

Ethanaminium, N,N,N-triethyl-, hydroxide: Human health tier II assessment

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CAS Number: 77-98-5



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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.

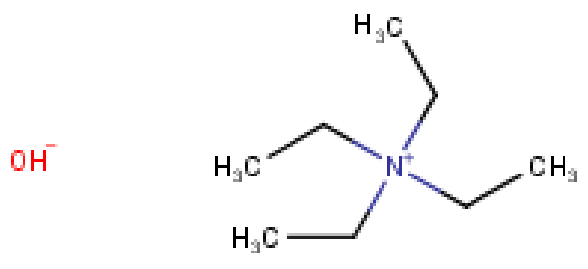
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Acronyms & Abbreviations

Chemical Identity

Synonyms	tetraethylammonium hydroxide (TEAH)
Structural Formula	
Molecular Formula	C ₈ H ₂₀ N.HO
Molecular Weight (g/mol)	147.26
Appearance and Odour (where available)	colourless, light yellow liquid
SMILES	<chem>C(C)N{+}(O{-})(CC)(CC)CC</chem>

Import, Manufacture and Use

Australian

The National Pollutant Inventory (NPI) holds data for all sources of the chemical in Australia.

Safety data sheets (SDS) indicate that the chemical has Australian site-limited uses, including as a:

- chemical intermediate; and
- phase-transfer catalyst.

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR) and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported commercial uses, including in:

- selective etching;
- oil and water based hydraulic fracturing;
- advanced ceramics; and
- flat panel display chemicals.

The chemical has reported site-limited uses, including:

- as an intermediate in photovoltaic chemicals;
- as a phase-transfer catalyst;
- as a trans-esterification catalyst; and
- in chemical synthesis.

Restrictions

Australian

This chemical is covered by the group entry for QUATERNARY AMMONIUM COMPOUNDS in Schedules 5 and 6 and by TETRAETHYLAMMONIUM entry in Schedule 4 of the Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP, 2019):

Schedule 6:

'QUATERNARY AMMONIUM COMPOUNDS except:

- a) when separately specified in these Schedules;
- b) when included in Schedule 5;
- c) dialkyl or dialkoyl quaternary ammonium compounds where the alkyl or alkoyl groups are derived from tallow or hydrogenated tallow or similar chain length (C16/C18) sources; or
- d) in preparations containing 5 per cent or less of such quaternary ammonium compounds.'

Schedule 5:

'QUATERNARY AMMONIUM COMPOUNDS in preparations containing 20 percent or less of quaternary ammonium compounds except:

- a) when separately specified in these Schedules;
- b) dialkyl or dialkoyl quaternary ammonium compounds where the alkyl or alkoyl groups are derived from tallow or hydrogenated tallow or similar chain length (C16/C18) sources; or
- c) in preparations containing 5 per cent or less of such quaternary ammonium compounds.'

Schedule 4:

'TETRAETHYLAMMONIUM'

Schedule 4 chemicals are described as 'Substances, the use or supply of which should be by or on the order of persons permitted by State or Territory legislation to prescribe and should be available from a pharmacist on prescription'. Schedule 4 chemicals are labelled with 'Prescription Only Medicine, or Prescription Animal Remedy' (SUSMP, 2019).

Schedule 5 chemicals are described as 'Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.' Schedule 5 chemicals are labelled with 'Caution' (SUSMP, 2019).

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, 2019).

International

No known restrictions specific to this chemical have been identified.

Quaternary ammonium compounds are listed in the Identification of Risk Assessment Priorities (IRAP) Canada as substances recommended for further scoping/problem formulation (Galleria Chemica).

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica):

Temporary Emergency exposure Limits (TEELs) defined by the US Department of Energy (DOE) for the chemical are reported as:

TEEL-1 = 1.2 mg/m³;

TEEL-2 = 13 mg/m³;

TEEL-3 = 79 mg/m³.

Health Hazard Information

Tetraethylammonium hydroxide (aqueous solution) is strongly basic (with pH >13 for a 35 % aqueous solution) clear colourless liquid. The systemic toxicity of tetraethylammonium hydroxide is considered to be due to the presence of the tetraethylammonium cation. The hydroxide ion is not considered to contribute to the systemic toxicity of the chemical.

Tetramethylammonium hydroxide (CAS No. 75-59-2) is a structural analogue of the chemical (REACH). Therefore, in the absence of toxicity data for the chemical, available data for this analogue were used as read-across for local effects. This report should be read in conjunction with the IMAP Human Health Tier II reports for tetraethylammonium (TEA) salts and tetramethylammonium hydroxide (NICNAS).

Toxicokinetics

The chemical can enter the body via oral, dermal and inhalation routes. Due to its high solubility in water and low molecular weight, uptake of the tetraethylammonium ion is mostly via passive diffusion from the gastrointestinal tract (GIT), respiratory tract and the skin. Elimination occurs mainly via the urine (REACH).

Acute Toxicity

Oral

The chemical has moderate acute toxicity based on results from animal tests following oral exposure. The median lethal dose (LD50) in rats is between 300–2000 mg/kg body weight. Hazard classification is warranted (see **Recommendation** section).

In an acute oral toxicity study conducted according to OECD Test Guideline (TG) 423, female Crl:WI (Han) rats (n=3/group) were treated with the chemical (35 % solution in water) by gavage at doses of 300 or 2000 mg/kg bw. Mortalities were recorded in 1/3 rats at 300 mg/kg bw and 3/3 rats at 2000 mg/kg bw between 2 to 4 hours post-treatment. Clinical signs observed included piloerection, hunched posture, lethargy, uncoordinated movements and tremors of the head. Red discolouration of the stomach and reduced thymus sizes were seen at gross pathological examination. The LD50 was determined to be between 300 and 2000 mg/kg bw (REACH).

Dermal

Based on the available limited information, the chemical is considered to have moderate acute dermal toxicity and warrants hazard classification.

In an acute dermal toxicity study (OECD TG 402) in Sprague Dawley (SD) rats (n=5/sex/dose), the chemical (35 % concentration in water) was semiocclusively applied at 2000 mg/kg bw for 24 hours. Mortality was recorded as 3/10 animals (2 males and 1 female). Observed effects included convulsions, vocalisation, wetness of the anogenital areas and chromorhinorrhoea (pigmented secretion from nose). Necrotic skin tissue with pale areas and slight oedema was observed at 24 hours post-treatment. A LD50 > 2000 mg/kg bw (equivalent to >700 mg/kg bw for pure chemical) was determined (REACH).

Inhalation

No data are available.

Corrosion / Irritation

Corrosivity

Based on the strong alkaline nature (pH >13) of the chemical and available data on the methyl analogue from studies conducted according to OECD TG 404 and 435, the chemical is considered to be corrosive. Hazard classification is warranted (see **Recommendation** section).

In a skin irritation study (OECD TG 404) in New Zealand White rabbits (n=3), 0.5 mL of 2.38 % aqueous solution of the analogue chemical elicited a severe, irreversible dermal reaction with necrosis in 1 animal (REACH).

Sensitisation

Skin Sensitisation

No data are available.

Repeated Dose Toxicity

Oral

Based on the available data on the TEA salts, and the limited available data on the chemical, the effects were not sufficient to meet the classification criteria for repeated dose toxicity.

In a 90-day study, TEAH (35 % in water) was administered in Crl:WI(Han) rats (n=10/sex/dose) at 0, 10, 30 or 100 mg/kg bw/day for 90 days. A no observed adverse effect level (NOAEL) of >100 mg/kg bw/day was reported based on the absence of adverse effects at the highest dose level tested. Effects observed at 30 and 100 mg/kg bw/day included: significant reduction in foregrip strength in males, increased creatinine and potassium levels in 100 mg/kg bw/day females and a trend towards lower body weight and body weight gain in 100 mg/kg bw/day males (REACH).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the available in vitro and in silico genotoxicity studies for the TEA salts, the chemical is not considered to be genotoxic.

Negative results were observed with TEAH in a bacterial reverse mutation assay (OECD TG 471) in *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537, and in *Escherichia coli* WP2 *uvrA* at concentrations up to 1250 µg/plate, with and

without metabolic activation (REACH).

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Based on the limited information available for TEA salts, the chemical is not expected to cause any reproductive or developmental toxicity.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic acute health effects (acute toxicity from oral and dermal exposure) and local effects (corrosivity).

Public Risk Characterisation

Given the uses identified for this chemical, it is unlikely that the public will be exposed. Hence, the public risk from this chemical is not considered to be unreasonable.

The chemicals are currently listed on Schedule 5 and 6 of the SUSMP for 'QUATERNARY AMMONIUM COMPOUNDS' and on Schedule 4 for 'TETRAETHYLAMMONIUM'. At concentrations greater than 5 %, a number of warning statements, first aid instructions and safety directions apply. The current controls are considered adequate to minimise the risk to public health posed by any potential use in domestic and cosmetic products.

Occupational Risk Characterisation

During product formulation, oral, dermal and ocular exposure may 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 chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic acute and local health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal and ocular exposure are implemented. Good hygiene practices to minimise oral exposure are expected to be in place. 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 the appropriate controls.

The data available support an amendment to the hazard classification in the HCIS (Safe Work Australia) (refer to **Recommendation** section).

NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that risk management recommendations are implemented and all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Consideration should be given to the revision of the Schedule 4 entry for the TETRAETHYLAMMONIUM to limit its use to therapeutics only.

Regulatory Control

Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2019).

Work Health and Safety

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

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Acute Toxicity	Not Applicable	Harmful if swallowed - Cat. 4 (H302) Harmful in contact with skin - Cat. 4 (H312)
Irritation / Corrosivity	Not Applicable	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 industry

Control measures

Control measures to minimise the risk from oral, dermal and ocular 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 chemicals are used. Examples of control measures that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- 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 chemicals.

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 help meet 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 chemicals 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 these chemicals has not been undertaken as part of this assessment.

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