Benzenesulfonic acid, dimethyl-, sodium salt: Human health tier II assessment

17 May 2013

CAS Number: 1300-72-7

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.

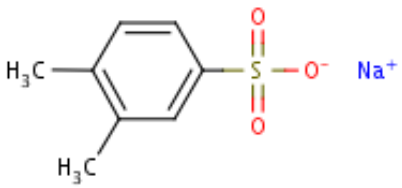
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	Xylenesulfonic acid, sodium salt Sodium xylenesulfonate Sodium xylenesulphonate Pentosan polysulfate sodium Sodium dimethylbenzenesulfonate
Structural Formula	 This is a UVCB with the relative positions of the methyl and the sulfonate groups varying
Molecular Formula	C8H10O3S.Na
Molecular Weight (g/mol)	208.21
Appearance and Odour (where available)	Odourless white powder or crystals
SMILES	c1(C)c(C)cc(S(=O)(=O)O{-}.[Na]{+})cc1

Import, Manufacture and Use

Australian

The chemical was reported during the 2002 High Volume Industrial Chemicals List (HVICL) compilation with a total reported introduction volume between 1000 and 9999 tonnes (NICNAS, 2002). Hydrotropes as a category, to which the chemical belongs, were reported to have an annual production of 1100 tonnes (40 % concentration) in Australia (OECD, 2005).

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information and in the OECD report (2005). The chemical is used as a hydrotrope in products to help solubilise otherwise water insoluble ingredients.

The chemical has reported cosmetic use including in:

- shampoos (up to 0.8 %).

The chemical has reported domestic use including in:

- laundry detergents (up to 1.375 %);
- hard surface cleaners (up to 0.9 %);
- machine dishwasher rinse aid (up to 5.5 %);
- hand dishwashing liquid detergents (1.2–5.5 %);
- toilet cleaners (at 0.2 %);
- solvent hand cleaners (at 0.8 %); and
- carpet cleaners (at 1 %).

The chemical has reported commercial use including in:

- professional cleaning/washing agents and additives;
- surface active agents;
- optical brightener products (at 3 %); and
- liquid sulfur textile dyes (7.5–50 %).

International

The following international uses have been identified through the European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; the Organisation for Economic Cooperation and Development Screening information data set International Assessment Report (OECD SIAR); Galleria Chemica; Substances in Preparations in Nordic countries (SPIN) database; the European Commission Cosmetic Substances and Ingredients (CosIng) database; and other sources via eChemPortal: the US Environmental Protection Agency's (EPA) Aggregated Computer Toxicology Resource (ACToR), the US National Library of Medicine's Hazardous Substances Data Bank (HSDB), and the US Department of Health and Human Service's Household Products Database (HHPD).

The chemical is used as a hydrotrope in products to help solubilise otherwise water insoluble ingredients.

The chemical has reported cosmetic use including in:

- liquid face and hand soap (10–15 %);
- shampoo (1–5 %);
- conditioner (1–5 %); and
- body washes (up to 0.5 %).

The chemical is listed in the US Cosmetic Ingredient Review (CIR) as a cosmetic ingredient found safe when used at concentrations up to 15 % (Galleria Chemica).

The chemical has reported domestic use including in:

- cleaning agents such as laundry liquids (1–10 %) and powders (0.1–0.5 %);
- hand dishwashing liquids (1–5 %);
- machine dishwasher rinse aid (1–5 %);
- concrete or hard surface cleaners (up to 5 %);
- pet care products; and
- car-cleaning products (1.3–6.3 %).

The chemical has reported commercial use including:

- in general cleaning products, and cleaning products for vehicles and facades;
- in water treatment products;
- in textile dyes (7.5–50 %);
- as an acidic recirculation cleaner (10–25 %);
- as a wetting agent for tanning leather (at 10 %);
- treating of metal surfaces;
- as an enzymatic recirculation cleaner in the food and dairy industry (at 4 %);
- as a floor stripper (2.7–9 %);
- in metal working fluids;
- in coolant system conditioners (at 6.9 %);
- in lubricants, greases and release products;
- in vinyl, plaster rubber restorer (at 0.2 %); and
- in fertiliser products.

The chemical is listed in the US Food and Drug Authority (US FDA) list as a food additive, as a sanitising agent for food contact surfaces, and in the US FDA list of 'indirect additives used in food contact substances' as a component of adhesives and paper or paperboard products (Galleria Chemica).

Restrictions

Australian

No known restrictions have been identified.

International

No known restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is 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

This chemical belongs to the chemical category hydrotropes assessed by the OECD (2005). Although the counter ion contributes to the physical and chemical behaviour of each individual hydrotrope, the toxicological properties are not expected to be affected by the difference in counter ion (i.e. sodium, ammonium, calcium or potassium) (OECD, 2005). In addition, hydrotropes may have a single methyl group on the sulfonated aromatic ring, two methyl groups (similar to the chemical under assessment), or a methylethyl group and these may be in a variety of isomeric forms (ortho, meta and/or para). This is not expected to have a major influence on chemical reactivity and behaviour. Therefore, if hazard data on specific health endpoints are not available on this chemical, data available on other hydrotropes were used in this assessment.

Toxicokinetics

Based on physical and chemical properties, it is expected that the chemical will be absorbed in significant amounts when administered orally. This is supported by clinical signs of toxicity in acute oral toxicity studies. In contrast, limited absorption is expected from dermal exposure. This is supported by a lack of clinical signs of toxicity in acute dermal toxicity studies (OECD, 2005). It is reported that the absorbed sulfonates are quickly distributed through living organisms and excreted rapidly (IUCLID, 2000).

Acute Toxicity

Oral

The chemical has low acute oral toxicity.

The oral LD50 is > 5000 mg/kg bw in rats (OECD, 2005).

For hydrotropes, the observed clinical signs of sublethal toxicity included decreased activity, weakness, diarrhoea, prostration, piloerection, ptosis (drooping eye lid), lachrymation, hypersalivation and anogenital staining, one to four hours after oral administration (OECD, 2005).

Dermal

The chemical has low acute dermal toxicity.

The dermal LD50 in rabbits is > 2000 mg/kg bw (REACH). No mortalities were observed at doses of 500 mg/kg bw or 2000 mg/kg bw. Observed sublethal effects included erythema and oedema at the site of application for 6/20 animals in the first week of the study, and in the second week slight cracking and dryness of the skin followed by desquamation (REACH).

Inhalation

No data are available for the chemical. Based on the data available for an analogue chemical, the chemical is likely to have low acute inhalation toxicity.

The inhalation LC50 for an aerosol of ammonium dimethylbenzenesulfonate (CAS No. 26447-10-9) is > 6.4 mg/L, based on a standard four hour exposure in rats (REACH).

Corrosion / Irritation

Skin Irritation

Based on the limited information available, the chemical is not considered a skin irritant.

The chemical is reported to slightly irritate the skin of rabbits. Following testing on intact and abraded rabbit skin (n = 6 females) for 24 hours, the chemical at a concentration of 30 % resulted in zero scores for erythema and oedema in all animals. The scores remained zero when the treatment was repeated every 24 hours (5 doses in total) (REACH).

In another study, six rabbits received the chemical in solution (details not available) as a single dose. The mean erythema scores reported were 1.3, 1.2 and 0.3 at 24, 48 and 72 hours, respectively (REACH).

Two studies testing the chemical at a concentration of 40 % on rabbit skin reported slight skin irritation (OECD, 2005). Detailed scores for erythema and oedema were not provided.

In addition, it has been shown that other hydrotropes (calcium dimethylbenzenesulfonate, CAS No. 28088-63-3 and sodium methylethylbenzenesulfonate, CAS No. 28348-53-0) are not skin irritants (OECD, 2005).

Eye Irritation

Based on the data available for the chemical (at 40 % concentration), and on the information available for similar chemicals, the chemical is considered to be an eye irritant.

The chemical is reported to be an eye irritant in one animal study. A study exposing the eyes of six rabbits to the chemical (40 % solution for 24 hours, and washed after 24 hours) showed positive responses in more than four animals. Maximum mean total scores were 13, 12.2, 5.0 and 2.0 at 1, 24, 48 and 72 hours, respectively (individual eye scores not available). Effects were generally reversible within 72 hours but slight erythema of the eye was still noticeable at 72 hours (OECD, 2005; REACH).

Studies with structurally and functionally similar chemicals (hydrotropes) had varied results, from mild or slight irritation to moderate irritation when tested according to OECD TG 405 (REACH). For example, a test with a 40 % solution of sodium methylethylbenzenesulfonate (CAS No. 28348-53-0) on three rabbits reported a maximum mean total score of 23.3 at 24 hours and found the chemical to be moderately irritating. Effects on the cornea, the iris and the conjunctivae were noted in all animals, with scores decreasing at 48 and 72 hours. The effects were fully reversible in seven days (REACH).

Sensitisation

Skin Sensitisation

No data are available for the chemical. Based on the data available for the analogue chemicals, the chemical is not considered a skin sensitiser.

Studies (OECD TG 406) using structurally and functionally similar chemicals (sodium methylethylbenzenesulfonate, CAS No. 28348-53-0; sodium methylbenzenesulfonate, CAS No. 12068-03-0) were not found to induce dermal sensitisation in guinea pigs (OECD, 2005; REACH).

Observation in humans

No skin sensitisation was observed in humans exposed to 0.5 % sodium methylethylbenzenesulfonate (CAS No. 28348-53-0) in 0.1 % solution of laundry detergent powder, using repeat patch testing

(OECD, 2005).

Repeated Dose Toxicity

Oral

Based on the data available, the chemical is not considered to cause serious damage to health by repeated oral exposure.

One study examined the effects of repeated oral administration of the chemical via diet in both mice (B6C3F1) and rats (Wistar) over a period of 13 weeks. The no observed adverse effect levels (NOAELs) were reported as > 2439 and > 2467 mg/kg bw/day for male and female mice respectively, based on no significant treatment related effects on animal body weight or food consumption up to and including the highest dosage. The NOAELs of > 1429 and > 1561 mg/kg bw/day for male and female rats, respectively, were reported based on no significant treatment related effects up to and including the highest dosage. Further to this, no treatment related lesions were observed at necropsy in the rats and mice at the highest dose, when compared with controls (OECD, 2005; REACH).

In another 13 week repeat dose oral study, the chemical was administered via the diet to Wistar rats. The NOAELs of 763 and 3534 mg/kg bw/day were established for female and male rats, respectively (OECD, 2005; REACH). Decrease in the relative spleen weight and some changes in the haematology were observed in female rats at the highest dose of 4092 mg/kg bw/day. No significant toxicological observations were made in male rats up to and including the highest dose of 3534 mg/kg bw/day.

Dermal

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

In a repeat dose study of 90 days (similar to OECD TG 411), the NOAELs were 440 and 550 mg/kg bw/day for male and female mice respectively, based on observations of epidermal hyperplasia at the treatment site at the highest dose of 1300 and 1620 mg/kg bw/day in males and females respectively. In male mice, an increase in the mean body weight and mean kidney weight (both < 10 % difference compared with the control group) were observed at the highest dose of 1300 mg/kg bw/day.

In a similar test with rats, NOAELs were established at ≥ 500 and ≥ 800 mg/kg bw/day for males and females respectively. A decrease in liver weight was observed in males at 60, 170 and 500 mg/kg bw/day. This decrease was not associated with any changes in the histopathology of the liver (OECD, 2005; REACH). No effects were observed in females at doses up to and including the highest dose of 800 mg/kg bw/day.

In a subchronic dermal toxicity study of 17 days (similar to the EPA OPP 82-2 guideline), NOAELs were reported as ≥ 1000 and ≥ 2000 mg/kg bw for male and female mice respectively, and ≥ 800 and ≥ 1030 mg/kg bw for male and female rats respectively. No significant treatment related effects were reported in rats and mice at doses up to and including the highest dose. However, there was some evidence of slightly higher relative liver weights in rats and mice that received the highest dose (REACH).

Inhalation

No data are available.

Genotoxicity

Based on the weight of evidence from in vitro data available for the chemical and in vivo data available for analogue chemicals, the chemical is not considered genotoxic.

The chemical showed negative results in some in vitro genotoxicity studies including bacterial mutagenicity (Ames) tests, mammalian chromosomal aberration tests, sister chromatid exchange assays and gene mutation tests with mouse lymphoma cells (OECD, 2005; REACH).

Positive results were reported for an in vitro mammalian sister chromatid exchange assay using Chinese hamster ovary cells. The chemical is reported to be clastogenic at concentrations > 1667 µg/mL without metabolic activation (OECD, 2005; REACH).

No in vivo genotoxicity data are available for the chemical. However, negative results were reported for two analogue chemicals (sodium methylethylbenzenesulfonate, CAS No. 28348-53-0 and calcium dimethylbenzenesulfonate, CAS No. 28088-63-3), using in vivo mouse micronucleus assays (REACH).

Carcinogenicity

Based on the data available, the chemical is not considered carcinogenic.

The chemical was not carcinogenic in rodents with NOAELs of 240 and 727 mg/kg bw/day established for rats and mice respectively, based on no observed carcinogenic activity up to and including the highest dose (240 and 727 mg/kg bw/day for rats and mice respectively). These studies were similar or equivalent to OECD TG 453 (combined chronic toxicity/carcinogenicity studies) (OECD, 2005; REACH).

Epidermal hyperplasia was observed at the site of chemical application at: 120 and 240 mg/kg bw/day in female rats; 364 and 727 mg/kg bw/day in female mice; and 364 and 727 mg/kg bw/day in male mice.

Reproductive and Developmental Toxicity

Based on the limited data available, the chemical is not considered to have reproductive or developmental toxicity.

No data are available for the chemical on reproductive or developmental toxicity. The OECD (2005) report on hydrotropes stated that despite the lack of specific studies on reproductive toxicity, some conclusions could be drawn from repeat dose studies that included examination of reproductive organs. In repeat dose dermal toxicity studies (13 weeks and two years) testing the chemical in both rats and mice, and in two 13 week repeat oral dose studies testing analogue chemicals in rats, there was no evidence of adverse effects on the reproductive organs of male or female rodents (OECD, 2005).

No developmental effects were noted in rats exposed (gestation days 6–15) to an analogue chemical (calcium dimethylbenzenesulfonate, CAS No. 28088-44-8) via oral gavage dosing of up to 3000 mg/kg bw/day. The NOAELs for maternal and developmental toxicity were > 3000 mg/kg bw/day (OECD, 2005; REACH).

Risk Characterisation

Critical Health Effects

The only critical effect to human health is the potential for eye irritation. Eye irritation was seen in animals when the chemical was applied as a 40 % solution.

Public Risk Characterisation

Considering that the chemical is used in cosmetics and domestic products, the main public exposure is expected to be through the dermal route. In Australia, the chemical is reported to be used in shampoos in concentrations up to 0.8 % and in domestic products (such as cleaning products) at 0.2–5.5 % concentration.

There are no use restrictions for this chemical in Australia. The low concentrations (up to 5.5 %) used in cosmetic/domestic products in Australia are not expected to lead to serious risk through ocular exposure.

In the United States, the Cosmetic Ingredient Review has recommended limitations on the use of this chemical in cosmetics of up to 15 % only in cosmetic formulations (Galleria Chemica).

Occupational Risk Characterisation

Given the critical health effects, the risk to workers from this chemical is considered high if adequate control measures to minimise occupational exposure to the chemical are not implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business, or an employee at a workplace, has adequate information to determine appropriate controls.

NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended amendment to the 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

Although the public may be exposed to the chemical through potential cosmetic and domestic uses, given the low concentrations used in cosmetic/domestic products, the risk to public health is not considered to be unreasonable.

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to eyes (Xi; R36)	Causes serious eye irritation - Cat. 2A (H319)

[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

Any cosmetic or domestic product 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 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 which may 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 assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of Safety Data Sheets for Hazardous Chemicals— Code of Practice* and *Labelling of Workplace Hazardous Chemicals—Code of Practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

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