Acetic acid, chloro-: Human health tier II assessment

24 April 2015

CAS Number: 79-11-8

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.

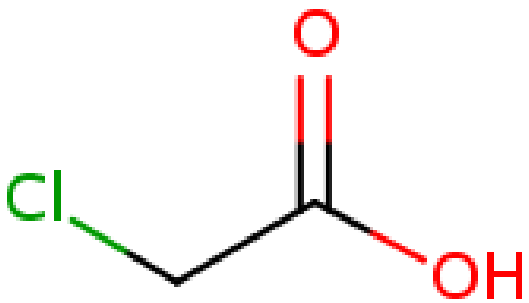
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	chloroacetic acid monochloroacetic acid
Structural Formula	
Molecular Formula	C2H3ClO2
Molecular Weight (g/mol)	94.49
Appearance and Odour (where available)	white crystalline solid
SMILES	C(=O)(O)CCl

Import, Manufacture and Use

Australian

The chemical is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of 1000–9999 tonnes. The chemical is used in manufacturing other chemicals.

International

The following international uses have been identified through:

- the European Union (EU) Registration, Evaluation, Authorization and Restrictions of Chemicals (REACH) dossiers;
- EU Summary Risk Assessment Report (RAR);
- Galleria Chemica;
- the Substances and Preparations in Nordic countries (SPIN) database;
- the European Commission Cosmetic Ingredients and Substances (CosIng) database;
- the United States (US) National Library of Medicines, Household Products Database;
- the US Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; and
- Ullman's Encyclopedia of Industrial Chemistry.

The chemical has cosmetic uses including:

- as a component in shampoo;
- as an exfoliant; and
- as a pH adjuster.

The chemical has site-limited uses as an intermediate in producing:

- other chemicals such as carboxymethylcellulose and thioglycolic acid;
- amphoteric surfactants;
- dyes;
- printing inks and paints; and
- lacquers and varnishes.

The chemical also has excluded uses such as in manufacturing crop protection chemicals or as a skin peeler or wart remover (keratolytic).

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 classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- T; R23/24/25 (Toxic by inhalation, in contact with skin and if swallowed)
- C; R34 (Causes burns)

Exposure Standards

Australian

The chemical has an exposure standard of 1.2 mg/m^3 (0.3 ppm) time weighted average (TWA) (Safe Work Australia).

International

The following exposure standards for chloroacetic acid are identified (Galleria Chemica):

An exposure limit of 1.0–4.0 mg/m^3 (0.3–1.0 ppm) TWA and 4.0–8.0 mg/m^3 (2.0 ppm) short-term exposure limit (STEL) in different countries such as Canada (British Columbia & Alberta), Ireland, Estonia, South Africa, Sweden, the United Kingdom, and the USA.

Health Hazard Information

Toxicokinetics

Studies in Sprague Dawley (SD) rats and Swiss-Webster mice have shown that chloroacetic acid is rapidly absorbed following oral exposure and rapidly eliminated, mainly through urinary excretion (half-life of up to 24 hours) (EU RAR, 2005). Rapid elimination was also observed in dermal, subcutaneous, and intraperitoneal (i.p.) exposure studies in SD rats and Swiss-Webster mice. It was suggested that chloroacetic acid metabolism occurs through two pathways:

1. initial glutathione conjugation then conversion into S-carboxymethylcysteine leading to thiodiacetic acid (the metabolite detected during urinary excretion)formation (EU RAR, 2005; NTP, 1992); or
2. dechlorination through glycolic acid formation which, in turn, is oxidised to carbon dioxide (EU RAR, 2005; NTP, 1992).

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase 'Toxic if swallowed' (T; R25) in the HSIS (Safe Work Australia). The information below, and details of the effects in humans (see **Observation in humans** section) support this classification.

The median lethal concentrations (LD50) in rats varied from 55–277.5 mg/kg bw while the LD50 in mice varied between 260–300 mg/kg bw (EU RAR, 2005).

In a study conducted in 10 female Wistar rats, chloroacetic acid was orally administered once by gavage at doses of 40, 63, 100, or 160 mg/kg bw. Deaths occurred between 120 minutes and 24 hours post-exposure (number of deaths and dose groups were not reported). Clinical symptoms that were observed in the moribund animals included neurobehavioural effects, lacrimation, and pulsing respiration. These effects were also observed in the surviving animals, but were less severe and reversible within 48 hours. Macroscopic changes in the decedents included discolouration of the liver, lungs, stomach, and spleen. These changes were not observed in the surviving animals. The LD50 value in this study was determined to be 90 mg/kg bw (EU RAR, 2005).

In a mouse study, a single oral dose of 320–380 mg/kg bw caused front paw rigidity, which was attributed to damage to the blood-brain barrier (BBB). The LD50 was calculated to be <320 mg/kg bw (EU RAR, 2005). In a separate mice study, tremors, respiratory depression, and convulsions were observed when male mice were orally administered chloroacetic acid at 300 mg/kg bw: (EU RAR, 2005).

Dermal

The chemical is classified as hazardous with the risk phrase 'Toxic in contact with skin' (T; R24) in the HSIS (Safe Work Australia). The information below and effects in humans (see **Observation in humans** section) supports this classification.

In a study conducted in female Wistar rats (six animals/dose), the chemical was administered under occlusion to the skin at the following doses and concentrations: 50 or 100 mg/kg bw at 1 % concentration; 200 or 400 mg/kg bw at 5 % concentration; and 200, 280, 400, or 2000 mg/kg bw at 40 % concentration. In the 40 % concentration groups, deaths occurred up to 24 hours post-administration and macroscopic changes in the lungs and bowels were observed at the 280, 400, and 2000 mg/kg bw doses. Moribund animals showed neurobehavioural effects, lacrimation, and respiratory difficulties. Forty-eight hours after exposure, the effects observed in the surviving animals were reversed and there were no observed macroscopic changes. The LD50 value was determined to be 305 mg/kg bw (based on a 40 % concentration) (EU RAR, 2005).

In another study conducted in six albino-Himalayan rabbits, a 50 % aqueous solution of the chemical was applied to occlusive skin at doses of 63, 125, 250, and 500 mg/kg bw. Deaths occurred up to 24 hours post-exposure (dose group not reported) and neurobehavioural effects, lacrimation, high respiratory frequency, and local irritation/corrosion in the highest dose group were observed. The LD50 value was determined to be 250 mg/kg bw (EU RAR, 2005).

Inhalation

The chemical is classified as hazardous with the risk phrase 'Toxic if inhaled' (T; R23) in the HSIS (Safe Work Australia).

The information below is not sufficient to allow determination as to whether the existing classification is appropriate. It is therefore not recommended that the existing classification for the chemical be amended.

In an acute inhalation study, Fischer 344 (F344) rats (six animals/sex/dose) were exposed to the chemical at a vapour concentration of 66 ppm (259 mg/m^3) for one hour. During exposure, the observations included squinting and slight lethargy. Transient urine-stained perineum and weight loss were also observed, but these effects were attributed as typical non-specific stress-related responses to chemical exposure. No deaths or exposure-related pathological changes occurred within the two week post-exposure period. The one-hour median lethal concentration (LC50) was reported as >66 ppm (259 mg/m^3) (EU RAR, 2005).

In another study conducted in rats, mice, and guinea pigs, mild lacrimation and nasal discharge were observed after a one-minute exposure to the chemical (EU RAR, 2005). No other details were provided.

Observation in humans

In an oral poisoning case, ingestion of a teaspoon of wart remover containing 80 % of the chemical by a 5-year-old girl was followed by immediate vomiting and collapse. After 1.5 hours, unmanageable metabolic acidosis and cardiac arrhythmias developed, with death eight hours later. Pulmonary and cerebral oedema, fatty infiltration of the liver, and marked gastric mucosal hyperaemia were observed during autopsy (EU RAR, 2005).

There were also numerous cases where dermal exposure to a molten form of the chemical occurred through accidental chemical splashing. In each case, third degree burns were apparent with a long recovery period (2–3 months) in surviving victims. In addition, emesis (nausea and vomiting), cardiovascular changes (cardiac shock and/or arrhythmia, premature ventricular contractions), metabolic acidosis, neurological symptoms (disorientation, agitation, cerebral oedema, loss of consciousness, alternation of excitation and depressive phases, coma), and hypokalaemia (low potassium levels) were observed. In some cases, the patients died between four hours to eight days post-exposure (EU RAR, 2005).

Corrosion / Irritation

Corrosivity

The chemical is classified as hazardous with the risk phrase ‘Causes burns’ (C; R34) in the HSIS (Safe Work Australia). The information below and in other sections of this report (see **Acute toxicity** section) supports the current classification.

Severe irreversible skin irritation was observed in six albino-Himalayan rabbits when the chemical (150–250 mg, based on a dose of 100 mg/kg bw, a bodyweight of 1.5–2.5 kg, and a 50 % solution of the chemical in 0.9 % NaCl) was applied to intact skin under occlusive conditions (EU RAR, 2005).

Sensitisation

Skin Sensitisation

A limited study in rabbit skin showed that the chemical did not have sensitising properties (induction: 5 % solution for 30 days; challenge: one drop of up to 50 % solution of the chemical) (EU RAR, 2005).

Due to the limitations of the study, the potential for skin sensitisation from exposure to the chemical cannot be accurately ascertained.

Repeated Dose Toxicity

Oral

In a 13-week study conducted in F344/N rats (20 animals/sex/dose) the chemical, in deionised water, was administered via gavage at doses of 0, 30, 60, 90, 120, or 150 mg/kg bw/d. Mortalities were observed in the 60 mg/kg bw/d group and higher (20/20 in the 120 and 150 mg/kg bw/d groups, 19/20 in the 90 mg/kg bw/d group, and 3/20 in the 60 mg/kg bw/d group). Cardiomyopathy was considered to be the main cause of death and was seen in both sexes in the 60 mg/kg bw/d group and above. Other effects observed in surviving animals included decreased heart weights and increased liver weights. Changes in biochemistry included a dose-related increase in aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in both sexes from the 60 mg/kg bw/d group and higher dose groups; increased thyroxine (T4) levels in males in the 90 mg/kg group

and higher dose groups; decreased plasma levels of total protein, calcium, and sodium from the 30 mg/kg bw/d group and higher dose groups; and a decreased lymphocyte count in males in all dose groups. The no observed adverse effect level (NOAEL) value was not derived from this study (EU RAR, 2005; NTP, 1992).

In another 13-week study conducted in B6C3F1 mice (20 animals/sex/dose), the chemical in deionised water was administered by gavage at doses of 0, 25, 50, 100, 150, or 200 mg/kg bw/d. All the males and two females in the highest dose group died (two males and one female died due to gavage trauma). In the decedents, hepatocellular cytoplasmic vacuolisation was found in five males and in one female. In the surviving animals, increased absolute and relative liver weights in females in the 100 and 200 mg/kg dose groups (but not in the 150 mg/kg group) and decreased serum cholinesterase activity in the 150 and 200 mg/kg groups were observed. No other treatment-related effects were found at necropsy in the surviving animals. In this study, the NOAEL value was determined at 100 mg/kg bw/d (EU RAR, 2005; NTP, 1992).

Other limited studies conducted in mice (B6C3F1) and rats (SD and Wistar) exposed to the chemical in the diet or in drinking water showed no treatment-related toxic effects (EU RAR, 2005; NTP, 1992). Due to the limited study design and the lack of reporting on the stability of the chemical in the diet studies, these studies were deemed unsuitable for characterising the hazard from chronic exposure to the chemical.

Based on the effects reported in these studies, a classification for chronic toxicity through repeated oral exposure is not warranted for the chemical.

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

The chemical was found to be non genotoxic based on various in vitro and in vivo studies.

In vitro studies

Negative results for genotoxic effects were observed in the following bacterial and mammalian studies:

- point mutations in *Salmonella typhimurium* strains (TA 98, TA 100, TA 104, TA 1535, TA 1537, and TA 1538) with or without exogenous metabolic activation;
- *Escherichia coli* strains (WP2*uvr*A and WP2*uvr*A/pKM101) with or without exogenous metabolic activation;
- chromosomal aberrations or sister chromatid exchanges in Chinese hamster lung fibroblast cells;
- Hypoxanthine-guanine phosphoribosyltransferase (HGPRT) assay with Chinese hamster V79 cells; and,
- DNA strand breaks in rat and mouse hepatocyte cultures or in human CCRF-CEM cells (EU RAR, 2005).

In vivo studies

There was no clastogenic activity in a micronucleus test with *Pleurodeles waltl* larvae. The chemical also tested negative for inducing sex-linked recessive lethal mutations in the germ cells of male *Drosophilia melanogaster*. There were no DNA strand breaks observed in the spleen, duodenum or the stomach of mice, or livers of mice and rats that were treated with the chemical (EU RAR, 2005).

Carcinogenicity

Based on an extensive two-year gavage studies on F344/N rats and B6C3F1 mice, the chemical was found to not have carcinogenic activity (NTP, 1992). This conclusion was also supported by other studies conducted in F344/N rats and ICR/Ha mice (EU RAR, 2005).

Reproductive and Developmental Toxicity

There was no indication that the chemical caused any reproductive or developmental effects (EU RAR, 2005).

Reproductive toxicity

There are no available reproductive toxicity studies on the chemical. However, in repeated dose toxicity studies, oral exposure to the chemical did not cause any treatment-related effects in the reproductive organs of B6C3F1 mice or F344/N rats (EU RAR, 2005).

Developmental toxicity

In a study conducted in pregnant Hsd:SD rats, the chemical did not cause mortalities nor any developmental effects at doses of up to 193 mg/kg bw/d. There were similar findings in a study conducted in pregnant Long-Evans rats exposed to the chemical by oral intubation at doses of up to 140 mg/kg bw (EU RAR, 2005).

Risk Characterisation

Critical Health Effects

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

Public Risk Characterisation

Although cosmetic use in Australia is not known, considering that the chemical could be used in cosmetics based on overseas information, the main public exposure is expected to be through dermal exposure. Inhalation and accidental ingestion may also be possible.

The risks from exposure to cosmetic products containing the chemical will depend on the type of cosmetic product (i.e. a rinse-off or a leave-on cosmetic product) and/or the concentration of the chemical. At higher concentrations, potential harm could be reduced through the use of strong warnings and safety directions on the label, although stronger statements relating to corrosivity and acute toxicity could further reduce the potential for harm. Where the function of the chemical is pH adjustment, the product will be buffered and only low concentrations of the free acid will be present.

Occupational Risk Characterisation

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 inhalation exposure are implemented. The chemical 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.

NICNAS Recommendation

Current risk management measures are considered adequate to protect 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

Work Health and Safety

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

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Toxic if swallowed (T; R25)* Toxic in contact with skin (T; R24)* Toxic by inhalation (T; R23)*	Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) Toxic if inhaled - Cat. 3 (H331)
Irritation / Corrosivity	Causes burns (C; R34)*	Causes severe skin burns and eye damage - Cat. 1B (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

Products containing the chemical should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, 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 storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which could 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 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 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 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 chemical 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 the chemical has not been undertaken as part of this assessment.

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