

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): N,N,N',N'-tetramethyl-4,4'-methylenedianiline
(Michler's base)

EC Number(s): 202-959-2

CAS Number(s): 101-61-1

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.*

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(Michler’s base)

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- The substance is proposed to be identified as substance meeting the criteria of Article 57 (a) of Regulation (EC) 1907/2006 (REACH) owing to its classification as carcinogen category 1B¹ which corresponds to classification as carcinogen category 2².

Summary of how the substance meets the Carcinogen 1B criteria

N,N,N',N'-tetramethyl-4,4'-methylenedianiline (Michler’s base) is listed as Index number 612-201-00-6 in Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (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 Michler’s base in Regulation (EC) No 1272/2008 shows that the substance meets the criteria for classification as carcinogen in accordance with Article 57 (a) of REACH.

Registration dossiers submitted for the substance: No (Registration dossiers were submitted for a substance that includes Michler’s base as impurity)

¹ 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.

² 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).

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:	202-959-2
EC name:	N,N,N',N'-tetramethyl-4,4'-methylenedianiline
CAS number (in the EC inventory):	101-61-1
CAS number:	Deleted CAS registry number: 30135-64-9
CAS name:	Benzenamine, 4,4'-methylenebis[N,N-dimethyl-
IUPAC name:	4,4'-methylenebis(N,N-dimethylaniline)
Index number in Annex VI of the CLP Regulation	612-201-00-6
Molecular formula:	C ₁₇ H ₂₂ N ₂
Molecular weight range:	254.4 g/mol
Synonyms:	Aniline, 4,4'-methylenebis[N,N-dimethyl-(6CI,7CI,8CI); Aniline, p,p'-methylenedi- (4CI); 4,4'-(Dimethylamino)diphenylmethane; 4,4'-Bis(dimethylamino)diphenylmethane; 4,4'-Bis(dimethylaminophenyl)methane; 4,4'-Methylenebis[N,N-dimethylaniline]; 4,4'-Methylenebis[N,N-dimethylbenzenamine]; 4,4'-Tetramethyldiaminodiphenylmethane; Arnold's base; Bis[4-(N,N-dimethylamino)phenyl]methane; Bis[4-(dimethylamino)phenyl]methane; Bis[p-(N,N-dimethylamino)phenyl]methane; Bis[p-(dimethylamino)phenyl]methane; Michler's Base; Michler's hydride; Michler's methane; N,N,N',N'-Tetramethyl-4,4'-methylenedianiline; N,N,N',N'-Tetramethyl-4,4'-diaminodiphenylmethane; N,N,N',N'-Tetramethyl-p,p'-diaminodiphenylmethane; NSC 36782; NSC 4892; NSC 9029;

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	Reduced Michler's ketone; Tetrabase; Tetramethyldiaminodiphenylmethane; p,p'-Bis(dimethylamino)diphenylmethane; p,p'-Tetramethyldiaminodiphenylmethane
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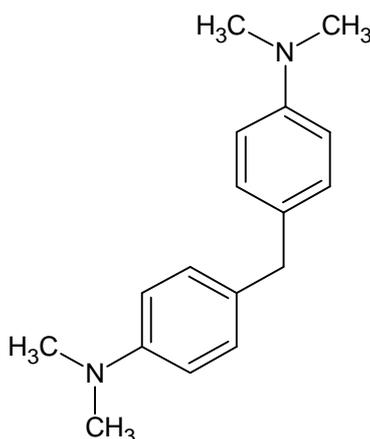
Structural formula:**1.2 Composition of the substance****Name:** N,N,N',N'-tetramethyl-4,4'-methylenedianiline**Description:** ---**Degree of purity:** see confidential Annex

Table 2: Constituents

Constituents	Typical concentration	Concentration range	Remarks
<i>N,N,N',N'</i> -tetramethyl-4,4'-methylenedianiline 202-959-2		See confidential Annex	Information from C&L notifications

Table 3: Impurities

Impurities	Typical concentration	Concentration range	Remarks
<i>No information available</i>			No impurities indicated in the C&L notifications

Table 4: Additives

Additives	Typical concentration	Concentration range	Remarks
<i>No information available</i>			No additives indicated in the C&L notifications

1.3 Physico-chemical properties

Table 5: Overview of physicochemical properties

Property	Value	Remarks
Physical state at 20°C and 101.3 kPa	solid	
Melting/freezing point	91.5°C	Lide, David. R.; Handbook of Chemistry and Physics 2009, 88 th , P3-50
Boiling point	427.7±30.0°C (1013.25 hPa)	Extracted from CAS; ⁽¹⁾
Water solubility	0.013 g/L (pH7 T= 25°C)	Extracted from CAS; ⁽¹⁾
Partition coefficient n-octanol/water (log value)	3.201 (T=25°C)	Extracted from CAS; ⁽¹⁾
Density	1.039 g/cm ³	Extracted from CAS; ⁽¹⁾

⁽¹⁾ calculated using Advanced Chemistry Development (ACD/Labs) software v11.02 (© 1994-2012 ACD/Labs)

2 HARMONISED CLASSIFICATION AND LABELLING

N,N,N',N'-tetramethyl-4,4'-methylenedianiline (Michler’s base) is listed as index number 616-011-00-4 in Annex VI, part 3 of Regulation (EC) No 1272/2008 as follows:

Table 6: Classification 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 statement code(s)	Suppl. Hazard statement code(s)		
N,N,N',N'-tetramethyl-4,4'-methylenedianiline	202-959-2	101-61-1	Carc. 1B Aquatic Acute 1 Aquatic Chronic 1	H350 H400 H410	GHS08 GHS09 Dgr	H350 H410	-	-	-

Table 7: Classification 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
N,N,N',N'-tetramethyl-4,4'-methylenedianiline	202-959-2	101-61-1	Carc. Cat. 2; R45 N; R50-53	T; N R: 45-50/53 S: 53-45-60-61	-	-

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

N,N,N',N'-tetramethyl-4,4'-methylenedianiline (Michler’s base) is listed as Index number 612-201-00-6 in Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (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 Michler’s base in Regulation (EC) No 1272/2008 shows that the substance meets the criteria for classification as carcinogen in accordance with Article 57 (a) of REACH.

PART II

INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS

1. MANUFACTURE, IMPORT, EXPORT

1.1 Manufacture process

Some data on manufacture methods for Michler’s base exist in the scientific literature³:

- Prepared by heating dimethylaniline with 40% formaldehyde and concentrated hydrochloride: Mekel, DE 1026322 (1958 to BASF); Hey, Sanderson, J. Chem. Soc. 1960, 3203;
- From dimethylaniline and diacetylperoxide: Horner et al., Ann. 626, 1 (1959);
- From dimethylaniline and tert-butylperbenzoate: Sosnovsky, Yang, J. Org. Chem. 25, 899 (1960)

1.2 Volumes

1.2.1 EU data

REACH Registration and C&L notification data

No registration had been submitted for Michler’s base by the time of submission of this report for identification of the substance as SVHC.

Overall 4 classification & labelling notifications on behalf of approx. 30 legal entities had been submitted for Michler’s base by that time.

Data from EU Member States

Of the Member States contacted, six provided responses, with only Sweden indicating the presence of Michler’s base on its market:

- Not registered by Dutch companies;
- Not on the market (manufactured or imported) in Finland;

³ Information & references from <http://www.drugfuture.com/chemdata/michler-s-base.html>

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- No information on use of Michler’s base on the Nordic SPIN database or on Denmark’s database on substances in consumer products (i.e. database on substances identified in consumer products in various Danish projects conducted during the last 10-15 years);
- No import to /export from Estonia of Michler’s base has been registered to customs authorities;
- No info held on the substance by the United Kingdom;
- Mixtures were imported in 2009 to Sweden from other MS, containing in total less than 0.1 tonnes of Michler’s base (Swedish Products Register, 2009). It cannot be excluded that Michler’s base is present as impurity in substance(s) included in the imported mixtures, as the use indicated in the registry was as colourant (see section 2.2 below).

Consultation with industry stakeholders

Questionnaires were sent to companies identified in ECHA’s classification & Labelling notifications database⁴ or from other sources on the internet. Furthermore, questionnaires were sent to industry associations, including four trade associations (ETAD, VdMi, CEPE, EuPIA) and six pulp and paper associations (CEPI, INTERGRAF, CEPIPRINT, EADP, FAEP, ENPA).

CEPE (European Council of producers and importers of paints, printing inks and artists’ colours) performed a survey with a negative result as results uses in coatings or inks. No information was directly available to INTERGRAF (International confederation for printing & allied industries). It was noted that EuPIA (the European Printing Ink Association) has published an “Exclusion List for Printing inks and Related Products” (EuPIA, 2011), which is a commitment of ink manufacturers not to use dangerous substances. It is a list that describes “substances previously used or relevant in the formulation of printing inks that must be avoided and which under normal established and foreseeable conditions of use in the manufacture and application of printing inks would cause a risk to health”. This list includes, among others, substances / mixtures with CMR 1A/1B classification. In that publication it is mentioned that the majority of raw materials used in printing inks are produced under commercial industrial conditions and may contain unavoidable impurities, mostly in small quantities. As some of these impurities may be on the exclusion list, every effort is made to ensure that they are at a minimum level. The EuPIA Exclusion List is by its nature a recommendation and does not constitute legal obligations. It is though reported by the Association to have the full support of all of its printing ink manufacturer members.

Only 1 company filled in the questionnaire. This company reported a very small volume of << 1 t imported as such from the United States in 2010. A small fraction of this volume was exported.

1.2.2 Non-EU data

The following information (and accordingly the references) is available from NTP (2011).

⁴ During the consultation, in principle only companies which had submitted single-substance notifications (i.e. not bulk notifications) were contacted. When the submission had been made by a group of Manufacturers / Importers, only the submitting legal entity was contacted.

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In 2009, Michler’s base was produced by one manufacturer each in China, Europe, and India (SRI 2009) and was available from 16 suppliers, including 10 suppliers in the United States (ChemSources 2009).

Commercial production in the United States began in the early 1920s (IARC 1982). U.S. production was approximately 800 t⁵ in 1974, decreasing to 400 t in 1977. Reports filed under the U.S. Environmental Protection Agency’s Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of Michler’s base totalled 250 t to 400 t in 1986 and 4 t to 200 t in 1990 (EPA 2004). No inventory update reports for Michler’s base were filed in 1994, 1998, or 2002.

2. USES

2.1 Uses according to the literature

Information on potential uses/applications of Michler’s base was retrieved from public on-line sources.

According to the NCI Thesaurus License as cited in NTP (2011), Michler’s base is used as **chemical intermediate in the manufacture of dyes and pigments**, including Methylene red, C.I. Basic Yellow 2, Basic Orange 14, Solvent Orange 15, and Solvent Yellow 34 (Society of Dyers and Colourists, 1956 in NCI, 1979 as cited in NTP, 2011). It appears that at least three of those substances (C.I. Basic Yellow 2, Basic Orange 14, Solvent Yellow 34) are on the EU market, as classification and labelling notifications have been received for them⁶. According to Gessner and Mayer (2005), Michler’s base can also be used for manufacturing of C.I. Basic Violet 3 (C.I. Basic Violet 3 is also on the EU market – see A.XV report on C.I. Basic Violet 3).

Michler’s base is also used as **chemical intermediate in the manufacture of its hydrochloric salt**. The latter is used as an analytical reagent for the determination of lead (NCI Thesaurus License as cited in NTP, 2011)

2.2 Identified uses in the EU

The company which responded to the questionnaire reported that Michler’s base is used as **chemical reagent in Research & Development**.

The information available at the Swedish Register indicates use (of the imported mixtures containing Michler’s base) as colouring agent in production of paper and paper products. As mentioned above, it cannot be excluded that Michler’s base is present as impurity in substance(s) included in the imported mixtures.

2.3 Releases from uses

The following information (and accordingly the references) is available from NTP (2011).

The routes of potential human exposure to Michler’s base are inhalation, ingestion, and dermal contact (NJDHSS 2009).

⁵ Values have been converted from lb and pounds (in the original reference) to approximate tonnes

⁶ This information is based on the CAS numbers provided for those dyes in Colour Index International

Although the compound is relatively non volatile, workers may be exposed via inhalation of dust. The potential for exposure is greatest among workers in the dye and chemical manufacturing industries (NCI 1979). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 4,140 workers potentially were exposed to Michler's base in the United States (NIOSH 1990).

US-EPA's Toxics Release Inventory reported environmental releases of 4,000 t ⁷ in 1988, 4 kg in 1995, and 0.4 kg in 1996. No more recent releases have been reported (TRI 2009).

3. ALTERNATIVES

At least for some of the dyes that are manufactured from Michler's base there seem to be alternative manufacturing methods available. Nevertheless, some of the alternative chemical intermediates (e.g. Michler's ketone) have also CMR (carcinogenic, mutagenic or reprotoxic) properties. For instance, C.I. Basic Violet 3 can be manufactured also via Michler's ketone or other intermediates, such as Michler's hydrol. As for Michler's hydrol, it is noted that, although it does not have a harmonised classification, its potential to elicit cancer may deserve further consideration on the basis of its structural similarity with Michler's ketone / Michler's base. Michler's hydrol is not self-classified as CMR according to the C&L notifications submitted to ECHA, while this substance has not been discussed in TC C&L in the past. In another example, C.I. Basic Blue 26 can also be manufactured via Michler's ketone (CMR substance).

4. REFERENCES

EuPIA (2011) Exclusion List for Printing inks and Related Products (7th edition revised http://cepe-myeteam.eudata.be/EPUB//easnet.dll/GetDoc?APPL=1&DAT_IM=104F19&DWNLD=2011-04-07_Exclusion_List_for_Printing_Inks_and_Related_Products_7th_edition_corr_Nov2011.pdf as of November 2011

NTP (2011), National Toxicology Program of U.S. Department of Health and Human Services, Report on Carcinogens, 12th edition, "4,4'-Methylenebis(N,N-dimethyl)benzenamine"

⁷ Values have been converted from lb (in the original reference) to approximate tonnes
