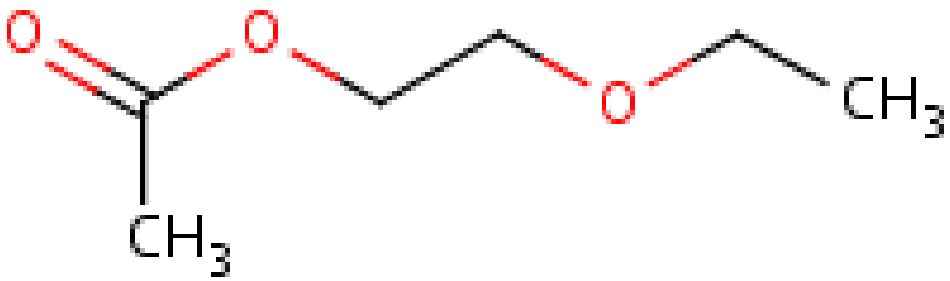
Chemical Name in the Inventory and Synonyms	**Ethanol, 2-methoxy-, acetate** Ethylene glycol, monomethyl ether acetate Methyl cellusolve acetate Acetic acid, 2-methoxyethyl ester EGMEA 2-MEA
CAS Number	110-49-6
Structural Formula	

	
Molecular Formula	C5H10O3
Molecular Weight	118.13

Chemical Name in the Inventory and Synonyms	**Ethanol, 2-ethoxy-** Ethylene glycol monoethyl ether 2-EE Cellosolve Oxitol EGEE
CAS Number	110-80-5
Structural Formula	

	
Molecular Formula	C4H10O2
Molecular Weight	90.1

Chemical Name in the Inventory and Synonyms	**Ethanol, 2-ethoxy-, acetate** Cellosolve acetate Ethylene glycol, ethyl ether acetate 2-EEA Acetic acid, 2-ethoxyethyl ester EGEEA
CAS Number	111-15-9
Structural Formula	

	
Molecular Formula	C6H12O3
Molecular Weight	132.16

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