Annex XV dossier

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR 1A OR 1B, PBT, vPvB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name(s): [4-[4,4'-bis(dimethylamino) benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride (C.I. Basic Violet 3) *

EC Number(s): 208-953-6

CAS Number(s): 548-62-9

Submitted by: European Chemicals Agency at the request of the European Commission

PUBLIC VERSION: *This version does not include the confidential annexes to Parts I and II.*

* **The substance is proposed only where it contains Michler's ketone (EC Number: 202-027-5) or Michler's base (EC Number: 202-959-2) ≥ 0.1% (wt/wt)**

CONTENTS

TABLES

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR 1A OR 1B, PBT, VPVB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name(s): [4-[4,4'-bis(dimethylamino) benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride (C.I. Basic Violet 3) [2]

EC Number(s): 208-953-6

CAS Number(s): 548-62-9

- The substance is proposed to be identified as substance meeting the criteria of Article 57 (a) of Regulation (EC) 1907/2006 (REACH) where it contains Michler's ketone (EC Number: 202-027-5) or Michler's base (EC Number: 202-959-2) ≥ 0.1%, owing to its classification as carcinogen category 1B[3] which corresponds to classification as carcinogen category 2[4].

Summary of how the substance meets the Carcinogen 1B criteria

[4-[4,4'-bis(dimethylamino)benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride (C.I. Basic Violet 3) with Michler's ketone ≥ 0.1% is listed as index number 612-205-00-8 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) as carcinogen, Carc. 1B (H350: "May cause cancer.") The corresponding classification in Annex VI, part 3, Table 3.2 (the list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is carcinogen, Carc. Cat. 2, R45 ("May cause cancer.")

Therefore, this classification of [4-[4,4'-bis(dimethylamino)benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride (C.I. Basic Violet 3) in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification as carcinogen in accordance with Article 57 (a) of REACH.

Michler's base (N,N,N',N'-tetramethyl-4,4'-methylenedianiline; EC Number: 202-959-2) is listed as Index number 612-201-00-6 in the CLP Regulation and classified in Annex VI, part 3, Table 3.1 as carcinogen, Carc. 1B (H350: "May cause cancer.") The corresponding classification in Annex VI, part 3, Table 3.2 of the CLP Regulation is carcinogen, Carc. Cat. 2, R45 ("May cause cancer.")

---

[2] The substance is proposed only where it contains Michler's ketone (EC Number: 202-027-5) or Michler's base (EC Number: 202-959-2) ≥ 0.1% (wt/wt)

[3] Classification in accordance with Regulation (EC) No 1272/2008 Annex VI, part 3, Table 3.1 List of harmonised classification and labelling of hazardous substances.

[4] Classification in accordance with Regulation (EC) No 1272/2008, Annex VI, part 3, Table 3.2 List of harmonised classification and labelling of hazardous substances (from Annex I to Council Directive 67/548/EEC).

According to Art. 10(1) of the CLP Regulation, specific concentration limits and generic concentration limits are limits assigned to a substance indicating a threshold at or above which the presence of that substance in another substance (or in a mixture) as an identified impurity, additive or individual constituent leads to the classification of the substance (or mixture) as hazardous.

For Michler's base no specific concentration limit is set in Annex VI of the CLP Regulation and therefore the generic concentration limit is to be used for the purpose of determining classification of substances (or mixtures) containing Michler's base. The generic concentration limit for carcinogens, Carc. 1B is 0.1%, as set out in Table 3.6.2 in Part 3 of Annex I to the CLP Regulation.

Therefore, the above classification of Michler's base in Annex VI to Regulation (EC) No 1272/2008 show that where the substance [4-[4,4'-bis(dimethylamino) benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride (C.I. Basic Violet 3) contains Michler's base ≥ 0.1% it also meets the criteria for classification as carcinogen in accordance with Article 57 (a) of REACH.

Registration dossiers submitted for the substance: Yes

PART I

JUSTIFICATION

1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

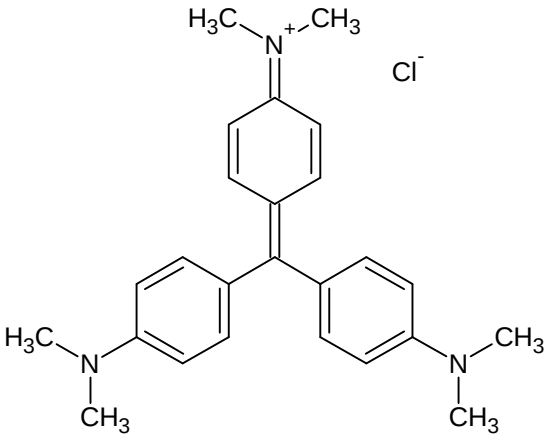
1.1 Name and other identifiers of the substance

Table 1: Substance identity

EC number:	208-953-6
EC name:	[4-[4,4'-bis(dimethylamino)benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride
CAS number (in the EC inventory):	548-62-9
Deleted CAS numbers:	– 7077-31-8 – 23355-47-7
CAS numbers indicated in the Colour Index International for Basic Violet 3	– 548-62-9 – 603-48-5 – 14426-25-6
CAS name:	Methanaminium, N-[4-[bis[4-(dimethylamino)phenyl]methylene]-2,5-cyclohexadien-1-ylidene]-N-methyl-, chloride (1:1)
IUPAC name:	4-{Bis[4-(dimethylamino)phenyl]methylidene}-N,N-dimethylcyclohexa-2,5-dien-1-iminium chloride
Index number in Annex VI of the CLP Regulation	612-204-00-2, 612-205-00-8
Molecular formula:	$C_{25}H_{30}ClN_3$
Molecular weight:	408 g/mol
Synonyms:	– C.I. Basic Violet 3 – Basic Violet 3 – Crystal Violet Technical – Crystal Violet USP – Gentersal – Gentian violet – Gentian Violet B

	– Gentiaverm – Genticid – Gentioletten – Hecto Violet R – Hectograph Violet SR – Hexamethyl violet – Hexamethyl-p-rosaniline chloride – Hexamethylpararosaniline chloride

Structural formula:



1.2 Composition of the substance

Name: [4-[4,4'-bis(dimethylamino)benzhydrylidene]cyclohexa-2,5-dien-1-ylidene] dimethylammonium chloride

Description: ---

Degree of purity: > 76 % - < 90 % (w/w) (according to information received in registration dossiers)

Table 2: Constituents

Constituents	**Typical concentration**	**Concentration range**	**Remarks**
[4-[4,4'-bis(dimethylamino)benzhydrylidene] cyclohexa-2,5-dien-1-ylidene] dimethylammonium chloride EC #: 208-953-6		> 76 % - < 90 %	According to information from registration dossiers.

Table 3: Impurities

Impurities	**Typical concentration**	**Concentration range**	**Remarks**
4,4'-bis(dimethylamino)benzophenone EC #: 202-027-5		See confidential Annex 3	According to information from registration dossiers.
N,N,N',N'-tetramethyl-4,4'-methylenedianiline EC #: 202-959-2		See confidential Annex 3	According to information from registration dossiers.
Further impurities: see confidential Annex 3			According to information from registration dossiers.

Table 4: Additives

Additives	**Typical concentration**	**Concentration range**	**Remarks**
None			According to information from registration dossiers.

1.3 Physico-chemical properties

No information available

2 HARMONISED CLASSIFICATION AND LABELLING

C.I. Basic Violet 3 with Michler's ketone ≥ 0.1%

[4-[4,4'-bis(dimethylamino)benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride (C.I. Basic Violet 3) is listed as index numbers 612-204-00-2 and 612-205-00-8 in Annex VI of Regulation (EC) No 1272/2008 as follows:

Table 5: Classification of C.I. Basic Violet 3 according to Part 3 of Annex VI, Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008

International Chemical Identification	**EC No**	**CAS No**	**Classification**		**Labelling**			**Spec. Conc. Limits, M-factors**	**Notes**
			Hazard Class and Category Code(s)	**Hazard statement code(s)**	**Pictogram, Signal Word Code(s)**	**Hazard state-ment code(s)**	**Suppl. Hazard statement code(s)**		
C.I. Basic Violet 3; 4-[4,4'-bis(dimethylamino) benzhydrylidene] cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride	208-953-6	548-62-9	Carc. 2 Acute Tox. 4 * Eye Dam. 1 Aquatic Acute 1 Aquatic Chronic 1	H351 H302 H318 H400 H410	GHS08 GHS05 GHS07 GHS09 Dgr	H351 H302 H318 H410	-	-	-
C.I. Basic Violet 3 with ≥ 0,1 % of Michler's ketone (EC no. 202-027-5)	208-953-6	548-62-9	Carc. 1B Acute Tox. 4 * Eye Dam. 1 Aquatic Acute 1 Aquatic Chronic 1	H350 H302 H318 H400 H410	GHS08 GHS05 GHS07 GHS09 Dgr	H350 H302 H318 H410	-	-	-

* *Indicates that the classification corresponds to the minimum classification for a category*

Table 6: Classification of C.I. Basic Violet 3 according to Part 3 of Annex VI, Table 3.2 (list of harmonized classification and labelling of hazardous substances from Annex I of Council Directive 67/548/EEC) of Regulation (EC) No 1272/2008

International Chemical Identification	**EC No**	**CAS No**	**Classification**	**Labelling**	**Concentration Limits**	**Notes**
C.I. Basic Violet 3; 4-[4,4'-bis(dimethylamino) benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride	208-953-6	548-62-9	Carc. Cat. 3; R40 Xn; R22 Xi; R41 N; R50-53	Xn; N R: 22-40-41-50/53 S: (2-)26-36/37/39-46-60-61	-	-
C.I. Basic Violet 3 with ≥ 0.1 % of Michler's ketone (EC no. 202-027-5)	208-953-6	548-62-9	Carc. Cat. 2; R45 Xn; R22 Xi; R41 N; R50-53	T; N R: 45-22-41-50/53 S: 53-45-60-61	-	E

Note E:

Substances with specific effects on human health (see Chapter 4 of Annex VI to Directive 67/548/EEC) that are classified as carcinogenic, mutagenic and/or toxic for reproduction in categories 1 or 2 are ascribed Note E if they are also classified as very toxic (T+), toxic (T) or harmful (Xn). For these substances, the risk phrases R20, R21, R22, R23, R24, R25, R26, R27, R28, R39, R68 (harmful), R48 and R65 and all combinations of these risk phrases shall be preceded by the word 'Also'.

C.I. Basic Violet 3 with Michler's base ≥ 0.1%

Michler's base (N,N,N',N'-tetramethyl-4,4'-methylenedianiline; EC Number: 202-959-2) is listed as Index number 612-201-00-6 in the CLP Regulation and classified in Annex VI, part 3, Table 3.1 as carcinogen, Carc. 1B (H350: "May cause cancer.") The corresponding classification in Annex VI, part 3, Table 3.2 of the CLP Regulation is carcinogen, Carc. Cat. 2, R45 ("May cause cancer.")

According to Art. 10(1) of the CLP Regulation, specific concentration limits and generic concentration limits are limits assigned to a substance indicating a threshold at or above which the presence of that substance in another substance (or in a mixture) as an identified impurity, additive or individual constituent leads to the classification of the substance (or mixture) as hazardous.

For Michler's base no specific concentration limit is set in Annex VI of the CLP Regulation and therefore the generic concentration limit is to be used for the purpose of determining classification of substances (or mixtures) containing Michler's base. The generic concentration limit for carcinogens, Carc. 1B is 0.1%, as set out in Table 3.6.2 in Part 3 of Annex I to the CLP Regulation.

Therefore, on such basis, the classification of C.I. Basic Violet 3 where it contains Michler's base ≥ 0.1% (wt/wt) is as follows:

Table 7: *Classification of C.I. Basic Violet 3 where it contains Michler's base ≥ 0.1% according to Art. 10 and Table 3.6.2 in Part 3 of Annex I to Regulation (EC) No 1272/2008 (CLP Regulation), on the basis of the entry with index number 612-201-00-6 in Part 3 of Annex VI to CLP Regulation, Table 3.1*

Substane name	**EC No**	**CAS No**	**Classification**		**Labelling**			**Spec. Conc. Limits, M-factors**	**Notes**
			Hazard Class and Category Code(s)	**Hazard statement code(s)**	**Pictogram, Signal Word Code(s)**	**Hazard state-ment code(s)**	**Suppl. Hazard statement code(s)**		
C.I. Basic Violet 3 with Michler's base ≥ 0.1%	208-953-6	548-62-9	Carc. 1B Acute Tox. 4 * Eye Dam. 1 Aquatic Acute 1 Aquatic Chronic 1	H350 H302 H318 H400 H410	GHS08 GHS05 GHS07 GHS09 Dgr	H350 H302 H318 H410	-	-	-

** Indicates that the classification corresponds to the minimum classification for a category*

Table 8: *Classification of C.I. Basic Violet 3 where it contains Michler's base ≥ 0.1% according to Art. 10 and Table 3.6.2 in Part 3 of Annex I to Regulation (EC) No 1272/2008 (CLP Regulation), on the basis of the entry with index number 612-201-00-6 in Part 3 of Annex VI to CLP Regulation, Table 3.2*

Substance name	**EC No**	**CAS No**	**Classification**	**Labelling**	**Concentration Limits**	**Notes**
C.I. Basic Violet 3 with Michler's base ≥ 0.1%	208-953-6	548-62-9	Carc. Cat. 2; R45 Xn; R22 Xi; R41 N; R50-53	T; N R: 45-22-41-50/53 S: 53-45-60-61	-	E

3 ENVIRONMENTAL FATE PROPERTIES

Not relevant for the identification of the substance as SVHC in accordance with Article 57(a).

4 HUMAN HEALTH HAZARD ASSESSMENT

See section 2 on harmonised classification and labelling.

5 ENVIRONMENTAL HAZARD ASSESSMENT

Not relevant for the identification of the substance as SVHC in accordance with Article 57(a).

6 CONCLUSIONS ON THE SVHC PROPERTIES

6.1 CMR Assessment

[4-[4,4'-bis(dimethylamino)benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride (C.I. Basic Violet 3) with Michler's ketone ≥ 0.1% is listed as index number 612-205-00-8 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) as carcinogen, Carc. 1B (H350: "May cause cancer.") The corresponding classification in Annex VI, part 3, Table 3.2 (the list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is carcinogen, Carc. Cat. 2, R45 ("May cause cancer.")

Therefore, this classification of [4-[4,4'-bis(dimethylamino)benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride (C.I. Basic Violet 3) in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification as carcinogen in accordance with Article 57 (a) of REACH.

Michler's base (N,N,N',N'-tetramethyl-4,4'-methylenedianiline; EC Number: 202-959-2) is listed as Index number 612-201-00-6 in the CLP Regulation and classified in Annex VI, part 3, Table 3.1 as carcinogen, Carc. 1B (H350: "May cause cancer.") The corresponding classification in Annex VI, part 3, Table 3.2 of the CLP Regulation is carcinogen, Carc. Cat. 2, R45 ("May cause cancer.")

According to Art. 10(1) of the CLP Regulation, specific concentration limits and generic concentration limits are limits assigned to a substance indicating a threshold at or above which the presence of that substance in another substance (or in a mixture) as an identified impurity, additive or individual constituent leads to the classification of the substance (or mixture) as hazardous.

For Michler's base no specific concentration limit is set in Annex VI of the CLP Regulation and therefore the generic concentration limit is to be used for the purpose of determining classification of substances (or mixtures) containing Michler's base. The generic concentration limit for carcinogens, Carc. 1B is 0.1%, as set out in Table 3.6.2 in Part 3 of Annex I to the CLP Regulation.

Therefore, the above classification of Michler's base in Annex VI to Regulation (EC) No 1272/2008 show that where the substance [4-[4,4'-bis(dimethylamino) benzhydrylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium chloride (C.I. Basic Violet 3) contains Michler's base ≥ 0.1% it also meets the criteria for classification as carcinogen in accordance with Article 57 (a) of REACH.

PART II

The underlying work for the development of Part II of this Annex XV report was carried out under contract ECHA/2010/174 SR27 by DHI[5] in collaboration with Risk & Policy Analysts Limited[6] and TNO[7]. The technical work on the current project has been led by DHI.

More detailed data on manufacture, uses and releases are provided in the confidential annex 2 to the report.

INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS

EXECUTIVE SUMMARY

Manufacture, Import, and Export

The study indicates that, presently, there is no manufacture of C.I. Basic Violet 3 (BV3) in the EU. Therefore, no information on specific manufacturing conditions was retrieved, including information on the process steps or conditions that determine the content of Michler's ketone (MK).

Based on the responses received from pre-registrants, the import into the EU is estimated at 210-230 tonnes per year, of which less than 18 tonnes is expected to contain Michler's ketone in concentrations of more than 0.1%. Furthermore, the retrieved information indicates that the trend in the import by the large companies is an unchanged demand whereas small companies experience a decrease in the market need for the substance.

Uses

The main uses of C.I. Basic Violet 3 are as a dye in ink applied in cartridges for printers and in ball pens and as dyestuff for paper colouring. Minor dyestuff uses include carbon papers (where dyestuff is suspended in wax and applied to a thin impregnated paper), staining of dried flowers/plants (dried plants dyed by immersion in a hot water solution of the dyestuff) and as a marker (i.e. where dyestuff is used to improve the visibility of a liquid). Furthermore, C.I. Basic Violet 3 is used in microbial and clinical laboratories (e.g. as stain to distinguish

[5] DHI, Agern Alle 5, 2970 Hørsholm, Denmark

[6] Risk & Policy Analysts Limited, Farthing Green House, 1 Beccles Road, Loddon, Norfolk, NR14 6LT, UK

[7] TNO, Schoemakerstraat 97, 2826 VK Delft, The Netherlands

gram negative from gram positive bacteria) in presumably thousands of laboratories and teaching institutions around Europe.

Releases from uses

It was not possible to obtain any information that can be used to estimate the degree of exposure during formulation and use phases. Therefore, exposure estimates were made on the basis of relative rough and conservative estimates using exposure modelling based on standard exposure scenarios. These estimates indicate that the main occupational exposure takes place in the formulation steps and that consumers are mainly exposed via the use of ink, e.g. in ball pens. The estimates also indicate that the exposure to the carcinogenic impurity Michler's ketone in C.I. Basic Violet 3 could come equally from the use of the relatively few tonnes of classified C.I. Basic Violet 3 (i.e. with a content of Michler's ketone >0.1%) and from the non-classified C.I. Basic Violet 3 with a content < 0.1%, which is used in higher tonnages, if the latter came with an average concentration of approx. 0.05%.

Conservative exposure estimates on the basis of exposure tools indicated that for the MK contained in BV3:

- the highest occupational exposure is expected to occur via the dermal route during paper dying, or via inhalation of dust or aerosols / dermal contact during formulation of dye or ink (conservative estimates: 70 µg/kg bw/d, assuming a content of MK of 0.5%); similar exposure is though expected for packaging (i.e. filling of mixtures in containers, such as ink cartridges and ball pens) (20 – 30 µg/kg bw/d)
- consumer exposure during the use of ball pens (oral – by sucking – or dermal)[8], as well as exposure during the use of coloured paper (e.g. by inhalation of air-suspended paper fibres), can occur, but it is estimated 10 - 100 times lower than occupational exposure[9] (0.14 µg/kg bw/d)
- releases to surface water are assumed to occur mainly at the formulation stage, during production of ink cartridges or coloured paper, and during recycling of printed paper (up to ~150 kg/y each, assuming MK=0.5% when >0.1% and 0.05% when <0.1%).

Monitoring studies have reported the presence of MK in ball pen inks, and in food packaging, although the source of the MK has not been concluded.

Current knowledge on alternatives

According to available information on possible alternatives, the substitution of BV3 would require R&D efforts, product re-design and/or process changes, at least in its ink-related applications. Substitution of its use in laboratories may require adaptation of analytical methods and international standards. For most minor uses, such as in tracing paper, staining of dried plants/flowers, or as a marker, it seems possible to replace BV3. However, while this appraisal by industry may be substantiated for the replacement of BV3 by other substances or processes, on the basis of available information the obvious and readily applicable alternative

[8] It is noted that the supply to general public of ball pens (mixture in containers) with ink containing > 0.1 BV3 where BV3 contains > 0.1 % MKis already prohibited in accordance with entry 28 of Annex XVII.

[9] Consumer exposure by contact with paper imprinted with inks containing BV3 or MK has not been assessed. However, it is assumed that exposure via this route is not higher than through the use of ball pens or stained paper.

to BV3 containing MK above the classification threshold of 0.1% would be the same substance containing MK below this threshold.

INTRODUCTION

C.I. Basic Violet 3 (CI 42555) (BV3) belongs to one of the oldest classes of synthetic dyes called triphenylmethane dyes, a class within the group of triarylmethane dyes (Thetford, 2000; Gessner and Mayer, 2005). The triphenylmethanes are classified as 1) diamino derivatives of triphenylmethane, i.e. dyes of the malachite green series (CI 42000 – CI 42175); 2) triamino derivatives of triphenylmethane, i.e. dyes of the fuchsine, rosaniline or magenta series (CI 42500 – CI 42800); 3) aminohydroxy derivatives of triphenylmethane (CI 43500 – CI 43570); and 4) hydroxy derivatives of triphenylmethane, i.e. dyes of the rosolic acid series (CI 43800 – CI 43875). Triphenylmethane dyes are recognised by brilliant hue and high tinctorial strength as well as by being relatively inexpensive and applicable to a wide range of substrates. However, triphenylmethane dyes are deficient in fastness properties and, therefore, the use of triphenylmethane dyes on textiles such as wool, silk and cotton has decreased as dyes from other classes with superior lightfastness and washfastness properties have become available (Thetford, 2000).

MANUFACTURE, IMPORT, AND EXPORT

Manufacture process

The manufacture of "crystallized methyl-violet" or "Crystal Violet", which today is recognised as C.I. Basic Violet 3, was developed by Kern and Caro in 1883 (Caro and Kern, 1883; Kern, 1883a; Kern, 1883b). The process (see Figure 1) is based on reaction of phosgene with dimethylaniline in the presence of zinc chloride forming 4,4'-bis(dimethylamino)benzophenone (Michler's ketone), which is further condensed with dimethylaniline and oxidised to give the dye (Colour Index, 1971; Thetford, 2000; Gessner and Mayer, 2005; ETAD, 2010).

Manufacture of C.I. Basic Violet 3 can also be conducted by condensing dimethylaniline with formaldehyde to 4,4'-methylenebis(N,N-dimethylaniline) (Michler's base), which is reacted with dimethylaniline and simultaneously oxidised to the dye by atmospheric oxygen in the presence of (dihydrodibenzotetraaza[14]annulene)iron and chloranil. Vanadium and molybdenum compounds and nitrous gases can also be used as oxidation catalysts together with chloranilin.

Finally, C.I. Basic Violet 3 can be produced by condensation of 4-dimethylaminobenzaldehyde with dimethylaniline or of 4,4'-bis(dimethylamino)diphenylmethanol (Michler's hydrol) with dimethylaniline and subsequent oxidation of the leuco base (Gessner and Mayer, 2005). Purification of triarylmethane dyes usually involves physical processes such as membrane filtration or chemical processes such as salting the mother liquors (Thetford, 2000).

In the synthesis of C.I. Basic Violet 3, Michler's ketone (which is classified as carcinogen 1B) is a crucial intermediate and the concentration in the final product is due to unreacted Michler's ketone (ETAD, 2010).

No further information was collected during this study with regard to the manufacture process as no manufacturers have been identified in the EU. Regarding content of Michler's ketone in C.I. Basic Violet 3, the feedback from respondents showed that most suppliers report a Michler's ketone content of less than 0.1%, i.e. below the level of classification of the mixture as carcinogenic. It thus seems possible to control the content of Michler's ketone in C.I. Basic Violet 3.

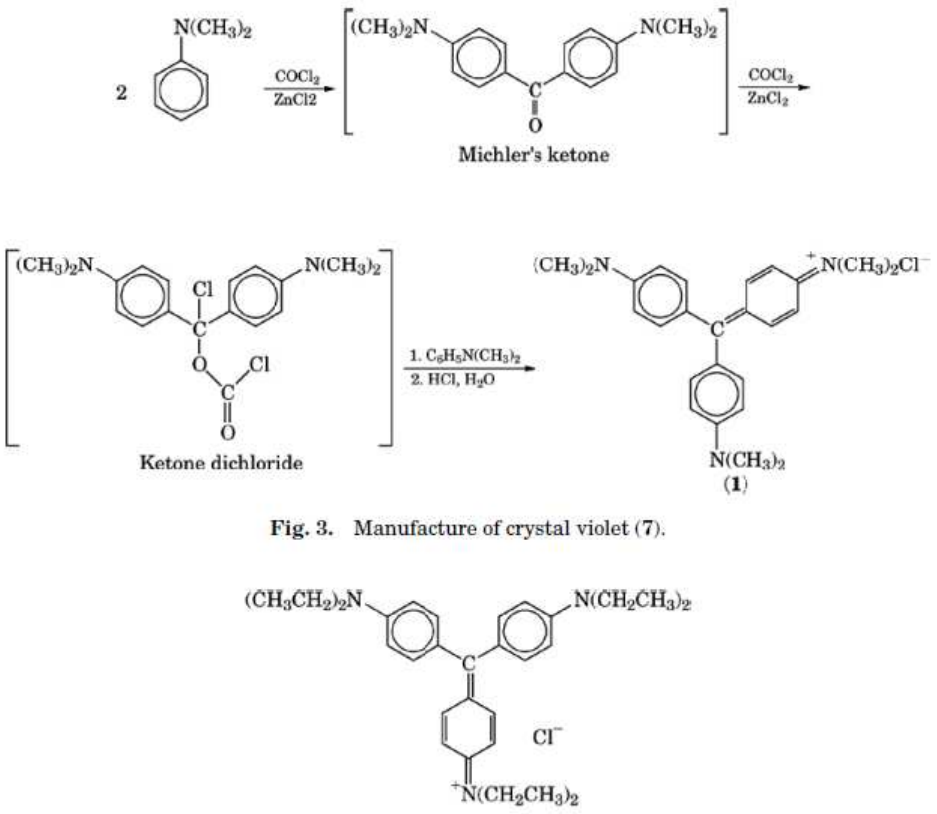


Fig. 3. Manufacture of crystal violet (**7**).

Figure 1. Illustration of the manufacture of C.I. Basic Violet 3 (Thetford, 2000).

Manufacture sites

No manufacturing sites for C.I. Basic Violet 3 were identified within the EU and therefore no information is available in terms of manufacturing volumes. C.I. Basic Violet 3 is imported to the EU as raw material, in mixtures or as articles.

Inquiries were sent to all pre-SIEF members for C.I. Basic Violet 3 and to competent authorities in the EU (sent by ECHA) and the associations the Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers (ETAD), European Pulp and Paper Chemicals Group, European Printing Ink Association (EuPIA) and EUROCOLOUR were contacted directly. Based on these inquiries, it was not possible to identify any production sites within the EU. According to the data obtained in this study, the production of C.I. Basic Violet 3 is located in India, China and to some extent in the US. For this reason, no information on manufacturing

processes was retrieved including conditions in the production that may have an impact on the content of Michler's ketone in C.I. Basic Violet 3.

As a reference point for elucidating historical production volumes, the U.S. International Trade Commission has reported the manufacture and sales of dyes as described in Thetford (2000). 1972 was the last year with statistics by chemical class, which revealed manufacture of 3,900 tonnes of triarylmethane dyes representing 4% of total dyestuff production in the United States. 185 triarylmethane dyes were listed in the Colour Index in 1972. From the late 1970s through the 1980s, the dye production in the US changed very little, which was also the case for the triarylmethane dyes. In 1981, methyl violet was the only triarylmethane dye for which statistics were available with an annual production of 725 tonnes. Furthermore, statistics were available for import of a few triarylmethane dyes in 1981, malachite green (163 t), methyl violet (40 t), new fuchsine (30 t) and other dyes totalling less than 15 t. According to Gessner and Mayer (2005), the di- and triphenylmethane dyes achieved considerable economic importance because of their colour strength and in 1993 approx. 9,000 tonnes of basic di- and triphenylmethanes dyes were sold. Some of the economically most important di- and triphenylmethane dyes were crystal violet and malachite green.

This study did not obtain any information on releases of C.I. Basic Violet 3 during manufacture.

Import into the EU

A major importer (IMP 1) with an unknown supply chain and a major dyestuff formulator (DF 1) being supplied by four different importers (IMP 2-510) were identified. These companies represent 80-90% of the annual import of C.I. Basic Violet 3 identified in this study. Furthermore, 10 additional companies were identified as importers.

One competent authority provided information regarding import of 75 tonnes of mixtures containing C.I. Basic Violet 3 in 2009, of which 28.8 tonnes were C.I. Basic Violet 3. The collected data from the pre-SIEF members revealed that an annual C.I. Basic Violet 3 import of less than 10 tonnes could be identified for that particular country. This indicates the degree of uncertainty related to the data identified through the pre-registered companies. Some pre-SIEF members responded that they used to import C.I. Basic Violet 3 but that this was no longer the case.

The total annual import into the EU identified from the pre-registrant responses was 210-230 tonnes. This tonnage is subject to quite some uncertainty and the actual tonnage may be somewhat greater. First of all, only approximately half of the pre-registrants provided feedback for the study and, therefore the 210-230 tonnes import should be regarded as a minimum. A few only representatives (OR) responded to the inquiries that they did not need to register until 2018 (1-100 t/y) and therefore could not currently provide data. Furthermore, a couple of pre-registrants stated that they were importing and/or using C.I. Basic Violet 3 without providing more detailed input (tonnages unknown). However, the general uncertainties

[10] Input for the study was received from three of these importers (IMP 2-4).

regarding unregistered import of mixtures and/or articles containing the substance have to be taken into account.

It is unknown whether all imported mixtures in containers (such as ink cartridges or ball pens), which contain BV3, are correctly registered (provided BV3 is imported in those mixtures at or above 1 t/y). Import of BV3 with articles, such as coloured paper or other stained articles, into the EU most likely takes place. However, no information is available on the volume of BV3 imported with these articles and the amount of the substance in articles rarely seems to exceed 0.1 % (w/w).

Less than 18 tonnes of the identified annual import of 210-230 tonnes of C.I. Basic Violet 3 contain more than 0.1% of Michler's ketone. Additional information on import is available in Confidential Annex 2. Based on the registrations received by the November 2010 deadline, it may be assumed that the identified maximum import tonnage of the substance with content of Michler's ketone above the defined level for registration is fairly reliable.

With regard to the content of Michler's ketone in C.I. Basic Violet 3, it was commented in a TC C&L meeting summary (European Commission, 2000) "that the content of Michler's ketone varied and nowadays seemed to be < 0.1%". This is in principle in accordance with the information collected in the study performed for the purpose of this report.

Furthermore, the retrieved information indicates that the trends in the import by the large companies show an unchanged demand whereas small companies experience a decrease in the market need for the substance. Additional information on these trends is available in the confidential Annex 2.

USES AND RELEASES FROM USES

Data from the literature

In literature, a whole range of uses have been described for triarylmethane dyes and triphenylmethane dyes in general as well as for C.I. Basic Violet 3 specifically. According to Gregory (1993) and Azmi et al. (1998) triphenylmethane dyes are used extensively in textile industries for dying of nylon, polyacrylonitrile-modified nylon, wool, silk and cotton. Some triphenylmethane dyes are used in medicine and for staining biological tissues (e.g. clinical laboratory analysis) while paper and leather industries are the main consumers. Furthermore, triphenylmethane dyes are used in plastic colouring, gasoline, varnish fats, oil and waxes. Food and cosmetic industries also use some of the triphenylmethane dyes. Thetford (2000) described the uses of triarylmethane dyes as being mainly confined to nontextile applications. Substantial quantities are used for preparation of organic pigments for printing inks and pastes and for the paper printing industry. Triarylmethanes dyes are used extensively in heat-, light- and pressure-sensitive recording materials for photocopying and photoimaging systems. Triarylmethane dyes are also used for specialty applications as for example in the manufacture of carbon paper and in inks for typewriter ribbons and ink jet printing. Triarylmethane dyes are suitable for the coloration of substrates such as paper, ceramics, leather, fur, anodized aluminium, waxes, polishes, soaps, plastics, drugs and cosmetics. Finally, several triarylmethane dyes are used as food colorants.

The uses of C.I. Basic Violet 3 included in the Merck Index (2001) were: dye for wood, silk, paper, in inks, as biological stain and therapeutic uses related to its anti-infective and antimicrobial properties. According to Gessner and Mayer (2005), the main uses of crystal violet are in inkjet inks, for the production of indelible pens, in formulation of stamping and hectographic inks and for dyeing of paper. Furthermore, it was described that crystal violet can be used as a component of navy blue and black dyes for polyacylonitrile fibers. According to Iqbal (2008) crystal violet was used in the formulation of inks, stamping pads, and typewriter ribbons as well as in pH-indicator solutions. Diamante et al. (2009) identified uses as colour additive that function as direct nonoxidative hair colorant as well as an acid-base indicator, as lab chemical for staining of bacteria and as an antiseptic. Furthermore, C.I. Basic Violet 3 was described as a class I medical device for use as a dye and stain. According to Confortin et al. (2010), crystal violet has widespread uses such as dyeing of textiles and paper, as an ingredient in inks for writing and drawing and in printing inks. ETAD (2010) regards the main use of C.I. Basic Violet 3 as being a paper dye with reference to a European-based paper dyes consortium. However, the companies represented in the consortium called European Pulp and Paper Chemicals Group responded that their members do not use C.I. Basic Violet 3 for paper dying. Among potential uses registered by companies in the Colour Index (2012)[11], for products (dyestuff) containing C.I. Basic Violet 3 include paper (widely used), use for printing inks, in newsprint tinting, and in spirit inks, use in various fibres and textiles (e.g. cotton, wool, silk, leather, acrylic, polyester, nylon, coir, feathers), as well as use in distempers, wood, lacquers, crayons, and soaps. The commercial product (dyestuff) may be a pure powder, a powder with diluents, a solution with or without diluents (personal communication with Society of Dyers and Colourists).

Moreover, it has not been possible to confirm some of the more commonly described main uses as dye for textiles/leather and for wood.

Data from the consultation with industry stakeholders

A summary of the data collected during the consultation is provided in Table 1.

Dyestuff formulation

Based on the input from the pre-registrants, it seems that C.I. Basic Violet 3 is predominantly used as a colorant in the formulation of dyestuff, which is further used in formulation of ink or colour, e.g. for paper dying. The main use of this ink is in cartridges and ball pens.

A Dye Formulator (DF 1) reported using C.I. Basic Violet 3 in the formulation of dyestuff, which was further used in the preparation of ink. More information is available in the confidential Annex 2. On the other hand, EuPIA (2010) reported that a survey among the major European printing ink companies showed that C.I. Basic Violet 3 was not used for formulation of printing inks in Europe. The whole EuPIA membership base was, however, not included in the survey.

[11] The registrations made / applications listed by some companies in the Colour Index database may some times be inaccurate / refer to a wider range of products (personal communication with Society of Dyers and Colourists)

Michler's ketone is on the exclusion list for printing inks and related products prepared by the Technical Committee of the European Printing Ink and Association (EuPIA, 2009).

Table 1: Summary of the main imports and uses of C.I. Basic Violet 3

IMP	**Annual tonnage**	**Reported use**	**Remarks**
IMP 1	120	Paper colouring	Supply chain unknown
IMP 2-5[12] and other importers	90-110	Ink	IMP 2-5 identified as suppliers by DF 1
IMP 6	0.3	Dyestuff for carbon paper, staining of dried plants and as a marker as well as unidentified uses	5 downstream users
Other importers	0.8	Laboratory use	-
Other importers	1.8	Unidentified uses	-
Ink formulators	90-110	-	-
Paper dye formulators	120	-	-

IMP 1 indicated that they were supplying C.I. Basic Violet 3 to formulators that use it in dyestuffs for the paper industry. No information was, however, available regarding the formulation of dyestuff for the paper industry. Moreover, the European Pulp and Paper Chemicals Group (2010) stated that their consortium members did not import or use C.I. Basic Violet 3.

Ink formulation and applications

Based on the information provided by the responding pre-registrants, approx. 90-110 tonnes of C.I. Basic Violet 3 contained in pre-formulated dyes were used annually for the formulation of inks for printing cartridges, ball pens and articles for printing and reproduction of recorded media. Information regarding the distribution of the total annual tonnage for these uses was not obtained. Of the total annual tonnage of C.I. Basic Violet 3 used in ink formulation, less

[12] Input for the study was received from three of these importers (IMP 2-4).

than 18 tonnes have a content of Michler's ketone of more than 0.1%. Additional information is available in the confidential Annex 2.

Regarding transformation of C.I. Basic Violet 3, the general feedback was that no transformation takes place during ink formulation.

Generally, very limited information was made available regarding future trends, environmental emissions or releases and occupational exposure. With regard to formulation of ink, the operational conditions were in a few cases described as a closed system process without occupational exposure.

A minor importer and ink formulator estimated that environmental release was <0.01 tonnes/year in terms of waste. It was further indicated that the processes, at which release and occupational exposure take place, are during weighing/charging, filling and cleaning, and the main routes of occupational exposure being inhalation and skin contact. The occupational exposure had not been measured, but was believed to be minimal based on controls employed and measurement of environment for other chemicals used in frequent operation. The applied risk management measures were local exhaust for weighing/charging as well as PPE gloves and overalls for all processes. The number of employees exposed was 10 for weighing/charging, 10 for filling and 10 for cleaning.

For the production of printing cartridges and ball pens, the main route of occupational exposure was described as dermal and by inhalation and the exposure level indicated as accidental/infrequent.

Paper dyeing/colouring

Based on personal communication with IMP 1, the annual import of C.I. Basic Violet 3 used in the paper industry was approx. 120 tonnes with a Michler's ketone content of less than 0.1%. No additional information was made available regarding paper colouring.

Other formulations and applications

A minor company (IMP 6) imported approx. 0.3 tonnes of C.I. Basic Violet 3 annually. The downstream uses were as dyestuff for carbon papers (dyestuff suspended in wax and applied to a thin impregnated paper), for staining of dried flowers/plants (dried plants dyed by immersion in a hot water solution of the dyestuff), as a marker (dyestuff to improve the visibility of the liquid) and other unidentified applications. The downstream supply chain consisted of four downstream users and one distributor, all located at the same country of the importer. The carbon paper represented 0.125 t/y of the substance with a concentration in the carbon paper of approx. 10% and the staining of dried plants/flowers represented 0.01 t/y with a maximum concentration in the dried plants/flowers of 3%. The use as a marker was 0.003 t/y with a probable concentration around 0.1% in the final formulation. The last category of other unidentified application represented approx. 0.2 t/y. For IMP 6, the trend was a further reduction of the market for C.I. Basic Violet 3. IMP 6 stated, however, that they could replace C.I. Basic Violet 3 in all of their applications. See more information in the section

regarding alternatives. Previously, IMP 6 had used C.I. Basic Violet 3 in own production (before 2008).

The information provided by the pre-registrants also indicate that C.I. Basic Violet 3 is also used in small amounts (but presumably very many sites) in laboratories and in formulations used in laboratories. Additional information is available in confidential Annex 2.

EXPOSURE SCENARIOS AND EXPOSURE MODELLING

For the scope of the current report, exposure modelling has been carried out for various uses of C.I. Basic Violet 3 and Michler's ketone. Both environmental, occupational and consumers exposure were considered. Calculations were carried out for different assumptions of the content of Michler's ketone in the imported C.I. Basic Violet 3:

- For the part of the tonnage, in which the content of Michler's ketone was stated to be > 0.1 wt%, calculations were carried out assuming a weight percentage of 0.1%, 0.5% and 1.0%, respectively.
- For the tonnage, in which the content of Michler's ketone was stated to be < 0.1 wt%, calculations were carried out assuming a content of Michler's ketone 0% and 0.05%, respectively.

The Excel version of EUSES was applied for the environmental exposure calculations. The life cycle stages: formulation, end-use and recycling phase were considered. Release estimates were primarily derived on the basis of the ERCSs. However, emission to the air was assumed negligible due to the very low vapour pressure of the substances. Both substances are neither readily nor inherently biodegradable under aerobic conditions. However, a primary biodegradation of C.I. Basic Violet 3 was assumed (some studies indicate that C.I. Basic Violet 3 can be primarily biodegraded).

Except for the recycling phase, ECETOC TRA was applied for the occupational exposure modelling. For the recycling phase, inhalation of paper dust containing residues of the substance was considered the most important exposure route. The consumer exposure was modelled by use of the consumer part of ECETOC TRA. For the cartridge use situation, which is not covered by ECETOC TRA, the ECETOC TRA calculation principles were applied, and some assumptions on the use pattern were made.

Besides the recycling phase, no risk management was assumed to be installed. For the recycling phase, it was assumed that workers wear gloves and protective clothing. No waste treatment of the waste water was assumed in the calculations. As this is probably not the actual use situation, it must be considered very conservative.

The following conclusions are drawn from the calculations:

C.I. Basic Violet 3

- The highest occupational exposure by inhalation was found in the formulation life-cycle stage, and the highest occupational dermal exposure was found for paper dying use. Apparently, the dermal exposure is higher than the inhalative exposure.
- The highest consumer exposure was calculated for the use of coloured paper. The consumer exposure was found to be lower than the occupational exposure.
- The highest concentration in the surface water was found for the formulation life-cycle phases and to some extend for the recycling phase.

Michler's ketone

- The highest occupational exposure was found for the formulation phase. Apparently, the inhalative exposure caused by inhalation of dust is the most important exposure pathway.
- The consumer exposure was found to be very similar for the various uses. The oral exposure was found to be the most important pathway - except for the use of cartridges. The highest exposure was found for the use of ball pens – mainly caused by sucking on the ball pens. The consumer exposure to Michler's ketone in recycled paper was found to be very similar. The consumer exposure – expressed as mg/kg bw/d - was found to be around 10-100 times lower than the occupational exposure.
- The concentration of Michler's ketone in the air was generally assessed to be low. The concentration of C.I. Basic Violet 3 in the air at the workplace was calculated to be up to 5 mg/m3. With a concentration of Michler's ketone between 0.05 wt% and 1.0 wt%, this corresponds to a concentration of 2-50 µg/m3 in the air at the workplace. For the consumer exposure, the concentration will be much lower – mainly caused by paper fibres in the air. The concentration of Michler's ketone in the indoor household air was assessed to be very low and is not expected to exceed 1 ng/m3.
- The highest concentration in the surface water was found for the formulation life-cycle phases and to some extent for the recycling phase.
- The threshold of 0.1 wt% (based on the classification criterion for Carc.1B) may lead to a significant underestimation of the import of and human and environmental exposures to Michler's ketone. Assuming e.g. a content of 0.05 wt% Michler's ketone in the unclassified imported C.I. Basic Violet 3 and a content of 0.5 wt% Michler's ketone in the classified (as Carc.1B) imported C.I. Basic Violet 3, the calculations show that the exposure to Michler's ketone from the classified and the non-classified C.I. Basic Violet 3 is almost the same.
- Regarding the exposure to C.I. Basic Violet 3 in recycled paper, it is very difficult so assess the importance of the content of Michler's ketone in the imported C.I. Basic Violet 3 as it may actually be formed in the paper recovering processes.

CURRENT KNOWLEDGE OF ALTERNATIVES

According to the received information on possible alternatives, it is not possible to replace C.I. Basic Violet 3 without major R&D work as well as product re-design and process changes. In addition it seems difficult to replace C.I. Basic Violet 3 in laboratories as alternative dyes need

be accepted in international standards before substitution can take place. However, for most minor uses, it seems possible to replace C.I. Basic Violet 3.

DF 1 stated that they were not working on replacement of C.I. Basic Violet 3 or C.I. Basic Violet 3-based mixtures/articles "because the substance is classified carcinogenic category 3". No further considerations were included in the response regarding alternatives to C.I. Basic Violet 3.

IMP 6 reported C.I. Basic Violet 4 and C.I. Basic Blue 7 as alternative components in basic dye mixtures. The main problem experienced with replacing C.I. Basic Violet 3 was the different shade of colour obtained. For the mentioned applications (as dyestuff for tracing papers and staining of dried flowers/plants and as a marker), it was possible to completely replace C.I. Basic Violet 3 and customers were already provided with the possibility to replace C.I. Basic Violet 3.

For the ink industry, the general trend was that no known alternatives had been identified. Additional information on alternatives is available in the confidential Annex 2.

RISK-RELATED INFORMATION

No manufacture sites were identified within the EU and therefore risks originating from manufacture were not addressed. The risk-related information thus focuses on the life-cycle steps from the import of C.I. Basic Violet 3, through the formulation steps and end uses stages to the waste phase.

Based on the identified uses, occupational and environmental exposures seem likely in the formulation of dyestuff/ink products and in the use of such products for printing and paper colouring. With respect to occupational exposure during formulation, the information indicates that risk management measures in place include closed systems and LEV supplemented by PPE. For widespread consumer use, the most significant area of interest is containers of mixtures (inks) with C.I. Basic Violet 3 such as ball pens, cartridges etc. as well as articles – mainly coloured paper - containing C.I. Basic Violet 3. Furthermore, the aspect of exposure to dried ink on paper can also be important to consider with regard to consumer use. No quantitative information on occupational and environmental exposures with regard to paper colouring, ink formulation, printing and consumer use was obtained in the course of the study. Therefore, conservative estimates were made for occupational, environmental and consumer exposures using exposure modelling based on standard exposure scenarios.

REFERENCES

Caro, H., Kern, A. 1883. Manufacture of dye-stuff. United States Patent Office, Letters Patent No. 290856.

Colour Index, third edition, volume 4. Bradford: Society of Dyers and Colourists. 1971. pp. 4391.

Colour Index International 2012. Society of Dyers and Colourists and American Association of Chemists and Colourists, www.colour-index.com

Diamante, C., Bergfeld, W.F., Belsito, D.V., Klaassen, C.D., Marks, J.G., Shank, R.C., Slaga, T.J., Snyder, P.W., Andersen, F.A. 2009. Final Report on the Safety Assessment of Basic Violet 1, Basic Violet 3 and Basic Violet 4. International Journal of Toxicology 28 (Suppl 3), pp. 193S-204S.

Environment Canada. 2010. Draft Screening Assessment for the Challenge Methylium, [4-(dimethylamino)phenyl]bis[4-(ethylamino)-3-methylphenyl]-, acetate (MAPBAP acetate), Chemical Abstracts Service Registry Number 72102-55-7. Environment Canada, Health Canada. http://www.ec.gc.ca/substances/ese/eng/challenge/batch8/batch8_72102-55-7.cfm

Environment Canada. 2010a. Screening Assessment for the Challenge Methanone, bis[4-(dimethylamino)phenyl]-(Michler's ketone), Chemical Abstracts Service Registry Number 90-94-8. Environment Canada, Health Canada. http://www.ec.gc.ca/substances/ese/eng/challenge/batch7/batch7_90-94-8.cfm

ETAD. 2010. Personal communication. The Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers.

EuPIA. 2009. Exclusion list for printing inks and related products. European Printing Ink Association.

EuPIA. 2010. Personal communication. European Printing Ink Association.

European Commission. 2000. Summary Record. Meeting of the Commission Working Group on the Classification and Labelling of Dangerous Substances. ECB Ispra 19 – 21 January 2000. European Commission, Directorate General JRC, Joint Research Centre, Institute for Health and Consumer Protection, European Chemicals Bureau. ECBI/19/00 – Rev. 1. http://ecb.jrc.ec.europa.eu/documents/Classification-Labelling/ADOPTED_SUMMARY_RECORDS/1900r1_cmr0100.pdf

European Pulp and Paper Chemicals Group. 2010. Personal communication.

Gessner, T., Mayer, U. 2005. Triarylmethane and Diarylmethane Dyes. In: Ullmann's Encyclopedia of Industrial Chemistry. Wiley-VCH Verlag GmbH & Co KGaA.

Gregory, P. 1993. Dyes and dyes intermediates. In: Kroschwitz, J.I. (Ed.), Encyclopedia of Chemical Technology Vol. 8. John Wiley & Sons, New York, pp. 544-545.

Iqbal, M. 2008. Textile Dyes. PCSIR Laboratories complex Karachi, Ministry of Science & Technology, Government of Pakistan. Rehbar Publishers Karachi.

Kern, A. 1883a. Manufacture of dye-stuff or coloring-matter. United States Patent Office, Letters Patent No. 290891.

Kern, A. 1883b. Manufacture of purple dye-stuff. United States Patent Office, Letters Patent No. 290892.

Personal communication with Society of Dyers and Colourists, February 2012.

The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals, Thirteenth Edition, O'Neil, M.J., Smith, A., Heckelman, P.E., Obenchain, J.R., Gallipeau, J.A.R., D'Arecca, M.A., Budavari, S. Merck & Co., Inc., Whitehouse Station, NJ, USA, 2001. ISBN: 0911910-13-1.

Thetford, D. 2000. Triphenylmethane and related dyes. In: Kirk-Othmer Encyclopedia of Chemical Technology. John Wiley & Sons, Inc.