Australian Government
Department of Health, Disability and Ageing
Australian Industrial Chemicals Introduction Scheme

Azo dyes based on 5-nitro-2-thiazolamine and toluenediamine derivatives

Evaluation statement (EVA00166)

16 December 2025

Table of contents

Contents

AICIS evaluation statement (EVA00166)

Subject of the evaluation

Azo dyes based on 5-nitro-2-thiazolamine and toluenediamine derivatives

Chemicals in this evaluation

CAS name	CAS number
C.I. Disperse Blue 82	12222-80-9
Ethanol, 2-[ethyl[3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]phenyl]amino]-, 1-acetate	15141-18-1
Ethanol, 2-[ethyl[3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]phenyl]amino]-	68516-81-4
1,2-Propanediol, 3-[ethyl[3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]phenyl]amino]-	69766-79-6
Benzenamine, *N*,*N*-diethyl-3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]-	70693-64-0
Ethanol, 2,2′-[[3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]phenyl]imino]bis-	72987-42-9

Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health risk.

Parameters of evaluation

Chemicals in this group are all azo dyes based on 5-nitro-2-thiazolamine and toluenediamine derivatives that are listed on the Australian Inventory of Industrial Chemicals (the Inventory).

This evaluation statement includes a human health risk assessment for all identified industrial uses of these chemicals. These chemicals have been assessed as a group based on their similar structure, metabolic pathways, physicochemical properties, and use profiles.

Chemicals in this evaluation will be referred to under the following CAS identities as follows:

- Disperse Blue 82 (CAS No. 12222-80-9)
- Disperse Blue 124 (CAS No. 15141-18-1)
- Disperse Blue 106 (CAS No. 68516-81-4)
- Disperse Blue 102 (CAS No. 69766-79-6)
- Disperse Blue 360 (CAS No. 70693-64-0)
- Disperse Blue 96 (CAS No. 72987-42-9).

Summary of evaluation

Summary of introduction, use and end use

Based on Australian and international use information, these chemicals have end use as textile (fabric) dyes and printing inks. These chemicals can be applied directly to the article or by sublimation transfer printing. These chemicals may be applied to, or introduced into Australia in, paper articles, leather articles and fabric, textile and apparel articles. Product types that may contain disperse blue dyes are clothing, footwear, nappies, seatbelts, furniture or any other products made of synthetic fabrics or leather.

Use of these chemicals may be declining due to restrictions in some jurisdictions. However, the available data indicates most of these chemicals are still commercially active internationally. Any direct end use of these dyes is primarily expected to be commercial. Domestic use of the dyes is not expected to be widespread.

Human health

Summary of health hazards

Data are available for Disperse Blue 360, Disperse Blue 124 and Disperse Blue 106. Chemicals with data represent all the toxicologically relevant features of chemicals in this group and have similar physicochemical properties. Therefore, the available data has been used to draw conclusions on health hazards for chemicals without data.

Azo dyes in this group may break down to release amine metabolites (see **Toxicokinetics** section). These smaller metabolites are expected to be more readily absorbed and may contribute to toxicity. Therefore, conclusions on toxicity were further supported by data on the azo reduction metabolites or chemicals structurally similar to the azo reduction metabolites. Based on the available data chemicals in this group:

- have low acute and dermal toxicity
- are slightly irritating to skin and eyes.

Chemicals in this group are expected to be extremely potent sensitisers based on animal and human data. In a local lymph node assay (LLNA) study on Disperse Blue 106, reported concentrations producing a 3 fold increase in lymphocyte proliferation (EC3) were below 0.02%. In a non-guideline biphasic LLNA study on Disperse Blue 106 and Disperse Blue 124, a concentration of 0.003% of either chemical elicited a significant increase in cell counts. Disperse Blue 124 and Disperse Blue 106 were also positive in Guinea pig maximisation tests. Disperse Blue dyes (including Disperse Blue 124 and Disperse Blue 106) are identified as strong skin sensitisers based on human patch test studies published in literature. Numerous and frequent clinical case reports of allergic contact dermatitis arising from dermal exposure to Disperse Blue dyes through garments are documented.

Based on the available data, chemicals in this group may cause systemic health effects following repeated exposure. In a 28 day study with Disperse Blue 360, adverse effects including in the blood and kidneys were reported in high dose animals and in 1–2 mid dose male or female animals, implying a dose response for some of those effects. Given the large dose spacing between the mid and high dose it was not possible to establish a true lowest observed adverse effect level (LOAEL) but it is considered likely to be < 300 mg/kg bw/day).

The mode of action for the toxicity is not known and cannot be inferred from information on metabolites. Given the uncertainty on the LOAEL and mode of action for repeated dose effects, classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) of the other chemicals in this evaluation is not proposed.

Positive results were reported for *in vitro* genotoxicity studies for Disperse Blue 360 in both bacterial reverse mutation and thymidine kinase mammalian gene mutation assays. Positive *in vitro* studies were reported for the common azo reduction metabolite 2-thiazolamine, 5-nitro- (CAS No. 121-66-4). Although results were negative in *in vivo* assays with Disperse Blue 360 there is some uncertainty whether these results fully negate the positive *in vitro* results.

In the absence of experimental data, the carcinogenic potential for these chemicals cannot be excluded. All chemicals of the group had alerts for genotoxic carcinogenicity in *in silico* tools. The significance of azo reduction in the mutagenicity and carcinogenicity of azo dyes generally is well established. However, the common azo-metabolite arising from degradation of chemicals in this group, 2-thiazolamine, 5-nitro- (CAS No. 121-66-4), is not classifiable as carcinogenic with the current data available.

There are no experimental data available to assess specific adverse effects on fertility/sexual function and foetal development.

No inhalation toxicity data were available for chemicals in this group.

For further details of the health hazard information see **Supporting information**.

Hazard classifications relevant for worker health and safety

These chemicals satisfy the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) for hazard classes relevant for work health and safety as follows. This does not consider classification of physical hazards and environmental hazards.

The specific target organ toxicity (repeated exposure) classification applies to CAS No. 70693-64-0 only.

Health hazards	Hazard category	Hazard statement
Skin Sensitisation	Skin Sens. 1A*	H317: May cause an allergic skin reaction
Specific target organ toxicity (repeated exposure)	STOT Rep. Exp. 2	H373: May cause damage to organs through prolonged or repeated exposure

*A specific concentration limit of 0.001% is recommended based on the potency observed in animal studies.

Summary of health risk

Public

Based on the available use information, the primary route of public exposure is expected to be through skin contact with articles dyed with these chemicals. Clothing (textiles) and footwear (leather) articles are considered to represent worst case exposure scenarios.

These chemicals are potent sensitisers and exposure to very low levels may elicit a skin sensitisation reaction. Numerous and frequent clinical case reports of allergic contact dermatitis arising from dermal exposure to Disperse Blue dyes through garments are documented. This includes evidence of Australians being sensitised to Disperse Blue 106 and Disperse Blue 124.

The European Union (EU) is proposing to restrict these dyes in a number of articles due to the risk of sensitisation elicitation. Risk based concentration values were derived for elicitation of an allergic reaction from exposure to these chemicals in clothing and leather. Elicitation reactions were well below the amount of disperse blue dyes in detected in textiles, which are generally greater than 30–50 mg/kg. Therefore, it is not possible to set a safe limit for these chemicals in articles with prolonged contact with skin and 24 hours a day use. Although exposure to these chemicals in other non-textile articles such as nappies were not calculated, the exposure and risk conclusions for textiles were used as read across for these articles.

Commercial use of one of these chemicals in textile printing ink has been reported in Australia. In addition, textiles and other products manufactured with these chemicals in other countries could be imported into Australia. There is currently no restriction for these chemicals in Australia.

Given the identified risks of skin sensitisation though presence in articles in contact with the skin, the evidence indicates that there is a risk to the public that requires management (see **Proposed means for managing risk** section).

Workers

During product formulation and packaging, 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 these chemicals at lower concentrations could also occur while using formulated products containing these chemicals. The level and route of exposure will vary depending on the method of application and work practices employed. Good hygiene practices to minimise incidental oral exposure are expected to be in place.

Given the sensitisation potential and potential systemic long term health effects, these chemicals could pose a risk to workers. Control measures to minimise dermal and inhalation exposure are needed to manage the risk to workers (see **Proposed means for managing risk** section).

Proposed means for managing risk

Inventory listing

To manage the risks to human health from the introduction and use of chemicals in this group, the Inventory listings should be varied under section 86 of the *Industrial Chemicals Act 2019* (IC Act).

The current terms of listing for Disperse Blue 360 (CAS No. 70693-64-0) are proposed to be varied to:

Term of listing	Details
Specific requirements to provide information to the Executive Director under section 101 of the IC Act	A person who introduces this chemical must tell the Executive Director the volume of introduction and end use of the chemical within 20 working days if: 1. The end use of the chemical has changed or is likely to change from use in textile (fabric) dyes and printing inks. 2. The chemical has begun to be used by anyone other than professional workers. 3. The introduction volume of the chemical exceeds 1 tonne per annum. 4. Manufacturing of the chemical has commenced in Australia. 5. Information has become available to the person as to an adverse effect of the chemical on the environment.

The proposed terms of listing for Disperse Blue 124 (CAS No. 15141-18-1), Disperse Blue 106 (CAS No. 68516-81-4), Disperse Blue 102 (CAS No. 69766-79-6), Disperse Blue 96 (CAS No. 72987-42-9), and Disperse Blue 82 (CAS No. 12222-80-9) include:

Term of listing	Details
Specific requirements to provide information to the Executive Director under section 101 of the IC Act	A person who introduces these chemicals must tell the Executive Director the volume of introduction and end use of the chemical within 20 working days if: 1. The end use of the chemical has changed or is likely to change from use in textile (fabric) dyes and printing inks. 2. The chemical has begun to be used by anyone other than professional workers.

Workers

Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the Hazardous Chemical Information System (HCIS) to include classifications relevant to work health and safety (see **Summary of health hazards** section).

Information relating to safe introduction and use

The information in this statement including recommended hazard classifications, should be used by a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

Recommended control measures that could be implemented to manage the risk arising from dermal and inhalation exposure to these chemicals include, but are not limited to:

- using closed systems or isolating operations
- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with these chemicals.

These control measures should be supplemented with:

- conducting health monitoring for any worker who is at significant risk of exposure to these chemicals, if valid techniques are available to monitor the effect on the worker's health.

Measures required to eliminate, or manage risk arising from storing, handling and using a hazardous chemicals depend on the physical form and the manner in which these chemicals are used.

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.

Model codes of practice, available from the Safe Work Australia website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Consumer products

Recommendation to Australian Competition and Consumer Commission

It recommended that the Australian Competition and Consumer Commission (ACCC) consider mechanisms under the Australian Consumer Law to address the identified safety risks posed by the presence of these chemicals in consumer goods.

Conclusions

The Executive Director is satisfied that the identified risks to human health from the introduction and use of the industrial chemicals can be managed.

The specific requirement to provide information as a term of the Inventory listing under Section 101 of the IC Act assists with managing the risks from introduction of the chemical. For Disperse Blue 360 (CAS No. 70693-64-0), the information currently required to be provided is no longer aligned with the risks identified in this evaluation statement. Therefore, a variation to the specific requirement to provide information as a term of the Inventory listing is necessary to manage the risks from introduction of the chemical (see **Proposed means of managing risk**). As this evaluation does not consider environmental risks current information requirements relevant to environmental risks have been maintained.

For the other chemicals in this evaluation the risk conclusions for the public were driven by the evaluation finding that these chemicals are expected to be used by professional workers only. Given that these chemicals are potent sensitisers it is important that the introduction and use of these chemicals in Australia are known so that the risks can be appropriately managed. Therefore, a variation to the listing for these chemicals, to add a specific requirement to provide information to identify new end use(s), is necessary to manage the risks to human health from the introduction or use of the industrial chemicals (see **Proposed means of managing risk**).

Note:

1. Obligations to report additional information about hazards under section 100 of the *Industrial Chemicals Act 2019* apply.
2. A person introducing these chemicals should be aware of their obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Grouping rationale

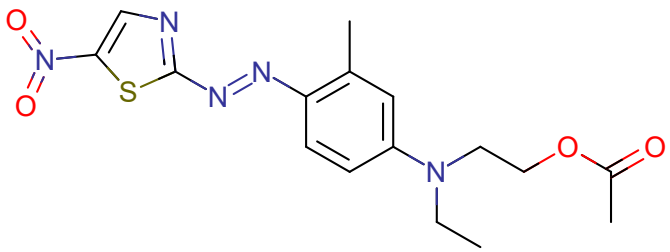
The group members are all azo dyes based on 5-nitro-2-thiazolamine and toluenediamine. These chemicals are grouped together based on their similar structure, metabolic pathways, physicochemical properties, and use profiles.

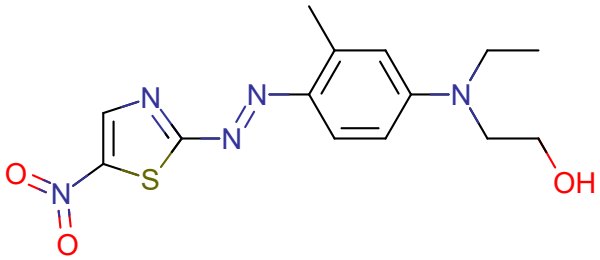
Chemical identity

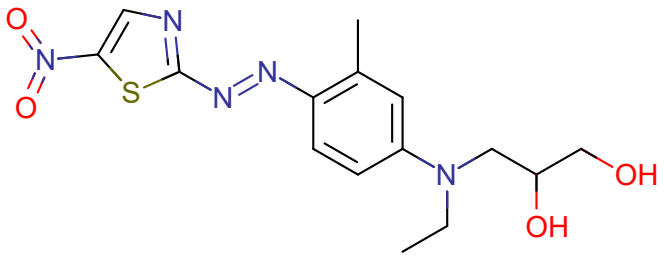
CAS number	12222-80-9
CAS name	C.I. Disperse Blue 82
Molecular formula	Unspecified
Associated names	Disperse Blue 102
Molecular weight (g/mol)	-
SMILES (canonical)	-

Additional chemical identity information

This chemical is a deleted CAS registration number and is expected to have the same chemical identity as Disperse Blue 102 (CAS No. 69766-79-6).

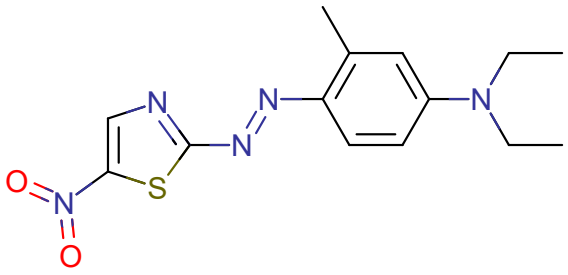
CAS number	15141-18-1
CAS name	Ethanol, 2-[ethyl[3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]phenyl]amino]-, 1-acetate
Molecular formula	$C_{16}H_{19}N_5O_4S$
Associated names	Disperse Blue 124
Molecular weight (g/mol)	377.42
SMILES (canonical)	O=C(OCCN(C1=CC=C(N=NC2=NC=C(S2)N(=O)=O)C(=C1)C)CC)C
Structural formula	

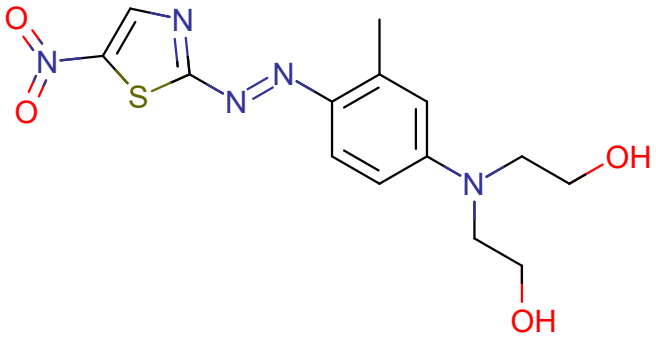
CAS number	68516-81-4
CAS name	Ethanol, 2-[ethyl[3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]phenyl]amino]-
Molecular formula	$C_{14}H_{17}N_5O_3S$
Associated names	Disperse Blue 106
Molecular weight (g/mol)	335.38
SMILES (canonical)	O=N(=O)C=1SC(N=NC2=CC=C(C=C2C)N(CC)CCO)=NC1
Structural formula	

CAS number	69766-79-6
CAS name	1,2-Propanediol, 3-[ethyl[3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]phenyl]amino]-
Molecular formula	$C_{15}H_{19}N_5O_4S$
Associated names	Disperse Blue 102 C.I. Disperse Blue 82
Molecular weight (g/mol)	365.41
SMILES (canonical)	O=N(=O)C=1SC(N=NC2=CC=C(C=C2C)N(CC)CC(O)CO)=NC1
Structural formula	

Additional chemical identity information

This chemical has a deleted CAS registration number (12222-80-9), which is also known as C.I. Disperse Blue 82.

CAS number	70693-64-0
CAS name	Benzenamine, *N*,*N*-diethyl-3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]-
Molecular formula	$C_{14}H_{17}N_5O_2S$
Associated names	Disperse Blue 360
Molecular weight (g/mol)	319.38
SMILES (canonical)	O=N(=O)C=1SC(N=NC2=CC=C(C=C2C)N(CC)CC)=NC1
Structural formula	

CAS number	72987-42-9
CAS name	Ethanol, 2,2′-[[3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]phenyl]imino]bis-
Molecular formula	$C_{14}H_{17}N_5O_4S$
Associated names	Disperse Blue 96
Molecular weight (g/mol)	351.38
SMILES (canonical)	O=N(=O)C=1SC(N=NC2=CC=C(C=C2C)N(CCO)CCO)=NC1
Structural formula	

Relevant physical and chemical properties

Data on physical and chemical properties of these chemicals is derived from the NICNAS 2015a report, ECHA 2019, SciFinder and publicly available information.

Chemical	DB 124	DB 106	DB 102*	DB 360	DB 96
Physical form	Powder	Powder	Powder	Powder	Powder
Melting point	-	-	-	> 224°C, decomposes during melting	-
Boiling point	545 ± 60°C (predicted)	550 ± 60°C (predicted)	> 500°C	> 225°C, decomposes before boiling	606 ± 65°C (predicted)
Vapour pressure	7.7×10^{-13} kPa at 25°C	-	1.37×10^{-15} kPa at 25°C	$< 4.7 \times 10^{-8}$ kPa at 25°C	-
Water solubility	4.6×10^{-6} mol/L at 25°C (predicted)	-	-	$< 1 \times 10^{-4}$ g/L at 20°C	-
pK_a	2.6 ± 0.5 (predicted)	14.6 ± 0.1 (predicted)	13.9 ± 0.2 (predicted)	2.8 ± 0.4 (calc.)	14.3 ± 0.1 (predicted)
log K_{ow}	2.57 ± 0.5 (predicted)	-	-	3.49 at 20°C	-

DB = Disperse Blue

*Disperse Blue 82 is not included in the table as it is expected to have the same chemical identity and physiochemical properties of Disperse Blue 102.

Introduction and use

Australia

There is currently limited information about the introduction, use and end use of these chemicals in Australia. Based on Australian information, Disperse Blue 360 has commercial use as a component of printing ink up to 2% (NICNAS 2015a). The ink is intended for printing an image onto substrate material which can be paper or cloth. Information provided to AICIS since 2020 indicates potential application to clothing in Australia.

Patch test data indicate that exposure to Disperse Blue 106 and Disperse Blue 124 has occurred in Australia (see **Skin sensitisation** section). This is likely through contact with textiles.

International

Disperse dyes are nonionic, water insoluble dyes with an affinity for hydrophobic fibers such as polyester. As such, they are used to mainly dye synthetic textiles such as polyester, cellulose acetate and nylon. The dye molecules are adsorbed onto the textile and then migrate into the textile fiber upon heating. They can also be used to print on substrate materials. Product types that may contain disperse dyes are clothing, footwear, nappies, seatbelts, furniture or any other products made of synthetic fabrics or leather (ECHA 2020a).

Measured and estimated concentrations of disperse dyes in textiles were between 10,000 and 100,000 mg/kg (ECHA 2020a).

The use of some of the disperse dyes in this evaluation may be declining due to recent restrictions introduced in Europe and voluntary phase-out by industry, see **International regulatory status**. However, there are several registrations for Disperse Blue 360 under ECHA REACH. The estimated tonnage band is 10–100 tonnes. In addition, the following 4 chemicals are reported as active under US Toxic Substances Control Act (TSCA) inventory notification rule (US EPA n.d.):

- Disperse Blue 106 (CAS No. 68516-81-4)
- Disperse Blue 102 (CAS No. 69766-79-6)
- Disperse Blue 360 (CAS No. 70693-64-0)
- Disperse Blue 96 (CAS No. 72987-42-9).

Both Disperse Blue 106 and 124 have historically been detected in clothing made from “black velvet” fabrics internationally (Hausen 1993). These same chemicals were also detected in leggings manufactured in Italy (Malinauskiene et al. 2012). However, more recent investigations into the presence of these two disperse blue dyes in textiles showed no detection of Disperse Blue 102 or 124 in synthetic garments available in Sweden (Carlsson et al. 2022).

Existing Australian regulatory controls

AICIS

Disperse Blue 360 (CAS No. 70693-64-0) is listed on the Australian Inventory of Industrial Chemicals (the Inventory) with the following specific requirement to provide information as a term of the Inventory listing.

Obligations to provide information apply. These obligations are:

1. *A person introducing this chemical must tell us in writing within 28 calendar days if any of the following circumstances have occurred in relation to their introduction (importation or manufacture):*
    a. *the introduction volume of the chemical exceeds 1 tonne per annum*
    b. *the chemical is applied to clothing textiles*
    c. *the chemical is used on products other than soft signage and promotional items*
    d. *information becomes available on the sensitisation, mutagenicity and/or carcinogenicity of the chemical*
2. *A person who introduces this chemical must tell us in writing within 28 calendar days if they become aware of any of the following circumstances, namely, that since the assessment under the Industrial Chemicals (Notification and Assessment) Act 1989:*
    a. *the function or use of the chemical has changed, or is likely to change, significantly;*
    b. *the amount of the chemical being introduced has increased, or is likely to increase, significantly;*
    c. *in the case of a chemical not manufactured, or proposed to be manufactured, in Australia at the time of the assessment—it has begun to be manufactured in Australia;*
    d. *the method of manufacture of the chemical in Australia has changed, or is likely to change, in a way that may result in an increased risk of an adverse effect of the chemical on occupational health and safety, public health or the environment;*
    e. *additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health or the environment.*

No specific controls are currently available for other chemicals in this evaluation.

Public

No specific controls are available for chemicals in this evaluation.

Workers

These chemicals are not listed on the Safe Work Australia Hazardous Chemical Information System (HCIS) (SWA n.d.).

No exposure standards are available for these chemicals in Australia (SWA n.d.).

International regulatory status

European Union

In the European Union (EU), disperse dyes including Disperse Blue 102 (identified under deleted CAS No. 12222-97-8), Disperse Blue 106 (CAS No. 68516-81-4) and Disperse Blue 124 (CAS No. 15141-18-1) are intended to be restricted and entered in Annex XVII to REACH. Based on an Annex XV proposal, the ECHA Risk Assessment Committee (RAC) and Socio-Economic Analysis Committee (SEAC) Opinion (ECHA 2020a) proposed a restriction that these chemicals shall not exceed detectable limits (30–50 mg/kg according to test method ISO 16373-1:2015 for dyestuffs in textiles (ISO 2015)) in the following articles placed on the market for the general public:

- clothing and related accessories
- textile, leather, fur, hide and synthetic leather articles other than clothing which come into contact with human skin under normal or reasonably foreseeable conditions of use to an extent similar to clothing
- disposable sanitary towels, napkins, tissues and nappies
- footwear.

The International Association for Research and Testing in the Field of Textile and Leather Ecology lists Disperse Blue 102, 106 and 124 on the restricted substance list for OEKO TEX® labelling standards due to skin sensitisation concerns, along with reproductive and developmental toxicity, mutagenicity and carcinogenicity, and skin irritation toxicological properties (OEKO-TEX n.d.).

Under the European Union Ecolabel scheme (Regulation (EC) No 66/2010) Disperse Blue 102, 106 and 124 are listed as dyes which shall not be used in textiles due to their potential sensitisation properties (EU n.d.)

The German Federal Institute for Risk Assessment (BfR) Opinion No. 041/2012 lists Disperse Blue 102, 106 and 124 as potentially sensitising dyes which should not be used in textiles on precautionary grounds. It was noted that these dyes were most commonly detected in samples of textiles suspected as being the trigger for contact dermatitis cases (BfR 2012).

Human exposure

Public

Available use information indicates that the public may be exposed to these chemicals through:

- prolonged exposure to articles containing the dyes
- young children being exposed by sucking the materials containing the dyes
- exposure by dermal contact or incidental ingestion of printed cardboards, papers or foils.

The most relevant exposure pathway from end use in clothing, footwear and related articles is a direct release of substances by migration from the article. The level of exposure from articles depends on a number of factors including exposure duration, exposure frequency,

surface weight and the amount of substance that migrates. Exposure through clothing (textiles) and footwear (leather) articles is considered to represent worst case scenarios with an assumption of high areas of body contact and 24 hours a day use. Exposure assumptions for clothing were considered indicative for non-textile articles such as nappies and other leather articles.

Exposure assumptions based on the ECHA restriction proposal are:

- Exposure duration = 24 h (both textiles and leather)
- Exposure frequency (n/day) = 3 (textiles) and 2 (leather)
- Surface weight textile = 0.2 kg/m^2 (textiles) and 0.9 kg/m^2 (leather)
- Surface contact 1:1 (both textiles and leather).

The conditions of use and manufacturing techniques may influence the migration factor of disperse dyes. Dye release may also be influenced by fabric type and weight, as well as washing and wearing of a textile which reduce release over time. A default migration value of 0.5% was developed by the "Textiles" Working Group established at the German Federal Institute for Risk Assessment (BfR 2012). However, in the recent ECHA RAC opinion on skin sensitising chemicals, a migration factor value of 5% for disperse dyes in textile and leather was considered more appropriate to cover any uncertainties (ECHA 2020).

Health hazard information

Data are available for Disperse Blue 360, Disperse Blue 124 and Disperse Blue 106. Chemicals with data represent all the toxicologically relevant features of chemicals in this group and have similar physicochemical properties. Therefore, the available data are considered suitable for drawing conclusions on hazards for chemicals without data.

Azo dyes in this group may break down to release amine metabolites (see **Toxicokinetics** section). These smaller metabolites are expected to be more readily absorbed and may contribute to toxicity. Therefore, conclusions on toxicity were further supported by data on the azo reduction metabolites or chemicals structurally similar to the azo reduction metabolite:

- 2-thiazolamine, 5-nitro- (CAS No. 121-66-4) (metabolite common to all chemicals)
- 1,4-Benzenediamine, N4,N4-diethyl-2-methyl-, monohydrochloride (CAS No. 2051-79-8) and 1,4-benzenediamine, 2-methyl (CAS No. 95-70-5) and its sulfate salt (considered representative of the toxicity of the toluenediamine metabolites).

Toxicokinetics

No toxicokinetic studies are available. However, azo dyes in this group may break down to release amine metabolites. Enzymatic reduction of the azo bond is expected to occur upon oral administration via intestinal and hepatic enzymes. Skin bacteria enzymes may also catalyse azo reduction reactions generating smaller aromatic amine metabolites (Stingley et al 2010; Collier et al 1993). These smaller amine metabolites are expected to be bioavailable, and due to their smaller size are more likely to be absorbed than parent chemicals. In addition to biological degradation mechanisms, photochemical degradation of azo dye linkages is also a potential degradation mechanism (Engel et al 2009).

Disperse Blue 124 (CAS No. 15141-18-1) can hydrolyse to Disperse Blue 106 (CAS No. 68516-81-4) (ECHA 2020b). Azo reduction of chemicals in this group may release the following metabolites:

- 2-thiazolamine, 5-nitro- (CAS No. 121-66-4) (common to all chemicals)
- a number of toluenediamine derivatives (CAS No. 50928-84-2; 131502-44-8; 2359-51-5, 148-71-0 and 2359-52-6).

Information is not available for all chemicals in this group. Based on the molecular weights of these chemicals (319–377 g/mol), low water solubility (Disperse Blue 360), and the partition coefficients (Log Kow < 4) absorption via the oral, dermal and inhalation routes is expected. Low vapour pressures and high boiling points indicate that these chemicals are expected to have minimal volatility, with inhalation only likely to arise from processes where dusts or aerosols are produced.

Acute toxicity

Oral

Based on the limited available data, these chemicals are likely to have low acute toxicity via the oral route.

In an acute oral toxicity study (good laboratory practice (GLP) compliance unknown) conducted in accordance with OECD TG 423, Crl:CD(SD) rats (3/sex/dose) were treated with a single dose (2000 mg/kg bw) of Disperse Blue 360 (CAS No. 70693-64-0) in both sexes. The median lethal dose (LD50) was reported to be > 2000 mg/kg bw. No clinical signs of toxicity were reported (NICNAS 2015a).

Dermal

Based on the limited available data, these chemicals are likely to have low acute toxicity via the dermal route.

In an acute dermal toxicity study (GLP compliance unknown) conducted in accordance with OECD TG 402, Crl:CD(SD) rats (5/sex/dose) were treated with a single dose (2000 mg/kg bw) of Disperse Blue 360 (CAS No. 70693-64-0) in peanut oil under semi-occlusive conditions. The LD50 was reported to be > 2000 mg/kg bw. No erythema or oedema were reported (NICNAS 2015a).

Inhalation

No data are available for chemicals in this group.

Corrosion/Irritation

Skin irritation

Based on the limited data available, chemicals in this group are likely to be slightly irritating to skin.

In a skin irritation study (GLP compliance unknown), similar to OECD TG 404, an undefined amount of Disperse Blue 106 (CAS No. 68516-81-4) in distilled water was applied to intact and abraded skin of 6 rabbits under semi-occlusive conditions. The following mean scores for individual animals were reported based on observations at 24 and 72 hours:

- 0.5 for erythema in 2/6 animals

- 0.5 for oedema in one animal.

All skin irritation effects resolved by 72 hours in all animals. No further details were provided (NICNAS 2015a).

Eye irritation

Based on the limited available data, chemicals in this group are likely to be slightly irritating to eyes.

In an eye irritation study (GLP compliance unknown), similar to OECD TG 405, Disperse Blue 106 (CAS No. 68516-81-4) (concentration not reported) was instilled into the eyes of 6 New Zealand White (NZW) rabbits. The eyes were observed at 24, 48, and 72 hours. Corneal dulling was noted in observation but was not scored. There was no iritis noted in any animal. The following mean scores for individual animals were reported based on observations at 24, 48 and 72 hours:

- conjunctival redness (1, 1.3, 0.3, 1, 0.3, 1.7)
- chemosis (1.7, 1.7, 0.6, 1, 1, 2).

All signs of irritation resolved by day 7, except for conjunctival redness that persisted in one animal. Follow up observation at 14 days was not performed (NICNAS 2015a).

In an *ex-vivo* rabbit nucleated eye test (GLP compliance unknown), Disperse Blue 360 (CAS No. 70693-64-0) was applied to 3 rabbit eyes, 2 additional eyes served as controls. Eyes were examined at 1, 2, 3 and 4 hour intervals following treatment. Corneal thickness and fluorescein uptake were measured. At 4 hours, no fluorescein uptake in any of the eyes was reported. Corneal thickness was increased in the treated eyes by 0.7, 3.2 and 9.4% at 1, 2 and 4 hour intervals respectively. These values were within historical controls and were reported not to be of statistical significance. Collectively due to the comparable effects in test and control eyes, the report concluded that the chemical was unlikely to have the potential to cause severe ocular irritancy *in vivo* (NICNAS 2015a).

Sensitisation

Skin sensitisation

Based on the data available for Disperse Blue 106 and Disperse Blue 124 and a common metabolic pathway releasing toluenediamine derivatives, chemicals in this group are skin sensitisers, warranting classification.

Based on an EC3 below 0.02% in a local lymph node assay (LLNA) study and a sensitisation rate in a guinea pig maximisation test (GPMT) of ≥ 60% following intradermal induction at > 0.1% but ≤ 1% (see ***in vivo*** section below), these chemicals are likely to have extreme potency (ECETOC 2003). The animal data is sufficient for sub-classification (Category 1A) and application of a specific concentration limit (SCL) of 0.001% (ECHA RAC 2020b). Although the human data alone does not enable sub-classification, a high frequency of positive responses are reported in patch test studies and the large number of case studies provide evidence that these dyes caused, either alone or jointly with other substances, the allergic contact dermatitis diagnosed in these patients.

In vivo

In a LLNA test conducted in accordance with OECD TG 429, 4, male, CBA/Ca strain mice received topical applications (0.005, 0.01, 0.025, 0.05, 0.1, and 0.25%) of Disperse Blue 106 (CAS No. 68516-81-4) in dimethyl sulfoxide (DMSO). No information in GLP was available. Two duplicate experiments were conducted with stimulation indices (SI) recorded (see **Table 1**). Reported concentrations producing a threefold increase in lymphocyte proliferation (EC3) for each experiment were 0.012% and 0.017%, respectively, indicating strong sensitisation potential (ECHA 2019; ECHA 2020b).

Table 1 – Summary of LLNA experiments

Concentration (% w/v)	Experiment 1: SI values (no units)	Experiment 2: SI values (no units)
0.005	*	0.9
0.01	2.6	*
0.025	5.5	5.2
0.05	6.6	9.4
0.1	8.2	9.1
0.25	9.2	*

*concentration not tested

In a non-guideline, biphasic (sensitisation challenge protocol) LLNA, 10 female BALB/c mice, were treated with either Disperse Blue 124 or Disperse Blue 106 (CAS No. 68516-81-4) in DMSO at concentrations of 0.003, 0.03, 0.3, 3.0, 10 and 30%. No information on GLP was available. No EC3 values were calculated in the study as no SI values were available. Analysis of sensitisation utilised cell counts, with the concentration of 0.003% of either chemical resulting in significant increases in cell count of treated animals, indicating strong sensitisation potential. However, this study had variations from OECD TG 429 and was not validated against a positive control (ECHA 2019; ECHA 2020b).

In a GPMT conducted similarly to OECD TG 406, intradermal induction was performed on 10, female, Pirbright white guinea pigs using 0.2% w/v of Disperse Blue 124 (CAS No. 15141-18-1) in Freund's complete adjuvant (FCA) and saline. No topical induction occurred. No information on GLP was available. The animals challenged via open epicutaneous elicitation with 1% of the chemical in acetone. After challenge, reactions were reported more than 60% of the animals. In a similar, non-GLP experiment, intradermal induction was conducted with 1.5% w/v of Disperse Blue 106 under similar conditions. Challenge with concentrations of 0.1, 0.3 and 1% resulted in extreme swelling and redness spanning the entre flanks of treated animals. After a recovery period of one week, challenge with a lower dilution of 0.001% in acetone on the opposite flank resulted in reactions in 100% of animals (ECHA 2019; ECHA 2020b).

In a previous NICNAS report, negative results for the skin sensitisation endpoint were reported for two chemicals in this group. However, it should be noted that these studies were considered to be of low reliability as study reports were not sighted. Disperse Blue 124 showed no skin sensitisation effects in a GPMT with challenge concentrations 10% and 25%. Similarly, in a Buehler test Disperse Blue 96 (challenge concentrations 25% and 50%) showed no evidence of sensitisation (NICNAS 2015a).

In silico

The profiling functionality of the OECD Quantitative Structure Activity Relationship (QSAR) Toolbox v4.5 was used to determine the presence of potential structural alerts for skin sensitisation. While the un-metabolised chemicals in this group did not display any mechanistic alerts for skin sensitisation, all had alerts for skin sensitisation when modelled with metabolism. Both skin metabolism simulators and rat liver simulators were applied. The rat liver simulators included azo reductase activity also present in the gut and the skin microbiota (NICNAS 2017). A number of predicted metabolites had structural alerts for protein binding for skin sensitisation Category 1A and Micheal addition.

The expert rule based systems, DEREK (Deductive Estimation of Risk from Existing Knowledge) Nexus (version 2.6.0) and METEOR Nexus (version 3.2.0), were used to estimate the skin sensitisation potential of these chemicals and their simulated metabolites via enzymatic reduction (catalysed by liver enzymes and enzymes in gut microflora) (Lhasa Limited). All chemicals in this group had plausible predictions for skin sensitisation. Simulated metabolites of these chemicals included anilines or aminopyridines substituted with hydroxyl or amino groups. These metabolites were also predicted to be skin sensitising, with predicted EC3 values (LLNA) ranging from 0.66 to 1.3%.

The QSAR modelling using OASIS-TIMES (Optimised Approach based on Structural Indices Set–TIssue MEtabolism Simulator) version 2.31.2 predicted all chemicals in this evaluation as strong skin sensitisers (Category 1A) using the GHS model for skin sensitisation. The predictions were within the applicability domain of the model.

Metabolites

Based on the available data, the common metabolite 2-thiazolamine, 5-nitro- (CAS No. 121-66-4) is a weak sensitiser (NICNAS 2017).

Although no data are available for the specific toluenediamine derivatives both 1,4-benzenediamine, N4,N4-diethyl-2-methyl-, monohydrochloride (CAS No. 2051-79-8) and 2,5-toluenediamine (CAS No. 95-70-5) are classified as skin sensitisers (NICNAS 2013; NICNAS 2015b). 2,5-Toluenediamine and its salt were strong sensitisers in available animal studies (NICNAS 2013). 1,4-benzenediamine, N4,N4-diethyl-2-methyl-, monohydrochloride (CAS No. 2051-79-8) has reported positive reactions in human case studies.

Observation in humans

Disperse Blue dyes are well established as skin sensitising chemicals (Militello et al. 2020). There are widespread and frequent reports of positive human patch test results for Disperse Blue 124 (CAS No. 15141-18-1) and Disperse Blue 106 (CAS No. 68516-81-4) including from a study in Melbourne, Australia. There are also extensive case reports detailing skin sensitisation from these two chemicals after exposure to textile and garments (ECHA 2019). A summary of sensitisation data (human patch tests) for Disperse Blue 106 and 124 are shown in **Table 2** and **Table 3**, derived from the ECHA reports (ECHA 2022; ECHA 2019). Further details for two of these studies are provided below.

A total of 2069 patients from general and occupational contact dermatitis clinics in Melbourne spanning from 1993–2006 were patch tested with a series of textile dyes, including Disperse Blue 106 and Disperse Blue 124 at 1% petrolatum. A mixture of Disperse Blue 106 and 124 at 1% each was also tested. Of the 2069 patients known to have a history of suspected

textile allergy, 178 had positive reactions to chemicals in the series. Of these positive reactions, 11.8% (21/178) and 11.2% (20/178) were attributable to Disperse Blue 106 and 124, respectively. Positive reactions occurred in 12.2% of patients (5/41) tested with the Disperse Blue mixture. Disperse Blue 124 and 106 and were the second and third most frequent allergens in this study (Slodownik et al. 2011).

The elicitation potential of purified and commercial forms of Disperse Blue 106 and Disperse Blue 124 was investigated in a dilution series patch test. Of the 21 patients 2 reacted to the lowest concentration tested (0.0003 µg/cm^2) for Disperse Blue 106. One of these also were positive to Disperse Blue 124 at lowest concentration tested (0.0003 µg/cm^2) (Ryberg et al. 2009).

Table 2 Summary of sensitisation (data) human patch testing with Disperse Blue 124 and 106 – consecutive dermatitis patients

Number of patients	Concentration and vehicle	Positive reactions (%)
1043	DB 124 1%, vehicle not reported	DB 124: 1.2% (12/1043)
3115	DB 124, 1% (vehicle not reported) DB 106, 1% (vehicle not reported)	DB 124: 3.4% DB 106: 2.8%
5085	DB 106, 1% (in petrolatum)	DB 106: 0.9%
427	DB 106 (vehicle and concentration not reported)	DB 106: 2.3%
327	DB 124, 1% (vehicle not reported) DB 106, 1% (vehicle not reported)	DB 124: 1.2% DB 106: 1.2%
982	DB 124, 0.1% (in petrolatum) DB 106, 0.1% (in petrolatum)	DB 124: 0.2% (2/982) DB 106: 0.2% (2/982)
2555	DB 124, 0.3% (in petrolatum) DB 106, 0.3% (in petrolatum) DB 106/124 mix , 0.35% and 0.2% (in petrolatum)	DB 124: 0.4% (8/2214) DB 106: 0.5% (11/2215) DB 106/124 mix: 0.7% (19/2555) (6 patients reacted to both)
1094 (children)	DB 124, 1% (in petrolatum) DB 106, 1% (in petrolatum)	DB 124: 1.8% DB 106: 4.0%
1098 (children)	DB 124 (vehicle and concentration not reported) DB 106 (vehicle and concentration not reported)	DB 124: 1.3% (14/1 098) DB 106: 3.0% (4/134)
3041	DB 124/106 mix (1% in petrolatum)	DB 124/106 mix: 1.3% (40/3041)
286	DB 124 (assumed 1% petrolatum) DB 106 (assumed 1% petrolatum)	DB 124: 7.3% (21/286) DB 106: 4.2% (12/286)
798	DB 124, 1% (in petrolatum)	DB 124: 3.6% (29/798)
1012	DB 124, 1% (vehicle assumed petrolatum)	DB 124: 2.2% (22/1 012)
670 (children)	DB 124 (assumed 1% in petrolatum)	DB 124: 0.7% (5/670)
576	DB 124, 1% (in petrolatum)	DB 124: 1.9% (11/576)
1043	DB 124 1%, vehicle not reported	DB 124: 1.2% (12/1043)
3115	DB 124, 1% (vehicle not reported) DB 106, 1% (vehicle not reported)	DB 124: 3.4% DB 106: 2.8%
5085	DB 106, 1% (in petrolatum)	DB 106: 0.9%
427	DB 106 (vehicle and concentration not reported)	DB 106: 2.3%
327	DB 124, 1% (vehicle not reported) DB 106, 1% (vehicle not reported)	DB 124: 1.2% DB 106: 1.2%

Number of patients	Concentration and vehicle	Positive reactions (%)
982	DB 124, 0.1% (in petrolatum) DB 106, 0.1% (in petrolatum)	DB 124: 0.2% (2/982) DB 106: 0.2% (2/982)
2555	DB 124, 0.3% (in petrolatum) DB 106, 0.3% (in petrolatum) DB 106/124 mix , 0.35% and 0.2% (in petrolatum)	DB 124: 0.4% (8/2214) DB 106: 0.5% (11/2215) DB 106/124 mix: 0.7% (19/2555) (6 patients reacted to both)
1094 (children)	DB 124, 1% (in petrolatum) DB 106, 1% (in petrolatum)	DB 124: 1.8% DB 106: 4.0%
1098	DB 124 (vehicle and concentration not reported) DB 106 (vehicle and concentration not reported)	DB 124: 1.3% (14/1 098) DB 106: 3.0% (4/134)
3041	DB 124/106 mix (1% in petrolatum)	DB 124/106 mix: 1.3% (40/3041)

Table 3 Summary of sensitisation (data) human patch testing with Disperse Blue 124 and 106 – selected dermatitis patients

Number of patients	Concentration and vehicle	Positive reactions (%)
3207	DB 124 0.3% (vehicle not reported) DB 106, 0.3% (vehicle not reported)	DB 124: 2.3% (28/1237) DB 106: 2.0% (25/1238)
2493	TDM, 6.6% (mixture of 6 disperse dyes, each 1.0%, and DB 106 and DB 124, each 0.3%) in petrolatum 83 positively patch-tested patients were then tested with: DB 124, 0.3 and 1% (in petrolatum) DB 106, 0.3 and 1% (in petrolatum)	TDM: 3.6% (1.3–18.2%; 90/2493) DB 124 (0.3%): 7.2% (6/83) DB 124 (1.0%): 10.8% (9/83) DB 106 (0.3%): 7.2% (6/83) DB 106 (1.0%): 15.7% (13/83) positive
2907	TDM 6.6% (in petrolatum) (6 disperse dyes, each 1.0%, and DB 106 and DB 124, each 0.3%). 94 TDM patients were then tested with: DB 124, 0.3% DB 124, 1.0% DB 106, 0.3% DB 106, 1.0%	TDM 3.7% (108/2 907) DB 124 (0.3%): 5.3% (5/94) DB 124 (1.0%): 8.5% (8/94) DB 106 (0.3%): 6.4% (6/94) DB 106 (1.0%): 13.8% (13/94)
277	DB 124, 1% (in petrolatum) DB 106, 1% (in petrolatum)	DB 124: 54.5% (84/154), DB 106: 28.6% (44/154) 39 reactions to both DB 124 and DB 106
671	DB 124, 1% (vehicle not reported) DB 106, 1% (vehicle not reported)	DB 124: 8.0% (n=665) DB 106: 8.3% (n=660)
2069	DB 124, 1% (in petrolatum) DB 106, 1% (in petrolatum) DB 124/106 mix, 1% (in petrolatum)	DB 124: 1.0% (20/2069) DB 106: 1.0% (21/2069) DB 124/106 mix: 0.3% (6/2069) 3 reactions to both DB 124 and DB 106
696	DB 124, 1% (in petrolatum) DB 106, 1% (in petrolatum) DB 124/106 mix, 1% (in petrolatum)	DB 124: 6.5% (17/263) DB 106: 7.2% (19/263) DB 124/106 mix: 7.7% (51/659)

Number of patients	Concentration and vehicle	Positive reactions (%)
577	DB 124 (assumed 1% petrolatum) DB 106 (assumed 1% petrolatum)	DB 124: 5.0% (29/577) DB 106: 5.9% (34/577)
6478 (130 with hand dermatitis specifically)	DB 124 (vehicle and concentration not reported) DB 106 (vehicle and concentration not reported)	DB 124: 49% (63/130) hand dermatitis patients 42% (130/307) no hand involvement DB 106: 50% hand dermatitis patients 49% no hand involvement
1986	DB 124, 1% (in petrolatum) DB 106, 1% (in petrolatum) DB 124/106 mix, 1% (in petrolatum)	DB124: 3.0% (55/1829) DB106: 3.5% (64/1847) DB 106/124 mix: 4.7% (52/1108) 46 reacted to both DB124 and DB106
103	DB124 (assumed 1% in pet.) DB106 (assumed 1% in pet.)	DB124: 6.8% (7/103) DB106: 6.8% (7/103)
271	DB 124, 1% (in petrolatum) DB 106, 1% (in petrolatum)	DB124: 11.8% (32/271) DB106: 12.2% (33/271) 31 reacted to both DB106 and DB124
159 (contact dermatitis patients and textile dye dermatitis patients)	DB124 (assumed 1% in pet.) DB106 (assumed 1% in pet.)	DB124: 3.8% (6/159) all patients 26.1% (6/23) patients with textile dye dermatitis DB106: 9.7% (16/164) all patients 57.1% (16/28) patients with textile dye dermatitis
100 (sensitised to textile dyes)	DB 124, 1% (in petrolatum)	DB124: 36% (36/100)
145 (suspected textile dermatitis)	DB 124, 1% (in petrolatum)	DB124: 8.3% (12/145)

Repeat dose toxicity

Oral

Based on the limited available data, chemicals in this group may cause systemic health effects following repeated exposure.

Disperse Blue 360 (CAS No. 70693-64-0) was recommended for GHS classification for specific target organ toxicity (Category 2) (NICNAS 2015a), based on a 28 day oral toxicity study (OECD TG 407) in rats. Adverse effects including changes in blood parameters indicative of anaemia and histopathological effects in kidneys were reported in rats at 1000 mg/kg bw/day (high-dose) and in 1–2 male or female rats at 150 mg/kg bw/day

(mid-dose), implying a dose response starting at 150 mg/kg bw/day for these effects. However, the mean body weights were also statistically significantly reduced in rats at high doses throughout the study and males at mid doses in the last 2 weeks, comparable with reduced food consumption. Given the large dose spacing between the mid and high dose it was not possible to establish a true LOAEL, but it is considered likely to be < 300 mg/kg bw/day (within the cut off for GHS classification for a 28 day study).

The mode of action for the toxicity is not known and cannot be inferred from information on metabolites. Given the uncertainty on the LOAEL and mode of action for repeated dose effects, classification of the other chemicals in this evaluation is not warranted.

Disperse Blue 360

In a 28 day study conducted in accordance with OECD TG 407 Crl:CD rats (5/sex/dose) were administered Disperse Blue 360 (CAS No. 70693-64-0) by gavage at 0, 15, 150, and 1000 mg/kg bw/day; 7 days per week. The NOAEL was reported to be 15 mg/kg bw/day (based on adverse effects observed in the 150 and 1000 mg/kg bw/day dose groups).

Effects in the 1000 mg/kg bw/day group included changes gait, ataxia, a hunched posture, dehydration, emaciation and pilo-erection in animals. Convulsion of hind legs was reported on a single occurrence in one animal. Reduced functional performance (limb grip strength) was noted along with increased startle reflex. At the end of the study, body weights of males and females were decreased by 42.4% and 31.4%, respectively. Food consumption was reduced for both sexes across all 4 weeks of the study (20–55% and 33–42% for males and females, respectively).

For the 1000 mg/kg bw day dose group, haematological effects indicative of anaemia were observed. This included reduced haemoglobin, erythrocyte count, haematocrit, mean corpuscular volume, and mean corpuscular haemoglobin. The animals in this dose group also exhibited statistically significant reductions in plasma glucose levels. In females, statistically significant effects such as reduced total plasma protein and albumin with a corresponding reduction in the albumin/globulin ratio was reported. Increases in plasma cholesterol in both sexes, inclusive of increased aspartate aminotransferase levels in males were also observed. Reported histopathological changes included atrophy of the thymus, cellular exfoliation and tubular basophilia in kidneys (with accumulation of granular pigment). For females, there was a corresponding reduction in relative thymus weight that was statistically significant. Additionally, animals in this dose group had hepatocyte enlargement with corresponding increased liver weights. In males, there were statistically significant reductions in plasma bilirubin levels.

No functional deficiencies or clinical signs of toxicity were reported in the 150 mg/kg bw/day group. At the end of the study, mean body weights of males were decreased 11.0%, no decreases in the body weights of females were observed in this group. Food consumption was reduced for males in week 4 of the study (by 17%). One male in this group experienced haematological effects indicative of anaemia. Males treated with 150 mg/kg bw/day also had statistically significant reductions in plasma glucose levels and plasma bilirubin levels. Histopathological changes were reported in various organs including the thymus, kidneys and liver, including tubular basophilia and vacuolation in the kidneys of females.

Mean body weights of males at the end of the study were decreased by 8.9% in the 15 mg/kg bw day dose group. Additionally, as in the other dose groups, there was a statistically significant reduction in plasma bilirubin levels at 15 mg/kg bw/day not attributed as a treatment related effect. No other changes were reported in the test animals from lowest dose group.

Metabolites

Limited data are available for the azo reduction metabolite 2-thiazolamine, 5-nitro- (CAS No. 121-66-4).

In non-guideline GLP sub-chronic studies, Fischer 344 (F344) rats (n=5/sex/dose) and B6C3F1 mice (n=5/sex/dose) were administered the chemical via diet for 6 weeks. Concentrations in the diet ranged from 375 to 4,000 ppm for rats and from 30 to 500 ppm for mice, respectively (equivalent to approximately 50–600 and 10–200 mg/kg bw/day). No effects were observed in mice. However slightly enlarged thyroids were seen in rats at higher doses. A dose related decrease in body weight gain was reported in male and female rats. (NICNAS 2017; NTP 1978).

In another non-guideline study, enlarged thyroids and lower accumulation of radioisotope iodine was observed in rats administered 2-thiazolamine, 5-nitro- at concentrations 0.06 to 0.1% via diet. No further details were available (NICNAS 2017).

No data are available for the toluenediamine derivative metabolites. 2,5-toluenediamine sulfate (CAS No. 615-50-9) caused myodegenerative changes in multiple organs in rats following repeated oral exposure at 20 mg/kg bw/day (the highest dose tested). The NOAEL for clinical pathology was reported to be 10 mg/kg bw/day despite transient, non-dose related increases in aspartate aminotransferase (AST) levels (NICNAS 2020; SCCP 2011).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on available data, the genotoxicity potential of chemicals reported in this evaluation statement cannot be ruled out. The chemical Disperse Blue 360 and the metabolite 2-thiazolamine, 5-nitro- (CAS No. 121-66-4) were positive in several *in vitro* assays. Disperse Blue 360 was negative in 2 *in vivo* assays. However, there is uncertainty whether these results fully negate the positive *in vitro* studies. These chemicals and their metabolites have positive QSAR predictions for genotoxicity *in vivo* and *in vitro*.

In vitro

Positive results for Disperse Blue 360 (CAS No. 70693-64-0) were reported in the following *in vitro* genotoxicity studies (NICNAS 2015a):

- Positive results for were reported in a bacterial reverse mutation assay (OECD TG 471) in *Salmonella typhimurium* strains TA1535, TA1537, TA98, TA100 with and without metabolic activation at concentrations of 5–5,000 µg/plate. A clear dose dependent increase in the number of revertant colonies was observed for all tested *Salmonella typhimurium* strains. In the same study, there were no statistically significant increases in the number of revertant colonies for *Escherichia coli* WP2uvrA^{-} under the same conditions with 5–5000 ug/plate;

- Positive results were reported in a mammalian gene mutation assay (OECD TG 476) in the thymidine kinase (TK) locus in mouse lymphoma cells L5178Y with metabolic activation from concentrations of 2 µg/plate up to 800 µg/plate.

In vivo

In a mammalian erythrocyte micronucleus test conducted in accordance with OECD TG 474, (deviation in standard oral route of administration) Crl:CD-1^{TM}(ICR)BR male mice (n=7/dose) were treated with Disperse Blue 360 (CAS No. 70693-64-0) via intraperitoneal injection (deviation from test guideline) at single doses of 50, 100 and 200 mg/kg bw. Positive and negative (arachis oil) controls were administered orally. The incidence of micronuclei in bone marrow polychromatic erythrocytes did not increase in any of the treated groups, indicating a lack of clastogenicity under the conditions of this study. Clinical signs of toxicity were reported in treated groups and premature death of one animal occurred in the high dose group. Although intraperitoneal administration would likely have led to exposure of the bone marrow, there was no evidence of the test chemical reaching the bone marrow as there were no statistically significant decreases in the polychromatic erythrocyte to normochromic erythrocyte (PCE/NCE*)* ratio. Therefore, there is uncertainty whether this result negates the positive *in vitro* studies (EFSA 2017; NICNAS 2015a).

In an unscheduled DNA synthesis (UDS) test conducted in accordance with OECD TG 486, Disperse Blue 360 (CAS No. 70693-64-0) was administered as a single dose via the intraperitoneal route to Crl:CR(SD)IGS BR male rats (n=4/dose) at 53.3 or 160 mg/kg bw. An upper dose of 160 mg/kg bw was chosen based on a range finding study where clinical signs of toxicity were reported at this dose and above. There were no signs of DNA damage in liver cells at any of the doses tested (NICNAS 2015a). The UDS assay is considered useful mainly for compounds that induce bulky DNA adducts or are positive in the Ames test. Therefore, there is uncertainty whether this result fully negates the positive *in vitro* studies (EFSA 2017; NICNAS 2015a).

Metabolites

The azo reduction metabolite 2-thiazolamine, 5-nitro- (CAS No. 121-66-4) was reported to be mutagenic in the following *in vitro* assays:

- bacterial reverse mutation assay (OECD TG 471) in *Salmonella typhimurium* strain TA100 with and without metabolic activation at concentrations greater than 100 µg/plate, but not in strains TA1535, TA1537, TA1538, and TA98 (IARC 1983).
- fluctuation test in *Klebsiella pneumonia* (no further details available) (IARC 1983).
- L5178Y mouse lymphoma cell forward mutagenesis assay with and without S9 activation (NICNAS 2017).
- mutagenicity assay in *Escherichia coli* (no further study details available) (OEHHA 1999; NICNAS 2017).

A NICNAS report on 1,4-benzenediamine, N4,N4-diethyl-2-methyl-, monohydrochloride (CAS No. 2051-79-8) indicated the chemical was not expected to be genotoxic based on negative *in vivo* assays for structurally similar chemicals 2,5-toluenediamine (CAS No. 95-70-5) and 2,5-toluenendiamine sulfate (2,5-TDS) (CAS No. 615-50-9) (NICNAS 2020).

In silico

Based on the mechanistic profiling functionality of the OECD QSAR Toolbox, structural alerts for DNA binding (nitrenium ion formation) and *in vivo* micronucleus formation (Aromatic

diazo, H-acceptor-path3-H-acceptor, and Nitro-aromatic) were identified for these chemicals in this group (OECD QSAR Toolbox version 4.2).

The genotoxicity potential of these chemicals in this group was predicted using DEREK Nexus (version 6.0.1) (Lhasa Limited). An alert for *in vitro* mutagenicity was reported for all group members. These alerts were considered plausible. Alerts for chromosomal damage for all group members were equivocal.

QSAR modelling using OASIS-TIMES (Optimised Approach based on Structural Indices Set–Tissue Metabolism Simulator) version 2.31.2 predicted that chemicals in this group and their metabolites induce chromosomal aberrations *in vitro*, micronucleus formation *in vivo*, and have positive predictions for *in vivo* liver in Transgenic Rodent mutation assay (TGR) (OASIS LMC). The predictions for the parent chemicals were within the applicability domain of the genotoxicity models and based on alerts for heterocyclic nitro compounds.

Carcinogenicity

No data are available on chemicals in this group. Based on the weight of evidence, the potential carcinogenic effects of these chemicals cannot be excluded.

In silico

All chemicals in the group had structural alerts for genotoxic carcinogenicity using the endpoint-specific profiling functionality of the OECD QSAR toolbox (v4.2). Alerts were based reactive oxygen species formation and generation of reactive on nitrenium ions. The highly reactive nitrenium ions covalently bind to DNA, provided that they are sufficiently stable to not undergo further reactions immediately. The stability of the nitrenium ion is correlated with mutagenicity, for example an Ames test with metabolic activation.

The knowledge based expert system DEREK Nexus version 6.0.1 (Lhasa Limited) utilised to predict the carcinogenic potential of these chemicals reported alerts for mammalian carcinogenicity with the alerts considered plausible.

Metabolites

The significance of azo reduction in the mutagenicity and carcinogenicity of azo dyes generally is well established. Azo reduction of chemicals in this group may release various arylamines (see **Toxicokinetics**).

The International Agency for Research on Cancer (IARC) determined that the azo-metabolite 2-thiazolamine, 5-nitro- (CAS No. 121-66-4) was '*Not classifiable as to its carcinogenicity to humans' (Group 3)* (IARC 1983). In a NICNAS report it was concluded that the carcinogenic potential cannot be ruled out (NICNAS 2017).

In a NICNAS report on 1,4-Benzenediamine, N4,N4-diethyl-2-methyl-, monohydrochloride (CAS No. 2051-79-8), this chemical was not considered to be carcinogenic based on genotoxicity data for the two analogue chemicals 2,5-toluenediamine (CAS No. 95-70-5) and 2,5-toluenendiamine sulfate (2,5-TDS; CAS No. 615-50-9), *in silico* modelling (QSAR) and metabolic reaction considerations. No *in vivo* toxicity studies were available for the chemical (NICNAS 2020).

Human health risk characterisation

Critical health effects

The critical health effect for risk characterisation is skin sensitisation.

Skin sensitisation includes two phases. The induction phase is the initial contact with a chemical that primes the immune system. The elicitation phase takes place after re-exposure to the same chemical that triggers the allergic reaction. A lower level of exposure is generally considered to be required for elicitation than for induction to occur (Palmer et al 2025).

There is vast amount of evidence of skin allergy from textiles containing Disperse Blue 106 and Disperse Blue 124 dyes (see **Sensitisation – Observations in humans**). The risk of induction of skin sensitisation from textiles is likely to be low (NICNAS 2019). However, there is evidence that part of the Australian population is already sensitised to disperse dyes or the amines they release (see **Sensitisation – Observations in humans**). Exposure to sensitising aromatic amines could potentially occur from other chemicals releasing the amines, such as black henna tattoo dyes or hair dyes (Akyüz and Ata 2008).

The elicitation threshold was determined to be 0.0003 µg/cm² based on a patch-test study (see **Skin sensitisation – Observations in humans**).

Public risk

The worst case exposure scenario for the public for articles with prolonged and extensive contact with skin are clothing for textile articles and footwear for leather articles. Exposure through clothing (textiles) and footwear (leather) articles is considered to represent worst case scenarios with exposure assumptions for clothing considered indicative for non-textile and leather articles such as nappies.

The risk based concentration values for elicitation of an allergic reaction in clothing (textiles) and footwear (leather) can be calculated using the following equations:

- *Limit in articles (**µg/cm²**) = elicitation threshold dose/(migration factor * contact surface *frequency of exposure)*
- *Limit in articles (**mg/kg**) = Limit in articles (µg/cm²)*10 000 (conversion factor cm² to m²) /(1000 (conversion factor µg to mg)* surface weight in* kg/m²*).*

Using exposure assumptions (see **public exposure** section) the derived risk based concentration values for elicitation of an allergic reaction were:

- 0.1 mg/kg or 1 mg/kg for textiles using migration factors of 5 and 0.5, respectively
- 0.033 mg/kg or 0.33 mg/kg for leather using migration factors of 5 and 0.5, respectively.

These elicitation levels are well below the typical detection limits for disperse blue dyes in textiles (30–50 mg/kg). Therefore, it is not possible to set a safe limit for these dyes in articles with prolonged contact with skin.

References

ACCC (Australian Competition and Consumer Commission) (n.d.-a) Safety guidance on concentrations of particular chemicals in certain consumer goods, ACCC website, accessed 27 May 2025.

ACCC (Australian Competition and Consumer Commission) (n.d.-b) Textiles recalled after tests for azo dyes, ACCC website, accessed 27 May 2025.

Akyüz M and Ata S (2008) Determination of aromatic amines in hair dye and henna samples by ion-pair extraction and gas chromatography–mass spectrometry, Journal of Pharmaceutical and Biomedical Analysis, Volume 47(1) 68-80, 10.1016/j.jpba.2007.12.011.

BfR (German Federal Institute for Risk Assessment) (2012) Updated BfR Opinion No. 041/2012: *Introduction to the problems surrounding garment textiles.*
Carlsson J, Åström T, Östman C, Nilsson U (2022) Disperse azo dyes, arylamines and halogenated dinitrobenzene compounds in synthetic garments on the Swedish market. Contact Dermatitis, 87(4):315-324. doi:10.1111/cod.14163.

Collier SW, Storm JE, Bronaugh RL (1993) Reduction of azo dyes during *in vitro* percutaneous absorption, *Toxicol Appl Pharmacol,* 118(1):73-9. doi:10.1006/taap.1993.1011. PMID: 8430426.

ECHA (European Chemicals Agency) (2019) *CLH report: 2-[N-ethyl-4-[(5-nitrothiazol-2-yl)azo]-m-toluidino]ethyl acetate; Ethanol, 2-[ethyl[3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]phenyl]amino]-, 1-acetate; C.I. Disperse Blue 124*, ECHA, accessed 25 November 2024.

ECHA (European Chemicals Agency) (2020a) *Committee for Risk Assessment (RAC), Committee for Socio-economic Analysis (SEAC) Opinion: on an Annex XV dossier proposing restrictions on Skin sensitising substances,* ECHA, accessed 27 May 2024.

ECHA (European Chemicals Agency) (2020b) *Committee for Risk Assessment (RAC) Opinion: proposing harmonised classification and labelling at EU level of 2-[N-ethyl-4-[(5-nitrothiazol-2-yl)azo]-m-toluidino]ethyl acetate; C.I. Disperse Blue 124,* ECHA, accessed 25 November 2024.

ECHA (European Chemicals Agency) (2022) *Committee for Risk Assessment (RAC) Annex 1 Background document to the Opinion proposing harmonised classification and labelling at EU level of 2-[ethyl[3-methyl-4-[(5-nitrothiazol-2-yl)azo]phenyl]amino]ethanol; (Disperse Blue 106),* ECHA, accessed 27 May 2025.

Engel E, Vasold R, Santarelli F, Maisch T, Gopee N, Howard P, Landthaler M, Baumler W (2009) Tattooing of skin results in transportation and light-induced decomposition of tattoo pigments – a first quantification *in vivo* using a mouse model. Experimental Dermatology 19 pp. 54-60.

EU (European Union) (n.d.) Commission Decision of 5 June 2014 establishing the ecological criteria for the award of the EU Ecolabel for textile products (notified under document C(2014) 3677) (Text with EEA relevance) (2014/350/EU)Text with EEA relevance, accessed 12 August 2025.

German Federal Institute for Risk Assessment (BfR) (2012) *Introduction to the problems surrounding garment textiles.* Updated BfR Opinion No. 041/2012, accessed 03 June 2025.

Hausen, B.M. (1993), Contact allergy to Disperse Blue 106 and Blue 124 in black “velvet” clothes. Contact Dermatitis, 28: 169-173. doi.org/10.1111/j.1600-0536.1993.tb03381.x

IARC (International Agency for Research on Cancer) (1983) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans – Some Food Additives, Feed Additives and Naturally Occurring Substances*. Vol 31: 71-78.

International Dialogue for the Evaluation of Allergens (IDEA) Project (2016) *Final Report on the QRA2. Skin Sensitisation Quantitative Risk Assessment for Fragrance Ingredients*, accessed 03 June 2025.

International Organization for Standardization (ISO) (2015) ISO 16373-1:2015 Textiles — Dyestuffs Part 1: General principles of testing coloured textiles for dyestuff identification, accessed 29 September 2025.

Malinauskiene L, Zimerson E, Bruze M, Ryberg K, Isaksson M (2012) Are allergenic disperse dyes used for dyeing textiles? Contact Dermatitis, 67(3):141-8. doi:10.1111/j.1600-0536.2012.02129.x. Epub 2012 Jul 2. PMID: 22748162.

Militello M, Hu S, Laughter M and Dunnick CA (2020) 'American Contact Dermatitis Society Allergens of the Year 2000 to 2020'. *Dermatol Clin*., 38(3):309-320. doi:10.1016/j.det.2020.02.011

National Institute of Public Health and the Environment (RIVM) (1999) *Cancer risk assessment of azo dyes and aromatic amines from garment and footwear*, Zeilmaker and co-workers. RIVM Report 601503014, accessed 03 June 2025.

National Toxicology Program (NTP) 1983. *Bioassay of 2-amino-5-nitrothiazole for possible carcinogenicity*. National Cancer Institute, Carcinogenesis, 53, accessed 12 August 2025

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2013), *1,4-Benzenediamine, 2-methyl-: Human health tier II assessment*, NICNAS, accessed 25 August 2025.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2015a) *Benzenamine, N,N-diethyl-3-methyl-4-[2-(5-nitro-2-thiazolyl)diazenyl]-*, NICNAS, accessed 22 November 2024.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2015b), *1,4-Benzenediamine, N4,N4-diethyl-2-methyl-, monohydrochloride: Human health tier II assessment*, NICNAS, accessed 25 August 2025.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2017) *IMAP Single Assessment Report – 2-Thiazolamine, 5-nitro-: Human health tier II assessment*, NICNAS, accessed 07 March 2025.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2019) *Risk assessment of sensitising aromatic amines as metabolites of azo dyes used in textiles*, NICNAS, accessed 29 May 2025.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2020) *IMAP Group Assessment Report – 1,4-Benzenediamine, 2-methyl-, sulfate: Human health tier II assessment*, NICNAS, accessed 07 March 2025.

OEKO-TEX (n.d.) *Restricted Substance List: OEKO-TEX®*, OEKA-TEX website, accessed 12 August 2025.

Palmer B, Gao Y, Ryan C, Kern P (2025) Skin sensitisation elicitation: Evaluation of the general threshold and considerations for use. Contact Dermatitis, 92(3): 197-208. doi:10.1111/cod.14718

Ryberg K, Goossens A, Isaksson M, Gruvberger B, Zimerson E, Persson L, and Bruze M. (2009): Patch testing of patients allergic to Disperse Blue 106 and Disperse Blue 124 with thin-layer chromatograms and purified dyes. Contact dermatitis 60 (5), 270-278. doi: 10.1111/j.1600-0536.2009.01538.x

SCCP (Scientific Committee on Consumer Safety) 2011) Opinion on Toluene-2,5-diamine and its sulfate, European Commission, accessed 15 September 2025.

Slodownik D, Williams J, Tate B, Tam M, Cahill J, Frowen K and Nixon R (2011), Textile allergy – the Melbourne experience. Contact Dermatitis, 65: 38-42. https://doi.org/10.1111/j.1600-0536.2010.01861.x

Stingley R, Zou W, Heinze T, Chen H and Cerniglia C (2010) Metabolism of azo dyes by human skin microbiota. *Journal of Medical Microbiology*, 59, pp. 108-114.

US EPA (United States Environmental Protection Agency) (n.d.) *TSCA Inventory Notification (Active-Inactive) Rule*, accessed 26 August 2025.