2,7-Naphthalenediol: Human health tier II assessment

24 April 2015

CAS Number: 582-17-2

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

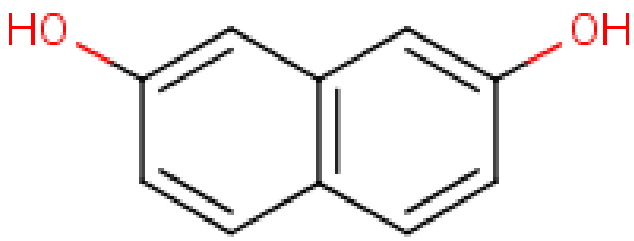
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	naphthalene-2,7-diol 2,7-dihydroxynaphthalene
Structural Formula	
Molecular Formula	C10H8O2
Molecular Weight (g/mol)	160.17
Appearance and Odour (where available)	Light grey, slightly yellow, amorphous powder
SMILES	c12c(cc(O)cc1)cc(O)cc2

Import, Manufacture and Use

Australian

The chemical is on the ‘List of chemicals used as dyes in permanent and semi-permanent hair dyes in Australia’ (NICNAS, 2007).

The chemical has reported cosmetic use in permanent hair dye preparations.

International

The following international uses have been identified through Galleria Chemica; the European Commission Cosmetic Ingredients and Substances (CosIng) database; the United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; and the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR).

The chemical has reported cosmetic use as a hair dye substance in oxidative and/or non-oxidative hair dye products.

Restrictions

Australian

No known restrictions have been identified.

International

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

- The Association of South East Asian Nations (ASEAN) Cosmetic Directive Annex III—Part 1: List of substances which cosmetic products must not contain except subject to restrictions and conditions laid down: ‘(a) the maximum authorised concentration in the finished cosmetic product as a hair dye substance in non-oxidative hair dye products is 1.0%; and (b) after mixing under oxidative conditions the maximum concentration applied to hair must not exceed 1.0%’;
- The European Union (EU) Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down: ‘(a) the maximum concentration in ready for use preparation is 1.0 %; (b) in combination with hydrogen peroxide the maximum use concentration upon application is 0.5 %; and (c) not to be used after 31.12.2009’; and
- New Zealand Cosmetic Products Group Standard—Schedule 5: Components cosmetic products must not contain except subject to the restrictions and conditions laid down: ‘(a) the maximum authorised concentration in the finished cosmetic product as a hair dye substance in non-oxidative hair dye products is 1.0%; and (b) after mixing under oxidative conditions the maximum concentration applied to hair must not exceed 1.0%’.

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

Toxicokinetics

The chemical, administered subcutaneously (20 mg in distilled water) or orally (60 mg in distilled water) to Wistar rats, was extensively excreted within 24 hours in the urine and faeces following subcutaneous treatment (>95 %) and in the urine following oral administration. The chemical was completely absorbed from the intestine following oral administration (EC SCC, 2000).

Following a 30-minute dermal application of the chemical to the intact clipped skin of rats, 0.93 % of the chemical was found to be absorbed over a period of 24 hours (EC SCC, 2000).

An in vitro percutaneous absorption study was conducted according to the Organisation for Economic Co-operation and Development Test Guideline (OECD TG) 428 using pig skin. The amount of chemical considered to be systemically available from a standard hair dye formulation (maximum of 1 % when applied to hair) is 6.1 and 4.31 µg/cm^2 in the absence and presence of hydrogen peroxide, respectively (SCCS, 2010).

Acute Toxicity

Oral

The chemical has low to moderate acute toxicity based on results from animal tests following oral exposure. The median lethal dose (LD50) values in rats and mice are 2160 and 720 mg/kg bw, respectively. Observed sub-lethal effects in rats included lethargy, pale extremities, hunched posture, rough fur, haemorrhagic oedema and hyperaemia of the lungs and the liver, haemorrhagic erosion in the stomach mucosa, partial hyperaemia of the duodenum with bloody-mucous content, collapse and death (SCCP, 2007; SCCS, 2010).

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Limited data are available. The chemical is not considered to be a skin irritant.

In a study conducted according to the OECD TG 404, 0.5 g of the chemical, moistened with 0.4 mL of water, was applied semi-occlusively to the shaved intact skin on one flank each of three male New Zealand White rabbits for four hours. The treated area was then washed with water and the animals were examined for skin irritation for up to 72 hours following patch removal. No signs of skin irritation were observed in the animals (SCCP, 2007; SCCS, 2010).

Eye Irritation

Limited data are available. The chemical is considered to be highly irritating and corrosive to the eyes, warranting hazard classification.

In a study conducted according to the OECD TG 405, 55.1 mg of the chemical (corresponding to a volume of 0.1 mL) was instilled into one eye of a male New Zealand White rabbit. Observations were made for up to 21 days following instillation. Two other rabbits initially assigned to this study were not treated due to the severity of ocular lesions observed during the study. The chemical induced corneal opacity (maximum grade 2) and epithelial damage (maximum 100 % of the cornea). Pannus (neovascularisation of the cornea) was observed on days 7, 14 and 21 following treatment with the chemical. Iridial irritation (grade 1) was observed at 24, 48 and 72 hours following treatment. Conjunctival irritation observed included redness (non-reversible), chemosis and discharge. The eyelids had reduced elasticity seven days after treatment and signs of necrosis (grey–white discolouration of the nictating membrane) were observed at 48 and 72 hours following treatment (SCCP, 2007; SCCS, 2010).

Sensitisation

Skin Sensitisation

Limited data are available. The chemical is considered to be a moderate skin sensitiser, warranting hazard classification.

In a local lymph node assay (LLNA) conducted according to the OECD TG 429, the chemical, in a 4:1 mixture of acetone and olive oil, was applied to the dorsal surface of both ear lobes of female CBA/CaOlaHsd mice (five animals/group) once daily for three consecutive days. The chemical at test concentrations of 0.5, 1, 2.5, 5, 25 or 50 % produced stimulation indices (SIs) of 1.6, 1.8, 1.4, 4.5, 12.4 or 4.2, respectively. The effective concentration needed to produce a three-fold increase in lymphocyte proliferation (EC3) was calculated to be 2.8 %, indicating moderate skin sensitisation potential (SCCP, 2007; SCCS, 2010).

Repeated Dose Toxicity

Oral

Limited data are available. The available data suggest that the chemical has low repeated dose toxicity based on results from an animal test following oral exposure. The effects were not sufficient to warrant hazard classification.

In a repeated dose toxicity study conducted according to the OECD TG 408, Wistar rats (10 animals/sex/group, except for the high dose group, which had 12 animals/sex) were administered 0, 70, 210 or 630 mg/kg bw/day of the chemical by oral gavage daily for 90 days. A recovery group with the same number of animals was treated at the high dose and observed for a further four weeks to determine the reversibility of treatment-related effects. Twelve treatment-related mortalities were recorded in the 630 mg/kg bw/day treatment and recovery groups. In the 210 and 630 mg/kg bw/day groups, excessive grooming of the snout

immediately post-gavage, salivation, lacrimation, nasal discharge, gasping and tremors were observed. The males in these two groups had significantly reduced haemoglobin and haematocrit values and significantly increased total bilirubin. In the 630 mg/kg bw/day group, males had significantly reduced erythrocytes and significantly increased serum ?-glutamyl transferase (GGT), while females had significantly higher mean corpuscular volume and haemoglobin (MCV and MCH), alanine transaminase (ALT) levels and total bilirubin. Haematological effects were completely reversed following the recovery period.

In the 630 mg/kg bw/day group, both sexes had significantly higher relative weights of the liver, spleen and kidneys. Significantly increased absolute liver and spleen weights were also observed in the females of this group. In the 210 mg/kg bw/day group, males had increased relative spleen weights, while females had increased liver and spleen weights. These effects were not reversible following the recovery period. Histopathological changes were observed in the liver and kidneys of animals in the 630 mg/kg bw/day group, including degeneration and necrosis of hepatocytes, bile duct hyperplasia and foci of erythropoiesis in the liver, increased extramedullary haematopoiesis with connective tissue proliferation in the spleen, and degeneration and necrosis of tubular epithelial cells in the outer medulla and cortex of the kidneys. These effects were reversible. A no observed adverse effect level (NOAEL) of 70 mg/kg bw/day was established for this study (SCCP, 2007; SCCS, 2010).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the available data from in vitro and in vivo studies, the chemical is not considered to be genotoxic.

In vitro studies

A bacterial gene mutation assay was conducted according to the OECD TG 471 using five *Salmonella typhimurium* strains (TA98, TA100, TA102, TA1535 and TA1537) up to a maximum concentration of 5000 µg/plate of the chemical, in the absence and presence of a rat liver metabolic activation system. Negative results were obtained from the study (SCCP, 2007; SCCS, 2010).

A mammalian cell gene mutation assay was conducted according to the OECD TG 476 using the mouse lymphoma L5178Y TK+ cell line. The chemical was tested up to maximum concentrations of 300 and 22.5 µg/mL in the absence and presence of a rat liver metabolic activation system, respectively. Negative results were obtained from the study (SCCP, 2007; SCCS, 2010).

A chromosomal aberration test was conducted according to the OECD TG 473 using the Chinese hamster fibroblast V79 cell line. The chemical was tested up to maximum concentrations of 200 and 1.5 µg/mL in the absence and presence of a rat liver metabolic activation system, respectively. In the absence of metabolic activation, the chemical induced a concentration-dependent increase in structural chromosomal aberrations in cells, indicating clastogenic potential in this study (SCCP, 2007; SCCS, 2010).

In vivo studies

In a mouse in vivo micronucleus assay in bone marrow cells conducted according to the OECD TG 474 using NMRI mice (five animals/sex/group), the chemical was administered at concentrations of 0, 18.75, 37.5 or 75 mg/kg bw by a single intraperitoneal (i.p.) injection. Bone marrow cells were collected 24 or 48 hours (for the 75 mg/kg bw group only) after administration of the chemical and the polychromatic erythrocytes (PCEs) for each mouse were examined. No increases in micronucleated PCEs were found, thus the chemical was concluded to be non-mutagenic in this study (SCCP, 2007; SCCS, 2010).

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Limited data are available. Based on the available data, the chemical is not expected to have reproductive and developmental toxicity potential.

In a reproductive and developmental toxicity study conducted according to the OECD TG 414, pregnant Wistar rats (25 animals) were administered 0, 65, 195 or 585 mg/kg bw/day of the chemical daily by oral gavage on gestational days (GDs) 5–19. All rats were euthanised on GD 20. In the 585 mg/kg bw/day group, two animals died, and significantly decreased maternal weight and reversible tremors and nasal discharge were observed. Lacrimation, nasal irritation, salivation, lethargy and significantly decreased food consumption were observed in the animals treated with 195 and 585 mg/kg bw/day of the chemical. The chemical treatment did not result in any adverse effects on pregnancy rates or significant incidences of malformation or birth defects. A reproductive and developmental NOAEL of 585 mg/kg bw/day was established in this study (SCCP, 2007; SCCS, 2010).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include local effects (eye irritation and skin sensitisation).

Public Risk Characterisation

The chemical is reported to be used in permanent hair dye preparations in Australia (NICNAS, 2007).

The ASEAN, EU and New Zealand have restricted the use of this chemical in cosmetics. Following a safety evaluation, the SCCS (2010) concluded that the chemical ‘as an ingredient in oxidative and non-oxidative hair dye formulations at a maximum on-head concentration of 1% does not pose a risk to the health of the consumer, apart from its sensitising potential’.

Currently, there are no restrictions in Australia for using this chemical in cosmetic products. In the absence of any regulatory controls, the characterised critical health effects, particularly skin sensitisation, have the potential to pose an unreasonable risk to the public given the identified uses.

Occupational Risk Characterisation

During product formulation, exposure might 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 local 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.

The data available support an amendment to the hazard classification in the HSIS (Safe Work Australia) (refer to **Recommendation** section).

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 cosmetic products (hair dye preparations) be managed through changes to the Poisons Standard, 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

Given the risk characterisation, it is recommended that the chemical be included in Schedule 6 of the Poisons Standard 2015—Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) for use in hair dye products.

Consideration should be given to the following:

- the chemical is an eye irritant;
- the chemical is a moderate skin sensitiser;
- overseas restrictions for use of the chemical in hair dyes where the maximum concentration allowed in the finished cosmetic product as a hair dye substance in non-oxidative hair dye products is 1.0 % and the maximum use concentration upon application is 1.0 % (after mixing under oxidative conditions); and
- the risk could be controlled by including warning statements on the label of hair dye formulations containing the chemical at any concentration.

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)	Causes serious eye damage - Cat. 1 (H318)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)

[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 exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- health monitoring for any worker who is at risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker's health;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

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

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

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

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

References

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