

HC Red 3 and HC Red 7: Human health tier II assessment

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Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Ethanol, 2-[(4-amino-2-nitrophenyl)amino]-	2871-01-4
Ethanol, 2-[(4-amino-3-nitrophenyl)amino]-	24905-87-1

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

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ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals, ethanol, 2-[(4-amino-2-nitrophenyl)amino]- (CAS No. 2871-01-4) and ethanol, 2-[(4-amino-3-nitrophenyl)amino]- (CAS No. 24905-87-1) are assessed together in this report because of their close structural similarities and metabolically related characteristics. The differences in chemical structure are limited to the relative position of the nitro group with respect to the ethoxylated amine. Similar or identical metabolites are expected. The chemicals in this group are secondary alkanolamine and thus prone to nitrosation. These chemicals have been grouped together for assessment due to their similar toxicological properties and uses.

The following synonyms and their corresponding CAS numbers will be used in this assessment:

- HC Red 3 (CAS No. 2871-01-4); and
- HC Red 7 (CAS No. 24905-87-1).

Import, Manufacture and Use

Australian

The chemicals are on the 'List of chemicals used in dyes in permanent and semi-permanent hair dyes in Australia' (NICNAS, 2007).

The chemicals have reported cosmetic use in permanent and semi-permanent 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; the US Household Products Database (HHPD); the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR); the Cosmetic Ingredient Review reports (CIR, 1992 & 2008); International Agency for Research on Cancer (IARC, 1993); Scientific Committee on Consumer Products (SCCS 2009; 2010 & 2012) reports; and the US National Library of Medicine Hazardous Substances Data Bank (HSDB).

The chemicals have reported cosmetic use as hair dyes in oxidative and semi-oxidative hair dye products.

The chemical, HC Red 3 has reported domestic use in furniture polish oil.

Restrictions

Australian

Substituted phenylenediamines are listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedules 6 and 10 (SUSMP, February 2017).

Schedule 6:

'PHENYLENEDIAMINES including alkylated, arylated and nitro derivatives not elsewhere specified in these Schedules:

a) in preparations packed and labelled for photographic purposes;

b) in preparations packed and labelled for testing water except tablets containing 10 mg or less of diethyl-para-phenylenediamine or dimethyl-para-phenylenediamine in opaque strip packaging provided the directions for use include the statement, "Do not discard testing solutions into the pool";

c) in hair dye preparations except when the immediate container and primary pack are labelled with the following statements:

KEEP OUT OF REACH OF CHILDREN, and

WARNING — This product contains ingredients which may cause skin irritation to certain individuals. A preliminary test according to the accompanying directions should be made before use. This product must not be used for dyeing eyelashes or eyebrows; to do so may be injurious to the eye.

written in letters not less than 1.5 mm in height; or

d) in eyelash and eyebrow tinting products when the immediate container and primary pack are labelled with the following statement:

WARNING — This product contains ingredients which may cause skin irritation to certain individuals, and when used for eyelash and eyebrow tinting may cause injury to the eye. A preliminary test according to the accompanying directions should be made before use.

written in letters not less than 1.5 mm in height.'

Schedule 6 chemicals are described as 'Substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label'. Schedule 6 chemicals are labelled with 'Poison' (SUSMP, February 2017).

Schedule 10:

'PHENYLENEDIAMINES, including alkylated, arylated and nitro derivatives, in preparations for skin colouration, tattooing and dyeing of eyelashes or eyebrows except when included in Schedule 6'.

Schedule 10 chemicals are 'substances of such danger to health as to warrant prohibition of sale, supply and use — substances which are prohibited for the purpose or purposes listed for each poison' (SUSMP, February 2017).

International

The chemicals, HC Red 3 and HC Red 7 are listed on the European Union (EU) Cosmetics Regulation 1223/2009 Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down (Galleria Chemica).

The HC Red 7 is listed on 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.

Under these restrictions, HC Red 3 may be used in non-oxidative hair dye products at a maximum concentration applied to hair of 3 % and in oxidative hair dye products at a maximum concentration of 0.45 %. The HC Red 7 may be used in non-oxidative hair dye products at a maximum concentration of 1 % (CosIng; Galleria Chemica).

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are not listed on the Hazardous Chemicals Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Toxicokinetics

The dermal absorption of the chemicals in this group in hair dye formulations was investigated in vitro and low percutaneous absorption was observed.

In an in vitro percutaneous study, an oxidative hair dye formulation containing HC Red 3 at 0.45 % (after mixing) was tested using 12 human skin samples from six donors. A mean amount of 0.365 % (0.333 $\mu\text{g}/\text{cm}^2$) of the applied dose was found in the receptor fluid within 24 hours post-exposure. The majority of the applied dose was rinsed off the skin surface (SCCS, 2012).

In a second study, a commercial hair dye formulation containing HC Red 7 at 0.86 % was tested on four human skin samples from two donors. A mean amount of 0.091 % (0.159 $\mu\text{g}/\text{cm}^2$) was found in the receptor fluid within 24 hours post-exposure. The majority of the applied dose (92.27 %) was rinsed off the skin surface (SCCS, 2009).

Acute Toxicity

Oral

The chemicals, HC Red 3 and 7 have low to moderate acute toxicity based on results from animal tests following oral exposure. The median lethal dose (LD50) in rats is 1250–5000 mg/kg bw.

Sprague-Dawley (SD) rats (n=5/sex/dose) were treated with HC Red 3 (10 % suspension in 3 % acacia) by gavage at doses of 1250 or 5000 mg/kg bw for male rats and 1250, 2500 or 5000 mg/kg bw for female rats. In males, no mortality at 1250 mg/kg bw was recorded, but mortalities were recorded as 5/5 males at 5000 mg/kg bw. In females, no mortality was recorded at 1250 mg/kg bw, while mortalities for 1/5 females at 2500 mg/kg bw and 5/5 females died at 5000 mg/kg bw was recorded. The LD50 was determined to be 1250–2500 mg/kg bw for males and 2500–5000 mg/kg bw for females (CTFA, 1991; CIR, 1992; SCCS, 2010; SCCS, 2012).

In another acute oral study, Fischer 344 (F344/N) rats (n=5/sex/dose) were orally administered single dose of HC Red 3 (1 % carboxymethyl cellulose in saline) at doses of 62, 125, 250, 500 or 1000 mg/kg. No mortality was reported. All treated animals had an orange to red discolouration of the urine, one day after administration (NTP, 1986; CIR, 1992).

In an oral study, two groups of four and five female SD rats were administered HC Red 7 (0.5 % solution of carboxymethylcellulose) by gastric gavage at doses of 300 or 2000 mg/kg bw. Mortalities were recorded (3/5) in the 2000 mg/kg bw/day dose groups. Observed sub-lethal effects included hypoactivity, sedation, dyspnoea, purple urine, purple to purplish red extremities, and piloerection. An LD50 of 2000 g/kg bw was reported (CIR, 2008; SCCS, 2009).

Dermal

No data are available for the chemicals.

Inhalation

No data are available for the chemicals.

Corrosion / Irritation

Skin Irritation

The chemicals in this group do not cause skin irritation.

In a skin irritation study, six New Zealand White (NZW) rabbits were topically administered an aqueous slurry of 500 mg HC Red 3 for 24 hours under non-occlusive conditions. Observations were recorded at 24 and 72 hours following exposure. No dermal irritation was observed (CIR, 1992; SCCS, 2010; SCCS, 2012).

In another study, 0.5 g of HC Red 7 was applied to the dorsal trunk of three NZW rabbits for 4 hours under semi-occlusive conditions. Observations were recorded at 1, 24, 48 and 72 hours following patch removal. No dermal irritation was observed (CIR, 2008; SCCS, 2009).

Eye Irritation

The chemicals in this group do not cause severe eye irritation.

HC Red 3 was reported to slightly irritate the eyes when tested in eyes of four NZW rabbits at a dose of 100 mg in powder form. Conjunctival redness, swelling and discharge were reported one hour after treatment. One rabbit had irritation with low-grade corneal opacity with ulcerations. All effects were reversible within 3 days (CIR, 1992; SCCS, 2010; SCCS, 2012).

HC Red 7 (0.1 g) was instilled in the conjunctival sac of eyes of three NZW rabbits. Observations were recorded at 1, 24, 48 and 72 hours after instillation. Palpebral and bulbar conjunctivae with enanthema (disruption of a mucous membrane) discharge and slight chemosis were reported at one hour after treatment. One rabbit had partial corneal opacity at 24 hours. All effects were reversible within 72 hours (CIR, 2008; SCCS, 2009).

Sensitisation

Skin Sensitisation

Based on the available data, the chemicals in this group are considered to be moderate to strong skin sensitisers. The effects observed in the local lymph node assays (LLNAs) are sufficient to warrant hazard classification (see **Recommendation** section).

In a guinea pig maximisation test (GPMT) study, 0.05 mL of 25 % HC Red 3 (0.1 % w/v in propylene glycol), was occlusively applied to shaved skin of female Hartley albino guinea pigs (n=10/group) for 48 hours. All injection sites were pre-treated with 10 % sodium lauryl sulfate in petrolatum, 24 hours before application of topical induction patches. Two weeks after the induction phase, challenge doses of 5 and 25 % HC Red 3 in propylene glycol, were applied to the test sites. Erythema and oedema were observed in 9/10 animals at 5 % and 10/10 animals at 25 % concentrations. No scores were reported (SCCS, 2012).

Two LLNAs were conducted according to OECD Test Guidelines (TGs) 409 and 429, using CBA female mice to test the sensitisation potential of HC Red 3 (SCCS, 2012).

In the first study, HC Red 3 in dimethyl sulfoxide (DMSO) was dermally applied at concentrations of 0, 0.25, 0.5, 1.0 or 2.0 % (w/v) to groups of five CBA mice. No positive responses in lymphocyte proliferation were measured at any dose tested. The author concluded that the concentrations used for this study were not high enough and that the sensitising potential could not be excluded.

In the second study, groups of three CBA mice were dermally treated with HC Red 3 at concentrations of 0, 0.1, 0.25, 0.5, 1.0 or 2.5 % (w/v) in acetone: olive oil (4:1), once daily for three consecutive days. Stimulation indices of 0, 0.5, 1.2, 1.9, 1.8 and 3.3 were reported, respectively. The estimated concentration to produce a three-fold increase in lymphocyte proliferation (EC3) was found to be approximately 2.2 %.

In an LLNA conducted according to OECD TG 429, HC Red 7 was a skin sensitiser in CBA mice. The HC Red 7 at concentrations of 0.5, 1, 2.5, 5 or 10 % (w/v) was topically administered once a day for five days. Stimulation indices of 0, 1.83, 2.54, 6.02, 3.19 and 3.90 were reported, respectively. An EC3 value of 1.2 % was determined (SCCS, 2009).

Repeated Dose Toxicity

Oral

Based on the available data, the chemicals are not expected to be harmful to health following repeated oral exposure.

In a 14-day subchronic toxicity study, Fischer 344 (F344/N) rats and B6C3F1 mice (n=5/sex/dose) were orally administered HC Red 3 at doses of 0, 62, 125, 250, 500 or 1000 mg/kg bw/day in rats and 0, 31, 62, 125, 250 or 500 mg/kg bw/day in mice. No mortality was recorded. In rats, dark thyroids were observed in 5/5 males at 1000 mg/kg bw/day; 2/5 males at 500 mg/kg bw/day and 2/5 males at 250 mg/kg bw/day. Maroon to orange stained urine was reported in all treated mice. No observed adverse effect levels (NOAELs) of 1000 mg/kg bw/day in rats and 500 mg/kg bw/day in mice were reported (SCCS, 2012).

In a 13-week study conducted according to the OECD TG 408, groups of SD rats (n= 10/sex/dose) were orally administered HC Red 7 at doses of 0, 50, 150 or 500 mg/kg bw/day, seven days/week. Hair loss and scabbing were observed in some treated animals. A dose-related statistically significant decrease in red blood cell count was reported in females of all treatment groups in week 13. Levels of alanine aminotransferase was significantly increased in males at 500 mg/kg bw/day. Absolute and relative liver weights were significantly increased in both sexes at 150 and 500 mg/kg bw/day. Spleen and ovarian weights were increased in high dose females, and thyroid weights were reduced in all treated females. Histopathological examination showed

increased haemosiderin deposits in spleens (6/10 males and 9/10 females) at 500 mg/kg bw/day. A NOAEL of 50 mg/kg bw/day was reported (SCCNFP, 2003; SCCS, 2009).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the weight of evidence from the available in vitro and in vivo genotoxicity studies, the chemicals are not considered to be genotoxic. Some in vitro genotoxicity tests indicated positive results, but all in vivo tests were negative.

In vitro studies

The available in vitro studies gave both positive and negative results for the chemicals (SCCS, 2009 and 2012).

In a bacterial point mutation assay conducted according to OECD TG 471, HC Red 3 gave positive results in *Salmonella typhimurium* strains TA98 and TA1537, at concentrations up to 5000 µg/plate, with or without metabolic activation (SCCS, 2012).

In a mammalian cell gene mutation assay compliant with OECD TG 476, HC Red 3 was tested on mouse lymphoma cells L5178Y (thymidine kinase (*tk*) locus) at concentrations up to 1000 µg/plate. The chemical did not induce mutations with or without metabolic activation (SCCS, 2012).

In a bacterial reverse mutation assay (OECD TG 471), HC Red 7 induced concentration-dependent, significant and reproducible increased in the number of revertants in *S. typhimurium* strains of TA98 and TA100 with or without metabolic activation (SCCS, 2009).

In an *in vitro* mammalian cell gene mutation test (*hprt*-locus), HC Red 7 was tested on L5178Y mouse lymphoma cells in two experiments at concentration up to 1972 µg/mL. The chemical was not mutagenic in mouse lymphoma cells with or without activation (SCCS, 2009).

In vivo studies

The available in vivo studies gave negative results (SCCS, 2009 and 2012).

In a mouse bone marrow micronucleus test (OECD TG 474), HC Red 3 was orally administered to albino CD1 mice (n=5/sex/group) as a single dose of 3000 mg/kg bw. While clinical signs of toxicity indicated systemic exposure, there was no increase in micronucleus incidences (SCCS, 2012).

In an unscheduled DNA synthesis (UDS) test conducted according to OECD TG 486, HC Red 7 was orally administered to male Wistar rats (n=4/dose) at doses of 0, 150 or 1500 mg/kg bw. Animals were euthanised 15 hours later. There was no DNA damage at any of the doses tested (SCCS, 2009).

Carcinogenicity

Based on the available data, HC Red 3 is not expected to be carcinogenic. HC Red 7 is expected to have similar effects based on its close structural and metabolic similarities.

In a two-year study in rats, groups of F344/N rats (n=50/sex/dose) were administered HC Red 3 (97 % purity) in corn oil at 0, 250 or 500 mg/kg bw/day by gavage, five days/week for 105 weeks. All animals were euthanised at 113-114 weeks. No changes in survival or mean body weights were observed. Some dose-related incidences of nephropathy were reported in female rats. All treated animals had pigmented kidneys and thyroids. Survival rate was reported as 34/50 at 250 mg/kg bw/day and 32/50 mg/kg bw/day at 500 mg/kg bw/day (for males) and 38/50 at 250 mg/kg bw/day and 34/50 at 500 mg/kg bw/day in females. Incidence of mammary gland fibroadenomas was significantly increased in females at 250 mg/kg bw/day (24/50), but not in high-dose females (11/50). Other effects were malignant adrenal gland pheochromocytomas and thyroid gland C-cell neoplasms in all male groups; uterine endometrial stromal sarcoma in all treated female groups; and mononuclear cell leukaemia in all treated groups. The US National Toxicology Program (NTP) concluded that there was no evidence of carcinogenicity for HC Red 3 in rats (CIR, 1992; IARC, 1993; NTP, 1986; SCCS, 2012).

In a mouse carcinogenicity study, groups of B6C3F1 mice (n=50/sex/dose) were administered HC Red 3 (97 % purity) in corn oil at 0, 125 or 250 mg/kg bw/day by gavage, five days per week for 104 weeks. Survival was reduced in all female groups due to reproductive tract infections. Increased incidences of hepatocellular adenomas and carcinomas were observed in male mice at 250 mg/kg bw/day (35/50). An increase in hepatocellular adenomas in males (6/50 at 125 mg/kg bw/day and 16/50 at 250 mg/kg bw/day) and hepatocellular carcinomas (9/50 at 125 mg/kg bw/day and 21/50 at 250 mg/kg bw/day) were reported. A variability of hepatic cell neoplasms in the males of this strain of mice and a lack of corresponding evidence for an increased incidence of hepatic neoplasms in female groups were reported. NTP concluded that 'due to poor survival rates, there was inadequate study of carcinogenicity for female mice' (CIR, 1992; IARC, 1993; NTP, 1986; SCCS, 2012).

The NTP and IARC have concluded that there was inadequate evidence in experimental animals and humans to classify HC Red 3 as a carcinogen (IARC, 1993; NTP, 1986).

Reproductive and Developmental Toxicity

The chemicals in this group do not cause specific reproductive or developmental toxicity based on results for HC Red 3 and HC Red 7. Any reproductive and developmental effects were only observed secondary to maternal toxicity.

In a prenatal development toxicity study conducted according to the OECD TG 414, pregnant female CrI:CD rats (n=40/dose) were given oral doses of HC Red 3 at 0, 50, 200, 500 or 1000 mg/kg bw/day during gestation days (GD) 6–20. Maternal toxic effects included were: purple or orange discolouration of urine in all treated animals; purple or red perivaginal and perinasal substance; orange amniotic fluid in females at 1000 mg/kg bw/day; and significantly reduced mean body weight at doses 200, 500 and 1000 mg/kg bw/day on GD 6–9 and 15–18. No significant changes in the foetal body weights, litter size, number of live and resorbed fetuses were reported. Some delays in ossification of hind limbs metatarsals and phalanges were observed at 1000 mg/kg bw/day. Two NOAELs of 200 mg/kg bw/day for maternal toxicity and 1000 mg/kg bw/day for developmental toxicity were reported (SCCS, 2012).

In a prenatal development toxicity study (OECD TG 414), HC Red 7 was orally administered to groups of 24 female SD rats at 0, 50, 200 or 800 mg/kg bw/day on days 6–15 after mating. All dams were sacrificed on day 20 of pregnancy. Hair loss and scabbing were reported in one female at 800 mg/kg bw/day. Reduced body weight gain was seen in the 200 and 800 mg/kg bw/day dose groups. Incidence of major skeletal and external/visceral abnormalities reported were 1, 4, 1 and 0 at 0, 50, 200 and 800 mg/kg bw/day, respectively. It was concluded that the chemical elicited dose-related maternal toxicity at 200 and 500 mg/kg bw/day. Two NOAELs of 50 mg/kg bw/day for maternal toxicity and 200 mg/kg bw/day for developmental toxicity were determined (SCCS, 2009).

Risk Characterisation

Critical Health Effects

The critical health effect for risk characterisation is skin sensitisation.

Public Risk Characterisation

In Australia, the chemicals are regulated through its inclusion in the 'PHENYLENEDIAMINES' chemical group of the SUSMP. The 'PHENYLENEDIAMINES' are listed on Schedules 6 and 10 of the SUSMP with restrictions and/or prohibitions on their use in specific cosmetic products. The Schedule 6 entry in the SUSMP allows phenylenediamines to be included in hair dye preparations and in eyelash and eyebrow tinting products, provided the label includes warning statements regarding skin and eye irritation (SUSMP, February 2017).

Current controls are considered adequate to minimise the risk to public health posed by hair dyes containing the chemical.

Occupational Risk Characterisation

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

Given the critical health effect, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise dermal exposure are implemented. The chemicals 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 HCIS (Safe Work Australia) (see **Recommendation** section).

NICNAS Recommendation

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

Regulatory Control

Public Health

Products containing the chemicals should be labelled in accordance with state and territory legislation (SUSMP, February 2017).

Work Health and Safety

The chemicals are recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Sensitisation	Not Applicable	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 chemicals should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from dermal 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 chemicals are used. Examples of control measures that 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 chemicals, 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 chemicals.

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 chemicals 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 these chemicals has not been undertaken as part of this assessment.

References

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) 2007. List of Chemicals used as Dyes in Permanent and Semi-Permanent Hair Dyes in Australia.

Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(2004)] Third edition. Accessed May 2017, http://www.nohsc.gov.au/pdf/Standards/approved_criteriaNOHSC1008_2004.pdf.

ChemID Plus Advanced. Accessed May 2017 at <http://chem.sis.nlm.nih.gov/chemidplus/>

Cosmetic Ingredient Review Expert Panel (CIR, 1992). Final report on the safety assessment of HC Red No.3. Journal of the American College of Toxicology; 11 Suppl 4. 509-519. Accessed May 2017 at <http://journals.sagepub.com/doi/abs/10.3109/10915819209141889?journalCode=ijta>

Cosmetic Ingredient Review Expert Panel (CIR, 2008). Final report on the safety assessment of HC Red No.7. International Journal of Toxicology 2008; 27 Suppl 1: 45-54

EC, 2012. EC List of 181 substances banned for use in hair dye products. Accessed June 2017 at file:///central.health/dfsuserenv/Users/User_19/patelj/Downloads/181_substances_en.pdf

European Chemicals Agency (ECHA) Classification and Labelling (C&L) Inventory. Accessed May 2017 at: <http://echa.europa.eu/information-on-chemicals/cl-inventory-database>

European Commission Cosmetic Ingredients and Substances (CosIng) Database. Accessed May 2017 at <http://ec.europa.eu/consumers/cosmetics/cosing/>

Galleria Chemica. Accessed May 2017 at <http://jr.chemwatch.net/galleria/>

Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Accessed at http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

Hazardous Substances Data Bank (HSDB). Accessed May 2017 at <http://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm>

International Agency for Research on Cancer (IARC) (1993). HC Red No. 3. Accessed May 2017 at <http://www.inchem.org/documents/iarc/vol57/05-hcr3.html>

National Toxicology Program (NTP) 1986. Toxicology and carcinogenesis studies of HC Red No 3 in F344/N rats and B6C3F mice. Accessed May 2017 at https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr281.pdf

Safe Work Australia (SWA). Hazardous Chemical Information System (HCIS). Accessed May 2017 at <http://hcis.safeworkaustralia.gov.au/>

Scientific Committee on Consumer Products (SCCP) 2010. Opinion on HC Red n° 3, COLIPA N° B50. SCCP/1293/10. Adopted at the 9th plenary meeting on 14th December 2010. Available at https://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_043.pdf

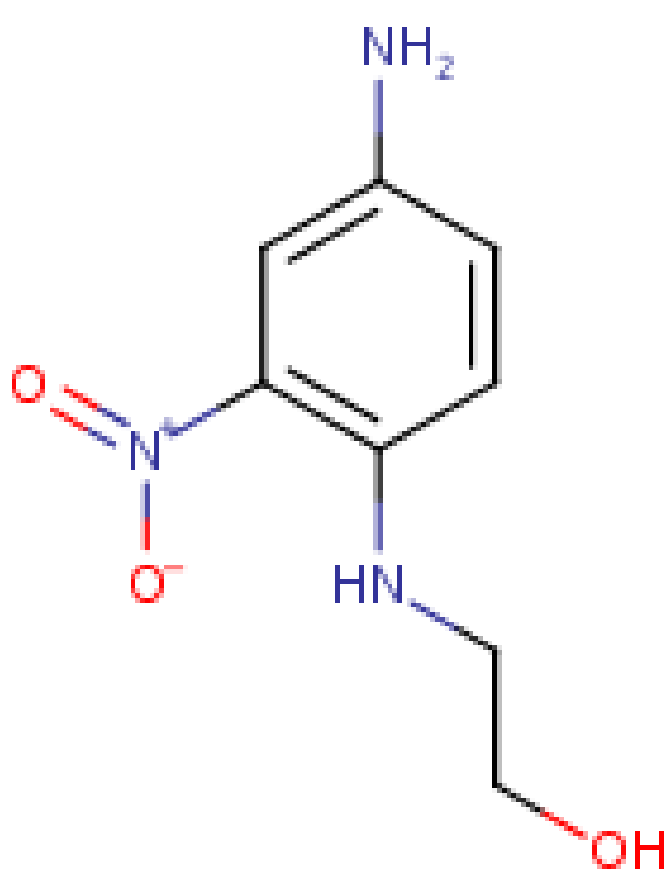
Scientific Committee on Consumer Products (SCCP) 2012. Opinion on HC Red n° 3, COLIPA N° B50. SCCP/1474/12. Adopted at the 16th plenary meeting on 18th September 2012. Available at https://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_107.pdf

Scientific Committee on Consumer Products and Non-Food Products intended for Consumers (SCCNFP) 2003. Opinion on HC Red n° 7, COLIPA N° B36. SCCNFP/0678/03. Adopted at the 24th plenary meeting on 24-25 June 2003. Available at http://ec.europa.eu/health/ph_risk/committees/sccp/documents/out209_en.pdf

Scientific Committee on Consumer Safety (SCCS) 2009. Opinion on HC Red n° 7, COLIPA N° B36. SCCS/1229/09. Adopted at the 5th plenary meeting of 8th December 2009. Available at http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_007.pdf

Therapeutic Goods Administration–Department of Health 2017. Standard for the Uniform Scheduling of Medicines and Poisons No. 16 (the SUSMP 16). Accessed May 2017 at <https://www.legislation.gov.au/Details/F2017L00057>

Chemical Identities

Chemical Name in the Inventory and Synonyms	Ethanol, 2-[(4-amino-2-nitrophenyl)amino]- HC Red 3 2-((4-amino-2-nitrophenyl)amino)ethanol
CAS Number	2871-01-4
Structural Formula	
Molecular Formula	C8H11N3O3
Molecular Weight	197.1

Chemical Name in the Inventory and Synonyms	Ethanol, 2-[(4-amino-3-nitrophenyl)amino]- HC Red 7 2-(4-amino-3-nitroanilino)ethanol
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Nc1cc(NCCO)ccc1[N+](=O)[O-]

https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-group-assessment-report?assessment_id=3482