Australian Government
Department of Health and Ageing
NICNAS

INVENTORY MULTI-TIERED ASSESSMENT AND PRIORITISATION (IMAP)

HUMAN HEALTH TIER II ASSESSMENT FOR

Ethane, chloro-

CAS Registry Number: 75-00-3

PREFACE

As part of the reform regarding assessment of Existing Chemicals, the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is implementing a new framework to address the human health and environmental impacts of industrial chemicals, not yet assessed, on the Australian Inventory of Chemical Substances (AICS).

The framework provides a more rapid, flexible and transparent approach for the assessment of existing chemicals.

The Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework was developed, with significant input from stakeholders, and will be applied in stages.

Stage One of this program, which will take three years, started 1 July 2012 and is examining 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This includes chemicals for which NICNAS already holds exposure information, chemicals identified as a concern or for which regulatory action has been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

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.

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

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

ACRONYMS & ABBREVIATIONS

ACToR	Aggregated Computational Toxicology Resource (US)
AICS	Australian Inventory of Chemical Substances
ASTDR	Agency for Toxic Substances and Disease Registry (US)
bw	bodyweight
CAS	Chemical Abstracts Service
CFR	Code of Federal Regulations (US)
CHO	Chinese hamster ovary
CosIng	Cosmetic Ingredients and Substances database (EU)
d	day
DNA	Deoxyribonucleic acid
EC	European Commission
EC3	Estimated concentration three
ECHA	European Chemicals Agency
ESIS	European Chemical Substances Information System
EU	European Union
EU RAR	European Union Risk Assessment Report
FDA	Food and Drug Administration (US)
FSANZ	Food Standards Australia and New Zealand
g	gram
g/mol	grams per mole
GHS	Globally Harmonized System of Classification and Labelling of Chemicals*
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GPMT	Guinea Pig Maximisation Test
h	hour
HGPRT	hypoxanthine guanine phosphoribosyltransferase
HPV	high production volume
HSDB	Hazardous Substances Data Bank
HSIS	Hazardous Substances Information System
HVICL	High Volume Industrial Chemicals List
IARC	International Agency for Research on Cancer
INCHEM	International Programme on Chemical Safety (also known as IPCS)
INCI	International Nomenclature of Cosmetic Ingredients
ip	intraperitoneal
IRIS	Integrated Risk Information System (US)
IUCLID	International Uniform Chemical Information Database
iv	intravenous
kg	kilogram
L	litre
LC50	median lethal concentration
LD50	median lethal dose
LCLo	lowest published lethal concentration
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOEL	lowest observed effect level
m^3	cubic metre
mg	milligram
mg/cm^3	milligrams per cubic centimetre
mg/kg bw/d	milligrams per kilogram bodyweight per day
min	minute
mL	millilitre
µg	microgram
µL	microlitre
(m)SDS	(material) Safety Data Sheet

NIOSH	National Institute for Occupational Safety and Health (US)
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOHSC	National Occupational Health and Safety Commission
NTP	National Toxicology Program (US)
OECD	Organisation for Economic Cooperation and Development
OEL	occupational exposure limit
PCBU	person conducting a business or undertaking
PEL	permissible exposure limit
PND	postnatal day
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
REACH	Registration Evaluation Authorisation of Chemicals (ECHA)
SD	Sprague Dawley
SIAP	SIDS Initial Assessment Profile (OECD)
SIAR	SIDS Initial Assessment Report (OECD)
SIDS	Screening Information Data Set (OECD)
SMILES	simplified molecular-input line-entry system
SPIN	Substances in Preparations In the Nordic countries
STEL	short-term exposure limits
STV	short-term value
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons (The Poisons Standard**)
TCLo	lowest published toxic concentration
TEEL	temporary emergency exposure limits
TSCA	Toxic Substances Control Act (US EPA)
TG	test guideline
TGA	Therapeutic Goods Administration
TLV	threshold limit values
TWA	time weighted average
UN	United Nations
US	United States of America
US EPA	United States Environmental Protection Agency
WHS	Work, Health and Safety
wt	weight
w/w	weight per weight

Glossary

NICNAS uses the IPCS Risk Assessment Terminology (IPCS, 2004) glossary, which includes:
Part 1: IPCS/OECD Key Generic Terms used in Chemical Hazard/Risk Assessment; and
Part 2: IPCS Glossary of Key Exposure Assessment Terminology.
The IPCS Risk Assessment Terminology can be accessed at:
http://www.who.int/ipcs/methods/harmonization/areas/ipcsterminologyparts1and2.pdf

*****Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Can be accessed at: http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

******The Poisons Standard (the SUSMP) can be accessed at: http://www.tga.gov.au/industry/scheduling-poisons-standard.htm

Ethane, chloro-

CAS No: 75-00-3

Chemical Identity

Synonyms	Chloroethane Ethyl chloride Aethylchlorid Aethylis Chloryl
Structural Formula	
Molecular Formula	C2H5Cl
Molecular Weight (g/mol)	65.5145
Appearance and Odour (where available)	A colourless gas at room temperature and pressure, with a pungent, ether-like odour and a burning taste.
SMILES	C(C)Cl

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 site-limited use including in the manufacture of chemicals.

The following uses have been identified through the National Pollutant Inventory (NPI).

The chemical has reported site-limited use including:
- as a blowing agent in foamed plastics;
- in the manufacture of ethyl cellulose, dyes, and other commercial chemicals; and
- as a refrigerant.

The chemical has reported commercial use including:
- as a solvent.

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

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 data set International Assessment Report (OECD SIAR), Galleria Chemica and the US Agency for Toxic Substances and Disease Registry (ATSDR) toxic substances portal.

The chemical has reported commercial use including:
- as a solvent for phosphorus, sulfur, fats, oils, resins, and waxes.

The chemical has reported site-limited use including:
- in the production of tetraethyllead and as an alkylating agent in the production of ethylcellulose and ethylhydroxycellulose, aluminium alkyls and other metal alkyls; and

- as a foam-blowing agent in polystyrene production.

The following non-industrial uses have been identified internationally:
- insecticide; and
- medicine (anaesthetic).

Restrictions

Australian

The chemical is on the Australia Government Department of Sustainability, Environment, Water, Population and Communities, National Pollutant Inventory (NPI); it has a threshold for emissions of 10 tonnes per year before it must be reported.

International

Health Canada, Consumer Product Safety Bureau, Cosmetics Division, Canada List of Prohibited and Restricted Cosmetic Ingredients (The Cosmetic Ingredient "Hotlist"), March 2011.

EU Cosmetic Directive 76/768/EEC Annex II: List of Substances which must not form part of the Composition of Cosmetic Products.

New Zealand Cosmetic Products Group Standard - Schedule 4: Components Cosmetic Products Must Not Contain.

Existing Worker 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.

Exposure standards

Australian

The chemical has an exposure standard of 2640 mg/m³ (1000 ppm) time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica):
An exposure limit (OEL, TWA, STEL, PEL or STV) of 25 – 2640 mg/m³ (9 - 1000 ppm) in different countries such as USA, United Kingdom, Japan, Canada, European Union and Switzerland.

Health Hazard Information

Toxicokinetics

The chemical is readily absorbed following inhalation (OECD, 2007). Human volunteers were reported to exhale approxmately 30% of an inhaled dose within 1 hour (IARC, 1991).

Acute Toxicity

Oral

There are no acute oral toxicity LD50 values available for the chemical. However, the chemical has the lowest published toxic doses of 250 mg/kg and 600 mg/kg for rats and mice respectively (RTECS).

Dermal

No data are available.

Inhalation

The chemical exhibits low acute toxicity in animal tests following inhalation exposure with no toxic effects in rodent studies (median lethal concentrations (LC50) > 19,000 ppm (OECD, 2007). A two hr LC50 of 152 mg/L (57600 ppm) has been reported in rodents (*ChemIDPlus Advanced).*

Observation in humans

The chemical produces neurological effects such as dizziness, analgesia and symptoms of intoxication after inhalation with effects seen at concentrations down to 13,000 ppm (OECD, 2007).

Corrosion / Irritation

Skin irritation

No animal test data are available. Irritant effects have been observed in humans (see below).

Eye irritation

The chemical is reported to cause epithelial damage to the eyes of rabbits (*ChemIDPlus Advanced).*

Observation in humans

Exposure to the chemical as a vapour has been reported to be irritating to the eyes, nose and throat with exposure to the chemical as a liquid being irritating to skin and eyes (OECD, 2007).

Sensitisation

Skin sensitisation

No animal test data available. Cases of contact dermatitis have been reported in humans (see below).

Observation in humans

There are a few reports of allergic contact dermatitis to the chemical.

Several separate cases of contact dermatitis have been reported where a medical aerosol containing the chemical has been applied. In the majority of these cases, subsequent re-exposure to the spray and patch tests revealed contact sensitisation to the chemical (Aberer, 1989; Bircher, 1994; Kriechbaumer, 1998; Van Ketel, 1976).

Patch tests performed on two patients with eczema were strongly positive for the chemical (Van Ketel, 1976).

However, in the absence of supporting data (animal tests or structural alerts for sensitisation), the human evidence is not considered sufficient to warrant a hazard classification. In addition, the expected rapid evaporation of the chemical would limit intense and prolonged contact with the skin and consequently contact sensitisation.

Repeat Dose Toxicity

Oral

Rabbits that were administered the chemical by gavage for 60 exposures at doses up to 1000 mg/kg bw showed no adverse effects from the treatment. No adverse treatment related effects were observed in rats during a 14 day oral study where animals were exposed to 0.57 g per 100 g of water (OECD, 2007).

Inhalation

Considering the LOECs for inhalation available from several rat studies (4000-19000 ppm), and based on the treatment related effects reported in various repeat-dose toxicity studies (predominantly limited to liver to bodyweight increases and overall bodyweight reductions) (OECD, 2007), the chemical is not considered to cause serious damage to health by repeated inhalation exposure.

Genotoxicity

The chemical is positive for genotoxicity *in vitro* however genotoxicity has not been demonstrated *in vivo*.

The chemical induced genetic mutations in *in vitro* tests on bacteria and Chinese hamster ovary cells, but in a mouse micronucleus assay did not show chromosomal damage *in vivo* at concentrations as high as 25,000 ppm. No consistent increase in S-phase DNA synthesis and genotoxic activity was seen in a unscheduled DNA synthesis assay (OECD, 2007).

Carcinogenicity

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

The chemical is classifed by the International Agency on Cancer (IARC) as *not classifiable as to its carcinogenicity to humans* (Group 3) (IARC, 1999).

The chemical was tested for carcinogenicity in a two-year study in rats and mice by inhalation at a concentration of 15,000 ppm. The chemical induced uterine carcinomas in mice with marginal increases also seen in the incidence of hepatocellular tumours in female mice and in the incidence of alveolar/bronchiolar tumours in male mice. There was a marginal increase in the incidence of skin tumours in male rats, and a few uncommon glial cell tumours occurred in female rats. No human data were available (IARC, 1999).

Reproductive and developmental toxicity

Based on the available data, the chemical is not considered to be a specific reproductive or developmental toxin. Skeletal variations observed in rat offspring were only observed at maternally toxic doses.

In a two-year study at 15,000 ppm in mice and rats no reproductive effects were seen, but at the same dose mice exposed for 14 days had a significantly longer oestrous cycle duration. This effect was attributed to stress, although effects on neuroendocrine function can not be ruled out.

Slight developmental toxicity (delayed ossification) was observed in mice when exposed to vapour from the chemical at a concentration of 5000 ppm for 6 h/d on days 6 through 15 of gestation (OECD, 2007). Although no maternal toxicity was observed in this study, toxic effects including reduced bodyweight has been observed in other inhalation animal tests (see **repeat dose toxicity**) at such doses.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (carcinogenicity) and local effects (potential skin sensitisation).

Although there is limited evidence of carcinogenicity in animal tests, the data are not sufficient to regard the chemical as probably carcinogenic to humans. The chemical may cause contact dermatitis in sensitive individuals particularly when the chemical is purposely applied to the skin.

Public Risk Characterisation

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

Occupational Risk Characterisation

During formulation of products, dermal, ocular and inhalation exposure of workers to the chemical may occur particularly where manual or open processes are used. This may include during 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. Dermal contact will be limited given the expected rapid evaporation of the chemical.

Given the critical systemic long-term and local 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.

Occupational Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This does not consider classification of physical hazards and environmental hazards.

	Approved Criteria (HSIS)[a]	*GHS Classification*
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)].

* Existing Hazard Classification. No change recommended to this classification.

Advice for industry

Control measures

Control measures to minimise the risk from dermal and inhalation 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 storage, handling and use of a hazardous chemical are dependent 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:

- use of closed systems or isolation of operations;
- use of local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimisation of manual processes and work tasks through automation of processes;
- work procedures that minimise splashes and spills;
- regular cleaning of equipment and work areas; and
- use of 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 selection of 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 hazardous chemical are prepared; and

- management of risks arising from storage, handling and use of 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 physical hazards of the chemical has not been undertaken as part of this assessment.

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