Ethanol, 2-[2-(2-butoxyethoxy)ethoxy]-: Human health tier II assessment

17 May 2013

CAS Number: 143-22-6

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.

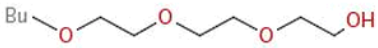
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	2-(2-(2-Butoxyethoxy)ethoxy)ethanol 3,6,9-Trioxa-1-tridecanol Butoxytriethylene glycol TGBE Triethylene glycol butyl ether
Structural Formula	
Molecular Formula	C10H22O4
Molecular Weight (g/mol)	206.28
Appearance and Odour (where available)	Colourless liquid with a mild smell.
SMILES	C(CCC)OCCOCCOCCO

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information.

The chemical has reported commercial or site-limited use, including as a:

- solvent; and
- softener.

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 Dataset Initial Assessment Report (OECD SIAR), Galleria Chemica, and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported domestic use. The chemical is reported to be present in a dishwasher cleaner (concentration not specified) (Household Products Database, US Department of Health and Human Services).

The chemical has reported commercial use in:

- brake fluid and;
- paint stripper formulations.

The chemical has reported site-limited use including as:

- a solvent; and
- an intermediate in plastination.

Restrictions

Australian

No known restrictions have been identified.

International

No known restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

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

Xi; R41 (Eye irritant, risk of serious eye damage).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

When data for ethanol, 2-[2-(2-butoxyethoxy)ethoxy]- (TGBE), are not available, data from other high boiling ethylene gycol ethers that are closely related to the chemical, with respect to molecular structure, physicochemical properties and toxicity, are included. Data for a mixture of high boiling ethylene glycols and their borate esters is also considered to be indicative of the toxicity of the chemical. The high boiling ethylene glycols considered are: triethylene glycol methyl ether (TGME; CAS No.: 112-35-6); triethylene glycol ethyl ether (TGEE; CAS No.: 112-50-5); polyethylene glycol methyl ether (MPEG350; CAS No.: 9004-74-4) and polyethylene glycol butyl ether (CAS No.: 9004-77-7); and substances which are a mixture of these chemicals.

Toxicokinetics

In an in vitro human skin study, the permeability of the chemical to human skin was determined to be low (22 ± 8.6µg/cm2/hr), which is around 1 % of the skin penetration rate of the shorter chain ethylene glycol monoalkyl ethers (OECD, 2002; REACH).

No metabolism data are available for the chemical. Based on data for TGME and diethylene glycol monobutyl ether acetate (CAS No. 124-17-4), the primary metabolite is likely to be 2-[2-[2-(2-butoxyethoxy)ethoxy]ethoxy] acetic acid. Metabolism to 2-butoxyacetic acid (2-BAA) is not expected (OECD, 2002).

Acute Toxicity

Oral

The chemical exhibits low acute toxicity in animal tests; the reported oral median lethal dose (LD50) in rats is > 2000 mg/kg bw. Observed sublethal dose effects included lethargy, ataxia, blood in the urogenital area and piloerection (OECD, 2002).

Dermal

The chemical exhibits low acute toxicity in animal tests; the dermal LD50 in rats is > 2000 mg/kg bw (REACH).

Inhalation

The chemical exhibits low acute toxicity in animal tests following inhalation exposure with no mortalities or toxic effects observed in rodent studies (median lethal concentration (LC50) > 2400 mg/L) (OECD, 2002).

Corrosion / Irritation

Skin Irritation

No skin irritation studies that have been conducted according to OECD Test Guideline (TG) 404 could be identified for the chemical. Slight to moderate irritation has been observed in rabbits following 24-hour exposure to the chemical.

Eye Irritation

The chemical is classified as hazardous with the risk phrase 'Risk of serious damage to eyes' (Xi; R41) in HSIS (Safe Work Australia). The available data support this classification. In an eye irritation study in rabbits, the chemical was found to be irritating to the eye, with inflamed conjunctiva, corneal opacity and iris damage observed at 24, 48 and 72 hours. Effects persisted for eight days with scars observed after this period (OECD, 2002, REACH).

Sensitisation

Skin Sensitisation

No data were available for the chemical. In general, glycol ethers are not skin sensitisers. Negative results seen for a test material containing a mixture of high boiling ethylene glycol ethers and their borate esters in a guinea pig maximisation test, supported a conclusion that the chemical is not a skin sensitiser (REACH).

Repeated Dose Toxicity

Oral

No data are available for the chemical. Considering the lowest observed adverse effect levels (LOAELs) available from 90-day rat studies (150–750 mg/kg bw/d) for other high boiling ethylene glycols reported in various repeat-dose toxicity studies, the chemical is not considered to cause serious damage to health by repeated oral exposure (REACH). Effects observed included reduced body weight, increased liver weights and slight histopathological changes in the liver (OECD, 2002).

Dermal

Considering the no observed effect level (NOELs) available from a 21-day study in rabbits (1000 mg/kg bw/d), the chemical is not considered to cause serious damage to health through repeated dermal exposure (REACH). No systemic effects were reported in the study. Mild to moderate desquamation and fissuring of skin was noted in most rabbits (OECD, 2002).

Inhalation

No data are available.

Genotoxicity

Overall, the data indicate the chemical has no mutagenic or genotoxic potential.

The chemical tested negative in an in vitro bacterial mutation test. Other high boiling ethylene glycols were negative in several in vitro (bacterial mutation, chromosome aberration, hypoxanthine guanine phosphoribosyl transferase assay) and in vivo (mouse micronucleus) tests for gene mutation and clastogenicity (OECD, 2002; REACH).

Carcinogenicity

No data are available for the chemical, however, considering similar chemicals (DEGBE (CAS No. 112-34-5) and EGBE (CAS No. 111-76-2), there is limited evidence of a carcinogenic effect (REACH).

Reproductive and Developmental Toxicity

No data for reproductive toxicity are available.

Testicular toxicity has been observed at high doses (1000 mg/kg bw/day or greater) with TGME and TGEE (OECD, 2002). However, given the absence of reproductive effects with shorter chain ethylene glycol monobutylethers (DEGBE (CAS No. 112-34-5) and EGBE (CAS No. 111-76-2), the chemical is not expected to produce reproductive effects (OECD, 2002).

The chemical did not produce developmental toxicity in rats when orally administered at 1000 mg/kg/day (highest dose used) from days 7–16 of gestation (OECD, 2002).

Risk Characterisation

Critical Health Effects

The critical health effect for risk characterisation is serious eye damage. The risk is reduced at lower concentrations.

The chemical does not produce the haemolytic effects observed with the shorter chain ethylene glycol butyl ether, 2-butoxyethanol.

Public Risk Characterisation

The only identified domestic use of the product is in a dishwasher cleaner. Provided that normal precautions are taken to avoid contact with eyes, the risk to public health is not considered to be unreasonable and further risk management is not considered necessary for public safety.

Occupational Risk Characterisation

During product formulation, dermal and ocular exposure of workers to the chemical may occur, particularly where manual or open processes are used. These may include transfer and blending activities, quality control analysis, and cleaning and maintenance of equipment. Worker exposure to the chemical at lower concentrations may also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the local health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise ocular 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.

Based on the available data, the exisiting hazard classification in HSIS is considered appropriate.

NICNAS Recommendation

Current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

Regulatory Control

Public Health

Considering the available information to indicate low public exposure from this chemical no regulatory controls are recommended.

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted 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]
Irritation / Corrosivity	Risk of serious eye damage (Xi; R41)	Causes serious eye damage - Cat. 1 (H318)

[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 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 storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and

- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

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

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

Obligations under workplace health and safety legislation

Information in this report should be taken into account to assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of Safety Data Sheets for Hazardous Chemicals— Code of Practice* and *Labelling of Workplace Hazardous Chemicals—Code of Practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

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