Australian Government

Department of Health and Ageing

National Industrial Chemicals Notification and Assessment Scheme

INVENTORY MULTI-TIERED ASSESSMENT AND PRIORITISATION (IMAP)

HUMAN HEALTH TIER II ASSESSMENT FOR

Ethaneperoxoic acid

CAS Registry Number: 79-21-0

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 four 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

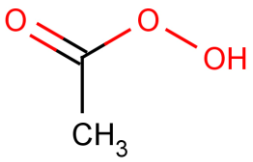
*Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Can be accessed at: http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

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

Ethaneperoxoic acid

CAS No: 79-21-0

Chemical Identity

Synonyms	Peracetic acid Peroxyacetic acid Acetic peroxide Acetyl hydroperoxide Estosteril
Structural Formula	
Molecular Formula	C2H4O3
Molecular Weight (g/mol)	76.1
Appearance and Odour (where available)	A clear, colourless liquid with a sharp, strong vinegar-like smell. In solution, the chemical can only exist in equilibrium with hydrogen peroxide (H2O2), acetic acid (HOAc) and water (referred to as 'the chemical in equilibrium').
SMILES	C(C)(=O)OO

Import, Manufacture and Use

Australian

The following Australian uses have been identified from NICNAS previous calls for information:

This chemical has reported domestic use including:
- Cleaning/washing agents and additives.

This chemical has reported commercial uses including:
- Used in paper industry;
- Oxidising agents;
- Water treatment;
- Horticultural/agricultural industries;
- Disinfection of medical devices and animal houses; and
- Beverage and food production.

The introduction volume in 2006 was between 100 -1000 tonnes.

International

The following uses have been identified from the Organisation for Economic Cooperation and Development (OECD 2008), Chemica Galleria and the Substances and Preparations In the Nordic countries (SPIN) database:

This chemical has reported domestic use including:
- Cleaning/washing agents and additives.

This chemical has reported commercial use including:
- Bleaching of paper pulp, textiles and waxes; and
- Sanitisers, disinfectants and sterilants in agriculture, food, beverage and medical industries at low

concentrations (1-15 %).

The chemical is permitted for use in United States Department of Agriculture National Organic Program as a synthetic substances allowed for use in organic crop production.

Restrictions

Australian

The chemical is listed in the Standard of the Uniform Scheduling of Medicines and Poisons (SUSMP) in Schedule 5 in concentrations of 10 per cent or less of the chemical and schedule 6 if more than 10 per cent.

Australia New Zealand Food Standards Code - Processing Aids:
- Permitted catalysts with a maximum permitted level of 0.7 mg/kg; and
- Permitted bleaching agents, washing and peeling agents and in water used as an ingredient in other foods.

International

No known restrictions have been identified.

Existing Worker Health And Safety Controls

Hazard classification

The chemical is currrently classified on the Hazardous Substances Information System (HSIS) (may be accessed at http://hsis.safeworkaustralia.gov.au/HazardousSubstance) with the following risk phrases:
Xn; R20/21/22 (Acute toxicity)
C; R35 (Corrosivity)

Exposure standards

Australian

No exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica):
A Time Weighted Average (TWA): 0.6 mg/m³ (0.2 ppm) [Finland]
A Short-Term Exposure Limit (STEL): 0.2 ppm [USA]

Health Hazard Information

Toxicokinetics

It is reported in the OECD (2008) that the chemical has limited absorption through skin and mucous membranes due to the high water solubility and low octanol-water partition coefficient although, due to its low molecular weight and small size, absorption could occur. Due to its high reactivity, systemic absorption of unreacted chemical is expected to be low and local effects at the site of application are expected to dominate.

During radioactive skin exposure studies, the chemical was excreted within 72 hrs, primarily via exhaled air (58 %), followed by urine (17 %) and faeces (6 %). In another study, degradation of the chemical was examined in rat blood. In blood diluted 1000-fold, the half-life of the chemical was < 5 minutes. It was reported that in undiluted blood, the half-life is expected to be several seconds or less. As a result, the distribution of the chemical would be very limited and it is not expected to be systemically available after exposure.

Acute Toxicity

Oral

Data available supports the current classification 'Harmful if swallowed (Xn; R22)' (Safe Work Australia 2012).

The chemical was reported to cause acute toxicity in rats, via the oral route with median lethal dose (LD50) values ranged between 185 - 3622 mg/kg bw based on the commercial product in equilibrium (4.89 % of the chemical, 19.7% H_2O_2, 10% HOAc) and (5.6% of the chemical, 26.9% H_2O_2, 7.6% HOAc) respectively (OECD, 2008). Acute toxicity effects include irritation and corrosion of tissues in contact with the test material.

Dermal

Data available supports the current classification 'Harmful in contact with skin (Xn; R21)' (Safe Work Australia 2012).

No dermal toxicity was observed in rats when exposed to solutions of 0.15-15%, while the chemical was reported to cause acute toxicity via the dermal route in rabbits (LD50 values of 1147 - 1957 mg/kg of the commercial product from 4.9% and 11.7 % of the chemical, respectively).

OECD (2008) reported that the dermal toxicity depends on the degree of skin damage caused by the different chemical solutions in equilibrium, since the corrosive properties of solutions may compromise the integrity of the skin.

Inhalation

The chemical is currently classified with the risk phrase 'Harmful by inhalation (Xn; R20)' (Safe Work Australia 2012). There are no data available to oppose this classification.

Corrosion / Irritation

Corrosivity

Data available supports the current classification "Causes severe burns (C; R35)" (Safe Work Australia 2012).

In dermal studies on rabbits, concentrations > 3.4% were corrosive, if contact time was greater than 45 minutes to the skin. Concentrations of 10 - 40% were corrosive for 3 minute exposure times. Concentrations between 0.013 – 0.34% of the chemical in equilibrium were considered slightly irritating, if contact time was greater than 45 minutes on the skin. A concentration of 5% for contact of 3 minutes was irritating (OECD 2008).

In eye studies, a concentration of 0.34% caused extreme irritation and severe irreversible corneal opacity, conjunctivitis, ulceration and iritis also occurred during a 24 hour exposure to the chemical. Concentrations of 0.15% of the chemical in equilibrium developed slight conjunctivitis during 24 hrs of exposure.

Observations in humans

At 0.5 % of the chemical (in equilibrium) used in hand wash, reports of skin irritation were found, while at a concentration of 0.2%, a burning sensation was reported only when small wounds were present; otherwise, no intolerance was found. When 0.1% of the chemical in equilibrium was applied to eyelids for 10 minutes, a slight burning sensation which disappeared during application was reported. Exposure to 2.8 mg/m³ (from combination of the chemical and hydrogen peroxide together) active oxygen for 4 minutes caused unbearable irritation, but was tolerated for 2 minutes of a 5-minute exposure.

The human findings on skin and eye irritation are supportive of the animal studies.

Sensitisation

Skin sensitisation

Studies from OECD (2008) and ECHA (2012) have shown the chemical has no skin sensitisation potential in guinea pigs.

Repeat Dose Toxicity

Oral

No systemic toxicity was observed with repeated dosing of the chemical in an equilibrium mixture. Mortality and other toxicological effects seen were due to local corrosive effects on the trachea and lungs.

There was no observed influence on behaviour, external appearance, body weight or food and no signs of toxicity in one repeat dose toxicity study where rats were treated with 10, 100 or 200 mg/litre of the chemical over a period of 90 days (ECHA, 2012).

In a GLP guideline study [OECD Guideline 408 (Repeated Dose 90-Day Oral Toxicity in Rodents] rats were exposed by gavage for 13 weeks to 5 % of the chemical diluted to various concentrations (0.25 mg/kg/day (0.018 %) to 7.5 mg/kg/day (0.55 %) of the component chemical). Due to mortality observed in the first weeks of the treatment period, dose-levels were reduced during the study. Mortality was observed in all treatment groups except the low dose group treated with 0.25 - 0.75 mg/kg/day. No relevant clinical, haematological, blood biochemical or histopathological findings were observed in the low dose group. Based on the results of this study, the no adverse effect level (NOAEL) was 0.25 - 0.75 mg/kg bw/day (component chemical). The only observed effects in the study were local effects that are concentration related (OECD 2009).

Dermal

No data are available.

Inhalation

No data are available.

Observation in humans

Long-term dermal exposure to 0.2% of the chemical in equilibrium for disinfection of hands resulted in no adverse effects on skin (OECD 2008).

Genotoxicity

The genotoxic potential of the chemical is summarised from the conclusion of the OECD (2008) report. Overall the data reveal the chemical has no mutagenic or genotoxic potential. The chemical is not expected to be systemically available and this could explain the lack of *in vivo* mutagenicity.

In vitro mutagenicity studies were performed to determine the activity of the component of the chemical in equilibrium (OECD 2008). Bacterial reverse mutation-assays, using different strains of *S. typhimurium*, required cytotoxic concentrations of the chemical and were considered to be non-mutagenic.

Chromosomal aberration studies using metabolic activation (with or without S9 mix) in human lymphocyte cells were positive only at cytotoxic concentrations.

Unscheduled DNA synthesis (UDS) induction and DNA repair assay by the chemical was investigated in human diploid foetal lung cells using concentrations of 0.2 to 32 ug/mL of the chemical. Although the highest dose was cytotoxic, no significant increase of UDS was detected using autoradiography, and DNA replication was reduced.

In vivo micronucleus studies in mice using single oral doses up to 7.8 mg/kg bw of the chemical by gavage, resulted in no significant differences between treatment group or controls. An *in vivo/ex vivo* UDS assay of rats receiving doses of 17 and 52 mg/kg bw of the chemical by gavage, also resulted in no significant difference between treatment groups. No genotoxic activity was found when using hepatocytes from rats in another *in vivo/ex vivo* UDS assay using doses of 52 and 104 mg/kg bw of the chemical.

Carcinogenicity

No data are available.

Reproductive and developmental toxicity

There is no evidence of reproductive toxicity and the developmental effects were only observed secondary to maternal toxicity, so the chemical is not a specific developmental toxin.

No reliable data on fertility are available. However, the chemical was observed to have no effect on reproductive organs from post-mortems of male and female rats following treatment with 5% of the chemical in equilibrium administered by daily gavage over a period of 13 weeks (OECD 2008). In another 90 day drinking water study, the degradation product of the chemical did not affect the reproductive organs and it was assumed that no systemic effect occurred due to rapid degradation of the chemical.

Developmental toxicity studies were performed in pregnant rats treated with 32-38% (w/w) of the chemical and 10 - 12% (w/w) hydrogen peroxide in drinking water with administered does levels of 100, 300 or 700mg of the chemical/litre (corresponding to 12.5, 30.4 ad 48.1 mg/kg bw/day of the chemical) from day 5 through to day 20 of gestation. There was no effect observed on reproduction, mortality of female or foetus, or macroscopic findings. From 12.5 mg/kg bw/day chemical onwards, reduction in water and food consumption was noted in dams. Severe reductions in drinking water, food consumption and absolute body weight were observed at the high dose. Although the foetal weights were reduced by 5% in the high dose group, there was also an increase of 13% in litter size which would have contributed to this discrepancy. A foetal weight reduction of 5% is not considered biologically relevant. The NOAEL for developmental toxicity was 300mg/L (30.4 mg/kg bw of the chemical) based on an increased incidence of poor and/or hypertrophic ossification (bone formation) in the presence of severe maternal effects (maternal NOAEL of 100mg/L (12.5 mg of the chemical /kg bw/day)).

Risk Characterisation

Critical Health Effects

The critical health effect for risk characterisation is corrosivity. The chemical is also expected to cause acute toxicity via the oral, dermal and inhalation routes.

Public Risk Characterisation

The chemical has known domestic uses in cleaning products and disinfection solutions. While the chemical is corrosive its use is currently adequately controlled for public exposure through scheduling.

Occupational Risk Characterisation

The health risks to workers from this chemical are controlled when correct classification and labelling are considered, and adequate control measures to minimise occupational exposure and protective clothing are implemented.

NICNAS Recommendation

The chemical is sufficiently assessed and risk managed provided the recommendation for classification

and labelling is followed.

Regulatory Control

Public Health

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

Work Health and Safety

The chemical is recommended for classification and labelling under the current Approved Criteria and adopted GHS as below. These do not consider classification of physical hazards and environmental hazards.

	Approved Criteria (HSIS)[a]	*GHS Classification*
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) Harmful if inhaled - Cat. 4 (H332)
Irritation / Corrosivity	Causes severe burns (C; R35)*	Causes severe skin burns and eye damage - Cat. 1 (H314)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

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

Advice for consumers

Products containing the chemical should be used according to 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:

- 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.

References

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