N-substituted anthraquinone-based dyes with limited data availability: Human health tier II assessment

03 July 2015

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Benzenesulfonamide, N-(4-amino-9,10-dihydro-3-methoxy-9,10-dioxo-1-anthracenyl)-4-methyl-	81-68-5
Benzenesulfonic acid, 3,3'-[(9,10-dihydro-9,10-dioxo-1,4-anthracenediyl)diimino]bis[2,4,6-trimethyl-, disodium salt	4474-24-2
2-Anthracenesulfonic acid, 4,4'-[(1-methylethylidene)bis(4,1-phenyleneimino)]bis[1-amino-9,10-dihydro-9,10-dioxo-, disodium salt	6471-01-8
1-Propanaminium, 3-[[4-[(2,4-dimethylphenyl)amino]-9,10-dihydro-9,10-dioxo-1-anthracenyl]amino]-N,N,N-trimethyl-, methyl sulfate	60352-98-9
Benzenesulfonic acid, [(9,10-dihydro-9,10-dioxo-1,4-anthracenediyl)bis(imino-4,1-phenyleneoxy)]bis-, disodium salt	70161-19-2
Benzenesulfonic acid, 2,2'-[(9,10-dihydro-5,8-dihydroxy-9,10-dioxo-1,4-anthracenediyl)diimino]bis[5-(1,1-dimethylethyl)-, disodium salt	83006-67-1

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 critical health concern for the chemicals in this group is the potential for carcinogenic effects following exposure.

All the chemicals in this group are diversely functionalised anthraquinones containing an anthracene-9,10- dione—an anthracene derivative with two ketone groups attached to the central benzene ring. The chemicals in this group could contain one or more functional groups that differ for each chemical, although all include amine substituents which are further N-substituted. These chemicals have similar physical–chemical properties and have similar uses. However, due to the range of

functional groups present in the chemicals being assessed, they are not considered to be toxicologically similar for local toxicity effects, including sensitisation.

Toxicological data for the chemicals in this group are limited. For such chemicals, NICNAS will commonly use the principles of 'read across' in accordance with the Organisation for Economic Co-operation and Development (OECD) Guidance on grouping of chemicals (OECD, 2014) based on known properties of similar chemicals (analogues). The quality of the data used depends on the similarity of the analogues to the chemicals.

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified.

International

The following international uses have been identified through:

- the European Union (EU) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) dossier;
- the Substances and Preparations in Nordic countries (SPIN) database;
- 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
- and other international assessments (Government of Canada, 2009a; Government of Canada, 2009b; Government of Canada, 2009c; Government of Canada, 2009d; Government of Canada, 2009e; Government of Canada, 2009f).

The chemical CAS No. 4474-24-2 has reported cosmetic use as a colourant.

The chemicals, CAS No. 4474-24-2 and CAS No. 70161-19-2, have reported domestic use in dishwashing liquid and tablets, carpet cleaners, and in stain removers.

The chemicals, CAS No. 81-68-5; CAS 6471-01-8; and CAS No. 70161-19-2, have reported domestic use as colourants in soaps and cleaning products.

The chemical, CAS No. 70161-19-2 has reported use as a textile dye.

The chemical CAS No. 83006-67-1 has reported use in the pigment/dye/ink industry sectors.

Restrictions

Australian

No known restrictions have been identified.

International

No known restrictions have been identified.

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

Based on a review of publicly available hazard information in accordance with the Inventory Multi-Tiered Assessment and Prioritisation (IMAP) Framework (NICNAS, 2013), a lack of empirical toxicokinetics and toxicological data were identified for all of the chemicals in this group. Hence, read across information from the following structurally-related chemicals will be considered in the current assessment:

- CAS No. 84-65-1 (anthraquinone) (NICNASa);
- CAS No. 2475-45-8 (C.I. Disperse Blue 1) (NICNASb);
- CAS No. 117-10-2 (Danthron) (NICNASc);
- CAS No. 81-49-2 (ADBAQ) (NICNASd); and
- CAS No. 114565-66-1 (NICNASe).

Based on the critical health effects of these chemicals, the focus of this assessment is carcinogenicity.

Toxicokinetics

Anthraquinones can enter the body via oral, dermal and inhalation routes. These compounds are generally lipophobic and hydrophobic (Jaskot & Costa, 1994). Although data for absorption, distribution, and metabolism for these chemicals are limited, anthraquinones can transform metabolically via one or two electron reductions facilitated by flavoenzymes in the presence of suitable electron donors (Bolton et al., 2000). Anthraquinones can undergo one-electron reduction by oxidoreductases (NADPH-cytochrome P450, NADH dehydrogenase, or xanthine oxidase) to produce semi-quinone free radicals. Upon auto-oxidation, these free radicals can produce cytotoxic reactive oxygen species (Doi et al., 2005). Ring hydroxylation could also occur as observed in the parent compound 9,10-anthracenedione (anthraquinone; CAS No. 84-65-1) (NICNASa). However, this metabolic process could be potentially sterically hindered (Doi et al. 2005).

Based on the read across information from amine-substituted anthraquinones (C.I. Disperse Blue 1 and ADBAQ), the chemicals in this group are likely to undergo metabolism similarly to aromatic amines. Metabolically, aromatic amines undergo ring oxidation, N-glucuronidation, N-acetylation, and N-oxidation (SCCNFP, 2002). The toxicity of these chemicals is largely influenced by N-oxidation, a process primarily mediated by cytochrome P450 enzymes, such as CYP1A2 and CYP3A4,

although other enzymes could also play a role. The resulting metabolic products are demonstrated to be highly reactive and are capable of DNA binding. However, the variable N-substitution in the chemicals in this group may have a range of effects on these metabolic routes.

Metabolically, the halogen- and nitro-bearing anthraquinones can undergo reductive dehalogenation and nitroreduction. Additionally, planar anthraquinones have been reported to be aryl hydrocarbon receptor (AhR) agonists (Amakura et al., 2014).

Doi et al. (2005) reported that the metabolism, toxicity and the target organs, especially for carcinogenicity associated with anthraquinones, are determined by the functional groups of the chemicals. The amino and methyl functional groups are ortho and para directors. The amino groups are considered strong activators, while the methyl groups are weak activators. Hence, an anthraquinone containing both functional groups is likely to be more reactive because of the ensuing additive effects (Doi et al., 2005). The order of mutagenicity of the functionalised anthraquinones has been reported to be NO2> OH>NH2 (Brown & Brown, 1976). Based on the data from all analogues, the target organs for toxicity can include the liver, kidney and urinary bladder, forestomach, intestines, and lungs (Doi et., 2005; NICNASa; NICNASb, NICNASd).

Sensitisation

Skin Sensitisation

Data are limited for the chemicals in this group.

The skin sensitisation potential for the chemical CAS No. 81-68-5 was investigated in an OECD Test Guideline (TG 406)-compliant study in Pirbright White guinea pigs. Intradermal and epicutaneous routes are used for induction exposure and the epicutaneous (occlusive) route was used for challenge exposure. During the induction phase, the animals were injected intradermally with 5 % or epicutaneously with 50 % of the chemical. During the challenge phase, the animals were exposed to 50 % of the chemical (REACH). Under these experimental conditions, the chemical did not induce skin sensitisation (REACH).

However, the parent anthraquinone and the structurally related chemical C.I. Disperse Blue 1 (see **Health hazard information** section), are skin sensitisers (NICNASa; NICNASb).

Genotoxicity

Based on the limited data available, it is not possible to draw a definite conclusion about the genotoxicity of the chemicals in this group. The metabolic reactions identified above are consistent with the mutagenic action of a range of aromatic amines. The data on the other anthraquinone derivatives assessed under IMAP are also ambivalent, without any clear evidence of genotoxicity. Although available data are neither sufficient nor adequately comprehensive for classification, a genotoxic mode of action cannot be ruled out for any of the chemicals in this group.

In an in vitro bacterial reverse mutation assay (OECD TG 471-compliant), the chemical CAS No. 81-68-5 gave a marginal or weak mutagenic response in *Salmonella typhimurium* strains TA 1537 and TA 98 with or without metabolic activation (REACH). The chemical, CAS No. 70161-19-2 also showed mutagenic response in vitro in micronucleus assay and in single cell gel/comet assay in normal human epidermal keratinocytes (NHEK) (Wollin & Gorlitz, 2003).

Several of the anthraquinone compounds are suggested to be mutagenic by three different mechanisms: direct frameshift mutations by certain derivatives bearing free hydroxyl groups; frameshift mutagenesis by certain derivatives with primary (and in a few cases, secondary) amine groups (potentiated by microsomal activation); and anthraquinones with one or more nitro groups showed least specificity with regard to *S. typhimurium* tester strains and to microsomal activation (all nitro-bearing anthraquinones tested were mutagenic) (Brown & Brown, 1976).

Limited data are available for the in vivo genotoxicity of the chemicals in this group.

Carcinogenicity

No data are available for the carcinogenic potential of the chemicals in this group. However, the structurally-related compounds, the parent anthraquinone and the substituted forms, C.I. Disperse Blue 1, Danthron, ADBAQ and CAS No. 114565-66-1 are carcinogens (NICNASa; NICNASb; NICNASc; NICNASd; NICNASe).

It has been suggested that functional group substitution of anthraquinones can influence both the toxicity and the target organs, especially for carcinogenicity (Doi et al., 2005; NICNASa; NICNASb; NICNASc; NICNASd). The target organs for carcinogenicity appear to differ for each functional group(s) as follows:

- liver, kidney and urinary bladder—parent anthraquinone (CAS No. 84-65-1);
- liver, and urinary bladder—amino group (NH_2);
- liver and kidney—methyl + amino groups (CH_3, NH_2);
- liver, kidney, urinary bladder, and intestines—amino + halogen groups (dibromo) (NH_2, Br);
- liver—nitro group (NO_2); and
- liver, urinary bladder, and intestine—hydroxyl group (OH).

In addition, anthraquinones have the potential to promote tumour induction in rodents. This was demonstrated by the increased incidence and multiplicity of colon and liver adenomas in mice following oral co-exposure to both a substituted anthraquinone (e.g. CAS No. 117-10-2) and a tumour initiator, the 1,2-dimethylhydrazine (DMH) (NICNASc).

There are no epidemiological studies available to demonstrate a direct association between exposure to anthraquinone dyes and human cancer. However, in two cohort studies, significant increases of oesophageal and prostate cancer were reported in workers in a Scottish dyestuff plant, and statistically significant risks were reported for lung and central nervous system cancers in workers in a New Jersey manufacturing plant that produced anthraquinone dyes and their intermediates, azo dyes and epichlorohydrin (NICNASd). However, these studies had a number of limitations including the small study size, the lack of exposure measurements and exposure to multiple chemicals (NICNASa; NICNASd). Therefore, no conclusion could be drawn from these studies as to their carcinogenicity.

Although the mechanism of action for the long-term systemic toxicity of the chemicals in this group (carcinogenicity) remains unclear, anthraquinones can interact directly with DNA via intercalation due to the size and planarity of the rings (Simi et al., 1995; ECHA, 2015). DNA intercalation has been suggested to be one of the mechanisms responsible for the toxicity of anthraquinones (Simi et al., 1995). However, these N-substituted anthraquinones are generally expected to be less planar than simple substituted anthraquinones, reducing the importance of this mechanism.

Quinones are highly redox active molecules capable of mediating formation of oxygen radicals via redox cycling, which results in lipid peroxidation, DNA damage and oxidation of protein thiols (Wolfe et al., 1990). In one study, a substituted anthraquinone (CAS No. 81-49-2; ADBAQ) was highly toxic following irradiation with visible and simulated solar light sources in *Daphnia magna*. The observed photosensitisation response is likely to be associated with the formation of highly reactive free radicals such as superoxide anion and singlet oxygen species, which could ultimately cause tissue damage. Levels of the reactive oxygen species were reduced after treatment with anti-oxidants such as vitamins C and E and beta-carotene (NICNASd). This suggests that oxidative DNA damage is likely to play a role in the toxicity of the chemicals in the group.

Additionally, the enzyme-mediated formation of active metabolites and the impurities produced during synthesis of anthraquinones could also play a role in the carcinogenity of the chemicals (Doi et al., 2005; ECHA, 2015). A genotoxic mode of action cannot be ruled out.

Considering the data obtained from the parent anthraquinone and the substituted anthraquinones (C.I. Disperse Blue 1, Danthron, ADBAQ and CAS No. 114565-66-1), the chemicals in this group potentially have carcinogenic properties.

Risk Characterisation

Critical Health Effects

Based on the limited data available, the chemicals have been identified as having the potential to cause a systemic long-term effect (carcinogenicity). Whilst the mechanism of action for the carcinogenicity of the anthraquinones is still unclear, a genotoxic mode of action cannot be ruled out. Other health hazards have not been considered in this assessment.

Public Risk Characterisation

Cosmetic and domestic

The chemical, CAS No. 4474-24-2, has been identified as having potential cosmetic use. The public could be exposed to the chemicals in this group if they are used in cosmetic products in Australia. The extent of current usage is unknown.

There is uncertainty regarding the safety of these chemicals in cosmetic and domestic products; therefore, a Tier III assessment, including consultation with industry to determine the extent of use and the availability of further sensitisation and carcinogenicity data, is recommended (see **NICNAS Recommendation**). In the absence of additional information, a conservative assessment based on Quantitative Structure Activity Relationship (QSAR) and inference from analogue information could be undertaken and relevant recommendations made.

Based on the results of the screening assessments, the Government of Canada has determined that the chemicals CAS No. 81-68-5, CAS No. 4474-24-2, CAS No. 6471-01-8, and CAS No. 60352-98-9 do not cause harm. However, for CAS No. 70161-1-2 and CAS No. 83006-67-1, the Government of Canada has implemented a Significant New Activity (SNAc) provision since the chemicals could have the potential to cause harm. Under the SNAc provision, any proposed new uses of the chemicals would be subject to further assessment or reassessment before new activities would be allowed (Government of Canada, 2009a; Government of Canada, 2009b; Government of Canada, 2009c; Government of Canada, 2009d; Government of Canada, 2009e; Government of Canada, 2009f).

Occupational Risk Characterisation

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

Overall, there is uncertainty regarding the hazards of these chemicals in the workplace; therefore, a Tier III assessment is required (see **NICNAS Recommendation**) to determine the appropriate occupational controls.

NICNAS Recommendation

The chemicals in this group are recommended for Tier III assessment to determine whether:

- risk management controls for domestic and cosmetic use are required;
- there are uses of the chemicals in Australia; and
- toxicological information is available that is not accessible in the publicly-available literature, to better characterise the hazards of the chemicals.

Regulatory Control

Advice for industry

Control measures

Control measures to minimise the risk from dermal 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 chemical is used. Examples of control measures which could minimise the risk include, but are not limited to:

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

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

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

Obligations under workplace health and safety legislation

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

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

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

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

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

References

Amakura Y, Yoshimura M, Takaoka M, Toda H, Tsutsumi T, Matsuda R, Teshima R, Nakamura M, Handa H, Yoshida T 2014. Characterization of natural aryl hydrocarbon receptor agonists from cassia seed and rosemary. Molecules 19(4) pp. 4956-4966.

Bolton JL, Trush MA, Penning TM, Dryhurst G, Monks TJ 2000. Role of quinones in toxicology. Chemical Research in Toxicology 13(3) pp. 135-160.

Brown JP and Brown RJ 1976. Mutagenesis by 9,10-anthraquinone derivatives and related compounds in Salmonella typhimurium. Mutation Research 40(3) pp. 203-224.

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

Doi AM, Irwin RD, Bucher JR 2005. Influence of functional group substitutions on the carcinogenicity of anthraquinone in rats and mice: analysis of long-term bioassays by the National Cancer Institute and the National Toxicology Program. Journal of Environmental Health, Part B Critical Reviews 8 (2) pp. 109-126.

ECHA 2015. CLH Report Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2. Substance name: anthraquinone (CAS No. 84-65-1). Accessed February 2015 at **http://www.echa.europa.eu/documents/10162/13626/clh_proposal_anthraquinone_en.pdf**

European Commission Cosmetic Ingredients and Substances (CosIng) Database. Accessed May 2015 at **http://ec.europa.eu/consumers/cosmetics/cosing/**

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

Government of Canada 2009a. Batch 3 Challenge Substances. Benzenesulfonamide, N-(4-amino-9,10-dihydro-3-methoxy-9,10-dioxo-1-anthracenyl)-4-methyl- (Disperse Red 86). Accessed October May 2015 at **http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/batch-lot-3/index-eng.php**

Government of Canada 2009b. Batch 2 Challenge Substances. Benzenesulfonic acid, 3,3'-[(9,10-dihydro-9,10-dioxo- 1,4-anthracenediyl)diimino]bis[2,4,6-trimethyl-, disodium salt (Acid Blue 80). Accessed October May 2015 at **http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/summary-sommaire/batch-lot-2/4474-24-2-eng.php**

Government of Canada 2009c. Batch 3 Challenge Substances. 2-Anthracenesulfonic acid, 4,4'-[(1-methylethylidene)bis(4,1-phenyleneimino)]bis[1-amino-9,10-dihydro-9,10-dioxo-, disodium salt (Acid Blue 127). Accessed October May 2015 at **http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/summary-sommaire/batch-lot-3/6471-01-8-eng.php**

Government of Canada 2009d. Batch 3 Challenge Substances. 1-Propanaminium, 3-[[4-[(2,4-dimethylphenyl)amino]-9,10-dihydro-9,10-dioxo-1-anthracenyl]amino]-N,N,N-trimethyl-, methylsulfate (PDDAM). Accessed October May 2015 at **http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/summary-sommaire/batch-lot-3/60352-98-9-eng.php**

Government of Canada 2009e. Batch 2 Challenge Substances. Benzenesulfonic acid, [(9,10-dihydro-9,10-dioxo-1,4-anthracenediyl) bis(imino-4,1-phenyleneoxy)]bis-, disodium salt (Acid Green 40:1). Accessed October May 2015 at **http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/summary-sommaire/batch-lot-2/70161-19-2-eng.php**

Government of Canada 2009f. Batch 2 Challenge Substances. Benzenesulfonic acid, 2,2'-[(9,10-dihydro-5,8-dihydroxy-9,10-dioxo-1,4-anthracenediyl)diimino]bis[5-(1,1-dimethylethyl)-, disodium salt (ADIBSS). Accessed October May 2015 at **http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/summary-sommaire/batch-lot-2/83006-67-1-eng.php**

Jaskot RH and Costa DL 1994. Toxicity of an anthraquinone violet dye mixture following inhalation exposure, intratracheal instillation, or gavage. Fundamental and Applied Toxicology 22(1) pp. 103-112.

Marrs TC, Colgrave HF, Cross NL, Edginton JAG, Morris BC 1988. Inhalation toxicity of a coloured smoke and the mutagenicity of its constituent dyes, solvent yellow 33 (CI 47,000) and disperse orange 11 (CI 60,700). Journal of Hazardous Materials 17 pp. 269-285.

National Cancer Institute (NCI) 1978. Bioassay of 1-amino-2-methylanthraquinone for possible carcinogenicity. Carcinogenesis Technical Report Series No.111 (NCI-CG-TR-111). U.S. Department of Health, Education, and Welfare. Accessed April 2015 at **http://www.ncbi.nlm.nih.gov/pubmed/12799680**

National Toxicology Program (NTP) 2002. NTP report on carcinogens background document for 1-amino-2,4-dibromoanthraquinone. Final. Accessed March 2015 at **http://ntp.niehs.nih.gov/ntp/newhomeroc/roc11/adbaqpub_no_appendices_508.pdf**

National Toxicology Program (NTP) Report on Carcinogens (RoC) 2014. Thirteenth Edition. 1-amino- 2,methylanthraquinone (CAS No. 82-28-0). Accessed March 2015 at **http://ntp.niehs.nih.gov/ntp/roc/content/profiles/aminomethylanthraquinone.pdf**

NICNAS 2013. Inventory Multi-tiered Assessment and Priorisation (IMAP) Factsheet 4: Leveraging international information. Accessed April 2015 at **http://www.nicnas.gov.au/chemical-information/imap-** assessments/imap-factsheets

NICNASa. Inventory Multi-tiered Assessment and Priorisation (IMAP): Human health Tier II assessment for 9,10-anthracenedione. Accessed May 2015 at **http://www.nicnas.gov.au**

NICNASb. Inventory Multi-tiered Assessment and Priorisation (IMAP): Human health Tier II assessment for 9,10-anthracenedione, 1,4,5,8-tetraamino-. Accessed May 2015 at **http://www.nicnas.gov.au**

NICNASc. Inventory Multi-tiered Assessment and Priorisation (IMAP): Human health Tier II assessment for 9,10-anthracenedione, 1,8-dihydroxy-. Accessed May 2015 at **http://www.nicnas.gov.au**

NICNASd. Inventory Multi-tiered Assessment and Priorisation (IMAP): Human health Tier II assessment for 9,10-anthracenedione, 1-amino-2,4-dibromo-. Accessed May 2015 at **http://www.nicnas.gov.au**

NICNASe. Inventory Multi-tiered Assessment and Priorisation (IMAP): Human health Tier II assessment for anthraquinone-based dyes with limited data availability. Accessed April 2015 at **http://www.nicnas.gov.au**

OECD (2014). Guidance on Grouping of Chemicals, Second Edition. Environment Directorate. Joint meeting of the Chemicals Committee and the Working party on Chemicals, Pesticides and Biotechnology. Series on Testing& Assessment No. 194. Accessed May l 2015 at **http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono(2014)4&doclanguage=en**

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

REACH Dossier (REACH). N-(4-amino-9,10-dihydro-3-methoxy-9,10-dioxo-1-anthryl)-4-methylbenzenesulphonamide (CAS No. 81-68-5). Accessed May 2015 at **http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances**

Safe Work Australia (SWA). Hazardous Substances Information system (HSIS). Accessed May 2015 at **http://hsis.safeworkaustralia.gov.au/HazardousSubstance**

Simi S, Morelli S, Gervasi PG, Rainaldi G 1995. Clastogenicity of anthraquinones in V79 and in three derived cell lines expressing P450 enzymes. Mutation Research 347(3-4) pp. 151-156.

SPIN (Substances in Preparations in Nordic Countries) Database. Available at **http://195.215.202.233/DotNetNuke/default.aspx**

The Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP) 2002. Opinion on the Safety Review of the Use of Certain Azo-Dyes in Cosmetics Products. SCCNFP/0495/01, final. Accessed April 2015 at **http://ec.europa.eu/health/archive/ph_risk/committees/sccp/documents/out155_en.pdf**

US Department of Health and Human Services, Household Products Database (HPD), health and safety information on household products. Accessed May 2015 at **http://householdproducts.nlm.nih.gov/**

US National Library of Medicine. Information on Hazardous Chemicals and Occupational Diseases. Haz-Map. Accessed March 2015 at **http://hazmap.nlm.nih.gov/index.php**

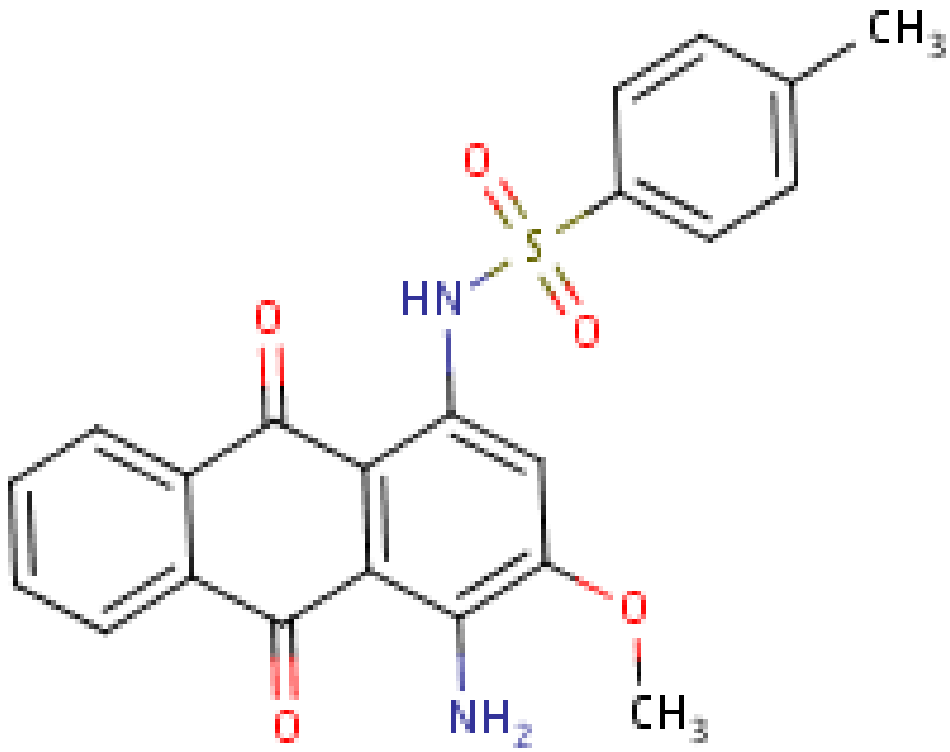
US National Library ofMedicine's Hazardous Substances Data Bank (HSDB). Accessed May 2015 at **http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB**

Wollin K, Gorlitz B 2003. Genotoxicity of textile dyestuffs in normal human epidermal keratinocytes and a three-dimensional reconstituted human epidermis model. Accessed May 2015 at **http://reconstructed-human-epidermis.com/resourcecenter/paperposter/**

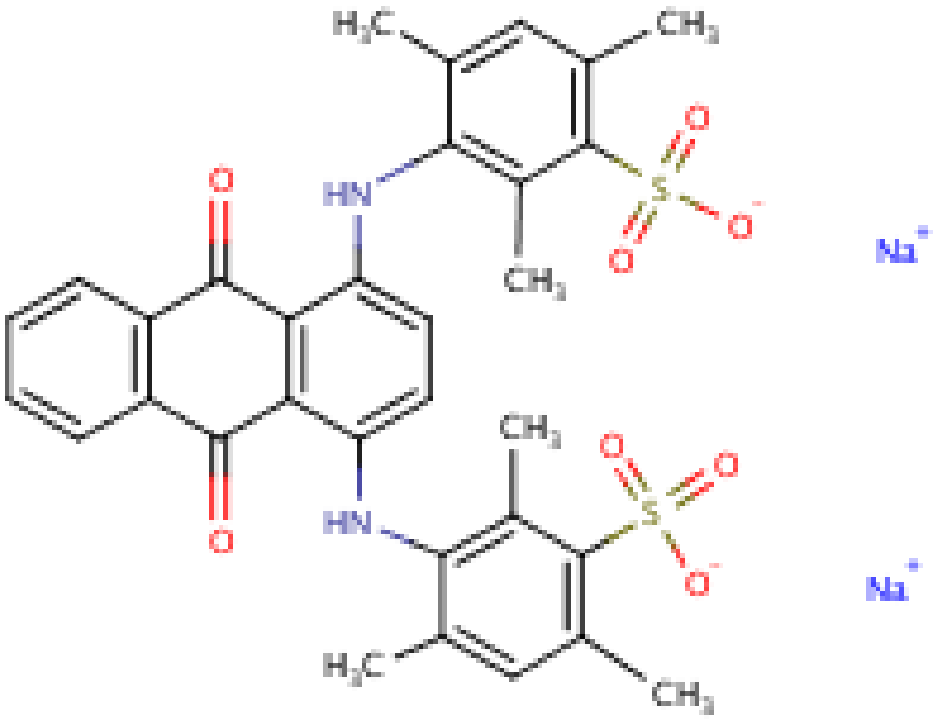
Last Update 03 July 2015

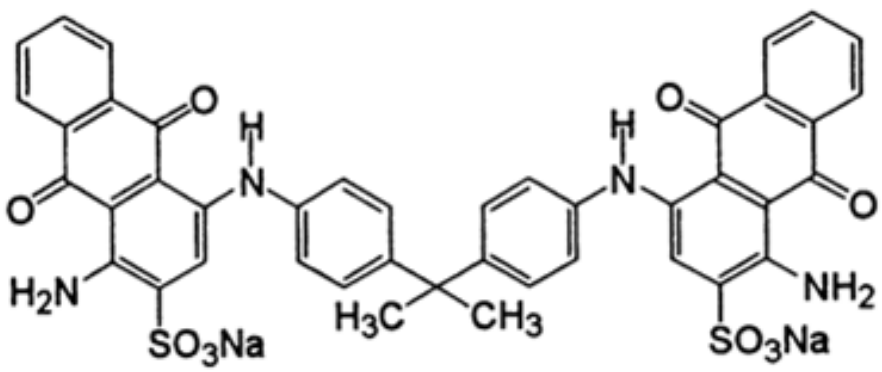
Chemical Identities

Chemical Name in the Inventory and Synonyms	**Benzenesulfonamide, N-(4-amino-9,10-dihydro-3-methoxy-9,10-dioxo-1-anthracenyl)-4-methyl-** C.I. Disperse Red 86 N-(4-amino-9,10-dihydro-3-methoxy-9,10-dioxo-1-anthryl)-4-methylbenzenesulphonamide p-toluenesulfonamide, N-(4-amino-3-methoxy-1-anthraquinonyl)-

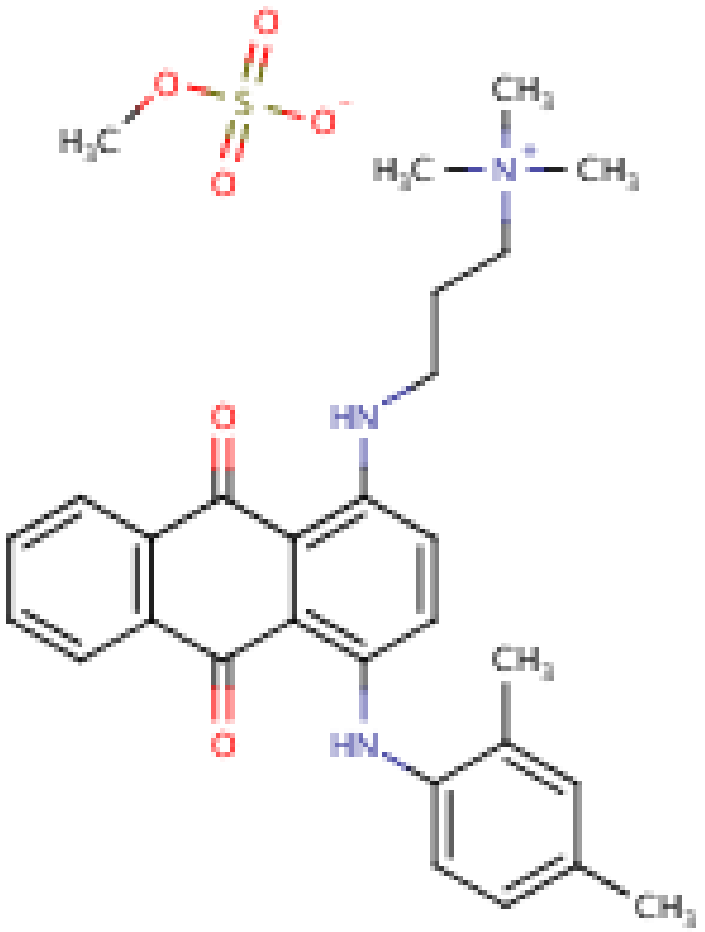
	Eastman Polyester Pink RL Terasil Brilliant Pink 2GL
CAS Number	81-68-5
Structural Formula	
Molecular Formula	C22H18N2O5S
Molecular Weight	422.459

Chemical Name in the Inventory and Synonyms	**Benzenesulfonic acid, 3,3'-[(9,10-dihydro-9,10-dioxo-1,4-anthracenediyl)diimino]bis[2,4,6-trimethyl-, disodium salt** C.I. Acid Blue 80 Alizarine Blue BL disodium 3,3'-((9,10-dihydro-9,10-dioxo-1,4-anthracenediyl)diimino)bis(2,4-,6-trimethylbenzenesulfonate) C.I. 61585 2-mesitylenesulfonic acid, 4,4'-(1,4-anthraquinonylenediimino)di-,disodium salt (8CI)
CAS Number	4474-24-2
Structural Formula	

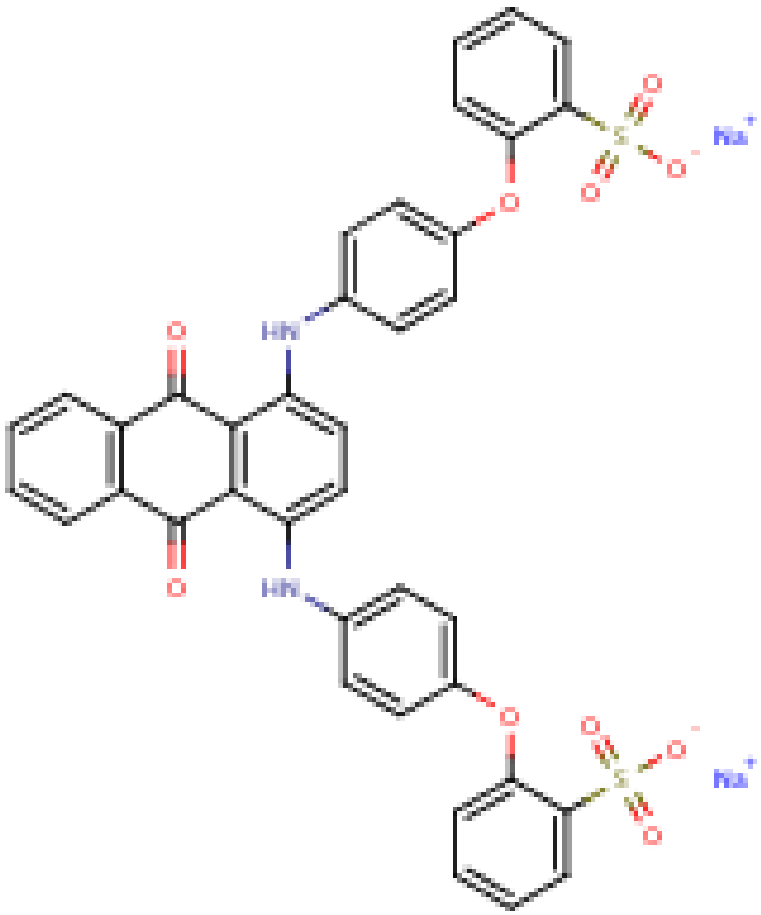
	
Molecular Formula	C32H30N2O8S2.2Na
Molecular Weight	678.69

Chemical Name in the Inventory and Synonyms	**2-Anthracenesulfonic acid, 4,4'-[(1-methylethylidene)bis(4,1-phenyleneimino)]bis[1-amino-9,10-dihydro-9,10-dioxo-, disodium salt** C.I. Acid Blue 127 disodium 4,4'-((1-methylethylidene)bis(4,1-phenyleneimino))bis(1-amino-9,10-dihydro-9,10-dioxoanthracene-2-sulphonate)
CAS Number	6471-01-8
Structural Formula	

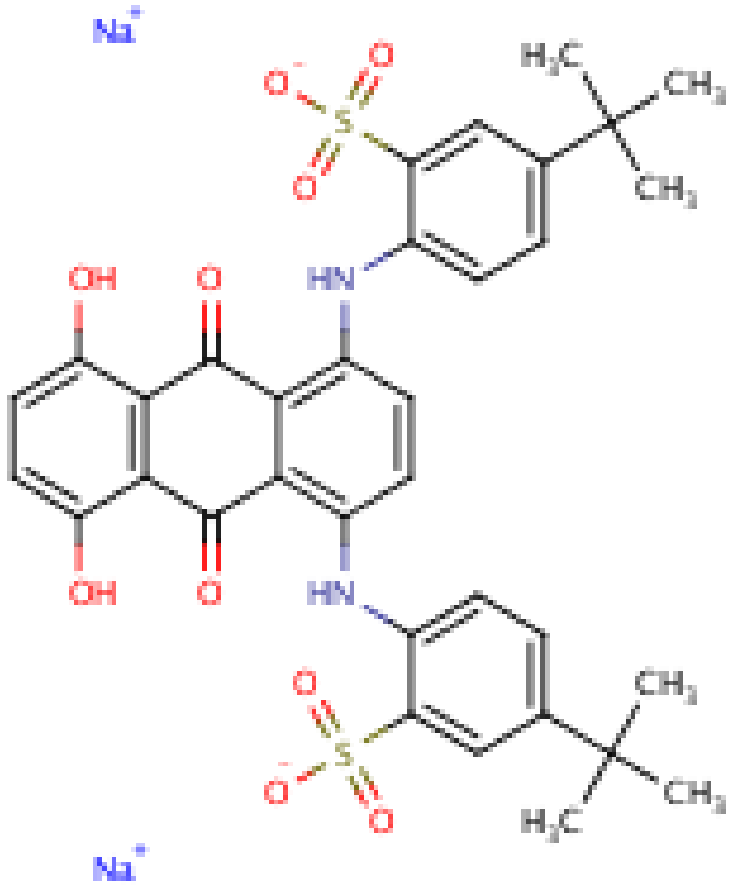
Molecular Formula	C43H32N4O10S2.2Na
Molecular Weight	392.47

Chemical Name in the Inventory and Synonyms	**1-Propanaminium, 3-[[4-[(2,4-dimethylphenyl)amino]-9,10-dihydro-9,10-dioxo-1-anthracenyl]amino]-N,N,N-trimethyl-, methyl sulfate** PDDAM (3-((4-((2,4-dimethylphenyl)amino)-9,10-dihydro-9,10-dioxo-1-anthryl)amino)propyl)trimethylammonium methyl sulphate
CAS Number	60352-98-9
Structural Formula	
Molecular Formula	C28H32N3O2.CH3O4S
Molecular Weight	553.68

Chemical Name in the Inventory and Synonyms	**Benzenesulfonic acid, [(9,10-dihydro-9,10-dioxo-1,4-anthracenediyl)bis(imino-4,1-phenyleneoxy)]bis-, disodium salt** disodium ((9,10-dihydro-9,10-dioxo-1,4-anthrylene)bis(imino-4,1-phenyleneoxy))bis(benzenesulphonate)

	Acid Green 40:1
CAS Number	70161-19-2
Structural Formula	
Molecular Formula	C38H26N2O10S2.2Na
Molecular Weight	778.72

Chemical Name in the Inventory and Synonyms	**Benzenesulfonic acid, 2,2'-[(9,10-dihydro-5,8-dihydroxy-9,10-dioxo-1,4-anthracenediyl)diimino]bis[5-(1,1-dimethylethyl)-, disodium salt** disodium 2,2'-((9,10-dihydro-5,8-dihydroxy-9,10-dioxo-1,4-anthrylene)diimino)bis(5-tert-butylbenzenesulphonate) ADIBSS
CAS Number	83006-67-1
Structural Formula	

	
Molecular Formula	C34H34N2O10S2.2Na
Molecular Weight	738.74

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