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

04 July 2014

CAS Number: 100-37-8

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.

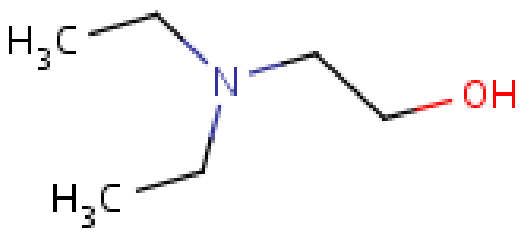
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	2-(Diethylamino)ethanol Diethylaminoethanol 2-Hydroxytriethylamine (2-Hydroxyethyl)diethylamine Diethyl ethanolamine
Structural Formula	
Molecular Formula	C6H15NO
Molecular Weight (g/mol)	117.19
Appearance and Odour (where available)	Colorless liquid
SMILES	C(O)CN(CC)CC

Import, Manufacture and Use

Australian

No specific Australian use, import or manufacture information has been identified.

International

The following international uses have been identified via the Registration Evaluation and Authorisation of Chemicals (REACH) Dossiers, the Organisation for Economic Cooperation and Development (OECD), Galleria Chemica, the Cosmetic Ingredients and Substances (CosIng) database, Personal Care Council Website (INCI Dictionary) & eChemPortal (Aggregated Computational Toxicology Resource (ACToR) and the Hazardous Substances Data Bank (HSDB)):

The chemical has reported cosmetic use:

- as a buffering agent in cosmetics.

The chemical has reported domestic use including:

- as a component of filler/sealing compounds and household cleaners/polishers (e.g. in shoe, leather, car).

The chemical has reported commercial use including:

- as a catalyst for the synthesis of polymers;
- as a pH stabiliser;
- as a component of corrosion inhibitors in closed systems, surface-active agents, cleaning/washing agents, cutting fluids, paint, lacquers and varnishes and surface treatment agents;
- in metal working fluids;
- as an additive in coatings, concrete and cement; and
- in the manufacture of emulsifying agents and special soaps.

The chemical has reported site-limited use including:

- as an intermediate in petroleum and gas processing chemicals; and
- in the production of pharmaceutical ingredients.

The chemical has reported uses as a food additive: use as a flavoring agents in Japan and Taiwan and in the USA up to 15 ppm is allowed; in steam contacting food except milk and milk products under US Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition.

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

Xn; R20/21/22 (Acute toxicity)

C; R34 (Corrosive)

Exposure Standards

Australian

The chemical has an exposure standard of 48 mg/m³ (10 ppm) Time Weighted Average (TWA).

International

48 - 50 mg/m³ (10 ppm) (OEL, TWA, STEL, PEL or STV) [USA (Alaska, Hawaii, Idaho, Michigan, Minnesota, Oregon, Tennessee, Vermont, Wyoming), Canada (Yukon), Norway, Switzerland, France, Greece, Ireland, Mexico, China, Argentina, Bulgaria, Czech Republic, Philippines, South Africa, Spain, Finland and New Zealand];

24 mg/m³ (5 ppm) MAK (Maximale Arbeitsplatz-Konzentration, or maximum allowed concentration) [Germany and Austria];

9.6 - 9.7 mg/m³ (2 ppm) (TWA, OEL, TLV or PEL) [USA (California), Canada (Alberta), Denmark, Iceland, Korea (South), Indonesian, Malaysia, Peru, Belgium and Singapore];

5 mg/m³ PDK (Predelno Dopustimaya Koncentraciya, or maximum allowed concentration) [Russia].

Health Hazard Information

Toxicokinetics

2-Diethylaminoethanol was rapidly absorbed via the oral route. It is also likely to be absorbed by dermal and inhalation routes. In the rat it was widely distributed to many tissues. It was primarily excreted unchanged via the urine in rats. Excretion via the faeces was also observed in rats, but to a lesser extent. Urinary excretion was also reported in humans (OECD, 2004).

The chemical has been reported to be rapidly absorbed via the oral route in humans and rats (Rosenberg et al., 1949 and Schulte et al., 1972). Rosenberg et al. (1949) reported that in humans, approximately 25% of the orally administered 2-diethyaminoethanol-HCl (5.6 g) was excreted unchanged in the urine within 48 hours. The plasma concentration peaked at 3 hours following oral administration and was almost undetectable after 8 hours.

In an oral gavage study with rats, radiolabeled 14C-2-diethylaminoethanol-HCl (68 or 679 mg/kg doses) was rapidly absorbed into the blood stream. With 68 mg/kg dose, the maximum concentration in the blood was reached in 30 minutes and with 679 mg/kg dose it was reached within 1 hour. The chemical was mainly excreted via the kidneys (of the 679 mg/kg bw dose, 40% was eliminated after 6 hours of application, 58.5% was eliminated within the first 24 hours and 90% was eliminated within 10

days after the application). In this study, autoradiography indicated that 2-diethylaminoethanol was widely distributed throughout the body after gavaging (Schulte et al., 1972).

Acute Toxicity

Oral

The data available support the current hazard classification in Australia: "Harmful if swallowed" (Xn; R22) (Safe Work Australia; HSIS).

The chemical was reported to cause acute toxicity via the oral route (median lethal dose (LD50) in rats = 1300 mg/kg bw) (JIHTAB, 1944).

Dermal

The data available support the current hazard classification in Australia: "Harmful in contact with skin" (Xn; R21) (Safe Work Australia; HSIS).

Rabbit dermal LD50 = 1260 mg/kg bw (Union Carbide Data Sheet, 1963) and guinea pig LD50 = 1000 mg/kg bw (JIHTAB, 1944).

Inhalation

The data available support the current hazard classification in Australia: "Harmful by inhalation" (Xn; R20) (Safe Work Australia; HSIS).

The mouse median lethal concentration (LC50) was reported to be 5000 mg/m³. Toxic effects include convulsions or effect on seizure threshold (GTPZAB, 1970). The rat lowest published lethal concentration (LCLo) = 4500 mg/m³/4 h (GTPZAB, 1970).

Observation in humans

The lowest published toxic concentration (TCLo) in humans = 200 ppm. Nausea or vomiting was reported at this dose (Toxicology of Drugs and Chemicals, 1969).

Corrosion / Irritation

Corrosivity

The available data support the current hazard classification in Australia: " Causes burns" (C; R34) (Safe Work Australia; HSIS).

Studies were performed in accordance to OECD Test Guideline (TG) 404, and reported that the chemical was corrosive to the rabbit skin after 4 hours of application, both occlusive and semi-occlusive (OECD, 2004).

Several other studies where the OECD TG were not followed demonstrated that the chemical has the potential of being severely irritating to the eyes or could cause serious damage to the eyes (OECD, 2004). Irreversible damage to corneal tissue and corrosion of the conjunctiva and eyelids were observed when 50 µl of the undiluted chemical was applied to the eye. These findings were also irreversible after 8 days (OECD, 2004).

Sensitisation

Skin Sensitisation

The chemical was not sensitising to the skin of guinea pigs (OECD, 2004).

The chemical was tested for skin sensitisation in guinea pigs using the method of Draize and the method of Magnusson and Kligman (OECD, 2004). The chemical was reported to be negative in both skin sensitisation methods. None of the 70 animals induced with 2-diethylaminoethanol showed signs of sensitisation.

Repeated Dose Toxicity

Oral

No data are available.

Dermal

No data are available.

Inhalation

No adverse systemic effects were reported in a 14-week inhalation toxicity study in rats.

Repeated exposure of rats to vapors of the chemical (up to 76 ppm or 0.365 mg/l) for 14 weeks caused local toxicity (irritation) at the upper respiratory tract and the eyes. However, systemic toxicity was not observed. No observed adverse effect concentration (NOAEC) for systemic toxicity = 0.365 mg/L (365 mg/m³ or 76 ppm) (OECD, 2004)). After inhalation exposure, the main finding described was respiratory irritation which led to noisy breathing (rales) and irritation of the eyes. The lowest observed adverse effect concentration (LOAEC) for local toxicity (irritation) to the respiratory tract was 0.120 mg/L (120 mg/m³ or 25 ppm). The NOAEC for local toxicity was 0.053 mg/L (53 mg/m³ or 10 ppm) based on a lack of histopathological effects in the nasal cavity at this dose. However, since an effect (rales) was seen at the lowest concentration a NOEC was not established (OECD, 2004).

Genotoxicity

Based on the data available, the chemical is not genotoxic.

The chemical was evaluated for mutagenicity in the *Salmonella* microsome preincubation assay using a standard protocol approved by the National Toxicology Program. Doses of 0, 33, 100, 333, 1000, 2500, and 3333 µg/plate were tested in four *S. typhimurium* strains (TA98, TA100, TA1535, and TA1537) in the presence and absence of metabolic activation. The chemical was negative in these tests and the highest ineffective dose level tested without total or slight clearing of the background lawn in any *S.* tester strain was 1000 µg/plate (OECD, 2004).

The chemical was also tested for its ability to induce micronuclei in bone marrow erythrocytes in mice in vivo using doses up to 500 mg/kg bw under guideline conditions and was found to be negative (OECD, 2004). The report also indicates that the highest dose tested was adequate since animals showed a hunched posture, piloerection, rales (an abnormal or pathological respiratory sound), irregular respiration and swollen abdomen. One animal was sacrificed *in extremis*. Data from the preliminary test indicated that the test substance can reach the bone marrow (OECD, 2004).

Carcinogenicity

While no reliable data are available, the chemical is not anticipated to be a carcinogen based on the negative data for genotoxicity (OECD, 2004) and lack of carcinogenicity for similar compounds such as Triethanolamine (OECD, 1996).

Reproductive and Developmental Toxicity

Based on the limited information available, the chemical is not likely to be a reproductive or developmental toxicant.

In a 14-week repeat dose toxicity study, inhalation of 365 mg/m³ (76 ppm) the chemical did not cause any adverse effects on the reproductive organs in rats under the conditions tested (OECD, 2004).

In pregnant rats treated with the chemical on gestational days 6 - 15 (6 hours/day) by gavage, the highest dose of 0.486 mg/L (100 ppm) produced maternally toxic effects (significant decrease in hypoplastic bones of the forepaw). There were no deaths observed in this study. No adverse developmental effects were reported at the lower dose of 0.160 mg/L (33 ppm). The NOAECs are 0.160 mg/L for maternal toxicity and 0.486 mg/L for developmental toxicity (OECD, 2004).

Risk Characterisation

Critical Health Effects

The main critical effect from exposure is corrosivity. The chemical may cause harmful effects if ingested, inhaled or in contact with skin.

Public Risk Characterisation

The chemical is used only as a buffering agent in cosmetics (CosIng) and therefore public exposure to higher concentrations of the chemical is not expected through cosmetic uses.

The chemical is also used in domestic products such as filler/sealing compounds and household cleaners/polishers. The concentration of the chemical in these domestic products in Australia is not known. The general public may be exposed to the chemical through dermal and/or inhalation routes when using domestic products containing the chemical. However, the concentration in these products is not considered to be high to cause corrosive effects based on the limited US information derived from the National Library of Medicine (NLM) Household Products Database.

Currently there are no restrictions in Australia to use this chemical in cosmetics or domestic products. If the concentrations in cosmetics and domestic products are low, corrosive effects are not expected. Therefore, further risk management is not considered necessary for public safety.

The current Australian exposure standard may require reconsideration, as in the repeat dose inhalation study, the presence of rales, albeit not severe, was observed in animals exposed at 10ppm, which is equivalent to the current exposure standard.

Occupational Risk Characterisation

Given the corrosive and harmful effects of the chemical, the risk to workers is considered high if adequate control measures to minimise occupational exposure to the chemical are not implemented. Inhalation exposure should be avoided to the extent possible. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or an employee at a work place has adequate information to determine appropriate controls for worker safety.

NICNAS Recommendation

The chemical is recommended for Tier III assessment to examine the adequacy of the current exposure standard. All other aspects have been sufficiently assessed at the Tier II level provided that the recommendations for classification and labelling are

followed.

Regulatory Control

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 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) Toxic if inhaled - Cat. 3 (H331)
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 domestic 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:

- protective clothing or protective equipment is used. The protective clothing or equipment should be designed, constructed, and operated to ensure that, the person handling the chemical (at concentrations greater than 25%) does not come into contact with the chemical; and
- 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

Arzneimittel-Forschung 1959. Drug Research. Vol.9, p.31. Cited in ChemIDPlus Advanced at http://chem.sis.nlm.nih.gov/chemidplus/

BASF AG 1969. Department of Toxicology, unpublished report (XVIII/320), 27 Jan 1969. Cited in OECD 2004, SIAR on Ethanol, 2-(diethylamino)- (100-37-8). Accessed October 2012 at http://webnet.oecd.org/hpv/UI/handler.axd?id=ce6dbeae-

BASF AG 1982. Department of Toxicology, unpublished report (82/18), 26.08.1982. Cited in OECD 2004, SIAR on Ethanol, 2-(diethylamino)- (100-37-8). Accessed October 2012 at http://webnet.oecd.org/hpv/UI/handler.axd?id=ce6dbeae-

Canada Ingredient Disclosure List . Diethylaminoethanol. Accessed October 2012 at http://laws-lois.justice.gc.ca/eng/regulations/SOR-88-64/index.html

Cosmetics Directive (CosIng). Diethyl ethanolamine. Accessed October 2012 at http://ec.europa.eu/consumers/cosmetics/cosing/

eChemPortal, Diethylaminoethanol (100-37-8). Accessed October 2012 at http://www.echemportal.org/echemportal/page.action?pageID=9

Galleria Chemica. Diethylaminoethanol (100-37-8). Accessed October 2012 at http://jr.chemwatch.net/galleria/

Gigiena Truda i Professional'nye Zabolevaniya 1970. Labor Hygiene and Occupational Diseases. Vol.14(11), p. 52. Cited in ChemIDPlus Advanced at http://chem.sis.nlm.nih.gov/chemidplus/

JIHT Journal of Industrial Hygiene and Toxicology 1944. Vol. 26, p. 269. Cited in ChemIDPlus Advanced at http://chem.sis.nlm.nih.gov/chemidplus/

JIHTAB Journal of Industrial Hygiene and Toxicology 1944. Vol. 26, p.269. Cited in ChemIDPlus Advanced at http://chem.sis.nlm.nih.gov/chemidplus/

JPETAB Journal of Pharmacology and Experimental Therapeutics 1948. Vol. 94, p. 249. Cited in ChemIDPlus Advanced at http://chem.sis.nlm.nih.gov/chemidplus/

OECD (1996). SIAR on Triethanolamine (102-71-6). Accessed October 2012 at http://webnet.oecd.org/hpv/ui/handler.axd?id=495476c1-4d29-4b46-9885-af845f9f6b7d

OECD 2004. SIAR on Ethanol, 2-(diethylamino)- (100-37-8). Accessed October 2012 at http://webnet.oecd.org/hpv/UI/handler.axd?id=ce6dbeae-dc52-43df-a418-783e79adf8d2

Personal Care Product Council. Diethylaminoethanol. Accessed October 2012 at http://www.ctfa-gov.org/jsp/gov/GovHomePage.jsp

REACH Dossier 2012. 2-diethylaminoethanol (100-37-8). Accessed October 2012 at http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d82d050-2753-1f77-e044-00144f67d249/AGGR-4d8c5b62-ed47-4269-82c3-c05d2ec38c56_DISS-9d82d050-2753-1f77-e044-00144f67d249.html#section_3_5

Rosenberg B et al. 1949. J. Pharmacol. Exp. Ter. 95 pp.18-27. Cited in OECD 2004, SIAR on Ethanol, 2-(diethylamino)- (100-37-8). Accessed October 2012 at http://webnet.oecd.org/hpv/UI/handler.axd?id=ce6dbeae-

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

Schulte KE et al. 1972. Arzneimittel-Forsch. 22 pp. 1381-1390. Cited in OECD 2004, SIAR on Ethanol, 2-(diethylamino)- (100-37-8). Accessed October 2012 at http://webnet.oecd.org/hpv/UI/handler.axd?id=ce6dbeae-dc52-43df-a418-783e79adf8d2

Toxicology and Applied Pharmacology 1968. Vol.12, p.486. Cited in ChemIDPlus Advanced at

http://chem.sis.nlm.nih.gov/chemidplus/

Toxicology of Drugs and Chemicals 1969. p. 216. Cited in ChemIDPlus Advanced at http://chem.sis.nlm.nih.gov/chemidplus/

Union Carbide Data Sheet 1963. Vol.6, p. 11. Cited in ChemIDPlus Advanced at http://chem.sis.nlm.nih.gov/chemidplus/

Zeiger E et al. 1987. Environ Mutagen. Vol. 9, pp. 1-110. Cited in OECD 2004, SIAR on Ethanol, 2-(diethylamino)- (100-37-8). Accessed October 2012 at http://webnet.oecd.org/hpv/UI/handler.axd?id=ce6dbeae-

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