MCL Report for: 1-hydroxy-4-(p-toluidino)anthraquinone (Solvent Violet 13)

Proposal for mandatory classification and labelling (MCL) based on Annex VI, Part 2 of the retained CLP Regulation (EU) No. 1272/2008 as amended for Great Britain

EC Number: 201-353-5

CAS Number: 81-48-1

Date: November 2023

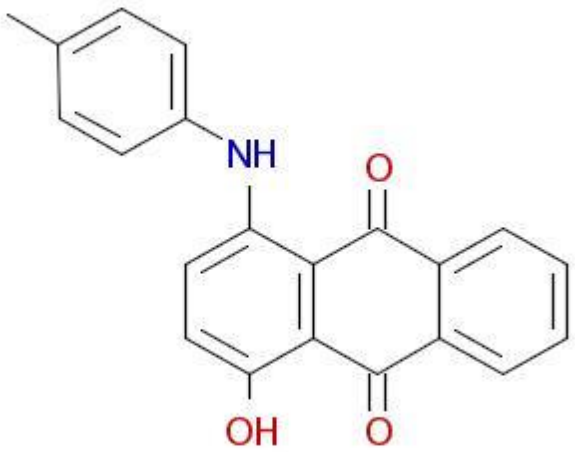
Contents

Identity of the substance

Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance (Source: ECHA, 2023)

Name(s) in the IUPAC nomenclature or other international chemical name(s)	1-hydroxy-4-((4-methylphenyl)amino)-9,10-anthracenedione 1-hydroxy-4-(4-methylanilino)anthracene-9,10-dione 1-Hydroxy-4-(p-toluidino)anthraquinone 1-hydroxy-4-(p-toluidino)anthraquinone 1-hydroxy-4-(p-tolylamino)anthracene-9,10-dione 1-Hydroxy-4-[(4-methylphenyl)amino]-9,10-anthraquinone 1-hydroxy-4-[(4-methylphenyl)amino]-9,10-anthraquinone 1-hydroxy-4-[(4-methylphenyl)amino]-9,10-dihydroanthracene-9,10- dione 1-hydroxy-4-[(4-methylphenyl)amino]-9,10-dihydroanthracene-9,10-dione 1-Hydroxy-4-p-toluidinoanthraquinone 9,10-Anthracenedione, 1-hydroxy-4-[(4-methylphenyl)amino]-
Other names (usual name, trade name, abbreviation)	C. I. Solvent Blue 90 C. I. Disperse Blue 72 C. I. Solvent Violet 13 Disperse Blue 72 Kenawax Violet ASPKenawax Blue 5RP Solvent Violet 13 Unisol violet A

	Keyplast Violet IRS Macrolex Violet B Macrolex Violett B Oracet Blue 640 Oracet Violet 580 Sandoplast Violet RSB Alizurol purple
ISO common name (if available and appropriate)	Solvent Violet 13
EC number (if available and appropriate)	201-353-5
EC name (if available and appropriate)	Not applicable
CAS number (if available)	81-48-1
Other identity code (if available)	Not applicable
Molecular formula	$C_{21}H_{15}NO_3$
Structural formula	
SMILES notation (if available)	Cc1ccc(Nc2ccc(O)c3C(=O)c4ccccc4C(=O)c23)cc1

Molecular weight or molecular weight range	329.4 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	≥ 50% ≤ 100% w/w

1.1 Composition of the substance

Table 1: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current MCL on GB MCL list (if applicable)
Solvent Violet 13	≥ 50% ≤ 100%	None

Table 2: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	Concentration range (% w/w minimum and maximum)	Current MCL on GB MCL list (if applicable)	The impurity contributes to the classification and labelling?
1,4-bis(p-tolylamino)anthraquinone (CAS 128-80-3)	≥ 0% ≤ 3%	Not on MCL list	No

Table 3: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	Function	Concentration range (% w/w minimum and maximum)	Current MCL on GB MCL list (if applicable)	The additive contributes to the classification and labelling?
N/A	N/A	N/A	N/A	N/A

2. Proposed mandatory classification and labelling

Table 5: Proposed mandatory classification and labelling according to the GB CLP criteria

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATEs	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current GB MCL list entry	No current GB MCL list entry.										
Proposed Classification	TBD	1-hydroxy-4-(p-toluidino)anthraquinone (Solvent Violet 13)	201-353-5	81-48-1	Skin Sens. 1B	H317	GHS07 Wng	H317	N/A	N/A	N/A
Proposed entry on the MCL list	TBD	1-hydroxy-4-(p-toluidino)anthraquinone (Solvent Violet 13)	201-353-5	81-48-1	Skin Sens. 1B	H317	GHS07 Wng	H317	N/A	N/A	N/A

Table 6: Reason for not proposing mandatory classification and status under public consultation

Hazard class	Classification / reason for no classification	Within the scope of public consultation
Explosives	Hazard class not assessed in this dossier	No
Flammable gases (including chemically unstable gases)	Hazard class not assessed in this dossier	No
Oxidising gases	Hazard class not assessed in this dossier	No
Gases under pressure	Hazard class not assessed in this dossier	No
Flammable liquids	Hazard class not assessed in this dossier	No
Flammable solids	Hazard class not assessed in this dossier	No
Self-reactive substances	Hazard class not assessed in this dossier	No
Pyrophoric liquids	Hazard class not assessed in this dossier	No
Pyrophoric solids	Hazard class not assessed in this dossier	No
Self-heating substances	Hazard class not assessed in this dossier	No
Substances which in contact with water emit flammable gases	Hazard class not assessed in this dossier	No
Oxidising liquids	Hazard class not assessed in this dossier	No
Oxidising solids	Hazard class not assessed in this dossier	No
Organic peroxides	Hazard class not assessed in this dossier	No
Corrosive to metals	Hazard class not assessed in this dossier	No
Acute toxicity via oral route	Hazard class not assessed in this dossier	No
Acute toxicity via dermal route	Hazard class not assessed in this dossier	No
Acute toxicity via inhalation route	Hazard class not assessed in this dossier	No
Skin corrosion/irritation	Hazard class not assessed in this dossier	No
Serious eye damage/eye irritation	Hazard class not assessed in this dossier	No
Respiratory sensitisation	Hazard class not assessed in this dossier	No
Skin sensitisation	**Skin Sens. 1B; H317**	Yes
Germ cell mutagenicity	Hazard class not assessed in this dossier	No
Carcinogenicity	Hazard class not assessed in this dossier	No
Reproductive toxicity	Hazard class not assessed in this dossier	No
Specific target organ toxicity-single exposure	Hazard class not assessed in this dossier	No
Specific target organ toxicity-repeated exposure	Hazard class not assessed in this dossier	No
Aspiration hazard	Hazard class not assessed in this dossier	No
Hazardous to the aquatic environment	Hazard class not assessed in this dossier	No
Hazardous to the ozone layer	Hazard class not assessed in this dossier	No

3. History of the classification and labelling

1-hydroxy-4-(p-toluidino)anthraquinone, also known as Solvent Violet 13, has not previously been considered for mandatory classification and labelling under GB CLP and does not have an existing entry on the GB MCL list. In the EU, 2723 notifiers have submitted self-classifications for this substance to ECHA's Classification and Labelling Inventory[1]. A breakdown of these notifications is provided below:

Table 7: Summary of the notifications submitted to the EU classification and labelling database (Source: ECHA, 2023).

Classification	Number of notifiers
Skin Sens. 1B; H317	26
Skin Sens. 1B; H317 **Aquatic Chronic 4; H413**	315
Skin Sens. 1; H317	33
Aquatic Chronic 4; H413	1
Not classified	2348

[1] Inventory checked October 2023. Available at https://echa.europa.eu/home

4. Justification that action is needed

The Health and Safety Executive, in its capacity as the Agency for UK REACH, has prepared a proposal to restrict certain hazardous substances in inks used for tattooing and permanent makeup (PMU) in accordance with Article 69(1) of UK REACH[2].

The proposed restriction applies to substances that have mandatory classification for various hazards, including skin sensitisation (H317). It also applies to substances that are prohibited for use in cosmetic products under Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products (as amended) (hereafter referred to as the Cosmetic Products Regulation). HSE considered if certain substances, which are brought into scope because they are listed in Annex II of the Cosmetic Products Regulation, should be derogated from the proposed restriction. Annex II of the Cosmetic Products Regulation prohibits the use of these substances in hair dyes. However, as they are also listed in Annex IV of the Cosmetic Products Regulation, they are permitted for use as colourants in some other cosmetic products. HSE has therefore reviewed the available hazard information on these substances and determined that for two of them (Pigment Red 83, CAS 72-48-0; and Solvent Violet 13, CAS 81-48-1) there is a potential concern for skin sensitisation. A mandatory classification for skin sensitisation (H317) would bring the substances into scope of the proposed restriction.

Therefore, HSE as the Agency for GB CLP (hereafter referred to as ‘the Agency’) has prepared this targeted report to propose the mandatory classification and labelling of Solvent Violet 13 for skin sensitisation. The substance has not been included in the proposed restriction derogation.

[2] Restrictions - HSE

5. Identified uses

Solvent Violet 13 is used in the production of plastic articles, in thermoprinting inks, in professional laboratories and in paper production (ECHA, 2023).

6. Data sources

This report was compiled from data in UK REACH registration dossiers and ECHA's dissemination platform (ECHA, 2023).

7. Physicochemical properties

Table 8: Summary of physicochemical properties (source: ECHA, 2023)

Property	Value	Reference	Comment (e.g., measured or estimated)
Physical state at 20°C and 101,3 kPa	Solid dark violet powder	Weiss, B. (2018) Seaber, J, A. (1994)	Visual inspection
Melting/freezing point	190°C	Heinz, U. (2018)	EC Test Procedure A.1
Boiling point	>300°C at 1028hPa	Heinz, U. (2018)	Differential scanning calorimetry
Relative density	The relative density of Solvent Violet 13 was not determinable owing to methodological limitations.	Opala, C. (2018)	Pycnometer method
Vapour pressure	3.25×10^{-9} Pa at 25°C	Dammers, S. (2018)	QSAR estimation (modified grain method)
Surface tension	Not determined (water solubility < 1mg/L at 20 °C)		
Water solubility	0.0093 mg/L in demineralised water at ambient temperature (24-25°C).	Az, R. (2014)	Flask method
Partition coefficient n-octanol/water	Log Pow: 4.26 at 25°C	Az, R. (2014)	Flask method
Flash point	Not applicable		Not applicable based on physical state (solid)
Flammability	Not flammable (burning index: 1)	Heinz, U., Keldenich, H-P. (2005)	VDI 2263 Blatt 1
Explosive properties	Not applicable		Not applicable; molecule does not contain chemical groups associated with explosive properties
Self-ignition temperature	Self-ignition was not observed up to the melting point	Heinz, U., Keldenich, H-P. (2005)	EC Test Procedure A.16

Property	Value	Reference	Comment (e.g., measured or estimated)
Oxidising properties	Not applicable		Not applicable; the molecule does not contain any chemical groups associated with oxidising properties.
Granulometry	No data		
Stability in organic solvents and identity of relevant degradation products	No data		
Dissociation constant	No data		
Viscosity	No data		

8. Evaluation of physical hazards

Not assessed.

9. Toxicokinetics (absorption, distribution, metabolism and excretion)

No experimental toxicokinetic data are available. The physicochemical properties of substances can inform on their potential to be absorbed dermally. Moderate octanol-water partition coefficient (log P_{ow}) values between -1 and 4 and relatively low molecular weights (MW) below 500 g/mol are most favourable for absorption. However, highly lipophilic small molecules (log P_{ow} > 4, and MW < 500 g/mol) that are also poorly soluble in water may also undergo dermal absorption.

The substance's Log P_{ow} of 4.26 indicates high lipophilicity, but its MW of 329.4 g/mol and low water solubility of 0.0093 mg/L (at 20 °C) suggest that dermal absorption cannot be excluded.

10. Evaluation of health hazards

10.1 Acute toxicity – oral route

Not assessed.

10.2 Acute toxicity – dermal route

Not assessed.

10.3 Acute toxicity – inhalation route

Not assessed.

10.4 Specific target organ toxicity – single exposure (STOT SE)

Not assessed.

10.5 Skin corrosion/irritation

Not assessed.

10.6 Serious eye damage/eye irritation

Not assessed.

10.7 Respiratory sensitisation

Not assessed.

10.8 Skin sensitisation

The potential for Solvent Violet 13 to induce skin sensitisation has been tested in four local lymph node assays (LLNA) in mice. Additionally, an older guinea pig maximization test (GPMT) is available.

Table 9: Summary of animal studies on skin sensitisation (source: ECHA, 2023)

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results
LLNA Guideline: OECD 429 (2010) Deviations: none GLP Reference: Anon, 2016	Mice, CBA/Ca, females Pre-screen test: 2 animals Main test & vehicle control: 5/group (20 in total)	Solvent violet 13 (1-hydroxy-4-(p-toluidino)anthraquinone) Purity: 97% Vehicle: dimethylformamide (DMF) Positive control: hexyl cinnamic aldehyde (HCA; CAS No. 101-86-0) in acetone/olive oil (4:1)	5, 10 & 25% Exposure: as per the test guideline (TG) (3 day topical) Treatment with tritiated (3H)-methyl thymidine (^{3}HTdR): 5 hours	**Sensitiser** Stimulation index (SI): 5% = 2.1 10% = 2.6 25% = 3.5 **EC3 = 16.7%** Positive & negative controls gave the expected results.
LLNA Guideline: OECD 429 (2010) Deviations: none GLP Reference: Anon, 2014	Mice, CBA/Ca, females Preliminary test: 2/group Main test: 4/group Vehicle control: 4/group	Solvent violet 13 (1-hydroxy-4-(p-toluidino)anthraquinone) Purity: 97.8% Vehicle: acetone/olive oil (4:1) Positive control: HCA in acetone/olive oil (4:1)	25% Exposure: as per TG (3-day topical administration)	**Sensitiser** Stimulation index (SI): **18.97 at 25% concentration** Positive & negative controls gave the expected results.

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance**	**Dose levels, duration of exposure**	**Results**
LLNA Guideline: OECD 429 (2010) Deviations: none GLP Reference: Anon, 2008	Mice, CBA/Ca, females Preliminary test: 4/group Main test: 5/group Vehicle control: 4/group	Solvent violet 13 (1-hydroxy-4-(p-toluidino)anthraquinone) Purity: 97.8% (solid) Vehicle: DMSO Positive control: HCA in acetone/olive oil (4:1)	20% Exposure: as per TG (3-day topical administration)	**Sensitiser** Stimulation index (SI): **5.33 at 20% concentration** Positive & negative controls gave the expected results.
LLNA Guideline: OECD 429 (2010) Deviations: none GLP Reference: Anon, 2008	Mice, CBA/Ca, females Preliminary test: 4/group Main test: 5/group Vehicle control: 4/group	Solvent violet 13 (1-hydroxy-4-(p-toluidino)anthraquinone) Purity: 97.3% Vehicle: DMSO Positive control: HCA	20% Exposure: as per TG	**Sensitiser** Stimulation index (SI): **4.25 at 20% concentration** Positive & negative controls gave the expected results.
GPMT Guideline: OECD 406 (1992) Deviations: none GLP Reference: Anon, 1994	Guinea pig, Pirbright White Strain (Tif: DHP) Main test: 5/sex/group Vehicle control: 10 female animals	Solvent violet 13 (1-hydroxy-4-(p-toluidino)anthraquinone) Purity: ~95% (solid) Vehicle: oleum arachidis (first induction); Vaseline (second induction, challenge)	Induction(s): 5% (3 pairs of intradermal injections; day 0); 50% (epicutaneous, occlusive; day 8) Challenge: 10, 20, 30 or 50% Exposure: 2 x induction (day 0 and 8); 24 h challenge (day 21)	**Non-sensitiser** **20 and 15% positive skin reactions** (24h and 48h after challenge, respectively) Positive & negative controls gave the expected results.

10.8.1 Short summary and overall relevance of the provided information on skin sensitisation

The skin sensitisation potential of Solvent Violet 13 has been investigated in four GLP- and OECD-compliant mouse local lymph node assays (LLNA), and one older guinea pig maximisation test (GPMT).

In the key LLNA, groups of 5 female CBA/Ca mice were treated with an epidermal application of 5, 10 or 25% test material in DMF in accordance with OECD TG 429; these concentrations used in the main test were determined in a pre-screen test. The negative control animals were treated in an identical fashion, concurrently with the main test, but exposed to the vehicle only, whilst the positive control experiment was conducted on a periodic basis by the same laboratory. The stimulation indices (SIs) determined from pooled lymph nodes (2 per animal) were 2.1, 2.6 and 3.5 at concentrations of 5, 10 and 25% (in DMF), respectively. The EC3 value was 16.7%.

Information from three additional LLNA studies is available, all of which employed a single concentration of the test material in vehicle (acetone/olive oil (4:1) in one study, and DMSO in the remaining two studies). All three studies yielded positive results (SI > 3), but, because of the single concentrations tested, did not inform on potency.

In the older guinea pig maximisation test (GPMT), groups of Pirbright White (Tif: DHP) guinea pigs underwent two induction exposure treatments – first (day 0), with 5% solution of test material (in oleum arachidis) administered as three pairs of intradermal injections (0.1 mL per injection), concurrently, into the right and left shaved neck of both the test and control group animals; and second (day 8), via epidermal application of 50% solution (w/w) of test material (in Vaseline) and applied on a filter paper patch to the neck of the test animals under occlusive conditions for 48 hours. Animals in the control group were treated with vehicle only. After 10 days, 100% of the test group animals showed mild-to-moderate epidermal irritation on the application site.

For the challenge exposure (day 21), the animals were treated with an epidermal application of 10, 20, 30 or 50% test material in vehicle (Vaseline) for 24 hours. Post-challenge, two reaction readings were taken, 24 and 48 hours after removing the dressings, and graded according to Draize scoring scale. The body weights were recorded at the start and end of the test.

The test animals showed limited indication of skin sensitisation – 20 and 15% of positive reactions at 24 and 48 hour reading, respectively, hence the GB CLP criterion of ≥ 30% positive reactions in an adjuvant guinea-pig test were not met.

10.8.2 Comparison with the GB CLP criteria

All four LLNA studies showed clear evidence of the induction of skin sensitisation, with SI values > 3. Therefore, the criterion for classification for skin sensitisation (SI ≥ 3 in a LLNA

conducted in accordance with OECD TG 429) is met. Information on potency was available from one of these studies (Anon, 2016), in which an EC3 value of 16.7% was derived. Since this EC3 value was > 2%, the criterion for classification in sub-category 1B is met. The three additional studies only used single concentrations and so do not allow a potency estimation.

An indication of skin sensitisation potential was also obtained in the GPMT, as up to 20% of animals showed skin reactions 24 hours after the challenge phase. However, this is below the cut-off of ≥ 30% animals in an adjuvant guinea-pig test with skin reactions that would lead to classification for skin sensitisation under GB CLP.

Considering the weight of evidence from the available LLNA data, and according to the GB CLP criteria, the substance meets the criteria for classification for skin sensitisation in Category 1B; H317.

10.8.3 Conclusion on classification and labelling for skin sensitisation

Solvent Violet 13 meets the classification criteria for Skin Sens. 1B; H317 (May cause an allergic skin reaction).

10.9 Specific target organ toxicity – repeated exposure (STOT RE)

Not assessed.

10.10 Germ cell mutagenicity

Not assessed.

10.11 Carcinogenicity

Not assessed.

10.12 Reproductive toxicity

Not assessed.

10.13 Aspiration hazard

Not assessed.

11. Evaluation of environmental hazards

Not assessed.

12. Evaluation of additional hazards

12.1 Hazardous to the ozone layer

Not assessed.

13. Additional labelling

No additional labelling is proposed.

14. References

ECHA (2017) Guidance on the application of the CLP criteria. Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, version 5.0, ref: ECHA-17-G-21-EN. Available at https://www.echa.europa.eu/

ECHA (2023) ECHA's dissemination website: http://echa.europa.eu/

UK REACH Agency (2023) Agency opinion on the Annex 15 dossier proposing restrictions on Substances in tattoo ink and permanent make-up. Available at https://www.hse.gov.uk/reach/restrictions/tattoo-inks/opinion.pdf

Further information

For information about health and safety, or to report inconsistencies or inaccuracies in this guidance, visit the Agency website.

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