Ethane, 1,1,2-trichloro-: Human health tier II assessment

17 May 2013

CAS Number: 79-00-5

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.

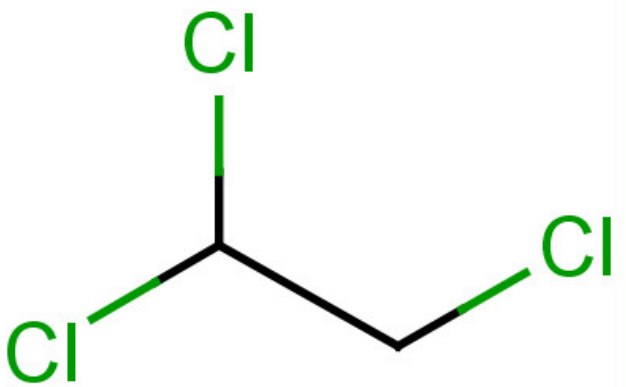
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	Ethane trichloride Vinyl trichloride 1,1,2-Trichloroethane beta-Trichloroethane
Structural Formula	
Molecular Formula	C2H3Cl3
Molecular Weight (g/mol)	133.405
Appearance and Odour (where available)	Transparent colourless liquid, with a sweet chloroform-like odour.
SMILES	C(Cl)(Cl)CCl

Import, Manufacture and Use

Australian

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

International

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

The chemical has reported domestic use including in:

- adhesives;
- lacquer and coating formulations; and
- aerosol paints.

The chemical has reported commercial use including:

- as a solvent in the manufacture of organic materials (fats, oils, waxes, resins).

The chemical has reported site limited use including:

- as an intermediate in the production of vinylidene chloride (1,1-dichloroethylene) and tetrachloroethanes.

Restrictions

Australian

No known restrictions have been identified.

International

US—California Proposition 65—No Significant Risk Levels (NSRLs) adopted in regulation for carcinogens. The NSRL for the chemical is 10 µg/d.

List of Substance Subject to Authorization, under REACH.

US TSCA Section 12(b)—List of Chemical Substances Subject to Export Notification Requirements.

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):

Carc.Cat.3; R40

Xn; R20/21/22

Xn; R66

Exposure Standards

Australian

TWA: 55 mg/m³ (10 ppm)

International

The following exposure standards are identified (Galleria Chemica):

An exposure limit (TWA) of 35–56 mg/m³ (8–10 ppm) and STEL (or KZG-W) of 30–275 mg/m³ (20–50 ppm) in different countries such as Argentina, Austria, Belgium, Brazil, Finland, Germany, Mexico, Philippines (skin), South Africa, Switzerland and United States of America (NIOSH, OSHA, TSCA and the following states Alaska, California, Hawaii, Idaho, Michigan, Minnesota, Oregon, Tennessee, Vermont, Wyoming).

Health Hazard Information

Toxicokinetics

The primary metabolites identified in rats and mice given 1,1,2-trichloroethane by gavage were chloroacetic acid, S-carboxymethylcysteine, and thiodiacetic acid (HSDB 2012).

Ethane, 1,1,2-trichloro- is rapidly absorbed across biological membranes in both humans and a variety of mammalian species following exposure. The half-life following inhalation in mice was determined to be 49.3 minutes (HSDB 2012).

Acute Toxicity

Oral

The chemical is currently classified with the risk phrase 'Harmful if swallowed (R22)' in Australia (Safe Work Australia, 2012). The data available support this classification.

The chemical has acute toxicity via the oral route (LD50 in mice = 378 mg/kg bw and in rats = 837 mg/kg bw) (OECD, 2000). In the mouse study a loss of righting reflex and sedation with irritation of the upper gastrointestinal tract and reddened or haemorrhagic lungs were seen, with deaths appearing to result from depression of the central nervous system (HSDB, 2012).

Dermal

The chemical is currently classified with the risk phrase 'Harmful in contact with skin (R21)' in Australia (Safe Work Australia, 2012). The data available on guinea pigs are consistent with this classification.

In an acute dermal toxicity study on guinea pigs, the chemical was found to have a Lowest Published Lethal Dose (LDLo) of 970 mg/kg. In a second study in guinea pigs, the chemical was also found to kill all the test animals at a dose rate of 232 mg/cm²

(0.5 ml applied to a 3.1cm² area of the back) (REACH, 2013).

In an acute dermal toxicity study on rabbits the chemical applied via the dermal route was reported to have an LD50 of 5377 mg/kg (HSDB, 2012).

Inhalation

The chemical is currently classified with the risk phrase 'Harmful by inhalation (R20)' in Australia (Safe Work Australia, 2012). The data available support this classification.

The chemical was reported to have moderate acute toxicity via inhalation (6 hours) (LC50 = 9000 mg/m³) in rats (SIAR 2000, HSDB 2012).

Observation in humans

Data on humans indicate that the chemical was a narcotic at low concentrations (OECD, 2000).

Corrosion / Irritation

Skin Irritation

The chemical is currently not classified as a skin irritant in Australia (Safe Work Australia, 2012). The data available support this classification.

When applied to the skin of rabbits the chemical showed mild irritation at a dose of 500 mg with 24 h exposure and severe irritation at a dose of 810 mg with 24 h exposure (OECD, 2000). Safework Australia criteria are based on a 500 mg amount of the test substance applied for 4 h.

Eye Irritation

The chemical is currently not classified as an eye irritant in Australia (Safe Work Australia, 2012). The data available support this classification.

The chemical was found to be a mild eye irritant at dose levels up to 500 mg with 24 h exposure.

Observation in humans

In humans, the chemical was reported to irritate the conjunctiva and the mucosa of the respiratory tract and the external skin (OECD, 2000).

Sensitisation

Skin Sensitisation

No data are available. The chemical was highlighted as a potential protein binder via nucleophilic substitution at a halogenated sp3 carbon atom (OECD toolbox). However, when reading across from all of the protein binding chemicals that could also potentially undergo nucleophilic substitution at a halogenated sp3 carbon atom and eliminating all the chemicals with

superfragments and where an alert was found for protein binding for skin sensitisation by OASIS v1.1, the chemical was predicted not to be skin sensitising (OECD toolbox).

Repeated Dose Toxicity

Oral

Based on the available information no hazard classification for repeat dose oral toxicity is recommended.

In a 90 day oral (drinking water) repeated dose toxicity study in mice, the chemical was present in the drinking water at concentrations of 20, 200 or 2000 mg/L. Daily intakes were estimated to be 0, 4.4, 46, and 305 mg/kg/day for males and 0, 3.9, 44, and 384 mg/kg/day for females. Effects reported included reductions in body weight gain (males), glutathione content (males), cytochrome P-450 content (females), aniline hydroxylase activities (females), haematocrit (females), haemoglobin (females), humoral immune status (both sexes) and increased alkaline phosphatase activity (both sexes). The NOELs for male and female mice in this study were 4.4 mg/kg bw/day and 3.9 mg/kg bw/day respectively (OECD, 2000).

In additional studies by gavage on rats and mice, the predominant effects seen were decreases in bodyweight and changes in liver biochemical parameters (European Commission, 2000).

Dermal

No data are available.

Inhalation

There are three inhalation studies available for the chemical where the animals were exposed for 6 months to a 15 ppm (15 mg/L) concentration. The studies were carried out on rats, rabbits and guinea pigs with no adverse effects seen in any of the species (OECD, 2000).

Observation in humans

In humans, this chemical was reported to cause gastrointestinal tract complaints, fatty degeneration of the kidneys and lung damage through prolonged exposure (OECD, 2000).

Genotoxicity

Although the chemical was found to have mixed results in a range of in vitro and in vivo tests and computer modelling (suggesting that interaction between the chemical and DNA could occur) the latest micronucleus test in mice in vivo showed negative results. Therefore the weight of evidence suggests that this chemical is not genotoxic.

The chemical produced negative results in a number of bacterial reverse mutation assays and DNA damage and repair assays all with and without metabolic activation. Unscheduled DNA synthesis due to the chemical was tested in a range of mammalian cells in vitro with both positive and negative results, although in in vivo the chemical did not cause unscheduled DNA synthesis. Positive results were seen in a gene mutation assay and a yeast cytogenetic assay without metabolic activation and showed indications of an aneuploidy-inducing effect. Positive results were also seen in a micronucleus test in vitro and a comet assay both in human lymphocytes with and without metabolic activation and in a mouse cell transformation assay performed without metabolic activation. Additional computer modelling and mechanistic studies indicated a potential for DNA binding (European Commission, 2000; OECD, 2000).

The chemical has also been tested in an in vivo mammalian erythrocyte micronucleus test according to OECD Test Guideline 474. This test was conducted in mice by gavage at doses up to 400 mg/kg bw, based on severe toxicity at 800 mg/kg in a

previous range-finding study. No increases in the number of micronucleated polychromatic erythrocytes in bone marrow cells were observed indicating that the chemical is not genotoxic in vivo (OECD, 2003).

Carcinogenicity

The chemical is currently classified with the risk phrase 'Limited evidence of a carcinogenic effect (R40)' in Australia (Safe Work Australia, 2012). The data available support this classification.

The chemical is classified by the International Agency on Cancer (IARC) as *not classifiable as to its carcinogenicity to humans* (Group 3).

The chemical was tested for carcinogenicity in a two year study in male and female mice and rats by oral administration and also in rats by subcutaneous injection. In the study by oral administration, the chemical produced hepatocellular neoplasms and adrenal phaeochromocytomas in mice of each sex but did not significantly increase the proportion of rats with neoplasms at any site relative to untreated controls. In the study in rats by subcutaneous injection, the chemical did not increase the incidence of neoplasms (IARC, 1999).

Reproductive and Developmental Toxicity

In a developmental toxicity study, the chemical was administered by gavage to mice on days 8 to 12 of gestation at dose of 350 mg/kg bw/day with no adverse effects on embryo/foetal viability, and/or postnatal growth and viability (OECD, 2000).

Risk Characterisation

Critical Health Effects

The critical effect for risk characterisation is carcinogenicity. The chemical also has acute oral, dermal and inhalation toxicity, as well as causing adverse effects following repeated oral exposure.

Public Risk Characterisation

No public exposure to the chemical is expected, based on the available use data.

Occupational Risk Characterisation

During product formulation, dermal and inhalation 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 during use of 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 critical long and short term systemic health effects of the chemical, the chemical may pose an unreasonable risk to workers if adequate control measures to minimise dermal and inhalation 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), e.g. employer, at a workplace has adequate information to determine appropriate controls.

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

NICNAS Recommendation

Current risk management measures are considered adequate for the protection of 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

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

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below:

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (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) Harmful if inhaled - Cat. 4 (H332)
Carcinogenicity	Carc. Cat 3 - Limited evidence of a carcinogenic effect (Xn; R40)*	Suspected of causing cancer - Cat. 2 (H351)

[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 dermal or inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls, which include: substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical are dependent on the physical form and the manner in which the chemical is employed. Examples of control measures which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automation of 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 be relied upon on its own 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 hazardous 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 chemical's physical hazards has not been undertaken as part of this assessment.

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The European Commision (EC) 2000. European Chemicals Bureau. International Uniform Chemical Information Database (IUCLID) on 1,1,2-trichloroethane (79-00-5).

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