Monoazo pigments that may release carcinogenic amines: Human health tier II assessment

12 December 2019

- Chemicals in this assessment
- Preface
- Grouping Rationale
- Import, Manufacture and Use
- Restrictions
- Existing Worker Health and Safety Controls
- Health Hazard Information
- Risk Characterisation
- NICNAS Recommendation
- References

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
2-Naphthalenecarboxamide, N-(4-chloro-2- methylphenyl)-3-hydroxy-4-[(2- methylphenyl)azo]-	21839-86-1
2-Naphthalenecarboxamide, 3-hydroxy-4-[(2- methyl-5-nitrophenyl)azo]-N-(3-nitrophenyl)-	6358-47-0
2-Naphthalenecarboxamide, N-(4- chlorophenyl)-3-hydroxy-4-[(2-methyl-5- nitrophenyl)azo]-	6410-30-6
2-Naphthalenecarboxamide, 3-hydroxy-4-[(2- methyl-5-nitrophenyl)azo]-N-phenyl-	6448-95-9
2-Naphthalenecarboxamide, N-(4-chloro-2- methylphenyl)-4-[(4-chloro-2- methylphenyl)azo]-3-hydroxy-	6471-51-8
2-Naphthalenecarboxamide, 3-hydroxy-4-[(2- methyl-5-nitrophenyl)azo]-N-(2-methylphenyl)-	6655-84-1
2-Naphthalenecarboxamide, 3-hydroxy-N-(4- methoxyphenyl)-4-[(2-methylphenyl)azo]-	104513-13-5



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

NICNAS has made every effort to assure the quality of information available in this report. However, before relying on it for a specific purpose, users should obtain advice relevant to their particular circumstances. This report has been prepared by NICNAS using a range of sources, including information from databases maintained by third parties, which include data supplied by industry. NICNAS has not verified and cannot guarantee the correctness of all information obtained from those databases. Reproduction or further distribution of this information may be subject to copyright protection. Use of this information without obtaining the permission from the owner(s) of the respective information might violate the rights of the owner. NICNAS does not take any responsibility whatsoever for any copyright or other infringements that may be caused by using this information.

ACRONYMS & ABBREVIATIONS

Grouping Rationale

Chemicals in this group are azo compounds that share a similar molecular structure and are part of a larger group of Naphthol AS pigments. These pigments contain the same basic structure of an aniline that is azo coupled to Naphthol AS, and are differentiated from each other by the presence of methyl, methoxy, nitro or chlorine groups at various positions of the phenyl groups (Herbst et al., 2005; Government of Canada, 2016).

The critical health concern for the chemicals in this group is the potential for carcinogenic effects following exposure to certain aromatic amines present as both impurities and breakdown products. The significance of azo-reduction in the mutagenicity and carcinogenicity of azo dyes is well established. Although the chemicals in this group are pigments and expected to be less bioavailable than dyes, there is still the potential for these chemicals to form carcinogenic break down products.

Several Napthol AS pigments including Pigment Red (PR) 112 (CAS No. 6535-46-2) have been published under IMAP as Tier I assessments (NICNASa). The chemicals in this group are differentiated from other Naphthol AS pigments by having the potential to undergo reductive cleavage of the azo linkage (N=N) to form one or more of the following carcinogenic and/or genotoxic aromatic amines:

- o-toluidine (CAS No. 95-53-4)
- 5-nitro-o-toluidine (CAS No. 99-55-8)
- 4-chloro-o-toluidine (CAS No. 95-69-2)

Based on data for PR 22 (see **Toxicokinetics** section), the 5-nitro-o-toluidine released from this chemical and PR 8, PR 17 and PR 114 may be further reduced to 2,4-toluenediamine (2,4-TDA—CAS No. 95-80-7).

These amines have been previously assessed by NICNAS (NICNASb; NICNASc; NICNASd; NICNASe).

In the European Union (EU), these aromatic amines are classified as carcinogens and are included in Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) list of 22 aromatic amines in Annex XVII Appendix 8 (European Commission, 2006) (see **International restrictions** section).

Import, Manufacture and Use

Australian

The chemicals PR 17 and PR 22 were identified as present in tattoo inks available in Australia (NICNAS, 2018).

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; Galleria Chemica; the European Commission Cosmetic Ingredients and Substances (CosIng) database; US Personal Care Products Council International Nomenclature Cosmetic Ingredients (INCI) directory; and the Colour Index Online.

The chemicals PR 7 and PR 22 have reported use as colouring agents in cosmetics. PR 7 is reported to be used in soaps at a concentration of 0.3 % and rinse off products (Commission of the European Communities, 1988).

For PR 22, to identify the colourant allowed for use in Japan, the INCI name Aka404 must be used. The chemical is not an approved colourant for the US or the EU. This INCI name may not be used for ingredient labelling in the US or the EU.

For PR 7 to identify the colourant allowed for use in the European Union (EU), the INCI Name CI 12420 must be used. The INCI Name may not be used for ingredient labelling in the US or Japan. The chemical is not an approved colourant for the US.

The chemicals PR 7, PR 8, PR 17 and PR 22 are reported as being used in tattoo and permanent make-up inks (Piccinini et al., 2015a).

The chemicals in this group also have reported use in the following:

- inks, toners and colourants (PR 8, PR 17 and PR 22);
- domestic and commercial paints and coatings (PR 8 and PR 22);

- textile printing and manufacturing (PR 8, PR 17, PR 22 and PR 114);
- packaging (PR 17, PR 22 and PR 114); and
- polymer preparations and compounds (PR 8 and PR 22).

Restrictions

Australian

No known restrictions have been identified for the chemicals.

The Australian Competition and Consumer Commission (ACCC) has published safety guidance on concentrations of particular aromatic amines, in clothing, textiles and leather articles in direct and prolonged contact with the human skin or oral cavity (ACCC, 2014). The guidance includes limits for aromatic amines, including those released by the chemicals in this assessment, in textile and leather articles that align with those in the European Union. The limit does not have a legislative basis and is provided for the information of suppliers who may be supplying products that contain aromatic amines.

International

PR 7 (CI 12420) is listed in the following (Galleria Chemica):

- European Union (EU) Cosmetics Regulation 1223/2009 Annex IV—List of colourants allowed in cosmetic products for use in rinse off products.
- New Zealand Cosmetic Products Group Standard—Schedule 6: Colouring Agents Cosmetic Products May Contain With Restrictions. The chemical is allowed exclusively in cosmetic products intended to come into contact only briefly with the skin.
- Association of South East Asian Nations (ASEAN) Cosmetic Directive Annex IV Part 1- List of colouring agents allowed for use in cosmetic products. The chemical is allowed exclusively in cosmetic products intended to come into contact only briefly with the skin.

Although listed on INCI, PR 22 is not included in these Annexes i.e. it is not a colouring agent allowed for use in cosmetic products in these countries.

Although azo dyes are restricted by Annex XVII to REACH Regulation for use in textiles and leather articles, azo pigments are not covered by this restriction. However PR 22 and PR8 were determined to be sufficiently soluble to yield detectable amounts of a listed amine. The Ecological and Toxicological Association of Dyes and Organic Pigments Manufacture (ETAD) recommends to its members a responsible approach to the management of these pigments (ETAD, 2008). The test materials specified may give positive results for aromatic amines. It is likely manufacturers would avoid these pigments due to the uncertain consequences of the positive outcome.

The Resolution ResAP(2008)1 on requirements and criteria for the safety of tattoos and permanent make-up (Council of Europe, 2008) lists the chemicals o-toluidine, 2,4-toluenediamine, 5-nitro-o-toluidine and 4-chloro-o-toluidine under the aromatic amines which should not be present or released from tattoos and permanent make-up products in concentrations that are technically avoidable according to good manufacturing procedures. These requirements have been imbedded by several European countries into their domestic legislative framework (Piccinini et al., 2015b).

A proposal for a restriction of substances in tattoo inks and permanent make up was published by the European Chemicals Agency (ECHA) in March 2019: This restriction proposal included the following assessed Naphthol AS pigments (with a proposed concentration limit of 0.1 %): PR 7, PR 17 and PR 22 (ECHA, 2017; ECHA, 2019).

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are not listed on the Hazardous Chemical 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

The chemicals in this group are Naphthol AS pigments with the potential upon cleavage of the azo bond to form carcinogenic amines.

Limited data is available for two of the chemicals in this group, PR 7 and PR 22. Due to their overall limited bioavailability, Naphthol AS pigments are expected to have similar toxicological profiles. For non-genotoxic and carcinogenic endpoints data from other Naphthol AS pigments, PR 23 (CAS No. 6471-49-4), PR 112 (CAS No. 6535-46-2), PR 170 (CAS No. 2786-76-7) and PR 268 (CAS No. 16403-84-2) has been included in the report. Read across from other Naphthol AS pigments both within and outside the group of chemicals considered in this assessment is justified based on limited bioavailability and similar toxicological profiles (Government of Canada, 2016; Sauer and Kreiling, 2019).

Toxicokinetics

Data available indicate a low overall bioavailability although there is some evidence of azo reduction.

Positive results in certain genotoxicity assays for PR 22 and PR 23 suggests the chemicals have a sufficient level of bioavailability or potential for degradation to elicit a genotoxic response (Government of Canada, 2016).

There is evidence that PR 22 present in tattoo inks is readily reduced by dithionite to form 2,4-toluenediamine (NICNAS, 2018).

The azo bond in PR 22 dissolved in organic solvents is cleaved following exposure to UVB and sunlight forming the aromatic amine 5-nitro-o-toluidine and also 4-nitrotoluene. When the skin from female SKH1 hairless mice tattooed with Pigment Red 22 were treated with a frequency doubled Nd:YAG laser at a wavelength of 532 nm the same aromatic amines were also detected (Engel, 2007; Engel, 2010).

Male F344 rats were administered a single oral dose of 5.3 mg/kg body weight (bw) of the related chemical PR 23. After 48 hours nearly all of the pigment was recovered from the faeces ($93 \pm 16 \%$). Even when animals were administered a 10 fold increase in the dose, none of the chemical was recovered from plasma, whole blood, liver, kidney or lungs (El Dareer, 1984).

In an anaerobic incubation with the bacterium *Shewanella* strain J18 142, low levels of azo reduction were observed for the related chemical PR112 (Government of Canada, 2016).

Acute Toxicity

Oral

Based on the available data for PR 7 and other Naphthol AS pigments, the chemicals in this group are expected to have low acute oral toxicity.

An LD50 of > 5000 mg/kg bw/day was reported for PR 7. No study details are available. (Commission of the European Communities, 1988).

In an OECD Test Guideline (TG) 401 (Acute Oral Toxicity) study, Wistar rats (n=5/sex) received by oral gavage a single dose of 5000 mg/kg bw of the analogue PR 11. Evidence of toxicity included reduced activity, abnormal posture and diarrhoea with stained faeces. No mortality occurred as a result of treatment with the chemical (REACHa).

In an acute oral toxicity study, rats (n=20/sex/dose) received by oral gavage a single dose of 6000 or 10000 mg/kg bw of the analogue, PR 23. Signs of toxicity included abnormal breathing, bulging eyes and abnormal posture. No deaths occurred in the treated animals (REACHb).

Dermal

Based on the available data for another Naphthol AS pigment, the chemicals in this group are expected to have low acute dermal toxicity.

In an OECD TG 402 (Acute Dermal Toxicity) study, male Wistar rats (n=5) received a single 24 hour occluded dose of 5000 mg/kg bw of PR 112. There were no clinical signs of toxicity and no deaths occurred as a result of treatment with the chemical (REACHa).

Inhalation

No data are available for the chemicals.

Corrosion / Irritation

Skin Irritation

Based on the available data for PR 7 and other Naphthol AS pigments, the chemicals in this group are expected to be at most slightly irritating to the skin.

In a non guideline study, repeated application of 100 mg of PR 7 on the intact skin of rabbits for 6 days produced no reactions. In another rabbit skin test a single treatment with 0.5 g applied as a paste with water was non-irritating (Commission of the European Communities, 1988). No other details are available.

In an OECD TG 404 (Acute Dermal Irritation) study, 0.5 g of the analogue, PR 112 was applied semi-occluded for 4 hours to the flank of New Zealand White (NZW) rabbits (n=3). Minor irritation was observed up to an hour after exposure, which resolved within 24 hours (REACHa).

In a dermal irritation study, 0.5 g of the analogue, PR 23 was applied for 24 hours to the intact and abraded shaved skin of rabbits (n=3/sex). The lowest possible irritation score was observed in the animals at 24 and 72 hours after the challenge (REACHb).

Eye Irritation

Based on the available data for PR 7 and other Naphthol AS pigments, the chemicals in this group are expected to be at most slightly irritating to the eyes.

In a non-guideline eye irritation study in rabbits, PR 7 was found to be practically non-irritating (Commission of the European Communities, 1988). No other details are available.

In an OECD TG 405 (Acute Eye Irritation) study, 0.1 g of the analogue, PR 112 was introduced into the conjunctival sac of NZW rabbits (n=3). Minor chemosis and conjunctival redness was observed, which resolved within 48 hours (REACHa).

In an eye irritation study, 0.1 g of the analogue, PR 23 was introduced into the conjunctival sac of rabbits (n=3/sex) and rinsed out 30 seconds after treatment. The lowest possible irritation score was observed in the animals from 1 to 7 days after challenge (REACHb).

Sensitisation

Skin Sensitisation

Limited data are available.

In a non-guideline sensitisation test in guinea pigs with 0.1 ml of a 10 % aqueous suspension of the analogue, PR 7, did not provoke any response either during the induction or upon challenge treatment (Commission of the European Communities, 1988). No other details are available.

In a local lymph node assay (OECD TG 429) in female CBA/Ca OlaHsd mice (n=5/dose), the analogue, PR 112, was found to be a not a skin sensitiser. Stimulation indices of 1.16, 1.15 and 0.68 were determined from treatment with the chemical at concentrations of 0.5 %, 10 % and 20 %, respectively (REACHa).

Repeated Dose Toxicity

Oral

Based on the available data for PR 22 and other Naphthol AS pigments, repeated oral exposure to the chemicals are not considered to cause serious damage to health.

In a combined repeated dose toxicity study with reproduction/developmental toxicity screening study (OECD TG 422), Sprague Dawley (SD) rats (n=12/sex at each dose) were dosed with Pigment Red 22 (CAS No. 6448-95-9) daily by gavage at 0, 100, 300 or 1000 mg/kg bw/day for 37 days in males and approximately 40 days in females. None of the animals died and there were no signs of toxicity based on clinical signs, body weights, food consumption, haematology, clinical chemistry, gross pathology or histochemical examination. A dose dependent increase in liver weights was observed in males and females, and this reached statistical significance at 1000 mg/kg bw/day. However, it is unclear whether the change in liver weights represents an adverse effect (Government of Canada, 2016).

Similar findings of low chronic toxicity were obtained from repeated dose and sub-chronic toxicity studies of analogue Naphthol AS pigments. In 28-day oral toxicity studies (OECD TG 407), no adverse effects were attributable to 2 Naphthol AS pigments at the highest doses tested. These doses were 1000 mg/kg bw/day by gavage for PR112, and 12500 ppm (approximately equivalent to 1000 mg/kg bw/day) in food for PR 170. PR 23 has been tested in a chronic feeding study in rats and mice (NTP 1992). The short-term and sub-chronic stages of this study indicated haemolysis and liver weight increases at a dietary concentration of 50 000 ppm in rats (equivalent to 2500 mg/kg-bw per day).

In a 17 day and 13 week feeding study of mice and rats, it was reported that PR 23 at a dose of 2500 mg/kg bw/day reduced haematocrit values, haemoglobin concentration, and erythrocyte count in male rats (NTP, 1992; Government of Canada, 2016).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Overall, the data on PR 22 and the related chemical PR 23 indicate some potential for genotoxicity in vitro. No in vivo data are available. Based on the limited data available for genotoxicity, a conclusion on the genotoxicity of the chemicals cannot be made.

In a standard Ames assay PR 22 was positive in *Salmonella typhimurium* strains TA98, TA100, TA1537 and Escherichia coli WP2 uvrA, with and without metabolic activation. Negative results were seen in *S. typhimurium* TA1535 with and without metabolic activation and *E. coli* WP2 uvrA without metabolic activation.

In an in vitro study, there was no increase in chromosomal aberrations or polyploidy in Chinese hamster ovary cells exposed to PR 22 with or without metabolic activation.

The related chemical PR 23 was reported to be mutagenic in *S. typhimurium* TA100, TA1537, and TA98 with and without exogenous metabolic activation (S9), but it was not mutagenic in strain TA1535. The chemical induced sister chromatid exchanges in Chinese hamster ovary cells in the absence of S9, but not with S9 activation. The chemical was negative for the induction of chromosomal aberrations in Chinese hamster ovary cells with or without metabolic activation (NTP, 1992). Similar results were observed for 5-nitro-o-anisidine (NICNASf), which is not classified as a carcinogen, and would be released from reduction of the azo bond.

Negative results were obtained in a number of in vitro genotoxicity studies with the analogue Naphthol AS pigments, PR112, PR 170 and PR 268 (Government of Canada, 2016). This indicates that the positive results observed with PR 22 and PR 23 may be due to release of the aromatic amine.

Carcinogenicity

No data were identified for any Naphthol AS pigments that release any of the 22 aromatic amines that are known carcinogens.

Carcinogenicity data are available for the analogue PR23. In a two year feeding study in mice and rats there was equivocal evidence for renal tumours and tubule hyperplasia at a feed concentration of 50 000 ppm in rats (dose equivalent to 2 500 mg/kg-bw per day). However, this data cannot be used to draw conclusions for the chemicals in this group as the potential metabolite 5-nitro-o-anisidine has uncertain carcinogenic potential (NICNASf).

Reproductive and Developmental Toxicity

Limited data are available.

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening study (OECD TG 422), Sprague Dawley (SD) rats (n=12/sex at each dose) were dosed with PR 22 by gavage at 0, 100, 300 or 1000 mg/kg bw/day for 37 days in males and approximately 40 days in females. No effect was observed on developmental or reproductive parameters up to highest dose (1000 mg/kg bw/day) (Government of Canada, 2016).

Risk Characterisation

Critical Health Effects

The critical health effects are the potential for carcinogenicity based on exposure to known carcinogenic amines as impurities in the pigments and reduction of the azo bond.

Public Risk Characterisation

Cosmetics

Two of the chemicals in the group, PR 7 and PR 22, have reported use as colouring agents in cosmetics overseas. However, available data do not indicate widespread use of the chemicals in cosmetics. PR 7 is used products intended to come into contact only briefly with the skin and, as a pigment, the chemical is less likely subject to metabolism by skin bacteria than similar dyes. Therefore the risk to the public is not considered to be unreasonable. If data becomes available indicating use in cosmetic ingredients in Australia further evaluation of the risks would be required.

Tattoo and permanent make-up inks

Several of the chemicals are reported as being used in tattoo and permanent make-up inks with PR 17 and PR 22 identified in tattoo inks available in Australia. In vivo studies have shown that PR 22 breaks down under laser irradiation to produce aromatic amines, while in vitro studies have demonstrated that UVB and sunlight also degrades this pigment to produce aromatic amines. Similar degradation is expected for all the chemicals in this assessment. Considering the potential breakdown products, are known carcinogens, the chemicals may pose an unreasonable risks to consumers if used in tattoo inks and permanent make-up. There are proposed restrictions for several of the chemicals in tattoo overseas (see **Restrictions** section).

Textiles

The public could be also be exposed to classified carcinogenic aromatic amines as impurities, or through the release of these aromatic amines as breakdown products from the chemicals in this group through:

- prolonged exposure to articles of clothing and leather goods containing the pigments;
- young children exposed by sucking the materials containing the pigment; and
- exposure by dermal contact or incidental ingestion of printed cardboards, papers or foils.

An international assessment of the risk of cancer caused by textiles and leather goods coloured with certain azo dyes concluded that, while consumer exposure is likely to be 'very low', the associated cancer risks give cause for concern. Although this assessment was not publicly available, the European Scientific Committee on Toxicity, Ecotoxicity and Environment (CSTEE) considers that the report adequately reviews the situation regarding the risk of cancer for consumers from fabrics dyed with azo compounds, and that its conclusions are, in general, acceptable (CSTEE, 1999). The CSTEE also supported the recommendation that using azo dyes with the potential to give rise to the 22 aromatic amines classified as Category 1 or 2 carcinogens according to Directive 76/769/EEC, should be restricted to the lowest possible levels or completely eliminated. Although the carcinogenic amines are expected to be less bioavailable from the pigments compared with the dyes, data for two pigments indicate that they are sufficiently soluble to yield detectable amounts of a listed amine (see **Restrictions** section).

In considering the NICNAS recommendation for previously assessed azo dyes, the ACCC conducted a market survey to determine if any dyes of concern had been used in manufacturing consumer goods supplied in Australia. The ACCC has negotiated several recalls of products based on the results of the surveys. The ACCC tested for the concentration of aromatic amines that could be released from the chemicals in this group. This testing is considered appropriate for the chemicals in this group.

The Australian Competition and Consumer Commission (ACCC) has published safety guidance on concentrations of particular aromatic amines in clothing, textiles and leather articles in direct and prolonged contact with the human skin or oral cavity (ACCC, 2014). The guidance includes limits for aromatic amines, including those released by the chemicals in this assessment, in textile and leather articles (see **Restrictions** section).

It is noted that the test methods to determine release of carcinogenic amines at above permitted levels would also be expected to give positive results for the pigments in this group and thus it is not likely these pigments are used in textiles claiming to meet EU requirements.

Occupational Risk Characterisation

During product formulation, dermal, ocular and inhalation 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 uncertainty in health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise dermal and inhalation exposure are implemented.

NICNAS Recommendation

Further evaluation of investigate the risk of the use of these pigments in tattoos should be undertaken.

Formulators and importers of tattoo inks should consider substituting alternative products for items that contain the chemicals.

Regulatory Control

Public Health

The need for further regulatory control for public health will be determined as part of any further evaluation of these chemicals.

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, ocular and inhalation 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

The Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers (ETAD) Information Notice No 6 (rev. 2008) https://etad.com/en/publications.html

[NTP] National Toxicology Program (US). 1992. Toxicology and Carcinogenesis Studies of C.I. Pigment Red 23 (CAS No.6471-49-4) in F344 Rats and B6C3F1 Mice (Feed Studies). Research Triangle Park (NC): US Department of Health and Human Services, National Toxicology Program. Technical Report Series No. 411. Available at: http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr411.pdf

Australian Competition and Consumer Commission (ACCC), 2014. Safety guidance on concentrations of particular chemicals in certain consumer goods, Oct 2014. Accessed October 2019 at https://www.productsafety.gov.au/publication/safety-guidance-on-concentrations-of-particular-chemicals-in-certain-consumer-goods

Colour Index Online. Accessed October 2019 at http://colour-index.com/

Commission of the European Communities, 1988. Reports of the Scientific Committee on Cosmetology(seventh series). Accessed November 2019 at http://aei.pitt.edu

Cosmetic Ingredients& Substances (CosIng) Database. European Commission. Accessed November 2019 at http://ec.europa.eu/consumers/cosmetics/cosing/

Council of Europe 2008. Resolution ResAP(2008)1 on requirements and criteria for the safety of tattoos and permanent makeup (superseding Resolution ResAP(2003)2 on tattoos and permanent make-up. Adopted by the Committee of Ministers on 20 February 2008 at the 1018th meeting of the Ministers' Deputies. Accessed November 2019 at https://search.coe.int/cm/Pages/result_details.aspx?ObjectID=09000016805d3dc4.

El Dareer SM, Tillery KF, Hill DL 1984. Investigations of the disposition of oral doses of some water-insoluble pigments. Bulletin of Environmental Contamination and Toxicology 32(1) pp. 171-174

Engel E, Spannberger A, Vasold R, König B, Landthaler M, Bäumler W. Photochemical cleavage of a tattoo pigment by UVB radiation or natural sunlight. J Dtsch Dermatol Ges. (2007) 5(7): 583-589

Engel E, Vasold R, Santarelli F, Maisch T, Gopee NV, Howard PC, Landthaler M, Bäumler W. Tattooing of skin results in transportation and light-induced decomposition of tattoo pigments – a first quantification in vivo using a mouse model.

29/06/2020

Experimental Dermatology. (2010) 19: 54-60

European Chemicals Agency (ECHA). Annex XV Restriction report. Substances in tattoo inks and permanentmake up. Accessed November 2019 at https://echa.europa.eu/documents/10162/49ca957f-86ca-5eda-1aed-

European Chemicals Agency (ECHA). Background document. Substances in tattoo inks and permanent make up. Accessed November 2019 at https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e180dff62a

European Commission 2006. Regulation (EC) No 1907/2006 of the European Parliament and of the Council (REACH). Accessed November 2014 at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do? uri=CONSLEG:2006R1907:20090627:EN:PDF

European Scientific Committee on Toxicity, Ecotoxicity and Environment (CSTEE) Opinion on Risk of cancer caused by textiles and leather goods coloured with azo-dyes (1999). Accessed October 2019 at http://ec.europa.eu/health/scientific_committees/environmental_risks/opinions/sctee/sct_out27_en.htm

Galleria Chemica. Accessed November 2019 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

Government of Canada (2016). Screening Assessment for Aromatic Azo and Benzidine-based Substance Grouping Certain Monoazo Pigments. Accessed November 2019 at http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=9C4DA306-1

Herbst W, Hunger K, Wilker G, Ohleier H, Winter R 2005. 'Azo Pigments' in Herbst W, Hunger K, Wilker G, Ohleier H, Winter(eds) Industrial Organic Pigments: Production, Properties, Applications. Wiley. Third Edition, pp183-419

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2018). Characterisation of tattoo inks used in Australia. Australian Government Department of Health. Accessed November 2019 at https://www.nicnas.gov.au/chemical-information/Topics-of-interest2/subjects/tattoo-inks-used-in-Australia/Characterisation-of-tattoo-inks-used-in-Australia

National Industrial Chemicals Notification and Assessment Scheme (NICNASa). Tier I Human Health Assessments. Accessed November 2019 at https://www.nicnas.gov.au

National Industrial Chemicals Notification and Assessment Scheme (NICNASb). Human health Tier II assessment for benzenamine, 2-methyl- (CAS No. 95-53-4). Australian Government Department of Health. Accessed November 2019 at https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessment-details?assessment_id=1158

National Industrial Chemicals Notification and Assessment Scheme (NICNASc). Human health Tier II assessment for 1,3benzenediamine, 4-methyl- (CAS No. 95-80-7). Australian Government Department of Health. Accessed November 2019 at https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessment-details?assessment_id=831

National Industrial Chemicals Notification and Assessment Scheme (NICNASd). Human health Tier II assessment for benzenamine, 2-methyl-5-nitro- (CAS No. 99-55-8). Australian Government Department of Health. Accessed November 2019 at https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessment-details?assessment_id=1354

National Industrial Chemicals Notification and Assessment Scheme (NICNASe). Human health Tier II assessment for benzenamine, 4-chloro-2-methyl- and its hydrochloride. Australian Government Department of Health. Accessed November 2019 at https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessment-details? assessment_id=1098

National Industrial Chemicals Notification and Assessment Scheme (NICNASf). Inventory Multi-tiered Assessment and Prioritisation (IMAP) Human Health Tier II Assessment for 5-Nitro-ortho-anisidine and its hydrochloride. Australian Government Department of Health. Accessed November 2019 at https://www.nicnas.gov.au

Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary. Accessed November 2019 at http://www.ctfa-gov.org/jsp/gov/GovHomePage.jsp

Piccinini P, Contor L, Pakalin S, Raemaekers T, Senaldi C (2015a). Safety of tattoos and permanent make-up: State of play and trends in tattoo practices. JRC Technical Report.

29/06/2020

IMAP Group Assessment Report

Piccinini P, Contor L, Pakalin S, Raemaekers T, Senaldi C (2015b). Safety of tattoos and permanent make-up. Compilation of information on legislative legislative framework and analytical methods, JRC Technical Report

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACHa) Dossier. 3-hydroxy-N-(o-tolyl)-4-[(2,4,5-trichlorophenyl)azo]naphthalene-2-carboxamide (CAS No. 6535-46-2). Accessed November 2019 at https://echa.europa.eu

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACHb) Dossier. 3-hydroxy-4-[(2-methoxy-5nitrophenyl)azo]-N-(3-nitrophenyl)naphthalene-2-carboxamide (CAS No. 6471-49-4). Accessed November 2019 at https://echa.europa.eu

Safe Work Australia. Hazardous Chemical Information System (HCIS). Accessed November 2019 at http://hcis.safeworkaustralia.gov.au/

Sauer U.G. and Kreiling R. The Grouping and Assessment Strategy for Organic Pigments (GRAPE): Scientific evidence to facilitate regulatory decision-making, Regulatory Toxicology and PharmacologyVolume 109, December 2019, 104501.

Serup et al. (2019) Identification of pigments related to allergic tattoo reactions in 104 human skin biopsies. Contact Dermatitis. First published: 18 October 2019.

The Poisons Standard October 2019. The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) No. 25. Accessed November 2019 at https://www.tga.gov.au/publication/poisons-standard-susmp

Last Update 12 December 2019

Chemical Identities

Chemical Name in the Inventory and Synonyms	2-Naphthalenecarboxamide, N-(4-chloro-2-methylphenyl)-3-hydroxy-4- [(2-methylphenyl)azo]-
CAS Number	21839-86-1
Structural Formula	

9/06/2020	IMAP Group Assessment Report
Molecular Formula	C25H20CIN3O2
Molecular Weight	429.90

Chemical Name in the Inventory and Synonyms	2-Naphthalenecarboxamide, 3-hydroxy-4-[(2-methyl-5-nitrophenyl)azo]- N-(3-nitrophenyl)- 3-hydroxy-4-((2-methyl-5-nitrophenyl)azo)-N-(3-nitrophenyl)naphthalene-2- carboxamide C.I. Pigment Red 114 C.I. 12351
CAS Number	6358-47-0
Structural Formula	

29/06/2020	IMAP Group Assessment Report
	H_3C NO_2 H_3C N N H_1 H_2 H_1 H_2
Molecular Formula	C24H17N5O6
Molecular Weight	471.42

Chemical Name in the Inventory and Synonyms	2-Naphthalenecarboxamide, N-(4-chlorophenyl)-3-hydroxy-4-[(2- methyl-5-nitrophenyl)azo]- C.I. Pigment Red 8 N-(4-chlorophenyl)-3-hydroxy-4-((2-methyl-5-nitrophenyl)azo)naphthalene-2- carboxamide C.I. 12335
CAS Number	6410-30-6
Structural Formula	

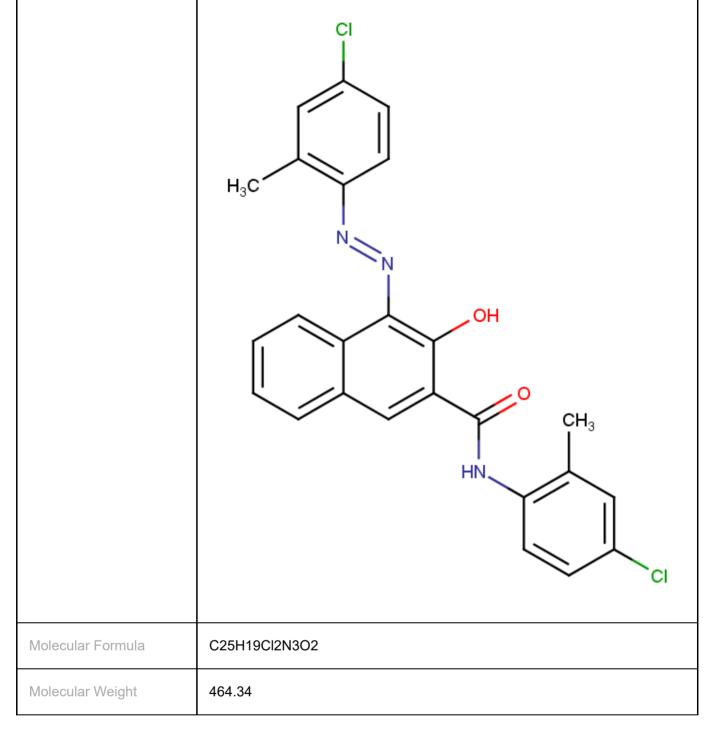
29/06/2020	IMAP Group Assessment Report
Molecular Formula	C24H17CIN4O4
Molecular Weight	460.87

Chemical Name in the Inventory and Synonyms	2-Naphthalenecarboxamide, 3-hydroxy-4-[(2-methyl-5-nitrophenyl)azo]- N-phenyl- 3-hydroxy-4-((5-nitro-o-tolyl)azo)-2-naphthanilide 3-hydroxy-4-((2-methyl-5-nitrophenyl)azo)-N-phenylnaphthalene-2- carboxamide C.I. Pigment Red 22 C.I. 12315 Aka404
CAS Number	6448-95-9
Structural Formula	

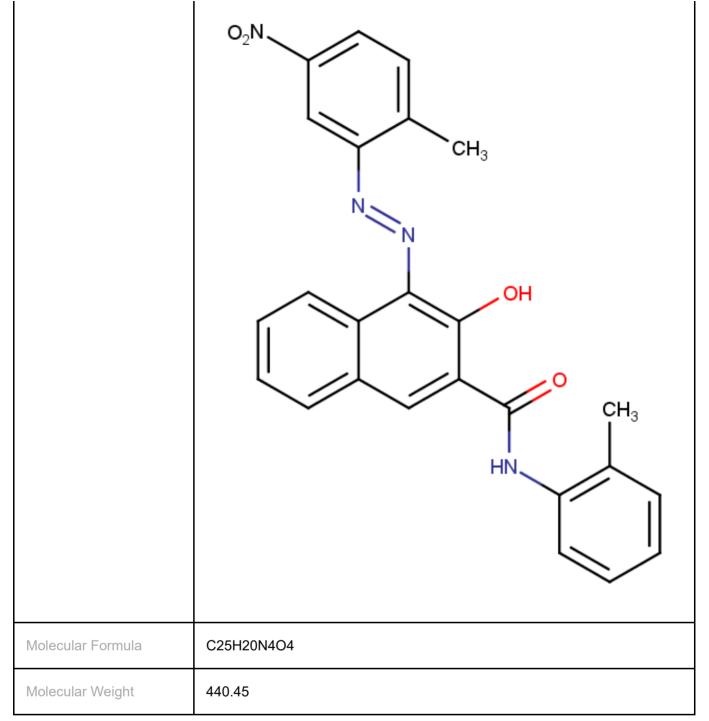
29/06/2020	IMAP Group Assessment Report
Molecular Formula	C24H18N4O4
Molecular Weight	426.43

Chemical Name in the Inventory and Synonyms	2-Naphthalenecarboxamide, N-(4-chloro-2-methylphenyl)-4-[(4-chloro- 2-methylphenyl)azo]-3-hydroxy- C.I. 12420 C.I. Pigment Red 7
CAS Number	6471-51-8
Structural Formula	

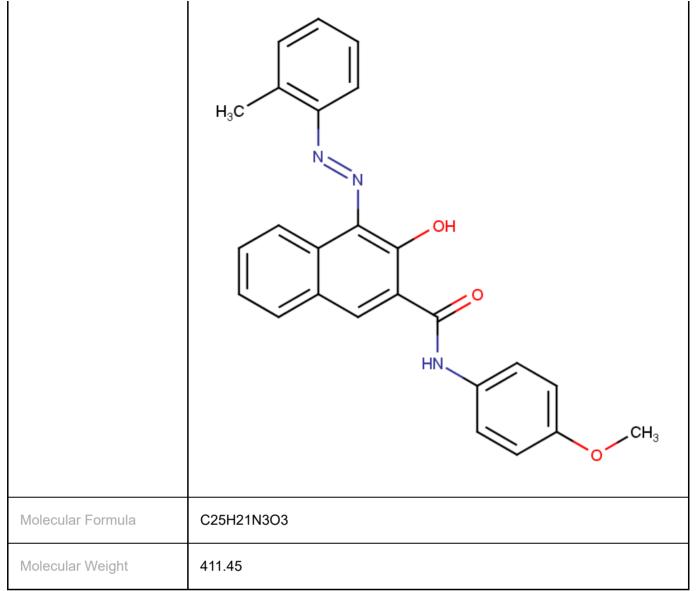




Chemical Name in the Inventory and Synonyms	2-Naphthalenecarboxamide, 3-hydroxy-4-[(2-methyl-5-nitrophenyl)azo]- N-(2-methylphenyl)- C.I. Pigment Red 17 C.I. 12390
CAS Number	6655-84-1
Structural Formula	



Chemical Name in the Inventory and Synonyms	2-Naphthalenecarboxamide, 3-hydroxy-N-(4-methoxyphenyl)-4-[(2- methylphenyl)azo]-
CAS Number	104513-13-5
Structural Formula	



Share this page