1,5-Naphthalenediol: Human health tier II assessment

13 February 2015

CAS Number: 83-56-7

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.

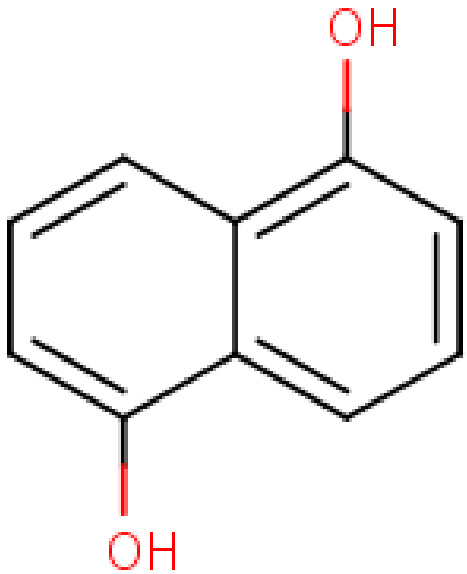
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	1,5-dihydroxynaphthalene naphthalene-1,5-diol C.I. 76625
Structural Formula	
Molecular Formula	C10H8O2
Molecular Weight (g/mol)	160.2
Appearance and Odour (where available)	Grey-white powder
SMILES	c1(O)c2c(c(O)ccc2)ccc1

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 cosmetic use in hair dyes (NICNAS).

International

The following international uses have been identified through: the European Union (EU) Registration, Evaluation and Authorisation of Chemicals (REACH) dossiers; Galleria Chemica; the Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; and the United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary.

The chemical has reported cosmetic use in hair dyes and colouring agents.

The chemical has reported commercial uses including as a photographic developer.

Restrictions

Australian

No known restrictions have been identified.

International

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

- EU Cosmetics Regulation 1223/2009 Annex III—List of Substances which cosmetic products must not contain except subject to the restrictions laid down (maximum authorised concentration in the finished cosmetic product is 1.0 % or 0.5 % when used in combination with hydrogen peroxide);
- New Zealand Cosmetic Products Group Standard—Schedule 5 Components cosmetic products must not contain except subject to the restrictions and conditions laid down; and
- The Association of Southeast 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.

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 1,5-naphthalenediol is used as a precursor for hair colours. It reacts with primary intermediates to form the final dye-stuff. The reaction is accelerated by adding an oxidising agent (e.g. hydrogen peroxide).

Toxicokinetics

Absorption and excretion

A study assessed the extent and rate of intestinal absorption and excretion of 1,5-naphthalenediol in rats following administration at 10 mg/kg body weight (bw) by oral gavage. Within 24 hours, 94.3 % and 6.2 % of the chemical was excreted via the urine and faeces, respectively (REACH).

The dermal absorption of 1,5-naphthalenediol was assessed according to the Organisation for Economic Co-operation and Development (OECD) test guideline (TG) 428 (skin absorption: in vitro method). Skin discs from pigs were exposed to hair dye formulations containing the test material (1 %) for 30 minutes to examine dermal penetration in vitro. Absorption was 1.81 ± 0.34 µg/cm² (0.88 ± 0.17 % of the applied amount) in the presence of H_2O_2 and 1.57 ± 0.35 µg/cm² (0.74 ± 0.17 % of the applied amount) in the absence of H_2O_2 under these test conditions (REACH).

These data suggest that the chemical has high oral absorption and low dermal absorption.

Distribution

The distribution of 1,5-naphthalenediol was examined in pregnant female rats. Animals received a single intravenous administration of 15 mg/kg bw test material on gestation day (GD) 19. The substance was distributed very rapidly within the animal. Thirty minutes following administration, the test material was distributed to the small intestine and kidneys. The lungs, blood vessels and placenta were also found to contain the radioactively labelled material. Minimal radioactivity was found in the foetuses (REACH).

Acute Toxicity

Oral

The chemical has low to moderate acute toxicity based on results from animal tests following oral exposure.

In an OECD TG 423 (acute oral toxicity) study, male and female Wistar rats were administered a single dose of 1,5-naphthalenediol at 2000 mg/kg bw by gavage. Animals were observed closely and numerous parameters assessed. No mortality occurred. Sublethal effects of dosing included hunched posture and piloerection, which resolved after 48 hours. The median lethal dose (LD50) was determined to be >2000 mg/kg body weight (bw) (SCCS, 2010; REACH).

In another acute toxicity study, Wistar rats were administered a single oral dose of the chemical at 100, 500, 800, 1000 or 1200 mg/kg bw. Animals were observed for clinical signs and mortality for 14 days. While 100 mg/kg bw was tolerated without

mortality or clinical signs, all other treated animals exhibited tremors, cramps and hunched posture prior to death. An oral LD50 of 660 mg/kg bw was determined for this chemical under these test conditions (REACH).

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

The chemical is reported to slightly irritate the skin in animal studies.

In an OECD TG 404 (acute dermal irritation/corrosion) study, 0.5 g of moistened 1,5 naphthalenediol was applied to the clipped back skin of three male New Zealand White rabbits, under semi-occlusive patches. The patch was removed after four hours and the skin was cleaned. The skin reactions were assessed at approximately one, 24, 48 and 72 hours (all animals) and seven days (2/3 animals) after removal of the chemical. In one animal, slight (24 hours) to well-defined (48, 72 hours) erythema, slight (one, 24 hours) to very slight (48 hours) oedema, and scaling (seven days) was observed following removal of the test material. No erythema, oedema or scaling was recorded in 2/3 animals. The chemical was found to cause slight irritation under these test conditions (SCCS, 2010; REACH).

A non-guideline study assessed the potential for the chemical to trigger skin irritation following a single dermal application to the ears of two New Zealand White rabbits. The substance was held in place by a plaster for 24 hours before being washed off. Under the conditions of this test, the chemical was not irritating to the skin of rabbits (REACH).

Eye Irritation

The chemical was reported to irritate the eyes when tested according to OECD TG 405. The available data are sufficient to warrant hazard classification (refer **Recommendation** section).

In an OECD TG 405 (acute eye irritation/corrosion) study, the chemical (39.7 mg in 0.1 mL) was instilled into one eye of three male New Zealand White rabbits. Eye irritation was assessed approximately one, 24, 48 and 72 hours and seven and 14 days after instillation. Conjunctival erythema was observed in all animals at one hour to seven days. Chemosis was also observed in all animals at one, 24 and 48 hours and in one animal also at 72 hours. Mean value of eye irritation scores for each animal were 3.0, 2.7, 2.7 for redness; and 1.7, 1.0, 1.0 for chemosis. No iridial irritation or corneal opacity was observed. Under these test conditions, 1,5 naphthalenediol was shown to be an ocular irritant (SCCS, 2010).

In a non-guideline eye irritation study, the test chemical (50 mg) was instilled into the conjunctival sac of one eye of each of two New Zealand White rabbits. Animals were observed for seven days. Slight conjunctival erythema was observed in both animals for up to 24 hours. Although few experimental details were provided, investigators reported that administration of the test material resulted in slight irritation in the eye of these rabbits (REACH).

Sensitisation

Skin Sensitisation

The chemical is a skin sensitiser.

A local lymph node assay (LLNA) was performed according to OECD TG 429 (skin sensitisation) using female CBA/J mice. Various concentrations of the test material were assessed across two experiments. The following stimulation index (SI) values were generated for these concentrations (% / SI): 0.25 / 1.4; 1 / 2.5; 2.5 / 2.8; 5 / 18.4; 25 / 16.7; 50 / 6.1. An EC3 (the concentration at which the SI is 3) of 3.4 % was calculated. Therefore, under these test conditions, 1,5 naphthalenediol was found to be a moderate skin sensitiser (REACH).

Repeated Dose Toxicity

Oral

In a 90-day oral gavage study in rats, a no observed adverse effect level (NOAEL) of 50 mg/kg bw/day was reported. Considering that the renal effects were seen at high doses and appeared to resolve spontaneously during the recovery period, the chemical does not warrant hazard classification.

An oral repeated dose toxicity study was conducted in accordance with OECD TG 408 (repeated dose 90-day oral toxicity in rodents). Male and female Wistar rats (12 animals per sex, per dose) were administered 1,5 naphthalenediol at concentrations of 0, 50, 100 or 300 mg/kg bw/day by oral gavage for 90 consecutive days. Animals were observed throughout the 90-day period and for 28 days thereafter. Two males and three females in the highest dose group died during the treatment phase.

Some haematological changes were observed; however, they were considered not to be a result of treatment as all statistically significant deviations from the control showed no relationship to dose. The following histopathological changes were observed:

- brown/black tubular pigment in the kidneys (11/12 males and 8/11 females at 300 mg/kg bw/day and 5/12 males at 100 mg/kg bw/day);
- hyaline casts (6/12 males and 2/11 females at 300 mg/kg bw/day and 2/12 males and 1/12 females at 100 mg/kg bw/day);
- corticomedullary basophilia (5/12 males at 300 mg/kg/day); and
- forestomach squamous cell hyperplasia (11/12 males and 6/11 females at 300 mg/kg bw/day and 3/12 males and 3/12 females at 100 mg/kg bw/day).

On the basis of these changes, a NOAEL of 50 mg/kg bw/day was established. Following the recovery period, some degree of renal pathology persisted in 2/5 males in the highest dose group. Limited forestomach effects remained in 2/5 females after the recovery period (REACH).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

The available data suggest that the chemical is not genotoxic.

In vitro

The chemical was investigated in a bacterial reverse mutation assay according to OECD TG 471 (bacterial reverse mutation test) for the induction of gene mutations in *Salmonella typhimurium* strains TA98, TA100, TA102, TA1535 and TA1537 at concentrations up to 5000 µg/plate in the presence or absence of metabolic activation. No revertant colonies were observed in any of the tester strains in the absence or presence of metabolic activation. Under these test conditions, the chemical was not genotoxic (SCCS, 2010).

A study conducted in accordance with OECD TG 473 (in vitro mammalian chromosome aberration test), investigated the potential for the chemical to induce chromosomal aberrations using Chinese hamster lung fibroblast (V79) cells. Cells were incubated with the chemical at various concentrations (0.1 - 10 µg/mL) for several time points, both in the presence and absence of metabolic activation. The test material caused an increase in the number of cells with structural chromosomal aberrations, indicating that the test material exhibited clastogenic activity under these test conditions (REACH).

Another in vitro study, conducted in accordance with OECD TG 476 (in vitro mammalian cell mutation test), assessed the potential for 1,5 naphthalenediol to induce mutagenicity in mouse lymphoma L5178Y cells. Cells were treated with the chemical at concentrations of 0.125 - 60 µg/mL in the presence or absence of metabolic activation, for four or 24 hours. Independent of the presence or absence of metabolic activation, no reproducible increase in the number of mutant colonies was observed. Under these test conditions, the chemical was considered not to be mutagenic in mouse lymphoma L5178Y cells (REACH).

In vivo

An in vivo genotoxicity study was performed in accordance with OECD TG 474 (mammalian erythrocyte micronucleus test). The chemical was administered to NMRI mice via intraperitoneal injection at 0, 12.5, 25.0 or 50.0 mg/kg bw and bone marrow cells were harvested and assessed for evidence of micronuclei. There was no biologically relevant increase in the number of micronucleated polychromatic erythrocytes compared with controls. Under these test conditions, the chemical was not clastogenic (REACH).

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Developmental toxicity

In an OECD TG 414 (prenatal developmental toxicity) study, pregnant Sprague Dawley (SD) rats were administered 1,5 naphthalenediol by oral gavage from day 6 to 15 post coitum at 0, 20, 60 or 360 mg/kg bw/day (30 animals per dose group). Females were euthanised on day 20 post coitum and the foetuses removed. Based on significantly decreased body weight gain at the highest test dose, the NOAEL for maternal toxicity was considered to be 60 mg/kg bw/day. The examined foetuses showed no treatment-related malformations (skeletal ossification in all groups was considered to be within normal range). The NOAEL for embryo or foetotoxicity was considered to be 360 mg/kg bw/day (SCCS, 2010; REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic acute effects (acute toxicity from oral exposure) and local effects (skin sensitisation). The chemical can also cause eye irritation.

Public Risk Characterisation

The chemical is reported to have cosmetic use in hair colourant formulations in Australia and overseas (NICNAS). Therefore, public exposure from this chemical can be expected.

The European Union and ASEAN, as well as New Zealand have prohibited the use of this chemical in cosmetics.

Considering the moderate skin sensitisation, moderate acute toxicity and eye irritation that could be caused by this chemical, there is a concern for its use in cosmetic products without any risk management measures.

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 systemic acute and 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 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

It is recommended that the chemical be listed in Schedule 6 of the *Poisons Standard* to restrict the use of this chemical in hair dye preparations in a similar manner as in the European Union, Canada and New Zealand.

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)	Causes serious eye irritation - Cat. 2A (H319)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
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 oral/dermal/ocular exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures 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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