Acetamide, 2-chloro-: Human health tier II assessment

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CAS Number: 79-07-2

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.

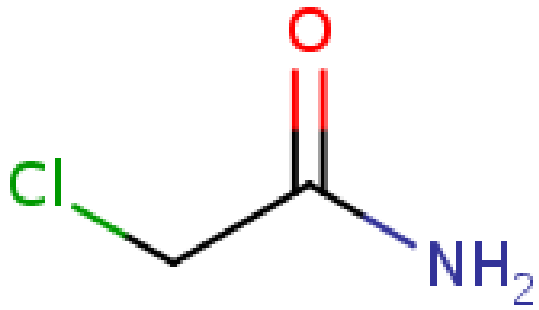
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	chloroacetamide 2-chloroacetamide 2-chloroethanamide alpha-chloroacetamide
Structural Formula	
Molecular Formula	C2H4ClNO
Molecular Weight (g/mol)	93.5
Appearance and Odour (where available)	Colourless to yellow crystals with characteristic odour
SMILES	C(N)(=O)CCl

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information was reported under previous mandatory and/or voluntary calls for information.

The chemical has been identified as being used in cosmetic products in Australia (Chow et al. 2013; Toholka, 2015).

International

The following international uses have been identified through:

- Galleria Chemica;
- the Substances and Preparations in Nordic countries (SPIN) database;
- the European Commission Cosmetic Ingredients and Substances (CosIng) database;
- the United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary;
- the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR);
- the US National Library of Medicine's Hazardous Substances Data Bank (HSDB);
- the Detergent Ingredients Database (DID);

- Ministry of Environment and Food of Denmark Environmental Protection Agency;
- The Pesticide Action Network (PAN) Pesticide Database; and
- various international assessments (CIR,1991; Danish EPA, 2001; SCCS, 2011).

The chemical has reported cosmetic use as a preservative, at concentrations less than 1 %, in bath preparations, body and hand preparations, cleansing products, eye makeup removers, neck and face preparations, foundations, hair conditioners, hair preparations, night skin care preparations, paste masks, personal cleanliness products, skin care preparations, suntan preparations, mascara and in other grooming aids. The concentration is restricted in some countries to 0.3 % (refer **International restrictions** section). There is recent reported use of the chemical in cosmetic products in the United States (Personal Care Products Council 2011).

The chemical has reported potential domestic use, as a preservative in detergents, paints, glues and emulsions. It is used in concentrations of less than 1 % and most often 0.2 – 0.5 %. Available North American databases do not give evidence for use of the chemical in consumer products, indicating the chemical is not likely to be widely available for domestic use.

The chemical has reported commercial use as a polymerisation control agent in the manufacture of paper/paperboard used in contact with foodstuffs and as a preservative in cutting oils and in the leather, textile, wood and plastics industries.

The chemical has reported non-industrial use as a microbiocide, herbicide and insecticide.

Restrictions

Australian

No known restrictions have been identified.

International

European Union (EU): Currently, chloroacetamide is authorised as a preservative in cosmetics products in entry 41 of Annex V to Regulation (EC) No 1223/2009, at a concentration up to 0.3 % w/w in ready for use preparations. However, in 2015, there was a consultation process on a proposal to remove entry 41 from Annex V,and to add the chemical to the list of substances prohibited in cosmetic products of Annex II to Regulation (EC) No 1223/2009 (European Commission, 2015). A decision had not been finalised at the time of the preparation of this assessment report.

The chemical is listed on the following (Galleria Chemica):

- New Zealand Cosmetic Products Group Standard—Schedule 7: Preservatives cosmetic products may contain with restrictions;
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient ‘Hotlist’) and;
- Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex VI – Part 1 – List of preservatives allowed for use in cosmetic products:

- Maximum authorized concentration 0.3 %;

- Conditions of use and warnings which must be printed on the label -Contains chloroacetamide.'

In 1991 the United States Cosmetic Ingredient Review (CIR) concluded that chloroacetamide is unsafe for use as a cosmetic ingredient (CIR, 1991).

The chemical is also subject to Significant New Activity (SNAc) provisions in Canada (Government of Canada).

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; R25 (acute toxicity)
- Xi; R43 (sensitisation)
- T; R62 (Reproductive Category 3) (Reproductive toxicity).

The sensitisation classification has a specific concentration limit for classification of ≥ 0.1 % in place of the default concentration limit of ≥ 1 %.

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Toxicological studies were performed on the chemical or a mixture of 70 % chloroacetamide and 30 % sodium benzoate, called CA 24.

Toxicokinetics

In a non-guideline study, the toxicokinetics of radiolabelled [1-^{14}C]-chloroacetamide was determined in male Wistar rats, by oral, dermal or intravenous (i.v) routes (10 animals/ application pathway) at a single dose level of 2 mg/kg bw. Chloroacetamide was detected in the blood, urine, faeces and tissues. Elimination from the blood occurred in a biphasic manner with half-lives of approximately 5 and 500 hours after i.v application, 5.6 and 520 hours after oral exposure and 6 and 180 hours after dermal exposure. The main route of elimination was determined to be via urinary excretion, at 87 %, 90 % and 43 % for i.v, oral and dermal exposure respectively, throughout the duration of the experiment. Radioactivity in faeces and cage wash amounted to 1.5 %, 3.6 % and 0.68 % of the applied dose after i.v, oral and dermal exposure respectively. Radioactivity could still be detected in the plasma of the animals upon termination for all exposure routes. Following oral treatment, 9 % of the administered radioactivity remained in tissues, with the greatest amounts detected in blood, heart, lungs, liver and spleen. Following dermal treatment, radioactivity was present in blood, liver, kidneys and untreated skin areas. At the site of application, 21.1 % of the radioactivity was found, with 11.8 % in other tissues. The applied radioactivity was reported to be absorbed via the oral and dermal routes at 96 % and 56 %, respectively (REACH; SCCS, 2011).

In another study, the bioavailability of [1-^{14}C]-chloroacetamide was determined in male Sprague Dawley (SD) rats by the dermal route, in accordance with Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 427. A group was also treated by the i.v route as a reference. Doses were formulated in an emulsion and a lotion for dermal exposure with an applied dose of 7.02 mg/kg bw in 5 animals, and 2 mg/kg bw in 6 animal for the i.v route. The half life determined for the dermal exposure was 3.9 ± 2 hours (emulsion), 2.1 ± 0.3 hours (lotion) which was significantly longer than that for the i.v exposure at 30.5 ± 2.7 minutes. The topical bioavailability was 53.5 and 48.3 % for emulsion and lotion, respectively (Kim, 2014).

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 available data support this classification.

In a study conducted in accordance with OECD TG 401, female Wistar rats were administered chloroacetamide at 0, 80, 125,160, 200 or 320 mg/kg bw as a single dose (10 animals/dose). The median lethal dose (LD50) was 138 mg/kg bw. Mortalities occurred at 125 mg/kg bw with 100 % mortality seen at doses above 200 mg/kg bw. Reported signs of toxicity include impaired balance, gasping breathing and bent posture (REACH).

A range of studies with minimal detail further support the classification, with reported LD50 values ranging from 70 - 370 mg/kg bw in rats, 150 - 155 mg/kg bw in mice, 122 mg/kg bw in rabbits and 31 mg/kg bw in dogs, with clinical observations not described (CIR, 1991; Danish EPA, 2001; HSDB; REACH; RTECS, SCCS, 2011).

Dermal

The chemical has low acute toxicity based on results from an animal test following dermal exposure.

In a study in accordance with OECD TG 402, SD rats were administered chloroacetamide at 2000 mg/kg bw (5 animals/ dose). The median lethal dose (LD50) in rats is > 2000 mg/kg bw. No effects attributed to the test substance were reported (REACH).

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

The chemical is reported to slightly irritate skin in animal studies. The effects were not sufficient to warrant hazard classification.

In a study conducted in accordance with OECD TG 404, 500 mg of chloroacetamide was applied to the shaved dorsal skin of New Zealand White rabbits (three animals) under semiocclusive conditions. The test substance produced slight erythema/eschar and slight oedema; the mean scores at 24, 48 and 72 hours post application were 1.6, 1.0 and 0.7, respectively, for erythema/eschar, and 1, 0.7 and 0.7, respectively, for oedema. After seven days, the animals were free of irritation (BG Chemie, 2000; HSDB; REACH).

In several other non-guideline studies, the chemical at concentrations up to 10 % did not induce any reported signs of irritation (CIR, 1991; Danish EPA, 2001; HSDB; REACH, RTECS). In a 30-day study (See **Repeat Dose Toxicity**), thickening and encrustation at the site of application was reported at doses above 25 mg/ kg bw/day (BG Chemie, 2000).

Eye Irritation

Based on the available data, the chemical is moderately irritating to the eye, warranting hazard classification (refer **Recommendation** section).

In a study conducted according to OECD TG 405, 100 mg chloroacetamide was instilled in the left conjunctival sac of New Zealand White rabbits (three animals). The average scores for cornea, iris/conjunctivae (redness) conjunctivae (chemosis) were given as 1.7/ 1/2.9/ 3, respectively. The effects were reversible within 21 days after application (HSDB; REACH; SCCS, 2011).

Several other non-guideline studies examined the chemical irritancy. Concentrations of the test chemical up to 3.5 % were tolerated with no signs of irritancy in rabbits (Danish EPA, 2001; SCCS, 2011). Redness of the conjunctivae was observed following a single application of a 10 % solution and upon daily application of 1 % ointment of the chemical for 12 days (SCCS, 2011).

Observation in humans

A 5 % solution of CA 24, a formulation of 70 % choroacetamide and 30 % sodium benzoate, was applied into the eyes of volunteers (no further information described). This corresponds to a chloroacetamide concentration of 3.5 %. Post-application, discomfort, lacrimation and blurred vision were reported. The effects lasted for 15 – 30 minutes (SCCS, 2011).

Sensitisation

Skin Sensitisation

The chemical is classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (R43) in the HSIS (Safe Work Australia). The positive results reported in guinea pig maximisation tests (GPMT) and observations of sensitisation in humans support this classification.

In a study conducted according to OECD TG 406, Dunkin-Hartley guinea pigs were given chloroacetamide at induction doses of between 0.003 - 0.3 % applied intradermally, followed by topical induction by applications of either between 0.3 - 30 % or 0.5 - 50 %. The challenge and rechallenge concentrations of 30 and 5 %, respectively, of the chemical in an aqueous polyethylene glycol (PEG) vehicle were topically applied to the clipped and shaved skin of the animals. Challenge concentrations of 30 % caused irritation responses; thus, results at 5 % were considered more robust. Positive reactions were seen for all induction doses for both challenge and re-challenge groups (REACH; SCCS, 2011).

The chemical is also reported to induce a positive response in studies similar to the GPMT following both intradermal and topical, as well as topical induction alone (five or 10 animals/dose). The minimum induction dose (sensitisation response seen in at least one animal) was determined as 500 ppm, and maximum induction dose (first induction concentration that maximally sensitised all animals in the dose group) as 5000 ppm (Yamano, 2005).

The chemical did not induce a sensitisation result in an LLNA at doses of 0, 10 or 25 % in DMSO (four animals/dose) (Yamano, 2005) and was negative in several non-guideline guinea pig studies (CIR, 1991; SCCS, 2011).

Observation in humans

Numerous reports are available, which demonstrate that the chemical can elicit contact allergies in humans.

In a 10 year retrospective study (2001–2010) of Australian patch testing data, 139 positive reactions (3 %) were reported out of 4576 patients tested at 0.2 % chloroacetamide in petrolatum (Toholka, 2015). In another Australian study, examining patch test data for the chemical tested at a concentration of 0.2 % in petrolatum from 1993–2006, the rate of chloroacetamide allergy was reported as 2.1 %, (Chow, 2013). These allergy prevalence rates are higher than those reported in a number of European countries (Chow, 2013).

A significant number of international studies have identified the chemical as a cause of contact allergy in both patch test volunteers and patients with suspected contact dermatitis (Marzulli, 1973; De Groot, 1986; CIR, 1991; Perrenoud, 1994; SCCS, 2011; REACH). Positive results ranged from 0 - 32 % of the populations. The lowest concentration eliciting sensitisation was 0.1 %. The best described study was a modified Draize patch test approach, performed on 147 volunteers (114 males and 33 females) with an aqueous solution of 0.5 % chloroacetamide to the skin. Treatment was repeated three times per week for

three weeks. After a two week non-treatment period, a challenge dose was applied. Positive reactions were seen in 47 of the patients, with a higher rate in females at 58 % when compared to males, at 25 % (CIR, 1991).

Several international occupational studies have also identified the chemical as a cause of contact allergies. Professions examined included hairdressers, shoe makers, metal workers and house painters (Hoegberg, 1980; Katsarou, 1995; Mancuso, 1996; SCCS, 2011; Schwensen, 2013). Positive results were observed following patch testing with concentrations as low as 0.1 % in petrolatum.

Repeated Dose Toxicity

Oral

Based on the available data, the chemical is not considered to be harmful to human health on repeated oral exposure. Classification for this endpoint was not considered relevant based on transient effects in the liver by both the oral and dermal routes. Specific treatment-related effects on the testes were considered more relevant for reproductive toxicity (See **Reproductive and Developmental Toxicity**).

In a 90-day study conducted according to OECD TG 408 in Wistar rats, the chemical was administered in the diet at levels equivalent to 0, 2, 10 and 50 mg/ kg bw/day (10 animals/ dose). Half of the animals were sacrificed at day 90, and the remaining animals observed for an additional 29-day recovery period before termination. A no observed adverse effect level (NOAEL) was reported at 10 mg/kg bw/day, based on effects at the highest dose. Reduced body weight gain was observed to be reversible within the recovery period. Haematological changes including elevated leukocyte count were also observed to be reversible within 29 days. At the highest dose in male animals, organ weights including those of the liver and testes were reduced and were persistently reduced through the recovery period. Reduced liver weight in females were reported to be reversible within 29 days. Histopathological changes in testes were reported as effects on fertility (See **Reproductive & Developmental Toxicity**) (BG Chemie, 2000; CIR, 1991; Danish EPA, 2001; SCCS, 2011; REACH).

In a 90-day study in SD rats, the chemical was administered in the diet at levels equivalent to 0, 12.5 or 50 mg/kg bw/day in feed. Reported effects were similar to other described studies including reduced testicular weight (See **Reproductive & Developmental Toxicity**) and liver changes. At the highest dose, fatty liver degeneration and atrophy were seen. Reduced body weight gain was reported at all doses. Increased thyroid weights were reported in females at the highest dose only. No NOAEL could be determined (BG Chemie, 2000; SCCS, 2011; REACH).

In a 90-day study in Wistar rats, at the same doses as in the previously reported study (10 animals/sex/dose), similar effects were reported including reduced body weight gain and male reproductive effects. No NOAEL could be determined (REACH).

In a non-guideline 28-day study, rats (strain unspecified) were dosed with chloroacetamide at 0, 5, or 20 mg/kg bw/day (five animals/dose). Reported effects at the highest dose included: increased protein concentrations in urine and dose dependent degenerative changes in the liver in addition to characteristic changes attributed to trichloroacetic acid in kidneys (no further information given) (SCCS, 2011; REACH).

Dermal

Based on the available data, the chemical is not considered to be harmful to human health following repeated dermal exposure. Classification for this endpoint was not considered relevant based on transient effects in the liver by the dermal route, similar to those seen by the oral route.

In a 90-day dermal study in male Wistar rats, no changes in body weight or organ histopathology were reported following exposure to the chemical at doses of 8.75 mg/kg bw/day and 35 mg/kg bw/day (SCCS, 2011; REACH). There were no details of the number of applications per week, or the examinations conducted.

In a well-performed 30-day study, female Yellow-Silver rabbits were administered chloroacetamide daily at 0, 2, 5, 50, 100, 200, or 400 mg/kg bw/day to the depilated skin of the neck. In all dose groups, encrustations, hardening and thickening of the treated area were reported. One mortality at 50 mg/kg bw/day was determined not to be treatment-related (further information not available). At 100 mg/ kg bw/day and greater, reduced weight gain and histopathological changes including fatty infiltration in the liver and myocardial tissues in addition to haemosiderin deposits in the spleen were observed all to be dose-dependent. The highest dose was lethal in three of five treated animals. An NOAEL was based on these effects at 50 mg/kg bw/day (BG Chemie, 2000; SCCS, 2011; HSDB; REACH).

Inhalation

No data are available.

Genotoxicity

Based on the weight of evidence from the available in vitro and in vivo genotoxicity studies, the chemical is not considered to be genotoxic.

Several in vitro studies produced negative results for gene mutation and clastogenicity including;

- several Ames mutagenicity test, in *Salmonella typhimurium* strains TA 98/ 100/ 1535/ 1537/ 1538;
- in vitro mammalian chromosome aberration test according to OECD TG 473 in Chinese hamster lung fibroblasts; and
- in vitro mammalian cell transformation assay in Syrian hamster embryo cells (SCCS, 2011; REACH).

A significant increase in the number of chromosome aberrations was induced at cytotoxic concentrations in an in vitro mammalian cell gene mutation assay according to OECD TG 476 in Chinese hamster lung fibroblasts. No effects were observed below cytotoxic concentrations (REACH).

In vivo studies provide further evidence to confirm the chemical is not genotoxic.

In an in vivo micronucleus test in accordance with OECD TG 474, Naval Medical Research Institute (NMRI) mice were dosed twice by oral gavage at 0, 1, 10 or 100 mg/kg bw (5/sex/dose). Polychromatic erythrocytes were examined for micronuclei with no reported significant increase in the incidence (SCCS 2011; REACH).

No structural or numerical chromosome aberrations or increase in the number of micronuclei were observed in an in vivo micronucleus test in Chinese hamsters (number of animals not reported) following two intraperitoneal (i.p.) injections of doses up to 35 mg/kg bw (SCCS, 2011).

In a dominant lethal test, male NMRI mice received a single i.p. injection of the chemical at doses up to 86 mg/kg bw and then were mated with three untreated females per week over a period of 10 weeks. No effect on the mutagenicity index was observed, although effects on fertility were reported (refer **Reproductive and developmental toxicity** section).

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

The chemical is classified as hazardous—Category 3 substance toxic to reproduction)—with the risk phrase 'Possible risk of impaired fertility' (Xn; R62) in the HSIS (Safe Work Australia). The available data support higher classification. Severe testicular effects seen in repeat dose studies appear to be associated with effects on male fertility. Whilst limited data are available, there is no evidence that the chemical causes specific developmental toxicity in the absence of maternal toxicity.

In a previously described 90-day study conducted according to OECD TG 408 (See **Repeat Dose Toxicity**), relevant histopathological changes in males at the highest dose (50 mg/kg bw/day) were depression and/or cessation of spermatogenesis and moderate proliferation of Leydig cells and other interstitial cells in the testes. Epididymal size was reduced, with marked absence of mature and immature sperms with only loose connective tissue present. These effects were reversible within the recovery period (BG Chemie, 2000; CIR, 1991; Danish EPA, 2001; SCCS, 2011; REACH).

In the 90-day studies (See **Repeat Dose Toxicity**), similar dose-dependent reproductive effects at the same doses (12.5 and 50 mg/kg bw/day) were reported. These include decreased testes weights in males and impaired spermatogenesis (BG Chemie, 2000; SCCS, 2011).

In a dominant lethal test described previously (refer **Genotoxicity** section), the number of resorptions, the mutagenicity index and the number of viable foetuses remained unchanged throughout the entire study. A reduction in the fertility index, number of implantations and foetuses were observed during the first three weeks of exposure; however, after week 4, the effects were no longer observed. These effects indicate toxic effects on male fertility during the first three weeks (SCCS, 2011).

In a combined developmental and reproductive toxicity study, doses were selected based on preliminary study findings of reduction in maternal organ weight as well as maternal and offspring body weight changes at the highest dose of 60 mg/kg bw/day.

Pregnant Wistar rats were dosed in two series:

- 0, 3, 12 or 48 mg/kg bw/day, daily during gestation day (GD) 7 through GD 17 to determine offspring effects;
- 0 or 24 mg/kg bw/day, daily during GD 14 to postnatal day (PD) two to determine effects on the reproductive systems of offspring.

In the first series, effects reported at the highest dose in offspring include: increased number of unossified sternebrae and forelimb phalanges as well as reduced body weight of viable foetuses. These effects were reported in the presence of maternal toxicity including; reduced body weight gain and organ weight (thyroid and gravid uteri).

In the second series, maternally toxic effects included reduced body weight gain and food consumption during late gestation. Offspring generation effects were limited to lower body weight in the highest dose group. No differences in the reproductive organs of offspring were noted. A NOAEL of 3 mg/kg bw/day was determined based on body weight reduction of dams (based on body weight reductions) and pups (based on ossified sternebrae and the number of ossified forelimb phalanges (SCCS, 2011).

In further developmental studies in rats, with administrations by the subcutaneous or i.p. routes, doses ranged between 20–2000 mg/kg bw/day. All studies included a single dose or two doses on consecutive days. Doses above 50 mg/kg bw/day were embryotoxic, with pup mortality being reported at 50 %. No malformations were reported (BG Chemie, 2000; Danish EPA, 2001, HSDB, SCCS, 2011, REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (reproductive toxicity), systemic acute effects (acute toxicity from oral exposure) and local effects (skin sensitisation and eye irritation). The chemical may also cause other harmful effects (non-reproductive) following repeated exposure from dermal and oral routes.

Public Risk Characterisation

The chemical has been identified as being present in cosmetic products in Australia. Based on international data, the use in domestic products is not considered to be widespread. The main route of public exposure is expected to be through the skin, and potential oral exposure from lip and oral hygiene products.

The chemical is considered to be a potential human sensitiser at use concentrations (CIR, 1991, SCCS, 2011), with relatively high prevalence of sensitisation to the chemical reported in Australia. Based on a conservative assumption that the chemical is available in all cosmetic products, the margin of safety for systemic effects has been calculated to be less than 100 (SCCS, 2011). Both the EU Scientific Committee on Consumer Safety (SCCS) and US CIR have concluded that the chemical is unsafe for use as a cosmetic ingredient (when used under current use conditions of 0.3 %) (CIR, 1991, SCCS, 2011).

Currently, there are no restrictions in Australia on using this chemical in cosmetics or domestic products. In the absence of further regulatory controls, the characterised critical health effects include systemic long-term, systemic-acute and local effects, which have the potential to pose an unreasonable risk under the identified uses.

Occupational Risk Characterisation

Given the critical systemic long-term, systemic acute and local health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise oral, dermal and ocular 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.

The data available support an amendment to the hazard classification in the HSIS (Safe Work Australia) (refer to **Recommendation** section). Given that several international occupational studies have identified the chemical as a cause of contact allergy, the specific concentration limit for sensitisation classification should be retained.

NICNAS Recommendation

Further risk management is required. Sufficient information is available to recommend that risks to public health and safety from the potential use of the chemical in cosmetics and/or domestic products be managed through changes to poisons scheduling, and risks for workplace health and safety be managed through changes to classification and labelling.

Regulatory Control

Public Health

Due to the toxicity profile of the chemical concentrations reported to be potentially in use, the chemical is recommended for scheduling in the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) to prohibit the sale, supply and use in cosmetic products. Matters to be taken into consideration include:

- the chemical is reported to be used in cosmetic products in Australia;
- the chemical is prohibited or restricted for cosmetic use overseas. The European Commision is currently considering prohibiting the chemical;
- the EU SCCS and US CIR have concluded that the chemical is unsafe for use as a cosmetic ingredient (when used under current use conditions of 0.3 %);
- allergy prevelance rates up to 3 % have been reported in Australia. These allergy prevalence rates are higher than those reported in a number of European countries; and
- the chemical may be harmful to male fertility and the liver following repeated oral and dermal exposure.

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.

The sensitisation classification should retain the specific concentration limit for classification of ≥ 0.1 %.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Toxic if swallowed (T; R25)*	Toxic if swallowed - Cat. 3 (H301)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to eyes (Xi; R36)	Causes serious eye irritation - Cat. 2A (H319)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)*	May cause an allergic skin reaction - Cat. 1 (H317)
Reproductive and Developmental Toxicity	Repro. Cat 2 - May impair fertility (T; R60)	May damage fertility - Cat. 1B (H360F)

[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 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 chemical is used. Examples of control measures that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- valid techniques are available to monitor the effect on the worker's health;
- 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.

References

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