# Benzenemethanaminium, N,N-dimethyl-N-[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]-, chloride: Human health tier II assessment

**05 February 2016**

## CAS Number: 121-54-0



## 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.

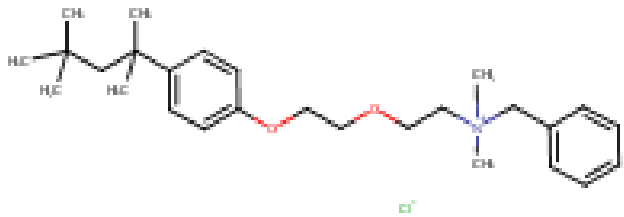
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

**Disclaimer**

Acronyms & Abbreviations

## Chemical Identity

| | |
|---|---|
| Synonyms | benzyldimethyl(2-(2-(p-(1,1,3,3-tetramethylbutyl)phenoxy)ethoxy)ethyl) ammonium chloride<br>benzethonium chloride<br>(2-(2-(4-diisobutylphenoxy)ethoxy)ethyl)dimethylbenzylammonium chloride<br>antiseptol<br>ammonium, benzyldimethyl(2-(2-(p-(1,1,3,3 -tetramethylbutyl) phenoxy)ethoxy)ethyl)-, chloride |
| Structural Formula |  |
| Molecular Formula | C27H42NO2.Cl |
| Molecular Weight (g/mol) | 448.08 |
| Appearance and Odour (where available) | Colourless to white crystals |
| SMILES | C(C)(C)(c1ccc(OCCOCCN{+}(C)(C)(.Cl{-})Cc2ccccc2)cc1)CC(C)(C)C |

## Import, Manufacture and Use

### Australian

No specific Australian industrial use information has been identified.

The following non-industrial uses have been identified in Australia:

- a preservative in sedative and analgesic veterinary products (Australian Pesticides and Veterinary Medicines Authority—APVMA); and
- in hospital grade disinfectants (Therapeutic Goods Administration—TGA).

### 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) Household Products Database; the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and various international assessments including from the National Toxicology Program (NTP) and the Scientific Committee On Cosmetic Products And Non-Food Products (SCCNFP, 2002).

The chemical has reported cosmetic uses:

- as a preservative and antimicrobial ingredient; and
- in surfactants.

The chemical is found in various cosmetic and personal care products such as creams, soap, mouthwashes, wipes and deodorants, at concentrations up to 1 % (US Household Products Database). The maximum authorised concentration in rinse-off and leave-on products when used as a preservative is 0.1 % (SCCNFP, 2003).

The chemical has reported domestic use in household cleaning products (at concentrations up to 0.28 % in some products) (US Household Products Database).

The chemical has reported commercial use in cleaning products for professional use.

The following non-industrial uses have been identified:

- as a topical anti-infective agent, detergent and spermicide in pharmaceutical products (reported concentrations of 3 % in preparations and 0.2 % in vaginal foams—HSDB);
- as an antiseptic agent in veterinary products (concentrations up to 0.1 %—HSDB);
- as a disinfectant in food processing; and
- to control algae in swimming pools.

## Restrictions

### Australian

This chemical is covered by the group entry for QUATERNARY AMMONIUM COMPOUNDS in Schedules 5 and 6 of the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP, 2015):

Schedule 6:

'QUATERNARY AMMONIUM COMPOUNDS **except**:

a) when separately specified in these Schedules;

b) when included in Schedule 5;

c) dialkyl or dialkoyl quaternary ammonium compounds where the alkyl or alkoyl groups are derived from tallow or hydrogenated tallow or similar chain length (C16/C18) sources; or

d) in preparations containing 5 per cent or less of such quaternary ammonium compounds.'

Schedule 5:

'QUATERNARY AMMONIUM COMPOUNDS in preparations containing 20 per cent or less of quaternary ammonium compounds **except**:

a) when separately specified in these Schedules;

b) dialkyl or dialkoyl quaternary ammonium compounds where the alkyl or alkoyl groups are derived from tallow or hydrogenated tallow or similar chain length (C16/C18) sources; or

c) in preparations containing 5 per cent or less of such quaternary ammonium compounds.'

Schedule 6 chemicals are described as 'Substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label'. Schedule 6 chemicals are labelled with 'Poison' (SUSMP, 2015).

Schedule 5 chemicals are described as 'Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.' Schedule 5 chemicals are labelled with 'Caution' (SUSMP, 2015).

### International

Using the chemical in cosmetics in the European Union is subject to the restrictions described in EU Regulation Annex V. This chemical may be used in rinse-off products and leave-on products other than oral products at a maximum concentration of 0.1 % (CosIng).

## Existing Work Health and Safety Controls

### Hazard Classification

The chemical is not listed on the Hazardous Substances Information System (HSIS (Safe Work Australia).

### Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

## Health Hazard Information

The chemical is a quaternary ammonium compound, thus possesses surface-active and detergent properties. The chemical is usually reported to be used at low concentrations in consumer products (HSDB; SCCNFP, 2003; US Household Products Database).

The chemical is expected to be a primary irritant to the skin (Cross and Singer, 1994). When data for the chemical are not available, health hazard information of cationic surfactants from the NICNAS IMAP group assessment (NICNASa) are considered indicative of the hazards of this chemical.

### Toxicokinetics

Toxicokinetic studies were conducted in Fischer 344/N (F344) rats by administering the chemical through intravenous and dermal routes (NTP, 1995):

- Twenty-four hours after a single intravenous dose of labelled chemical, 50 % of the radiolabel was found in the faeces and 2 % in the urine. The elimination half-life of the chemical from the blood was 110 minutes.
- When rats were topically exposed to the chemical at doses of 0.15 or 1.5 mg/kg bw (non-occlusive patches), results showed that peak elimination took place 24 to 48 hours later in the urine and 48 to 72 hours later in the faeces. Urinary excretion represented 1 to 2 % of the dose, and faecal excretion about 45 % of the dose. Some residual radiolabel could not be washed off the skin at the site of application.
- Repeated dermal studies in rats exposed for ten days showed that total excretion of the chemical was 25 % on the last day, suggesting some accumulation of the chemical.

The urinary excretion was likely to be underestimated in these studies (NTP, 1995).

In an in vitro dermal absorption study, 1 % solution of the chemical was applied on human and rat dermatomed skin membranes. The total amount absorbed in 24 hours was 4.14 % (4.14 µg/cm$^2$) in human skin and 16.4 % in rat skin. Although the absorption was higher in rat skin, total absorption of the chemical was poor in both cases (SCCNFP, 2002).

When a formulation containing the chemical at 0.1 % (in 'GMS-cream') was tested on human dermatomed skin, the total absorption within 24 hours was 4.72 % or 0.094 µg/cm$^2$.

The chemical is closely related to nonylphenols, assessed under NICNAS IMAP framework (NICNASb), as its degradation can give rise to octylphenols.

### Acute Toxicity

Oral

The chemical has moderate acute oral toxicity based on the available animal data, warranting hazard classification.

Median lethal dose (LD50) values of 295 and 420 mg/kg bw were reported in rats (SCCNFP, 2002).

Other LD50 values available include 368, 420, 450 or 665 mg/kg bw in rats (CIR, 1985) and 338 mg/kg bw in mice (ChemIDPlus). Observed sublethal effects included severe depression in rats (CIR, 1985).

### Dermal

Only limited data are available, showing no mortalities or systemic toxicity following acute dermal exposure.

The chemical was applied to the skin of C57BL/6 mice (n = 3 per dose) in a single dose of 8.75, 17.5, 35, 70, 140 or 280 mg/kg bw (duration not stated). At the two highest doses, severe blistering occurred. No mortalities were reported. Moderate local reactions were observed at 35 and 70 mg/kg bw, and no skin reactions were observed at the two low doses. Ten days later, spotted depigmentation was observed in two mice exposed at 140 mg/kg bw (CIR, 1985).

### Inhalation

No data are available.

## Corrosion / Irritation

### Skin Irritation

Based on the available information, the chemical is considered to be at least irritating to the skin, warranting hazard classification (see **Recommendation** section). The available data are not sufficient to warrant a higher hazard classification, although cationic surfactants can be corrosive (NICNAS).

The chemical is reported to exhibit 'a graded skin irritation response dependent on concentration' (Cross and Singer, 1994).

In an acute dermal irritation study in mice (see **Acute Toxicity: Dermal** section), local effects included severe blistering at the two highest doses of 140 and 280 mg/kg bw and moderate skin reactions at 70 and 35 mg/kg bw (CIR, 1985).

In a dermal toxicity study, six male rabbits were exposed daily to a solution of 0.1 % of the chemical, five days per week, for four weeks. No sign of irritation was observed (CIR, 1985).

In a skin irritation study in human volunteers, five female subjects were topically exposed to 0.15, 0.31, 0.63, 1.25, 2.5 and 5 % of the chemical in water, under an occlusive dressing. A total of four applications were made. Three of the subjects exhibited irritated skin at 0.63 % and above. The concentration of 0.31 % was considered as an appropriate level for a repeated insult patch test (see **Skin Sensitisation** section) (SCCNFP, 2002).

### Eye Irritation

Based on the available information, the chemical is considered to be at least irritating to the eyes, warranting hazard classification (see **Recommendation** section). At concentrations above 0.03 %, the chemical can elicit ocular irritation in animals. The available data are not sufficient to warrant a higher hazard classification.

A Draize test was conducted on three groups of albino rabbits (n = 3/group), with 0.1 mL of the chemical instilled into the conjunctival sac of one eye of each rabbit. In the first group, the treated eye was not rinsed. In the second and third groups, the treated eyes were rinsed two and four seconds after instillation, respectively. Irritation scores were not reported but a maximum tolerated concentration (concentration at which no corneal or iridic lesions were present on the seventh day of reading following exposure) of 0.5 % was established for the chemical (CIR, 1985).

A cologne stick containing 0.5 % of the chemical was found to be minimally irritating to the eyes of three rabbits. Maximum scores (after one hour of exposure to seven days) were 4, 4 and 6 (out of 110) (CIR, 1985).

In a test conducted according to the OECD TG 405, a 0.1 % solution of the chemical caused minimal irritation to the eyes of New Zealand White rabbits (SCCNFP, 2002).

The threshold concentration, defined as the highest concentration not producing eye irritation in at least three rabbits (n = 5/dose), was reported to be 0.03 % (CIR, 1985). Based on this study, the chemical was reported to be irritating at concentrations of 0.03 % and above (NTP, 1995).

### Observation in humans

The chemical was topically applied at concentrations of 0.1, 0.2 or 0.5 % under occlusive patches to the skin of 100 volunteers. No irritation was observed at 0.1 and 0.2 %, but at 0.5 % the chemical caused irritation in 51 subjects. The extent of irritation was not provided (Cross & Singer, 1994).

A female patient exhibited 'severe, long-standing labiitis and vulvitis' (inflammation of the vulva) after using a preparation containing unknown concentration of the chemical. A negative patch test result determined that it was not due to an allergic reaction (Cross and Singer, 1994).

Exposure to the chemical at concentrations above 7.5 % is reported to cause 'corrosive injuries' (HSDB).

## Sensitisation

### Skin Sensitisation

Only limited data are available due to corrosive/irritation properties of the chemical. The chemical is not expected to be a skin sensitiser at concentrations below 0.3 %.

A repeated insult patch test was conducted on 152 human subjects using the chemical at 0.3 % in aqueous solution (the highest non irritating concentration—see **Skin Irritation** section). The induction phase consisted of ten topical applications of the chemical under occlusive dressing for 24 hours, three times a week. The challenge phase consisted of patches applied to the original and virgin sites, approximately 14 days after the last induction application. During the induction phase, six subjects showed mild to well-defined erythema and one subject exhibited mild to marked responses. Apart from the subject showing mild to marked responses (considered to be a reactive individual), only negative results were observed after the challenge phase (SCCNFP, 2002).

## Repeated Dose Toxicity

### Oral

Based on the available data, the chemical is not expected to cause severe effects to health following repeated oral exposure.

In a 28-day study, rats were administered the chemical in the diet at doses of 0, 100, 200, 500 or 2500 ppm (equivalent to 0, 1.7, 8, 40 or 200 mg/kg bw/day). At the highest dose, signs of toxicity included growth retardation, caecum enlargement and signs of liver damage. In males, decreased serum inorganic phosphorus levels were observed at 500 and 2500 ppm and regarded as treatment-related. A supplementary study was reconducted under the same conditions and resulted in the same observations, apart from no decrease in serum inorganic phosphorus levels. Based on the later study, a no observed adverse effect level (NOAEL) of 40 mg/kg bw/day was determined (SCCNFP, 2002).

In a two-year study, groups of rats (n = 5/sex/dose) were administered the chemical at 0, 50, 200, 1000, 2500 or 5000 ppm in the diet (equivalent to 0, 4, 16, 80, 200 or 400 mg/kg bw/day). Mortality was observed at the highest dose. Testicular atrophy and caecum enlargement were reported at 2500 and 5000 ppm. At 1000 ppm, only caecum enlargement was observed (SCCNFP, 2002).

In a one-year study, groups of three dogs were fed with the chemical at 0, 5, 100 or 500 ppm (equivalent to 0, 0.4, 8 or 40 mg/kg bw/day). No changes were observed in growth rate, haematology or gross or microscopic pathology. The NOAEL was considered >40 mg/kg bw/day (SCCNFP, 2002).

### Dermal

Based on the available data, the chemical is not expected to cause severe systemic health effects following repeated dermal exposure.

In a 16-day study, groups of F344/N rats (n = 5/sex/dose) were topically administered the chemical at doses of 0, 6.3, 12.5, 25, 50, or 100 mg/kg bw/day, five days a week. None of the treated animals died during the study. Rats treated with 50 or 100 mg/kg bw/day had significantly lower final mean body weight and body weight gain compared with the controls. Both relative and absolute thymus weights were decreased at high doses (at 100 mg/kg bw/day in males and from 50 mg/kg bw/day in females). Minimal to mild epithelial hyperplasia (proliferative lesion of the skin at the site of application) was observed at the lowest dose. At high doses (50 and 100 mg/kg bw/day), ulcerative, necrotising inflammation of marked severity of the epidermis and chronic inflammation of mild to moderate severity of the dermis and subcutaneous tissues were observed (NTP, 1995).

In a 13-week study, groups of F344/N rats (n = 10/sex/dose) were topically exposed to the chemical at doses of 0, 1.56, 3.13, 6.25, 12.5 or 25 mg/kg bw/day, five days per week. No mortalities occurred during the study. At the highest dose, the final mean body weight and body weight gain in males were significantly lower compared with the controls. At the site of application, irritation, inflammation and ulceration were observed at 3.13 mg/kg bw/day and above. At 25 mg/kg bw/day, absolute and relative weights were significantly lower for the thymus of males and significantly higher for the right kidney of females, compared with controls. Hypercellularity of the myeloid fraction in the bone marrow (increase in haematopoietic cells relative to adipocytes) was observed at 25 mg/kg bw/day, and regarded as a secondary effect of inflammation. There was no evidence of systemic toxicity and a NOAEL was not determined (NTP, 1995).

### Inhalation

No data are available.

## Genotoxicity

Based on the available negative in vitro genotoxicity data, the chemical is not expected to be genotoxic. Supporting this, cationic surfactants were also reported to be not genotoxic (NICNASa).

The following in vitro genotoxicity data are available for the chemical (NTP, 1995):

- negative results were reported for a bacterial gene mutation assay (Ames test) in *Salmonella typhimurium* strains TA 98, 100, 1535 and 1537, at doses up to 100 µg/plate, with or without metabolic activation;
- no statistically significant increases in chromosome aberrations were observed in a chromosome aberration test in Chinese hamster ovary (CHO) cells exposed to doses up to 9.6 µg/mL; and
- negative results were reported in a sister chromatid exchange (SCE) assay in CHO cells exposed to doses up to 30 µg/mL.

No in vivo genotoxicity data are available on the chemical.

## Carcinogenicity

Based on the available data, the chemical is not expected to be carcinogenic by the dermal route of exposure. No oral carcinogenicity studies are available.

In a two-year study, groups of F344/N rats (n = 60/sex/dose) were topically administered the chemical at 0, 0.15, 0.5 or 1.5 mg/kg bw/day, five days per week. The treatment did not affect the survival rate of rats compared with controls. Reddening of the skin at the site of application was observed in all treated groups. Treatment-related non-neoplastic lesions were observed at the site of application: at 1.5 mg/kg bw/day, the occurrence of epithelial hyperplasia in males (12/56) and females (32/53) was significantly different from the control groups (1/52 and 2/51, respectively), with minimal severity in males and mild severity in females. Sebaceous gland hyperplasia was observed in a small number of males at 0.5 mg/kg bw/day (2/55) and 1.5 mg/kg bw/day (2/56), and females treated at any dose, but the incidence was statistically significant only in females at the highest dose (30/53). Epidermal ulceration was observed in females at all doses, with statistical significance at the highest dose (19/53). Keratoacanthomas (benign tumours similar to squamous cell carcinomas) were reported in one male at 0.5 mg/kg bw/day and one male at 1.5 mg/kg bw/day. A sebaceous gland carcinoma was observed in a male at 0.5 mg/kg bw/day. Incidences of these neoplastic lesions were not significantly increased (NTP, 1995).

In another two-year study, groups of B6C3F1 mice (n = 60/sex/dose) were topically exposed to the chemical at doses of 0, 0.15, 0.5 or 1.5 mg/kg bw/day, five days per week. No change in survival was observed in treated mice, compared with controls. Reddening of the skin at the site of application was observed in all treated groups of males, and in females at 0.15 mg/kg bw/day. Treatment-related non-neoplastic lesions consisted of epithelium hyperplasia of minimal to mild severity. The incidence was statistically significant in males at 0.5 (16/50) and 1.5 mg/kg bw/day (23/50), and in females at 1.5 mg/kg bw/day (22/53). Subcutaneous sarcomas were reported in one control female and in one female at 1.5 mg/kg bw/day. One haemangioma (benign tumour of endothelial cells lining blood vessels) was observed in a female of the control group. None of the neoplastic lesions observed were statistically significant (NTP, 1995).

## Reproductive and Developmental Toxicity

Based on the results of a more recent rat study (SCCNFP, 2002), the chemical is not considered to cause specific reproductive or developmental toxicity effects. Any reproductive and developmental effects were observed secondary to maternal toxicity.

In a teratogenicity study on Sprague Dawley (SD) rats (n = 24/dose), the chemical was administered by gavage at doses of 0, 10, 30, 100 or 170 mg/kg bw/day on gestation days (GD) 6–15. Signs of maternal toxicity occurred at the highest dose, including mortality, gastrointestinal lesions (in animals that died), body weight loss, alopecia, hypersalivation, fur staining, hypothermia, ptosis (drooping of the upper eyelid) and abnormal faeces. There was no effect on the number of resorptions, litter size or foetal viability. No malformations were observed in foetuses (SCCNFP, 2002). A NOAEL of 100 mg/kg bw/day for maternal toxicity and 170 mg/kg bw/day for teratogenicity was determined in this study.

A series of reproductive toxicity and teratogenicity studies were conducted with the chemical, using oral doses up to a maximum of 35.6 mg/kg bw/day (SCCNFP, 2002):

- In pregnant New Zealand (NZ) White rabbits (n = 15/dose) given 1, 3 or 10 mg/kg bw/day of the chemical on gestation days (GD) 7–19, signs of maternal toxicity and increased incidence of supernumerary ribs were reported at 3 and 10 mg/kg bw/day. Maternal and pup mortality increased at the highest dose. No teratogenic effects were reported (supernumerary ribs were considered as secondary to maternal toxicity) and a NOAEL of 1 mg/kg bw/day for maternal toxicity and embryotoxicity was determined in this study;
- In another study in pregnant NZ White rabbits (n = 15–27/dose) orally administered doses of 1.1, 3.6 or 35.6 mg/kg bw/day on GD 7–19, maternal and foetal mortalities increased at the highest dose. There was a dose-related increase in foetal resorption at all doses, but it was statistically significant only at the highest dose. A NOAEL of 3.6 mg/kg bw/day for maternal toxicity and embryotoxicity was established in this study;
- In pregnant Long Evans rats (n = 20/dose) given oral doses of the chemical at 1.1, 3.6 or 35.6 mg/kg bw/day on GD 6–15, the highest dose induced a decrease in maternal body weight, an increase in the number of smaller pups, and an increase in the number of skeletal malformations. The incidence of reduced ossification (skeletal variaations) increased in all treated groups;

- In another study with pregnant Long Evans rats (n = 18–20/dose) given oral doses of the chemical at 1.1, 3.6 or 35.6 mg/kg bw/day on GD 6–15, effects were observed only at the highest dose, including lower maternal body weights, increased variation of skeletal ossification and increased incidence of skeletal malformations. No teratogenic effect was observed and a NOAEL of 3.6 mg/kg bw/day for maternal toxicity and embryotoxicity was determined in this study;
- In rats given oral doses of 1.1, 3.6 or 35.6 mg/kg bw/day on GD 15 through lactation day 20, there were slight decreases in foetal viability at all doses and in postnatal survival at 3.6 and 35.6 mg/kg bw/day. These effects could be related to maternal toxicity; and
- In rats treated with oral doses of 1.1, 3.6 or 35.6 mg/kg bw/day prior to and during mating, gestation and lactation, the highest dose induced growth depression, increased irritability, respiratory distress in parents and decreased viability and body weight of pups. There were no effects on reproductive parameters.

Based on the results of these studies, the SCCNFP (2002) stated that 'there was no evidence of benzethonium chloride effect on fertility and reproductive performance, nor in peri- or postnatal studies in rats at the highest chemical dose used (35.6 mg/kg bw/day)'.

# Risk Characterisation

## Critical Health Effects

The critical health effects for risk characterisation include skin and eye irritation and systemic acute effects from oral exposure.

## Public Risk Characterisation

Although use in cosmetic and/or domestic products in Australia is not known, the chemical is reported to be used overseas at concentrations up to 0.1 % in cosmetic products (CosIng; SCCNFP, 2002) and 0.28 % in some domestic products (US Household Products Database). These concentrations are expected to be representative of the maximum use concentrations in similar products in Australia.

Considering the range of domestic, cosmetic and personal care products that may contain the chemical, the main route of public exposure is expected to be through the skin, inhalation from products applied as aerosols, and potential oral exposure from lip and oral hygiene products.

The chemical is covered by the listing on Schedules 5 and 6 of the SUSMP for 'QUATERNARY AMMONIUM COMPOUNDS'. At concentrations greater than 5 %, a number of warning statements, first aid instructions and safety directions apply.

Currently, there are no restrictions in Australia on using this chemical in concentrations below 5 %, including in cosmetics or domestic products.

Based on the latest toxicokinetic studies available, the SCCNFP established a margin of safety (MOS) of 257 for the chemical when used at concentrations up to 0.1 % in leave-on cosmetics (SCCNFP, 2003). This MOS supported the conclusion that the chemical could be considered safe for use as a preservative in all types of leave-on cosmetics (SCCNFP, 2003).

Provided that normal precautions are taken to avoid prolonged skin contact and with available controls for quaternary ammonium compounds, the risk to the public posed by cosmetic/domestic products containing the chemical at low concentrations ($\leq$5 %) is not considered to be unreasonable.

## Occupational Risk Characterisation

During product formulation, dermal and ocular exposure may occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise 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 a recommendation for new classification in the HSIS (Safe Work Australia) (refer to **Recommendation** section).

# NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

## Regulatory Control

### Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2015).

### 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 | Harmful if swallowed (Xn; R22) | Harmful if swallowed - Cat. 4 (H302) |
| Irritation / Corrosivity | Irritating to eyes (Xi; R36) Irritating to skin (Xi; R38) | Causes serious eye irritation - Cat. 2A (H319) Causes skin irritation - Cat. 2 (H315) |

[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 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 that could minimise the risk include, but are not limited to:

- 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

Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(2004)] Third edition. Accessed at http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/258/ApprovedCriteria_Classifying_Hazardous_Substances_NOHSC1008-2004_PDF.pdf

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