Butanedioic acid, sulfo-, 1,4-bis(2-ethylhexyl) ester, sodium salt: Human health tier II assessment

01 July 2016

CAS Number: 577-11-7

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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.

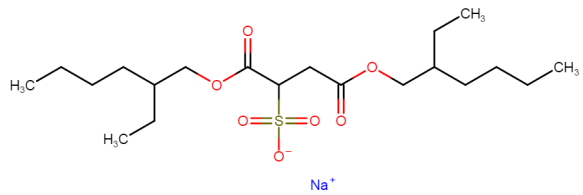
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	ducosate sodium dioctyl sodium sulfosuccinate diethylhexyl sodium sulfosuccinate succinic acid, sulfo-1,4-bis(2-ethylhexyl)ester, sodium salt di(2-ethylhexyl)sulfosuccinic acid, sodium salt
Structural Formula	
Molecular Formula	C20H38O7S.Na
Molecular Weight (g/mol)	444.56
Appearance and Odour (where available)	White, wax-like solid.
SMILES	C(=O)(C(CC(=O)OCC(CCCC)CC)S(=O)(=O)O{-}.[Na]{+})OCC(CCCC)CC

Import, Manufacture and Use

Australian

The following Australian industrial use was reported under previous mandatory and/or voluntary calls for information.

The chemical has reported domestic use as a surface-active agent.

The total volume introduced into Australia, as reported under previous mandatory and/or voluntary calls for information, was <100 tonnes per annum.

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

- agricultural or veterinary use as an active constituent not requiring evaluation by the Australian Pesticides and Veterinary Medicines Authority (APVMA);
- as a stool softening agent by the Therapeutic Goods Administration (TGA); and
- as a food additive, with a maximum permitted level (MPL) of 10 mg/kg, by Food Standards Australia New Zealand (FSANZ).

International

The following international uses have been identified through:

- the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers;
- the European Commission Cosmetic Ingredients and Substances (CosIng) database;
- the US Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary;
- the Organisation for Economic Co-operation and Development (OECD) High Production Volume (HPV) chemical program;
- the US Department of Health and Human Services Household Products Database (HPD);
- the US National Library of Medicine's Hazardous Substances Data Bank (HSDB);
- Galleria Chemica;
- the Substances and Preparations in Nordic countries (SPIN) database; and
- various international assessments (CIR, 2013; CIR, 1998).

The chemical is indicated as having cleansing, emulsifying, hydrotropic and surfactant functions and has reported cosmetic use in:

- fragrances and air fresheners;
- deodorants and hair sprays;
- bath oil and skin cream or moisturising products;
- nail and hair-colouring products; and
- eye make-up products.

The chemical has reported domestic use, including in liquid and pump spray household and automobile washing and cleaning products.

The chemical has reported commercial use, including in:

- lubricants and greases;
- metal working and hydraulic fluids;

- corrosion inhibitors; and
- manufacturing adhesive or polymeric coatings.

The chemical has reported site-limited use, including in the manufacture of other chemicals (an intermediate).

Restrictions

Australian

While no known restrictions have been identified, the chemical is listed in the *Poisons standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) under 'Docusate sodium (dioctyl sodium sulfosuccinate)' in Appendix B, as not requiring control by scheduling for any use, due to low toxicity (SUSMP, 2016).

International

No known restrictions have been identified.

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 dialkyl sulfosuccinate salt produced through the esterification of 2-ethylhexanol (CAS No. 104-76-7) and sulfosuccinic acid (CIR, 2013; CIR, 1998). As it contains two ester linkages, it is considered to be sensitive to hydrolysis via chemical or enzymatic processes, with hydrolysis resulting in the formation of 2-ethylhexanol and sulfosuccinic acid.

Toxicokinetics

In a toxicokinetics study in rats, 5 mg/mL solution of the chemical was administered by oral gavage (single dose) to one animal at 1 mL and another at 2 mL. A further two animals were administered 10 mg of the chemical intravenously. One animal was

administered the radiolabelled chemical by oral gavage (single dose) at 10 mg/kg bw. Analysis of the results demonstrated the chemical was effectively absorbed (at least 65 %), extensively metabolised (to form 2-ethylhexanol derivatives), and excreted (approximately 2/3 through urine; 1/3 through faeces) (REACH). Similar results were reported in a toxicokinetics study in rabbits (REACH), although only limited details are available for this study.

In an oral toxicokinetics study in humans, 200 mg of the chemical was administered as liquid-containing capsules to two male volunteers. Similarly to studies in rats and rabbits, the chemical was well absorbed following ingestion, with 2-ethylhexanol derivatives formed on metabolism of the chemical (REACH). However, in contrast to the animal studies, excretion of the administered dose occurred primarily through the faeces (70 %), with 25 % excreted in urine, with similar results reported in comparative oral and intravenous toxicokinetics studies in dogs (one animal/dose/exposure route) administered single doses of either 10 mg/kg bw of the chemical, or 4 mg/kg bw of the radiolabelled chemical (REACH).

Acute Toxicity

Oral

Based on the weight of evidence of results from animal tests following oral exposure, the chemical is considered to have low acute oral toxicity.

In a study conducted in rats according to OECD Test Guideline (TG) 401, the median lethal dose (LD50) was reported to be >2100 mg/kg bw (REACH).

In several other acute toxicity studies in rats, the oral LD50 values were reported to be between 3080 - 4200 mg/kg bw, while in two other studies, no mortalities were reported up to the highest doses tested (LD50 values of >1300 and >1400 mg/kg bw, respectively) (REACH).

Although an LD50 value in rats of 1900 mg/kg bw was reported in one early study, only limited study details are available (CIR, 1998; Olsen et al, 1962).

Dermal

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

In a study on five New Zealand White (NZW) rabbits, a single dose of the chemical was applied to clipped, unabraded skin at 10 000 mg/kg bw. The dermal LD50 value was reported to be >10 000 mg/kg bw. No mortalities were reported. Local effects of skin irritation were noted (CIR, 2013; REACH).

In another study of limited reliability (due to low numbers of animals), the dermal LD50 in rabbits was reported to be 2525 mg/kg bw (REACH).

Inhalation

Limited data are available.

The chemical is reported to have a median lethal concentration (LC50) value of 20 mg/L following a 96-hour exposure period. No further study details are available (REACH).

Corrosion / Irritation

Skin Irritation

Based on the available experimental data, the chemical is considered to be a skin irritant. There is sufficient evidence to warrant hazard classification. While effects indicative of corrosivity have been reported in several studies, these followed co-exposure to other substances or use at prolonged exposure times.

In a skin irritation study conducted according to OECD TG 404, 0.5 mL of a 70 % solution of the chemical was applied, under occlusive conditions, to the shaved skin of three white Russian rabbits for a four hour exposure period. A mean irritation score of 7.8 (out of a maximum score of 8) was reported based on observations recorded at 1, 24, 48 and 72 hours after exposure (REACH). Severe erythema and oedema were still observed in all animals at the end of the 14-day observation period, with formation of scars reported in 2/3 animals. While scar formation may indicate corrosive effects, it was reported that the presence of 15 % ethanol (diluted with 5 % methanol) in the solution potentially increased the irritancy of the test substance.

In another study conducted according to test guidelines, 0.5 mL of the chemical (>97 % purity) was applied under occlusive conditions, to the shaved and intact skin of six NZW rabbits for a 24-hour exposure period. A primary irritation score of 3.83/4 was reported, with the chemical considered to be strongly irritating to the skin (REACH; CIR, 2013). Erythema and oedema were still observed at the end of the 72-hour observation period; reversibility was not assessed in this study.

In other studies, the chemical applied as a 2 % patch on the skin of rabbits for 24 hours resulted in irritation scores of 3.7/8 (intact skin) and 1.7/8 (abraded skin), while 5 % of the chemical applied to intact abdominal skin in rabbits produced a burn after two to four 24-hour applications, and 25 % produced a burn after one 24-hour application. Additionally, application of 1, 5 and 25 % of the chemical to abraded rabbit skin for three days caused moderate to severe irritation (CIR, 2013; CIR, 1998).

Eye Irritation

Based on the available experimental data, the chemical is considered to be a severe eye irritant. There is sufficient evidence to warrant hazard classification.

In an eye irritation study conducted according to OECD TG 405, 0.1 mL of a 70 % solution of the chemical was applied to the right eye of three white Russian rabbits; the left eye served as the control. The test substance was washed out of the eye after a 72-hour exposure period. An irritation index of 46.67/110 was reported based on mean irritation scores recorded at 1, 24, 48 and 72 hours after application (REACH). Effects, including turbidity of the cornea (reported as irreversible damage), were still visible at the end of the 21-day observation period.

In another eye irritation study, 0.1 mL (equivalent to 0.1 g) of the chemical (>97 % purity) was applied to the eyes of three NZW rabbits (exposure period not specified). The chemical was reported to cause moderate eye irritation based on observations at 24, 48 and 72 hours after application (REACH). Effects on the cornea, iris and conjunctivae were still observed at the end of the 72-hour observation period; reversibility was not assessed in this study.

A 10 % solution of the chemical was also reported to have been used as a positive control in an eye irritancy test in rabbits, with severely irritating effects (CIR, 2013; CIR, 1998).

Observation in humans

In addition to being a potential skin and eye irritant following a single exposure, the chemical is also reported to be a cumulative irritant based on effects observed in human irritation and skin sensitisation studies (see also **Skin sensitisation** section).

In several four-day cumulative irritancy tests conducted in humans, application of products containing the chemical resulted in a primary irritation index (PII) range of 0.25-0.80 at a chemical concentration of 2.94 %, a PII range of 1.78-1.85 at 0.25 % and a PII of 0.04 at 0.1 % (CIR, 2013; CIR, 1998).

In a 21-day cumulative irritancy test in seven volunteers, daily application of a product containing 1.13 % of the chemical (of 84 % purity) under occlusive conditions resulted in a total irritation score of 324/578, with the average score of 46.3/84 per subject (CIR, 2013; CIR, 1998).

Skin irritation reactions were reported in six patients following application of a orthopaedic plaster cast lined with a wool containing the chemical (CIR, 2013; CIR, 1998). Subsequent patch testing was conducted in these six patients using the four chemicals used to manufacture the wool (the other three chemical are not identified) at concentrations of 1, 10, and 100 %. Application of the chemical produced positive irritancy reactions in all patients. The other three chemicals used in the

manufacturing process did not cause irritation. In a follow-up patch testing study, a product containing the chemical was applied to the skin of 18 volunteers (eight with normal skin and 10 with non-inflammatory skin disease). No irritation or allergic reactions were reported in any of the subjects exposed to the chemical at 1 and 10 %. However, at 100 %, the chemical produced skin irritation reactions in 12/18 volunteers.

In a separate study, no irritation effects were reported following a single application of the chemical at 2.5 % in a formulation (occlusive patch) for a 24-hour period (CIR, 2013).

Sensitisation

Skin Sensitisation

While no skin sensitisation studies in animals are available, several human studies have been conducted. Based on the available information, the chemical is not considered to be a skin sensitiser. However, cumulative irritancy effects are reported.

In a skin sensitisation patch test in humans, 0.3 g of a 2.5 % solution of the chemical was applied to the back or forearms of 100 volunteers for 24-hour periods over 10 alternate days (induction phase). After a one-week rest period, 0.3 g of a 1 % solution was applied to different sites on the back or forearms of the volunteers for a 24-hour period (challenge phase). Observations were recorded after removal of the challenge patch. No sensitisation reactions were reported in any of the subjects at the challenge sites. However, mild erythema was reported in 19/100 individuals during the induction phase (REACH).

The chemical was also reported not to induce skin sensitisation effects in several human repeated insult patch tests (HRIPTs) at concentration up to 5 %. However, mild irritation reactions were reported in some individuals during the induction phase (CIR, 2013). Similar results were observed in a HRIPT of a 50/50 dilution in distilled water of an eyebrow pencil containing 2.5 % of the chemical and another HRIPT of a product containing 0.1 % of the chemical (reported as 84% purity) (CIR, 2013; CIR, 1998).

Repeated Dose Toxicity

Oral

Based on the available information from experimental studies, repeated oral exposure to the chemical is not considered to cause serious damage to health.

In a repeated oral dose toxicity study in Charles River rats (20 animals/sex), conducted similarly to OECD TG 408, the chemical was administered in diet at 750 mg/kg bw/day for 90 days. No significant differences in body weights, absolute organ weights, clinical blood chemistry or urinalysis were reported between the treatment and control group animals. No deaths were reported and no gross pathological findings were noted at necropsy. A no observed adverse effect level (NOAEL) of 730 mg/kg bw/day was reported for this study (REACH).

In another study in rats (12 animals/group), the chemical was administered in diet at 0.5, 1.04, or 1.5 % for 26 weeks. Decreased body weight gains were reported in females of the 1.04 and 1.5 % groups after three weeks of treatment. Deaths were reported in two control animals and four animals of the 1.5 % group, with haemorrhagic gastroenteritis noted in 2/4 animals that died at the highest dose. No other effects were noted. A NOAEL of 0.5 % and a lowest observed adverse effect level (LOAEL) of 1.04 % were reported for this study (CIR, 2013).

In other repeated dose oral toxicity studies, no adverse effects were reported in rats fed =1250 mg/kg bw, in dogs fed 100-250 mg/kg bw, or in monkeys fed 125 mg/kg bw of a product containing the chemical for 24 weeks. However, in a four-month study in male rats, the chemical was reported to be very toxic (no further details available) when fed at 2, 4, or 8%, while reduced body weight gains were reported in rats fed =1 % of the chemical for 2 years (CIR, 2013; CIR, 1998). It is noted that due to the use of formulated products containing the chemical, the effects reported in the above studies cannot be solely attributed to the test chemical.

Dermal

Based on the limited data available, repeated dermal exposure to the chemical is not considered to cause serious systemic damage to health.

In a 13-week dermal toxicity study in female Sprague Dawley (SD) rats (n=8), the chemical (4 mL/kg of a 0.00126 % formulation, equivalent to 0.05 mg/kg bw/day) was applied to the shaved intact skin for five days/week for 67 days. A statistically significant increase compared to control animals in white blood cell count was reported at week 13, in addition to a decrease in serum aspartate aminotransaminase activities at week seven. However, these values were considered to be within the range for historical controls. One animal was reported to have fluid-filled kidneys at necropsy. There was no significant difference from control animals in body weight gain, organ weight, survival or urinalysis parameters, although observations of minimal to moderate skin irritation were reported in animals throughout the 67-week study period (CIR, 2013; CIR, 1998). As this test was conducted using a formulation containing the chemical, any adverse effects reported cannot be solely attributed to the chemical being assessed in this report.

Inhalation

No reliable data are available.

Several repeated inhalation toxicity studies in animals are available. However, these were conducted using formulated products containing the chemical, with very little information regarding the composition of the product (CIR, 2003; CIR, 1998). Any adverse effects reported in these studies cannot be solely attributed to the chemical being assessed in this report.

Genotoxicity

Although two well-conducted in vitro experimental studies are available, the results are inconclusive, and as no in vivo studies are available, there is insufficient evidence to determine the genotoxic potential of the chemical.

In an in vitro bacterial reverse mutation assay (Ames test) conducted according to OECD TG 471, the chemical did not induce mutations in *Salmonella typhimurium* strains TA98,TA100, TA1535, TA1537 or TA102, both in the presence or absence of metabolic activation, at test concentrations up to 5000 µg/plate (REACH).

In an in vitro mammalian chromosome aberration test conducted according to OECD TG 473 in Chinese hamster ovary (CHO) cells, a significantly increased frequency of cells with chromosomal aberrations was reported at doses ≥120 ug/mL only in the presence of metabolic activation. No significant difference was observed in the absence of metabolic activation. While the study concluded that the chemical was able to induce chromosome aberrations in CHO cells, the authors also noted that effects were observed at doses very close to the threshold of toxicity, and that aberration induction is likely to be associated with an indirect mechanism (REACH).

Carcinogenicity

No reliable data are available.

The only available carcinogenicity information is from a six month study investigating colorectal carcinogenesis in male F344 rats. Animals were administered the chemical in diet at 0 or 1 %, in addition to a weekly single subcutaneous injection of 1,2-dimethylhydrazine (a chemical known to induce colon tumours in experimental animals). No statistically significant difference between test and control group animals were reported in regards to frequency or progression of tumours (REACH; CIR, 2013). However, due to the study design and the very limited study details available, these results are insufficient to determine the carcinogenic potential of the chemical.

Reproductive and Developmental Toxicity

The chemical is the sodium salt of the diester of 2-ethylhexanol (CAS No. 104-76-7) and sulfosuccinic acid, with hydrolysis of the chemical resulting in formation of 2-ethylhexanol at a ratio of 2:1 (CIR, 1998). 2-Ethylhexanol has been assessed (NICNAS) and is reported to cause developmental toxicity, but not teratogenicity, in rats following treatment via the oral route. These

effects were noted in the absence of signs of marked maternal toxicity. The NOAEL for developmental toxicity was reported to be 130 mg/kg bw/day. 2-Ethylhexanol is also classified as a Category 3 hazardous substance toxic to reproduction, with the risk phrase ‘Possible risk of harm to the unborn child’ (Xn; R63) in HSIS (Safe Work Australia).

The available data on the chemical indicate that it is not a specific reproductive or developmental toxin. While some developmental effects were seen in a study using a very high dose of the chemical, this dose is outside the dose range considered relevant for developmental toxicity studies.

Reproductive Toxicity

In a three-generation reproductive toxicity study in rats, the chemical was administered in diet, daily, at 0.1, 0.5 or 1 % (approximately equivalent to 50, 250 and 500 mg/kg bw/day, respectively) to 30 animals/sex/group. Parental (F0 generation) animals were treated from approximately seven weeks of age, continuously throughout mating, gestation and lactation, until animals were necropsied (duration of exposure was six months for F0 males and five months for F0 females). Additionally, first generation (F1) and second generation (F2) animals were exposed to the test material in utero, while nursing, continuously from when they were weaned to test diets, throughout mating, gestation, and lactation, until animals were necropsied (total duration of exposure for F1 and F2 animals is not clear). At 0.5 %, a reduction in body weights for parental males of all generations and for F1 and F2 females was reported, which correlated with lower pup weights at this dose level, compared to control animals, in all three generations. No adverse effects on growth, developmental or reproductive performance were reported despite the reduced pup weights. A no observed effect level (NOEL) of 0.1 % was established for parental animals and offspring based on reduced body weights, while a NOEL of 1 % was reported for reproductive parameters (REACH; CIR, 1998).

In a two-generation reproductive toxicity study in albino rats, the chemical was administered at 0.5 and 1 % (approximately equivalent to 250 and 500 mg/kg bw/day, respectively) in diet (16 animals/sex/group), from weaning onwards (REACH). For most of the matings, the test material was removed from the diet of the dam the day before they were expected to deliver the litters. Pups were then placed on respective control or treatment diets after weaning. However, for two of the matings (the first mating of the F0 generation to produce F1a pups, and the second mating of the F2 generation to produce F3b pups), dams were continuously fed throughout the study, including during lactation, and pups were weaned directly on the respective diets. For these two matings, the lactation indices were lower than control values, with mean weight of F1a and F3b pups at weaning reported to be decreased with increasing dietary dose level administered to the dams. Additionally, a decreased viability index was reported in F3b pups. While all pups were examined for gross defects, only pups from the first mating of the F2 animals were selected for necropsy examination. From these pups, it is reported that 2 animals/sex/litter that were the smallest or appeared the least healthy were excluded from necropsy. The study concluded that the type and frequency of skeletal abnormalities observed in foetuses did not differ significantly between test and control group animals, and that the lower survival rate and mean body weights of the F1a and F3b pups is attributable to nutrition deficiencies resulting from taste aversion of the test material secreted into the milk of the dams during lactation. However, as the F1a and F3b pups were not examined at necropsy, there is insufficient evidence to discount that maternal exposure to the chemical during lactation may cause adverse developmental effects in offspring.

Developmental Toxicity

In a developmental toxicity (teratogenicity) study in pregnant SD rats, the chemical was administered in diet at 1.0 and 2.0 % (equivalent to 1074 and 1983 mg/kg bw, respectively) to 22 and 20 animals, respectively, on gestational days (GD) 6-15 (REACH; CIR, 2013). At GD 21, dams were euthanised and foetuses removed from examination. The only maternal sign of toxicity observed was a statistically significant reduction in weight gain of 2.0 % group animals during GD 6-15, although weight gain of dams did not differ significantly across any of the groups during GD 15-21 (REACH). While the occurrence of implantation resorptions was significantly higher (depending on statistical method of calculation) in the 2.0 % group, there was no significant difference between any of groups in regards to occurrences of viable foetuses, foetal weight or litter size (of viable foetuses).

However, statistically significant increases in the occurrence of foetal morphological observations including exencephaly (development of the brain outside the skull) and anophthalmia (the absence of one or both eyes) were reported at the 2.0 % dose level. Statistically significant increases in the occurrence of foetal skeletal observations were also reported at this dose level, including incomplete or lack of ossification of the cranial bones (which can be linked to the occurrence of exencephaly) and absent or less developed ribs.

A NOAEL of 1.0 % was reported for this study, with the dose level of 2.0 % considered to be 'a near toxic or toxic dietary level' based on the reduced maternal body weight gain during GD 6-15. However, considering the lack of difference in maternal body

weight gain during GD 15-21, there is concern that the observed foetal abnormalities at this dose may not be secondary non-specific consequences of the reduced maternal body weight gain during GD 6-15.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include skin and eye irritation.

Public Risk Characterisation

Currently, there are no restrictions in Australia on using this chemical in cosmetics or domestic products.

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 sprays or aerosols, and potential eye exposure from eye make-up products. The chemical is also reported to be used in a cosmetic product that is likely to result in exposure to the mucous membrane (CIR, 2013). However, no further details on this product are available. Reported use of the chemical in a bath oil is also a potential concern in regards to all routes of exposure (CIR, 2013; HPD).

Although concentration levels of the chemical used in consumer products in Australia are not known, the chemical is reported to be used in domestic products overseas at concentrations ranging from 0.01 - 5.0 % (HPD), with a maximum reported use concentration in cosmetic products at 4.4 % in a leave-on eye make-up product (CIR, 2013). The chemical is also reported to be used in leave-on skin moisturising products. Although use concentrations of the chemical are not specifically reported for these products, a concentration range of 0.0002 - 4.4 % is reported for cosmetic products that are expected to result in dermal exposure (CIR, 2013). The concentration of the chemical used in bath oil products is not reported (CIR, 2013; HPD).

The US Cosmetic Ingredients Review (CIR) Expert Panel evaluated the use of the chemical in cosmetic products in 1998 and 2013. Both reviews acknowledged that the chemical is a cumulative irritant and that 'care should be taken to avoid irritancy in formulations intended for prolonged contact with the skin' (CIR, 1998), concluding that use of the chemical in cosmetics is 'safe in the present practices of use and concentration in cosmetics described...' (in the 2013 CIR review) '...when formulated to be non-irritating' (CIR, 2013).

While the chemical is reported to be used at concentrations up to 0.25 % in cosmetic products that may be aerosolised (CIR, 2013), there are insufficient data from inhalation exposure studies to determine the risk from use of these products. However, the CIR panel evaluated the risk of incidental inhalation exposure of the chemical from hair sprays, and concluded that, based on the available information (including the chemical and biological properties of the chemical), incidental inhalation is not considered to be a significant route of exposure that could lead to local respiratory or systemic effects (CIR, 2013).

Occupational Risk Characterisation

Given the critical health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise 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

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.

Assessment of the chemical is considered to be sufficient provided that risk management recommendations are implemented and all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

Inclusion of the chemical in Appendix B of the SUSMP is considered inappropriate, as the chemical cannot be considered to be of low toxicity based on the results of this assessment.

Appropriate scheduling and labelling should be undertaken to mitigate risk when the chemical is used in domestic and cosmetic products. Due to the toxicity profile at the concentrations reported to be potentially in use, this chemical should be considered for listing in the Schedules of the SUSMP to ensure appropriate labelling. Exemptions to scheduling might be applicable at low concentrations. Matters to be taken into consideration include:

- the known uses of the chemical;
- although there is no information to confirm the maximum use concentration of the chemical in cosmetic and domestic products in Australia, it is reported to be used in cosmetic and domestic products overseas at concentrations up to 4.4 and 5.0 %, respectively (CIR, 2013; HPD);
- the chemical is a skin irritant and a severe eye irritant;
- dermal irritation has been observed in humans (studies and case reports) following repeated application of products containing the chemical at <5 %; and
- the CIR recommendation that products containing dialkyl sulfosuccinate salts (including this chemical) must be formulated to be non-irritating, based on the panel's conclusion that surfactant formulations containing the chemical would most likely produce irritation effects (CIR, 2013).

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]
Irritation / Corrosivity	Risk of serious eye damage (Xi; R41) Irritating to skin (Xi; R38)	Causes serious eye damage - Cat. 1 (H318) 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 or 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 that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- 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[s] 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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Last update 01 July 2016

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