Ethanol, 2,2'-[(4-amino-3-nitrophenyl)imino]bis- and its monohydrochloride: Human health tier II assessment

03 July 2015

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Ethanol, 2,2'-[(4-amino-3-nitrophenyl)imino]bis-	29705-39-3
Ethanol, 2,2'-[(4-amino-3-nitrophenyl)imino]bis-, monohydrochloride	94158-13-1

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**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemical, ethanol, 2,2'-[(4-amino-3-nitrophenyl)imino]bis-, monohydrochloride (CAS No. 94158-13-1) is a salt resulting from ethanol, 2,2'-[(4-amino-3-nitrophenyl)imino]bis- (CAS No. 29705-39-3; referred to as the parent base in this report) reacting with a single molecule of hydrochloric acid. The parent base and its salt have been grouped together for assessment due to their similar toxicological properties and uses.

Import, Manufacture and Use

Australian

The salt is on the ‘List of chemicals used as dyes in permanent and semi-permanent hair dyes in Australia’, with reported cosmetic use in semi-permanent hair dye preparations (NICNAS, 2007).

No specific Australian use, import, or manufacturing information has been identified for the parent base.

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 Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary, and the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR).

The chemicals have reported cosmetic uses as hair dye substances in oxidative (permanent) and non-oxidative (semi-permanent) hair dye products.

Restrictions

Australian

No known restrictions have been identified.

International

The use of the chemicals in this group as cosmetics in the European Union (EU) is subject to the restrictions described in the EU Cosmetics Regulation 344/2013 (as an amendment to the listing under Annex III of Regulation 1223/2009). These chemicals may be used as a hair dye substance in ready-for-use preparations of non-oxidising hair dye products at a maximum concentration of 2.5 % (as hydrochloride). Additionally, after mixing under oxidative conditions (i.e. with hydrogen peroxide), the maximum concentration applied to hair must not exceed 1.25 % (as hydrochloride) (CosIng).

The chemicals in this group are also listed with the same use restrictions as described above for the EU on the following (Galleria Chemica):

- the Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex III—Part 1; and
- the New Zealand Cosmetic Products Group Standard—Schedule 5.

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are 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 hazards of both the parent base (ethanol, 2,2'-[(4-amino-3-nitrophenyl)imino]bis-; CAS No. 29705-39-3) and its salt (ethanol, 2,2'-[(4-amino-3-nitrophenyl)imino]bis-, monohydrochloride; CAS No. 94158-13-1) were assessed together using the toxicological data available (SCCP, 2007). Where data are unavailable for the parent base, the data available for the salt are considered relevant for the hazard assessment due to the structural similarity of the two chemicals. However, the monohydrochloride salt could have different properties from the parent base with respect to local effects.

Toxicokinetics

The chemicals are expected to have slow dermal absorption but fast oral absorption. The absorbed fraction is extensively excreted within 24 hours.

The salt was applied to the skin of Sprague Dawley (SD) rats at the following concentrations: (a) 2 % in a hair dye formulation without hydrogen peroxide; (b) 2 % in a hair dye formulation with hydrogen peroxide; and (c) 6.66 % in solution. The formulation or solution was left on the skin for 30 minutes and then rinsed with a shampoo formulation followed by water. Only 2–3.7 % of the salt was reported to be absorbed through the skin, with the majority (96.3–98 %) removed from the skin after rinsing. The dermal absorption was 0.86–1.13 μg/cm^2. Most of the absorbed dose was excreted within the first 24 hours following application (78–90 %) and excretion was mainly via the urine (57–62 %). When orally administered at concentrations of 20.4 or 21 mg/kg bw to SD rats (three animals/sex/group), 92 % of the salt was excreted within the first 24 hours. The excretion was mainly via the urine (46 %) and faeces (54 %). Less than 0.015 % of the salt remained in the tissues 72 hours after administration (SCCP, 2007).

A hair dye formulation containing the salt was applied to five healthy female volunteers' washed hair for 15 minutes at a concentration of 15.13 mg/kg bw. The salt was not detected in the serum or the urine following application. Thus, it was concluded that the absorption was close to zero; less than 0.0195 mg/kg bw of the amount applied (SCCP, 2007).

Acute Toxicity

Oral

The chemicals are expected to have low acute toxicity based on results from animal tests following oral exposure. The median lethal dose (LD50) in CFY (remote SD) rats for the salt was 2120 mg/kg bw. Observed sub-lethal effects included lethargy, piloerection, diuresis, purple staining of the urine and external extremities, ataxia, increased lacrimation and decreased respiratory rate (SCCP, 2007).

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Limited data are available. The available data suggest that the chemicals at low concentrations are not irritating to the skin.

In a skin irritation study, 0.5 mL of the salt at a 2.5 % concentration was applied occlusively to the intact or abraded dorsal skin of three albino rabbits for 24 hours. No skin irritation effects were observed immediately after patch removal, or at 24 and 48 hours later. However, it is noted that the test concentration used in this study was too low for hazard classification (SCCP, 2007).

Eye Irritation

Limited data are available. The available data suggest that the chemicals at low concentrations are not irritating to the eyes.

In an eye irritation study with three albino rabbits, 0.1 mL of the salt at a 2.5 % concentration was instilled into one eye of each animal. The treated eyes were washed with distilled water 10 seconds after instillation of the salt. No eye irritation effects were observed during the seven-day observation period following treatment. However, it is noted that the test concentration used in this study was too low for hazard classification (SCCP, 2007).

Sensitisation

Skin Sensitisation

Based on the available data, the chemicals are considered to be moderate skin sensitisers, warranting hazard classification.

In a local lymph node assay (LLNA) conducted according to the Organisation for Economic Co-operation and Development Test Guideline (OECD TG) 429, the salt, in a mixture of water/acetone (1:1) with olive oil (3:1) or in dimethyl sulfoxide (DMSO), was applied to the surface of the ear of female CBA/J mice (five animals/group) once daily for three consecutive days. The salt at test concentrations of 0.5, 1.5, 5 or 10 % in water/acetone/olive oil produced stimulation indices (SIs) of 1.3, 2.2, 1.2 or 1.4, respectively. The estimated concentration needed to produce a three-fold increase in lymphocyte proliferation (EC3) could not be calculated as all values were below three. The salt, at test concentrations of 0.5, 1.5, 5 or 10 % in DMSO, produced SIs of 1.5, 1.8, 2.1 or 3.5, respectively. The EC3 was 8.2 %, indicating a moderate skin sensitisation potential (SCCP, 2007).

In a guinea pig maximisation test with 20 female Pirbright guinea pigs, the sensitisation potential was tested by pair-wise intradermal injections (two injections of Freund's complete adjuvant (FCA) and two injections of the salt at a 3 % dilution) on the clipped shoulder of each animal. On the following day, 6–8 hours before dermal induction, the animals were pre-treated with 10 % sodium lauryl sulfate. A topical induction patch using 3 % of the salt was then applied for 24 hours. A second intradermal induction (two injections of 3 % of the salt in FCA) was performed 48 hours later. A challenge with 1, 2 or 3 % of the salt in FCA 14 days after the last exposure did not result in dermal responses, although it is noted that both the induction and challenge concentrations were very low. This study was considered inadequate for hazard classification (SCCP, 2007).

In a Landsteiner-Draize guinea pig sensitisation test with female Pirbright guinea pigs (15 test animals and 10 control animals), the sensitisation potential was tested by an intradermal injection of 0.1 mL of a commercial product, Kardinalrot (containing 84 % of the parent base) at a 1 % dilution on the shaved shoulder of each test animal. Both test and control animals were challenged by an intradermal injection of 0.1 mL of Kardinalrot (1 % dilution) on the untreated flanks of each animal four weeks after the induction. No dermal responses were observed, although it is noted that the test concentrations used in this study were too low. This study was considered inadequate for hazard classification (SCCP, 2007).

Repeated Dose Toxicity

Oral

The available data suggest that the chemicals have low to moderate repeated dose toxicity based on results from animal tests following oral exposure. The effects observed were not sufficient to warrant hazard classification.

In a repeated dose toxicity study conducted according to OECD TG 408, Wistar rats (12 animals/sex/group) were administered Kardinalrot (a product containing 84 % of the parent base) at concentrations of 0 or 10 mg/kg bw/day by oral gavage, once daily for 90 days. Discolouration of the urine was observed in the treated animals. In the treated females, reduced absolute and relative spleen weights were observed, whereas in the treated males, significant increases in the relative spleen and relative kidney weights were observed. Slight activation of the thyroid epithelium was observed in 10 treated males and one treated female. A lowest observed adverse effect level (LOAEL) of 10 mg/kg bw/day was established in this study (SCCP, 2007).

In a separate repeated dose toxicity study conducted according to OECD TG 408, Wistar rats (15 animals/sex/group) were administered Kardinalrot (a product containing 84 % of the parent base) at concentrations of 0, 75, 150 or 300 mg/kg bw/day by oral gavage, once daily for 90 days. Two mortalities were recorded in the 300 mg/kg bw/day group. Urine discolouration was observed in all animals treated with 150 or 300 mg/kg bw/day of the chemical and in some animals treated with 75 mg/kg

bw/day. The discolouration was reversed following a four-week recovery period. Increased absolute spleen weights in the females in the 150 mg/kg bw/day group, increased relative spleen weights in the females in the 75, 150 and 300 mg/kg bw/day groups, increased relative kidney weights in the animals in the 300 mg/kg bw/day groups and significant decreases in brain weights in the females in the 75, 150 and 300 mg/kg bw/day groups were observed. Dose-dependent increases in thyroid weights with dark discolouration were observed in the treated animals. In the males in the 150 and 300 mg/kg bw/day groups, activation of thyroid epithelium was observed, accompanied by follicular cell hypertrophy at the 300 mg/kg bw/day dose. In the 300 mg/kg bw/day group, liver cell hypertrophy was also observed. A LOAEL of 75 mg/kg bw/day was established in this study (SCCP, 2007).

Dermal

Limited data are available. The available data suggest that the chemicals are not expected to have systemic toxicity based on results from an animal test following repeated dermal exposure.

The salt was applied dermally at concentrations of 0, 0.013, 1, or 2 % (in a volume of 0.05 mL/animal) to NMRI mice (75 animals/sex/group), three times a week for 18 months. Dose-dependent body weight reduction was observed in all treated males for the first three months and in males treated with 2 % of the salt throughout the study. However, no signs of toxicity or histopathological effects were observed (SCCP, 2007).

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. Positive results were seen in some in vitro genotoxicity tests, but all in vivo tests were negative.

In vitro studies

A bacterial point mutation assay was conducted according to OECD TG 471 in five *Salmonella typhimurium* strains (TA98, TA100, TA1535, TA1537 and TA1538) up to a maximum concentration of 5000 µg/plate of the parent base, in the absence and presence of a rat liver metabolic activation system. Negative results were obtained from the study (SCCP, 2007).

A mammalian cell gene mutation assay was conducted according to OECD TG 476 in the mouse lymphoma L5178Y cell line (thymidine kinase (tk) locus). The salt was tested up to a maximum concentration of 3200 µg/mL in the absence and presence of a rat liver metabolic activation system, respectively. Significant increases in mutation frequency were observed in the absence of metabolic activation, indicating the clastogenic potential of the salt (SCCP, 2007).

An in vitro micronucleus assay was conducted according to OECD TG 487 in the human lymphocytes from two healthy, non-smoking female donors. The salt was tested up to maximum concentrations of 1556 and 2413 µg/mL in the absence and presence of a rat liver metabolic activation system, respectively. Dose-dependent increases in the frequencies of micronucleated binucleated (MNBN) cells were observed in both the absence and presence of metabolic activation. The salt was considered to be genotoxic in this study (SCCP, 2007).

In vivo studies

In an in vivo micronucleus assay in bone marrow cells in NMRI mice (five animals/sex/group), the parent base was administered at concentrations of 0, 375, 750 or 1500 mg/kg bw by oral gavage. Bone marrow cells were collected 24 or 48 hours (for the 1500 mg/kg bw group only) after administration of the parent base and the polychromatic erythrocytes (PCEs) for each rat were examined. No increases in micronucleated PCEs were found, thus the parent base was concluded to be non-mutagenic in this study (SCCP, 2007).

In a comet assay (single cell gel electrophoresis) in B6C3F1 mice (five males/group), the salt was administered at concentrations of 0, 1000 or 2000 mg/kg bw by oral gavage twice, with 20 hours between the two treatments. The animals were

euthanised four hours after the last treatment to evaluate DNA damage. The salt resulted in an increased percentage of cells with low molecular weight DNA at concentrations up to 2000 mg/kg bw in the urinary bladder, indicating cytotoxic potential. However, the examination of 100 nuclei per organ indicated that the salt did not induce DNA damage in the urinary bladder, liver, duodenum or blood of the mice. Thus, the salt is concluded to be non-genotoxic in this study (SCCP, 2007).

Carcinogenicity

No carcinogenicity studies are available for the chemicals, except for a dermal study conducted using the salt at low concentrations. The data available do not provide sufficient information to make a conclusion on the carcinogenicity of the chemicals. Based on the available genotoxicity data and mechanistic information, the chemicals are not considered to be carcinogenic.

The salt was applied dermally at concentrations of 0, 0.013, 1, or 2 % to NMRI mice (75 animals/sex/group), three times a week for 18 months (refer to **Repeated dose toxicity** section). Lymphatic leucosis was observed in both control and treated animals and was not considered to be treatment-related. No differences in the occurrence or frequency of tumours were observed between the control and treated animals. Under the conditions of this study, the salt was not considered to be carcinogenic. However, it is noted that the concentrations used in this study were considered to be too low to detect any carcinogenic effects (SCCP, 2007).

Experimental in vitro and in vivo genotoxicity data (refer to **Genotoxicity** section) showed that the chemicals are not considered to be genotoxic. However, Quantitative Structure–Activity Relationship (QSAR) modelling using OASIS–TIMES (Optimized Approach based on Structural Indices Set–TIssue MEtabolism Simulator) resulted in positive results for in vitro and in vivo genotoxicity, except for a negative result for in vitro Ames test. It should be noted that the chemicals were out of the applicability domain of the models. If a prediction is out of the applicability domain of the model, it indicates that there is greater uncertainty about the reliability of the models, since the performance statistics from the training set might not be applicable to the chemical. Thus, QSAR model predictions for the chemicals will not outweigh the negative results for genotoxicity in the weight of evidence analysis of the carcinogenic potential of the chemical.

Nitroaniline derivatives can be metabolically activated to reactive electrophiles as an initial step in a carcinogenic mechanism of action. This usually involves the activation of N-hydroxylamine metabolites with enzymatic reaction and the eventual formation of pro-carcinogenic nitrenium ions. The highly reactive nitrenium ions can covalently bind to DNA, provided that they are sufficiently stable to not undergo further reactions. The stability of the nitrenium ions is correlated with mutagenicity, for example in an Ames test with metabolic activation (Benigni & Bossa, 2011). For the parent base, the Ames test results were negative, indicating a lower likelihood of carcinogenic potential. In the parent base, the nitro group is in the *meta*-position compared with the tertiary amine, which is not likely to be hydroxylated, and *ortho*-position to the primary amine. Studies showed that *para*-substituted nitrobenzene derivatives are more mutagenic compared with *ortho*- or *meta*-isomers (Vance & Levin, 1984; Shimizu & Yano, 1986; Assman et al., 1997). The nitro group of the chemicals is attached in an *ortho*-position to the primary amine, which could disrupt the activation of the N-hydroxylamine metabolites. Therefore, compared with other nitroaniline derivatives, the chemicals are less likely to be carcinogenic.

Reproductive and Developmental Toxicity

Based on the available data, the chemicals are not expected to have reproductive or developmental toxicity.

In a one-generation reproduction toxicity study conducted according to OECD TG 415, HanBrl:WIST rats (24 animals/sex/group) were administered the salt once daily by oral gavage at concentrations of 0, 30, 100 or 300 mg/kg bw/day during pre-mating (70 days for males, 14 days for females), mating, gestation, and (in females only) lactation. The offspring were treated once daily up to postnatal day (PND) 21. No treatment-related mortalities were observed. Urine discolouration was observed in the treated animals. Dose-dependent increases in red discoloured thyroids and increases in follicular cell hypertrophy in the thyroids were observed in the treated adults. No reproductive effects were observed in this study. A no observed adverse effect level (NOAEL) of 300 mg/kg bw/day was established for reproductive effects (SCCP, 2007).

In a prenatal development toxicity study conducted according to OECD TG 414, HanBri:WIST rats (22 pregnant females/group) were administered the salt at concentrations of 0, 30, 100 or 300 mg/kg bw/day by oral gavage, once daily on gestational days (GDs) 6–20. No treatment-related mortalities were observed. Urine discolouration was observed in the 300 mg/kg bw/day group,

which subsequently led to discoloured fur and tails. No developmental effects were observed, thus a NOAEL of 300 mg/kg bw/day was established in this study (SCCP, 2007).

Risk Characterisation

Critical Health Effects

The critical health effect for risk characterisation is skin sensitisation.

Public Risk Characterisation

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

The ASEAN, EU and New Zealand have restricted the use of these chemicals in cosmetics. Currently, there are no restrictions in Australia for using these chemicals in cosmetic products. The risks could be mitigated by implementing concentration limits for use in hair dyes to address the risk of skin sensitisation.

Occupational Risk Characterisation

During product formulation, dermal 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 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 local health effects, 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.

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 chemicals 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 chemicals 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 chemicals should be included in the Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons) with an appropriate concentration cut-off (exemption) for hair dye use.

Consideration should be given to the following:

- the chemicals are moderate skin sensitisers;

- overseas restrictions for use of the chemicals 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 2.5 % and the maximum use concentration upon application is 1.25 % (after mixing under oxidative conditions); and
- the risk could be controlled by including warning statements on labels for hair dye formulations containing the chemical at any concentration.

Work Health and Safety

The chemicals are 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]
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 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 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 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

Assman N, Emmrich M, Kampf G and Kaiser M, 1997. Genotoxic Activity of Important Nitrobenzenes and Nitroanilines in the Ames Test and Their Structure-Activity Relationships. Mutat. Res. 395, 139–144.

Benigni R and Bossa C, 2011. Mechanisms of Chemical Carcinogenicity and Mutagenicity: A Review with Implications for Predictive Toxicology. Chem. Rev. 111, 2507–2536.

ChemIDPlus Advanced. Accessed April 2015 at **http://chem.sis.nlm.nih.gov/chemidplus/**

CosIng. Cosmetic Ingredients and Substances. Accessed April 2015 at **http://ec.europa.eu/consumers/cosmetics/cosing/**

Galleria Chemica. Accessed April 2015 at **http://jr.chemwatch.net/galeria/**

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

Personal Care Products Council (INCI Dictionary). Accessed April 2015 at **http://www.ctfa-gov.org/jsp/gov/GovHomePage.jsp**

Scientific Committee on Consumer Products (SCCP) 2007. Opinion on HC Red no 13 (Colipa No B31). SCCP/1075/07. Accessed April 2015 at **http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_104.pdf**

Shimizu M and Yano E, 1986. Mutagenicity of Mono-Nitrobenzene Derivatives in the Ames test and Rec Assay. Mutat. Res. 170, 11–22.

US Environmental Protection Agency's Aggregated Computational Toxicology Resource (ACToR). Accessed April 2015 at **http://actor.epa.gov/actor/faces/ACToRHome.jsp**

Vance WA and Levin DE, 1984. Structural Features of Nitroaromatics That Determine Mutagenic Activity in Salmonella typhimurium. Environ. Mutagen 6 (6), 797–811.

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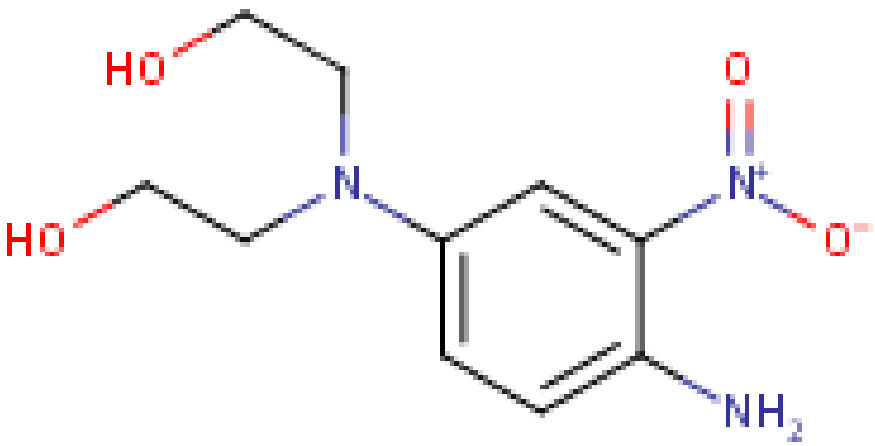
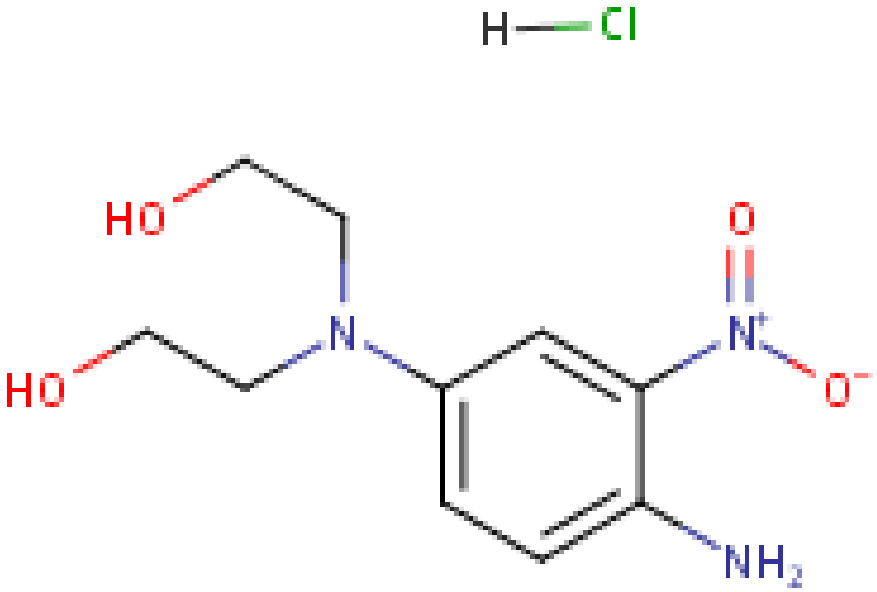
Chemical Identities

Chemical Name in the Inventory and Synonyms	**Ethanol, 2,2'-[(4-amino-3-nitrophenyl)imino]bis-** HC Red No. 13
CAS Number	29705-39-3
Structural Formula	
Molecular Formula	C10H15N3O4
Molecular Weight	241.245

Chemical Name in the Inventory and Synonyms	**Ethanol, 2,2'-[(4-amino-3-nitrophenyl)imino]bis-, monohydrochloride** 2,2'-((4-amino-3-nitrophenyl)imino)bisethanol hydrochloride HC Red No. 13
CAS Number	94158-13-1

Structural Formula	
Molecular Formula	C10H15N3O4.ClH
Molecular Weight	277.71

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