Ethanol, 2-propoxy-: Human health tier II assessment

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CAS Number: 2807-30-9

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	Ethylene glycol monopropyl ether 2-(propyloxy)ethanol Propyl cellosolve n-Propyl Oxitol glycol 2-propoxyethan-1-ol
Structural Formula	
Molecular Formula	C5H12O2
Molecular Weight (g/mol)	104.15
Appearance and Odour (where available)	Volatile liquid
SMILES	C(CC)OCCO

Import, Manufacture and Use

Australian

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

International

The following international use information was obtained through the Organisation for Economic Cooperation and Development (OECD), the Substances and Preparations In the Nordic countries (SPIN) database and European Union Registration Evaluation Authorisation of Chemicals (REACH) dossiers.

This chemical has reported commercial uses including:

- in a variety of surface coatings, cleaners and intermediates;
- in coalescing agents in water-based coatings and printing applications; and
- textile printing and leather finishing.

The chemical has reported domestic use. The chemical is reported to be present in a range of home maintenance products such as floor coatings and adhesives (spray and liquid) up to a concentration of 13% (Household Products Database, US Department of Health and Human Services).

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 classified as hazardous with the following risk phrases in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

Xn; R21 (Acute toxicity)

Xi; R36 (Irritation)

Exposure Standards

Australian

No specific exposure standards are available.

International

The following are identified (Galleria Chemica):

Time Weighted Average (TWA): 110 mg/m³ (25 ppm) [Canada, Denmark, Iceland]

TWA: 86 mg/m³ (20 ppm) [Germany, Spain, Switzerland]

TWA: 45 mg/m³ (10 ppm) [Sweden]

Short-Term Exposure Limit (STEL): 90 mg/m³ (20 ppm) [Sweden]

STEL: 170 mg/m³ (40 ppm) [Switzerland]

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). Further, rapid conversion of the aldehyde by aldehyde dehydrogenase produces 2-propoxy acetic acid (PAA), the predominant urinary metabolite.

In general, monosubstituted glycol ethers are absorbed through the skin with the absorption rate decreasing with increasing molecular weight (NICNAS, 1996). Study data on the extent of absorption was equivocal although absorption was observed in all cases (IPCS 2009; REACH, 2011).

Acute Toxicity

Oral

The chemical is reported to be of low acute toxicity via the oral route ((median lethal dose (LD50) > 2000 mg/kg bw)) (IPCS, 2009; OECD, 2006; REACH, 2011).

Dermal

The chemical is classified as hazardous in Australia with the risk phrase 'Harmful in contact with skin' (R21). The data available (LD50 = 1300 mg/kg bw in rabbit) support this classification. Observed effects included prostration, hypothermia and haemoglobinuria and gross changes in the kidney, spleen, intestines and/or liver. (IPCS 2009, OECD, 2006; REACH, 2011)

Inhalation

No lethality has been reported in acute inhalation studies in rats at the highest vapour concentration administered (2132 ppm). However gross haemolysis and pathological changes in kidneys, liver and lungs were observed (IPCS 2009; OECD, 2006; REACH, 2011).

Overall

Signs of acute toxicity in rats and rabbits are consistent with haemolysis and non-specific central nervous system depression typical of organic solvents in general. The metabolite, PAA, is responsible for red blood cell haemolysis in rodents. However the effects of haemolysis were reversible and appear to be species dependent. PAA is reported to cause nearly complete haemolysis of red blood cells from rats at 5 mM, but had no effect on human red blood cells (Boatman *et al*.,1993).

Corrosion / Irritation

Skin Irritation

The chemical is reported to be slightly irritating to skin in animal studies, particularly following repeated exposure. Effects were not sufficient to warrant a hazard classification (IPCS 2009; REACH, 2011).

Eye Irritation

The chemical is classified as hazardous in Australia with the risk phrase 'Irritating to eyes' (R36). The data available support this classification. Effects observed including conjunctival redness and oedema, iritis and clouding of the cornea were reported to be reversible by two weeks but not within 7 days (IPCS 2009, REACH 2011).

Sensitisation

Skin Sensitisation

In general, monoalkyl glycol ethers do not appear to be sensitisers (NICNAS, 1996). The negative results seen for the chemical from several skin sensitisation animal studies support a conclusion that the chemical is not a skin sensitiser (IPCS, 2009; OECD, 2006; REACH, 2011).

Repeated Dose Toxicity

Oral

In a six-week oral gavage study in rats, a lowest observed adverse effect level (LOAEL) of 195 mg/kg bw day was reported. At this dose haemosiderin in the kidney was observed in 20% of animals. Effects consistent with haemolysis including effects in the liver, kidney and spleen were observed at higher concentrations (390, 780 and 1560 mg/kg bw/day). Histopathological changes were also observed in the stomach at the top doses (IPCS, 2009; OECD, 2006; REACH, 2009).

Dermal

No data are available.

Inhalation

In a 14-week repeated dose toxicity study in rats, the no observed adverse effect concentraion (NOAEC) was reported to be 100 ppm (425 mg/m³). Effects consistent with haemolysis including effects in the liver, kidney and spleen were observed at higher concentrations (200 and 400 ppm). The NOAEC for haemolytic effects of 100 ppm was also confirmed in additional studies (IPCS, 2009; OECD, 2006; REACH, 2011).

A separate study established an NOAEC of >784 ppm for pulmonary function (OECD, 2006).

Genotoxicity

In general, monethylene glycol ethers are not genotoxic (OECD, 2006; NICNAS, 1996). The negative results for the chemical from several *in vitro* and *in vivo* genotoxicity studies supports a conclusion that the chemical is not a genotoxicant (OECD, 2006; REACH, 2011).

Carcinogenicity

No carcinogenicity data are available for the chemical.

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 actions for the observed tumours (OECD, 2006; SCHER, 2008) and the similar effects observed with the two chemicals in acute and chronic toxicity studies, 2-butoxyethanol is considered a suitable analogue for the chemical for this endpoint.

Reproductive and Developmental Toxicity

Results of developmental toxicity studies conducted in both rabbits and rats via inhalation exposure indicate that the chemical is not teratogenic. Skeletal variations observed in the offspring of rats were only observed at maternally toxic doses (haemolysis) and no effects were observed in the offspring of rabbits even at maternally toxic doses. The NOAECs for developmental toxicity are greater than 500 ppm or 2125 mg/m³ (rabbit), 100 ppm or 425 mg/m³ (rat) (IPCS, 2009; OECD, 2006; REACH, 2011).

Although certain short chain monoethylene glycol ethers such as 2-methoxyethanol (CAS No. 109-86-4) are known reproductive toxicants, the ability of the glycol ethers to cause testicular toxicity decreases with increasing chain length.

It is considered that alkoxyacetic acid metabolites are responsible for testicular toxicity. The chemical's metabolite PAA has been reported to be toxic to pachytene spermatocytes at a concentration of 20 mM and slightly toxic at 10 mM. This toxicity is reported to be significantly lower (four-fold) than toxicity observed with methoxyacetic acid (MAA), the metabolite of 2-methoxyethanol (OECD, 2006).

There was no effect of PAA on testicular weights or morphology in rats treated with 776 mg/kg bw/day by gavage for 4 days (OECD, 2006). In addition, no significant effect of treatment on weights or histology of reproductive organs were observed in repeat dose toxicity studies (described above) with the chemical.

Other Health Effects

Neurotoxicity

In a 14 week repeated dose toxicity study in rats, the NOAEC for neurotoxic effects was reported to be > 400 ppm (1700 mg/m3) with no effects observed at the highest dose of 400 ppm.

Risk Characterisation

Critical Health Effects

The critical health effects, for risk assessment are acute toxicity via the dermal route of exposure and eye irritation.

Although the chemical is also reported to cause haemolysis and associated organ toxicity in rats, the severity of effects differs markedly between species, with humans appearing to be the least sensitive. Modelled data demonstrate that even at saturated concentrations of 2-butoxyethanol (a more potent haemolytic agent than 2-propoxyethanol) it is not possible to reach haemolytic blood concentrations of the relevant metabolite in humans by the inhalation route of exposure (NICNAS, 1996; OECD, 2006).

Public Risk Characterisation

Although the use of this chemical in domestic products in Australia is not known, the chemical is reported to be used in domestic products overseas at concentrations up to 13%. 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 domestic products containing the chemical is expected to be minimal at concentrations reported internationally (up to 13%).

The chemical does not appear to affect pulmonary function.

Occupational Risk Characterisation

Given the critical health effects the risk to workers from this chemical is considered low, particularly at concentrations below 25%, 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 undertaking (PCBU) at a workplace has adequate information to determine appropriate controls. The existing hazard classification is considered adequate for determining appropriate controls to protect workers handling the chemical.

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 public health and workers. However, a modified entry in the SUSMP for the specific chemical may be appropriate, as explained below.

Regulatory Control

Public Health

At present, the chemical falls 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, so it is recommended that a separate listing for 2-propoxyethanol be considered.

Work Health and Safety

The chemical is recommended for classification and labelling under the current Approved Criteria and adopted Globally Harmonised System (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 in contact with skin (Xn; R21)*	Harmful in contact with skin - Cat. 4 (H312)
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

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. 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.

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