Ethanol, 2-(hexyloxy)-: Human health tier II assessment

07 December 2012

CAS Number: 112-25-4

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.

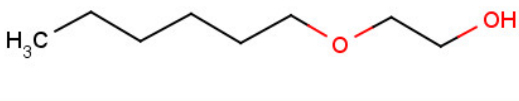
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	2-Hexyloxyethanol Ethylene glycol n-hexyl ether Ethylene glycol monohexyl ether Hexyl cellosolve EGHE
Structural Formula	
Molecular Formula	C8H18O2
Molecular Weight (g/mol)	146.23 g/moles
Appearance and Odour (where available)	Water-white liquid Odourless
SMILES	C(CCCCC)OCCO

Import, Manufacture and Use

Australian

This chemical was reported to be used as solvent (NICNAS, 2006).

International

The following international use information was obtained through The Organisation for Economic Co-operation and Development's (OECD) SIDS Initial Assessment Report (SIAR), REACH Dossier, Substances in Preparations In the Nordic

countries (SPIN), CosIng, and European Chemicals Agency (ECHA).

This chemical has reported commercial or site-limited uses including:

- coalescing agent in latex paints and cleaners;
- colouring agent and as a component of cleaning/washing agents; and
- high boiling solvent.

The chemical has reported domestic use. The chemical is reported to be present in a range of domestic cleaning products (spray and liquid) up to a concentration of 5% (Household Products Database, HHPD). It is also reported that the chemical may be present in some consumer products at the 1-10% range (OECD, 2006).

Restrictions

Australian

The chemical falls within the scope of ethylene glycol monoalkyl ethers, which are listed on Schedule 6 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) for preparations containing more than 10% glycol ether. Schedule 6 chemicals are labelled with "Poison". These are 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.

International

No known restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is currently classified on the Hazardous Substances Information System (HSIS) (may be accessed at http://hsis.safeworkaustralia.gov.au/HazardousSubstance) with following:

Xn; R21/22 (Acute toxicity)

C; R34 (Corrosion)

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Toxicokinetics

The chemical is reported to be a substrate for alcohol dehydrogenase isozyme ADH-3, which catalyses the conversion of the terminal alcohol to an aldehyde (which is a transient metabolite). In general for monosubstituted glycol ethers further rapid conversion of the aldehydes by aldehyde dehydrogenase produces alkoxyacetic acids, which are the predominant urinary metabolites (OECD, 2006).

In general, monosubstituted glycol ethers are absorbed through the skin with the absorption rate decreasing with increasing molecular weight (NICNAS, 1996). The chemical is reported to be rapidly absorbed through the skin in animal studies (rodent and rabbit) (REACH, 2011).

Acute Toxicity

Oral

The chemical is classified in Australia as 'Harmful if swallowed'. The data available (lethal dose, 50% (LD50) = 738 mg/kg bw) supports this classification. Signs of toxicity included sluggishness, unsteady gait, and prostrated appearance (OECD, 2006; REACH, 2011).

Dermal

The chemical is classified in Australia as 'Harmful in contact with skin'. The data available (LD50 = 721 mg/kg bw) supports this classification. Signs of toxicity included salivation, sluggishness, unsteady gait, skin irritation and ulceration, and comatose appearance (OECD, 2006; REACH, 2011).

Inhalation

The chemical is reported to be of low toxicity via inhalation with no lethality and toxic effects observed in studies in rodents (median lethal concentration (LC50) > 85 ppm) (OECD, 2006; REACH, 2011).

Overall

Signs of acute toxicity consistent with haemolysis observed with other monoethylene glycol ethers (NICNAS, 2006) were not observed (OECD, 2006; REACH, 2011).

Corrosion / Irritation

Corrosivity

The chemical is classified in Australia as a corrosive. The data available supports this classification (REACH, 2011). Data from three studies were available.

The chemical was reported as having a corrosive potential in the EpiDerm skin corrosivity test.

A single administration of the chemical was applied at three separate sites on each the of six rabbits tested. The exposure period at the three sites was three minutes, 60 minutes or four hours, followed by a 14-day observation period. Immediately

following a three-minute exposure period, all six animals were free of skin irritation. Subsequently, two animals exhibited moderate erythema with very slight or slight oedema and four animals exhibited slight erythema with little or no oedema. By seven days post-dose, one animal exhibited subepidermal tissue damage with eschar, which persisted to study termination (14 days post-dose). The irritation of the remaining animals subsided to slight erythema in one animal or no irritation in four animals. There was evidence of irreversible alteration of the tissue at one of the six 3- minute exposure sites.

Immediately after a 60-minute exposure, three of the six animals exhibited moderate erythema with very slight edema; the remaining three animals had only very slight (barely perceptible) erythema without oedema. Within 24 hours, three animals exhibited subepidermal tissue damage, which persisted with eschar and scarring to 14 days post-dose. Within 72 hours, one additional animal exhibited subepidermal tissue damage, which persisted with eschar to seven days post-dose; and another animal exhibited superficial tissue damage, which persisted with eschar to 14 days post-dose. The remaining animal was free of all skin irritation by the termination of the study at 14 days post-dose. There was evidence of irreversible alteration of the tissue at three of the six 60-minutes exposure sites.

In a third study a 4-hour application of 0.5 ml of the chemical to occluded rabbit skin resulted in minor to moderate erythema on 5 out of 6 rabbits and moderate oedema on 4. After one day, necrosis was apparent on three females and persisted through seven days. No erythema or oedema remained after seven days. Four rabbits exhibited desquamation.

Corrosive chemicals are also considered to cause irreversible effects on the eyes. This is supported by the available eye irritation data for the chemical (REACH, 2011).

Respiratory Irritation

There are no valid respiratory irritation studies available for the chemical. While other monoethylene glycol ethers are respiratory irritants there is no evidence of irritant effects in acute and repeat dose inhalation studies in animals for hexyloxy ethanol.

Sensitisation

Skin Sensitisation

There are no valid sensitisation studies available. In general monoethylene glycol ethers do not appear to be sensitisers (NICNAS, 1996).

Repeated Dose Toxicity

Oral

There are no valid repeat dose toxicity oral studies available.

Dermal

The chemical was evaluated in an 11 day repeated dose dermal study (nine applications, 6 h/day) at doses of 44, 222 and 444 mg/kg bw in rabbits. Effects observed were considered to mainly relate to the corrosive nature of the chemical, although effects in haematology parameters including decreased haemoglobin and haematocrit was reported with changes statistically significant at the top dose.

Inhalation

In a 90 day repeated dose inhalation study in rats performed at exposure levels of 20, 41, or 71 ppm (120, 245, or 425 mg/m³), the no-observed adverse effect concentration (NOAEC) for the chemical was reported to be 41 ppm (245 mg/m³). Increased liver weights and

changes to liver enzymes were observed at the top dose. No effects on red blood cells or histologic changes in the liver or kidney were noted (OECD, 2006).

Overall

Based on the acute toxicity findings and repeat dose inhalation study, the chemical is not considered to be as potent a haemolytic agent as other monoethylene glycol ethers such as 2-butoxyethanol (CAS no 111-76-2).

Genotoxicity

In general, monoethylene glycol ethers are not genotoxic (OECD, 2006; NICNAS, 1996). The negative data available from several *in vitro* genotoxicity studies for the chemical supports this (OECD, 2006; REACH, 2011).

Carcinogenicity

There are no valid carcinogenicity studies available.

Reproductive and Developmental Toxicity

No developmental effects were noted (even at concentrations that produced maternal toxicity) in rabbits and rats exposed to the chemical by inhalation (OECD, 2006).

Although certain short chain monoethylene glycol ethers such as 2-ethoxyethanol (110-80-5) are known reproductive toxicants, the ability of the glycol ethers to cause testicular toxicity decreases with increasing chain length (OECD, 2006). As 2-butoxyethanol (111-76-2), which has a shorter chain than the chemical, has been shown not to be a reproductive toxicant (OECD, 2006; NICNAS, 1996) the chemical is also considered not to be toxic to the reproductive system.

Risk Characterisation

Critical Health Effects

The critical health effects for risk assessment are acute toxicity (oral and dermal routes of exposure) and corrosivity. Unlike other monoethylene glycol ethers such as 2-butoxyethanol there is no evidence of respiratory irritation or haemolysis.

Public Risk Characterisation

Although its use in domestic products in Australia is not known, the chemical is reported to be used in domestic cleaning products overseas at concentrations up to 5%. It is also noted from overseas data that the chemical may be present in some consumer products at the 1-10% range. The chemical is currently listed on Schedule 6 of the Poisons Schedule for preparations containing more than 10% glycol ether. At concentrations greater than 10% a number of first aid instructions and safety directions relating to skin and eye contact apply.

Provided that normal precautions are taken to avoid prolonged skin and eye contact, the public health risk posed by cleaning and cosmetic products containing the chemical is expected to be minimal at concentrations less than 10%. At higher concentrations, potential harm is reduced through the use of strong warnings and safety directions on the label, although stronger statements relating to corrosivity may further reduce potential for harm.

Occupational Risk Characterisation

Given the critical health effects, the risk to workers from this chemical is considered high if adequate control measures to minimise occupational exposure to the chemical are not implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) 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 considered to be fully assessed at the Tier II level with current risk management measures considered adequate for the protection of workers. Further strengthening of the existing risk management measures for public health may further reduce potential for harm.

Regulatory Control

Public Health

At present, the chemical is listed on the SUSMP under 'ethylene glycol monoalkyl ethers'. However, the health effects of the members of this class of chemicals vary significantly, so it is recommended that a separate listing for the chemical be considered. Consideration should be given to the following:

- that no data were available to indicate at what concentration the chemical would not cause irritation to skin and eyes;
- under Worker Health and Safety (WHS) legislation, the chemical would be classified as an irritant at concentrations between 5 and 10%;
- the chemical is known to be used overseas in domestic cleaning products up to a concentration of 5%; and
- a chemical with a similar classification profile to this chemical is included in the SUSMP with warning statements relating to corrosivity.

Work Health and Safety

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

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)* Harmful in contact with skin (Xn; R21)*	Harmful if swallowed - Cat. 4 (H302) Harmful in contact with skin - Cat. 4 (H312)
Irritation / Corrosivity	Causes burns (C; R34)*	Causes severe skin burns and eye damage - Cat. 1 (H314)

[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

The chemical or products containing the chemical should be used according to the label instructions.

Advice for industry

Work Health and Safety (WHS) legislation in each Australian state and territory imposes obligations on manufacturers and importers of hazardous chemicals to ensure that the chemicals are correctly classified, correctly labelled and (material) safety data sheets ((m)SDS) are prepared for those chemicals. These include:

- the (m)SDS for the chemical, or products and mixtures containing the chemical, must contain accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of a chemical, as well as instructions on the safe storage, handling, use and disposal of the chemical (a review of physical hazards of the chemical has not been undertaken as part of this assessment); and
- a copy of the (m)SDS must be easily accessible to employees.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals to meet duties under the WHS Regulations are provided in the *Preparation of Safety Data Sheets for Hazardous Chemicals—Code of Practice* and *Labelling of Workplace Hazardous Chemicals—Code of Practice*, respectively.

To comply with the WHS legislation, a person conducting a business or undertaking (PCBU) at a workplace must manage risks arising from storage, handling and use of a hazardous chemical. Other duties may apply to a PCBU involved in the storage, handling and use of hazardous chemicals at a workplace. Refer to the WHS legislation in the relevant jurisdiction for further information.

Guidance on managing risks from hazardous chemicals are provided in the *Managing Risks of Hazardous Chemicals in the Workplace—Code of Practice*.

It is recommended that a PCBU should ensure that:

- equipment be designed, constructed, and operated so that, the person handling the chemical does not come into contact with the chemical and is not exposed to a concentration of the chemical that is greater than the workplace exposure standard for the chemical;
- equipment used to handle the chemical retains the chemical, without leakage, at all temperatures and pressures for which the equipment is intended to be used and dispenses or applies the substance, without leakage, at a rate and in a manner for which the equipment is designed.

References

NICNAS 2006. Australian High Volume Industrial Chemicals List (AHVICL). Accessed November 2012 at http://www.nicnas.gov.au

NICNAS Priority Existing Chemical Report for 2-butoxyethanol (1996) Electronic version for the web, accessed in October 2012 at www.nicnas.gov.au.

OECD 2006. SIAR category assessment for monoethylene glycol ethers. Accessed October 2012 at http://webnet.oecd.org/hpv/UI/handler.axd?id=c0edaa0e-2885-4ebe-a102-135ed2bc2da3

REACH Dossier 2011. 112-25-4. Accessed October 2012 at http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed October 2012 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance

Substances in Preparations in Nordic Countries (SPIN). Accessed October 2012 at http://fmp.spin2000.net

US Department of Health and Human Services, Household Products Database, Health and safety information on household products. Accessed October 2012 at http://householdproducts.nlm.nih.gov/

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