National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

4,4'-bis(diethylamino)benzophenone

EC No 202-025-4

CAS RN 90-93-7

Evaluating Member State(s): The Netherlands

Dated: 15 December 2022

Evaluating Member State Competent Authority

Bureau REACH on behalf of the Ministry of Infrastructure and the National Institute for Public Health and the Environment
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Year of evaluation in CoRAP: 2021

The substance evaluation was terminated without requesting further information from the registrant under an Article 46(1) decision due to change in status of the registration dossier (cease of manufacture in accordance with Article 50(3) of the REACH Regulation).

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B, the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

The Substance, **4,4'-bis(diethylamino)benzophenone**, EC No 202-025-4 was originally selected for substance evaluation to clarify concerns about:

- (suspected) Mutagenicity

- (suspected) Carcinogenicity

During the evaluation no other concern was identified.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Close structural analogue - used for read-across - 4,4'-bis(dimethylamino)benzophenone (Michler's ketone) (EC No. 202-027-5, CAS RN 90-94-8), was placed on the Candidate List of substances of very high concern, for Authorisation (published in accordance with Article 59(10) of the REACH Regulation) on June 18, 2012, for the concern of Carcinogenicity and suspected Mutagenicity.

Close structural analogue - used for read-across - N,N,N',N'-tetramethyl-4,4'-methylenedianiline (Michler's base) (EC No. 202-959-2, CAS RN 101-61-1), was placed on the Candidate List of substances of very high concern for Authorisation (published in accordance with Article 59(10) of the REACH Regulation) on June 18, 2012 for the concern of Carcinogenicity.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State to the following conclusions, as summarised in the table below.

Table 1

CONCLUSION OF SUBSTANCE EVALUATION	
Conclusions	**Tick box**
Need for follow-up regulatory action at EU level	
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	X

4. FOLLOW-UP AT EU LEVEL

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Table 2

REASON FOR REMOVED CONCERN The concern could be removed because	Tick box
Clarification of hazard properties/exposure	
Actions by the registrants to ensure safety, as reflected in the registration dossiers (cease of manufacture)	X

Before submission of the Draft Decision to MSC for decision making, all registrants of the Substance had ceased manufacture in accordance with Article 50(3) of the REACH Regulation and the substance evaluation was terminated because no relevant registrant exists as addressee of the DD. Therefore, as there were no longer any uses within the scope of substance evaluation, the risk-based concerns were removed. At the time of finalising this report, there were no other active registrations within the scope of substance evaluation. The evaluating MSCA is of the opinion that the concern for Mutagenicity and Carcinogenicity remains unresolved since no additional information was requested to further clarify the concern due to the termination of the substance evaluation decision making process.

The evaluating MSCA recommends that further assessment of the Mutagenicity and Carcinogenicity hazards shall be undertaken in the event of new future registrations of the Substance.

If new registrations are submitted, the SEv process may restart by including the substance again in the CoRAP.

5.2. Other actions

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Not applicable.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

The Substance was originally selected for substance evaluation to clarify concerns about:

- Mutagenicity
- Carcinogenicity

Table 3

EVALUATED ENDPOINTS Endpoint evaluated	Outcome / conclusion
Mutagenicity	Concern unresolved. The evaluating MSCA concluded that further information was required to clarify the concern regarding Mutagenicity. However, due to termination of the manufacturing and import of the substance, no additional information was requested, and the substance evaluation process was terminated.
Carcinogenicity	Concern unresolved. The evaluating MSCA concluded that further information was required to clarify the concern regarding Carcinogenicity. However, due to termination of the manufacturing and import of the substance, no additional information was requested, and the substance evaluation process was terminated.

7.2. Procedure

Due to initial grounds of concern for mutagenicity and for carcinogenicity, the Member State Committee agreed to include the Substance (EC No 202-025-4, CAS RN 90-93-7) in the Community rolling action plan (CoRAP) to be evaluated in 2021. The Netherlands' competent authority ('the evaluating MSCA') was appointed to carry out the evaluation.

The evaluating MSCA completed its evaluation considering that further information is required to clarify the following concerns: mutagenicity. Therefore, the eMSCA prepared a draft decision for submission to ECHA under Article 46(1) of the REACH Regulation to request further information in March 2022.

In April 2022 ECHA sent the draft decision to the registrants with the invitation to comment. No comments from the registrants were received.

In August 2022 the last remaining active registrant informed the eMSCA that production was ceased in accordance with Article 50(3) of the REACH Regulation, and thus their registration would be revoked. ECHA informed the registrant and the evaluating MSCA that as the registration was revoked and as there were no other registrants of the substance at that time, the substance evaluation decision making process related to the draft decision was terminated and no further information was requested.

Therefore, the substance evaluation was terminated without a decision requesting for additional information.

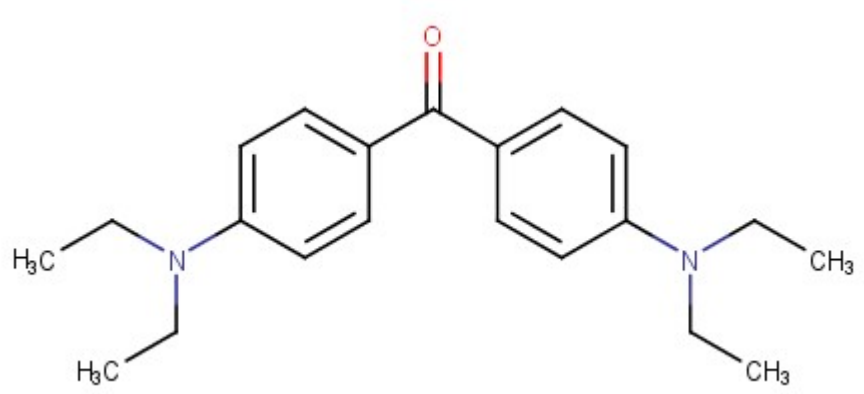
7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	4,4'-bis(diethylamino)benzophenone
EC number:	202-025-4
CAS number:	90-93-7
Index number in Annex VI of the CLP Regulation:	606-073-00-0
Molecular formula:	$C_{21}H_{28}N_2O$
Molecular weight range:	324.5 g/mol
Synonyms:	Michler's ethylketone Michler's ethyl ketone Bis(4-(diethylamino)phenyl)methanone Methanone, bis[4-(diethylamino)phenyl]- Bis[4-(diethylamino)phenyl]methanone 4,4'-Bis(diethylamino) benzophenone 4,4'-(Tetraethyldiamino)benzophenone p,p'-Bis(diethylamino)benzophenone p,p'-(Tetraethyldiamino)benzophenone DEAB Trade name: Omnirad EMK

Type of substance X Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:



UVCB substance

Not applicable.

7.4. Physico-chemical properties

Table 5

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Solid (particulate/powder)
Melting point	Assessed by OECD TG 102: 96.3 °C
Boiling point	Assessed by OECD TG 103: > 300 °C.
Density	Assessed by OECD TG 109: relative density is 1.11 (T=20ºC)
Vapour pressure	Assessed by OECD TG 104: <0.13E-7 Pa (T=20°C) <0.72e-7 Pa (T=25ºC)
Water solubility	Assessed by OECD TG 105: 0.0998 mg/L (pH7, T=20ºC)
Partition coefficient n-octanol/water (Log K_{ow})	Assessed by OECD TG117: 5.2 (T=35ºC)
Flammability	not highly flammable
Explosive properties	not applicable
Oxidising properties	not applicable
Granulometry	Laser scattering/diffraction: 90% of the particles < 115 µm; 50% < 49 µm and 10% < 13.5 µm. MMAD 51.6 µm with a geometric standard deviation of 0.267.
Stability in organic solvents and identity of relevant degradation products	not applicable
Dissociation constant	not applicable

7.5. Manufacture and uses

7.5.1. Quantities

At the start of the substance evaluation process, the tonnage was reported to be 1-10 tonnes per annum. The evaluating MSCA found this to be incorrect for the Lead Registrant, who subsequently updated the dossier, adapting the tonnage to 10-100 tpa. However, during the data generation phase all registrants ceased manufacture of the Substance in accordance with Article 50(3) of the REACH Regulation and therefore all registrations were revoked.

At the time of finalising this report, there were no active registrations within the scope of substance evaluation.

7.5.2. Overview of uses

Table 6

USES	Use(s)
Manufacture	Manufacture of dye
Formulation	• Formulation of ink, toners, adhesives, sealants, coatings, paints, thinners, paint removers, polymer preparations and compounds; • Mixing or blending in batch processes; • Transfer of substance or mixture (charging and discharging) at dedicated facilities;
Uses at industrial sites	• Use of reactive processing aid at industrial site (no inclusion into or onto article); • Transfer of substance or mixture (charging and discharging) at dedicated and non-dedicated facilities; • Mixing or blending in batch processes; • Industrial spraying; • Roller application or brushing; • Treatment of articles by dipping and pouring; • Low energy manipulation of substances bound in materials and/or articles; • High (mechanical) energy work-up of substances bound in materials and/or articles; • Use of reactive process regulators in polymerisation processes at industrial site (inclusion or not into/onto article)
Uses by professional workers	• Widespread use leading to inclusion into/onto article (indoor); • Roller application or brushing; • Mixing or blending in batch processes; • Transfer of substance or mixture (charging and discharging) at non-dedicated facilities; • Transfer of substance or mixture (charging and discharging) at dedicated facilities; • Roller application or brushing; • Non industrial spraying; • Treatment of articles by dipping and pouring; • Low energy manipulation of substances bound in materials and/or articles; • High (mechanical) energy work-up of substances bound in materials and/or articles;
Consumer Uses	N/a, but eMSCA considers it likely due to its presence in ink, toners, adhesives, sealants, coatings, paints, thinners and paint removers;
Article service life	• Widespread use of articles with low release (indoor and outdoor), e.g., vehicles, machinery, mechanical appliances, stone, plaster, cement, glass and ceramic articles, packaging; • Toys intended for children's use (and child dedicated articles) • Fabrics, textiles and apparel; • Leather, metal, rubber, wood, plastic and paper articles; • Other (intended to be released): Use of a ballpoint pen and cartridge

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

The Substance is not listed in Annex VI of CLP.

7.6.2. Self-classification

- In the registration(s): no self-classification.
- The following hazard classes are in addition notified among the aggregated self-classifications in the C&L Inventory:
  - Skin Irrit. 2 – H413
  - Eye Irrit. 2 – H319
  - Carc. 2 – H351
  - STOT SE 3 – H335 (inhalation)
  - Aquatic Acute 1 – H400
  - Aquatic Chronic 1 – H410
  - Aquatic Chronic 2 – H411
  - Aquatic Chronic 4 – H413

7.7. Environmental fate properties

Not evaluated.

7.8. Environmental hazard assessment

Not evaluated.

7.9. Human Health hazard assessment

The following information was evaluated by the eMSCA:

7.9.1. Mutagenicity

Following its assessment of the available relevant information on the Substance, the evaluating MSCA has identified the following potential hazard:

a) Potential mutagenicity

The available information suggests that the Substance may have properties potentially leading to classification for mutagenicity and carcinogenicity according to the CLP Regulation (EC) 1272/2008.

Evidence on the Substance

One Ames test is performed with the Substance, with a negative result. No other data on genetic toxicity are available.

Evidence based on related (analogue) substances

The potential hazard for mutagenicity is derived from mutagenicity data from two analogues of the Substance (Table 7).

• The Substance is a close structural analogue of 4,4'-bis (dimethylamino) benzophenone (EC number 202-027-5; CAS RN 90-94-8; also known as Michler's Ketone).

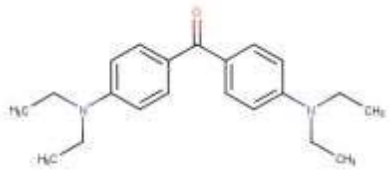
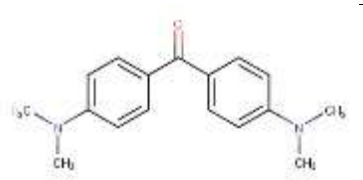
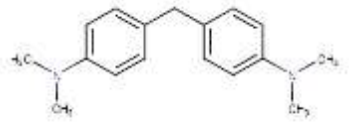
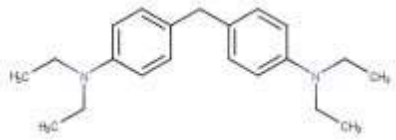
• The Substance is also an analogue of 4,4'-methylenebis (N,N-dimethyl benzenamine, also known as Michler's Base) (EC number 202-959-2; CAS RN 101-61-1).

Furthermore, both analogous substances:

• have a harmonized classification as Carcinogen cat. 1B - and Michler's ketone is additionally also classified as Mutagen cat. 2;

• are identified as a Substance of Very High Concern (SVHC).

Table 7.

Name	**EC number / CAS RN**	**Harmonized classification**	**Structural formula**
4,4'-bis(diethylamino) benzophenone Michler's ethyl ketone (the Substance)	EC 202-025-4 CAS RN 90-93-7	-	
4,4'-bis(dimethylamino) benzophenone Michler's Ketone	EC 202-027-5 CAS RN 90-94-8	Eye Dam. 1 Carc. 1B Muta. 2	
4,4'-methylenebis (N,N-dimethylbenzenamine) Michler's Base	EC 202-959-2 CAS RN 101-61-1	Carc. 1B Aq. Acute 1 Aq. Chronic 1	
4,4'- methylenebis (N,N-diethylbenzenamine) Michler's Ethyl Base	Not registered CAS RN 135-91-1	-	

- QSAR information on mutagenicity and carcinogenicity

The evaluating MSCA generated QSAR predictions for the Substance, the structural analogues (Michler's ketone and base) as well as for the Michler's Ethyl Base (CAS RN 135-91-1; i.e., the Substance without the ketone functionality).

This was done to show that the identified structural alert(s) related to potential mutagenicity and carcinogenicity are present in the Substance (aromatic dialkylamine groups) with or without the benzophenone functionality, and that the di-ethyl substitution of the aromatic amine (in the Substance and in Michler's Ethyl Base) gives identical QSAR results as the (experimentally proven) mutagens and carcinogens Michler's Ketone and Michler's Base (with di-methyl substitution of the aromatic amine functionality).

All four substances (Table 7) are N-substituted aromatic amines and share similar structural alerts (the aromatic dialkyl-amine functionality) for mutagenicity/ carcinogenicity (OECD QSAR toolbox, VEGA QSAR models, Derek Nexus). The similar alerts are an indication that all four substances are likely to be able to cause mutagenicity and carcinogenicity via the same mechanism.

The OECD QSAR Toolbox (v4.5, 2021) has a number of different profilers that alert for potential mechanisms causing mutagenicity and carcinogenicity. The Substance shows alerts relevant for mutagenicity and carcinogenicity in the following profiles:

• DNA binding by OECD – reactivity via SN1-mechanism

• Carcinogenicity (genotox) alerts by ISS – Aromatic mono- and di-alkylamine

• In vitro mutagenicity (Ames) alerts by ISS – Aromatic mono- and di-alkylamine

• In vivo mutagenicity (Micronucleus) by ISS– Aromatic mono- and di-alkylamine

• Oncologic Primary Classification – Aromatic amine type compounds

• Protein binding alerts for CA by OASIS – reactivity via AN2 mechanism

Both close structural analogues, Michler's ketone and Michler's base, as well as the analogue Michler's ethyl base, have completely similar alert profiles as the Substance, given above.

The VEGA QSAR software (also used to generate REACH Annex III alerts) predicts that the Substance and three analogues are all both mutagenic and carcinogenic as given in the summary table 8 below.

The high reliability score (1.0) for the CONSENSUS mutagenicity model prediction for Michler's Ketone and Base is based on the experimental data available in the model's training data sets (as also indicated for all other model predictions for Michler's Ketone and Base).

Table 8

	The Substance	**Michler's ketone**	**Michler's base**	**Michler's ethyl base**
CAS RN	90-93-7	90-94-8	101-61-1	135-91-1
VEGA Mutagenicity Models[1]				
CONSENSUS	+ (0.6)	+ (1.0)	+ (1.0)	+ (0.6)
CAESAR	+ (mod)	+ (exp)	+ (exp)	+ (mod)
SarPy/ IRFMN	+ (mod)	+ (exp)	+ (exp)	+ (mod)
ISS	+ (mod)	+ (exp)	+ (exp)	+ (mod)
KNN/read across	+ (mod)	+ (exp)	+ (exp)	+ (mod)
VEGA Carcinogenicity Models[2]				
CAESAR	- (low)	+ (exp)	+ (exp)	+ (good)
ISS	+ (good)	+ (exp)	+ (exp)	+ (good)
IRFMN/Antares	+ (good)	+ (exp)	+ (exp)	+ (good)
IRFMN/ISSCAN-CGX	+ (good)	+ (exp)	+ (exp)	+ (good)
IRFMN (oral class.)	+ (good)	+ (exp)	+ (exp)	+ (good)
IRFMN (inhal class.)	+ (good)	+ (exp)	+ (exp)	+ (good)

[1] Mutagenicity (Ames) models and versions included in VEGA QSAR Application version 1.1.5 b48: CONSENSUS model (v1.0.3), CAESAR (v2.1.13), SarPy/IRFMN (v1.0.7), ISS (v1.0.2), KNN/Read-Across (v1.0.0).

[2] Carcinogenicity models and versions included in VEGA QSAR Application version 1.1.5 b48: CAESAR (v2.1.9), ISS (v1.0.2), IRFMN/Antares (v1.0.0), IRFMN/ISSCAN-CGX (v1.0.0), IRFMN (oral) (v1.0.0), IRFMN (inhalation) (v1.0.0).

All models, except for the CAESAR Carcinogenicity model, predict the Substance to be mutagenic and carcinogenic. The negative prediction from the CAESAR carcinogenicity model is the only prediction which is considered by the VEGA QSAR Software to be of 'low' quality where all other model predictions for carcinogenicity are considered 'good'.

Furthermore, the Derek Nexus software (version 2.2, Knowledgebase 2021) has been applied to the Substance and the three analogues:

• it correctly predicts the mutagenicity *in vitro* (Ames), *in vivo* (mammalian) as well as carcinogenicity (mammalian) to be plausible for Michler's base (in line with the experimental data for Michler's base);

• it predicts the Michler's ethyl base to be mutagenic (*in vitro* as well as *in vivo*), due to the presence of the aromatic amine or amide alert. This alert is also visibly present in the registered Substance as well as Michler's Ketone but does not produce an alert in the predictions for those chemicals;

• it does not predict mutagenicity or carcinogenicity for Michler's ketone, even though Michler's ketone is a confirmed carcinogen and tested positive in different *in vitro* and *in vivo* mutagenicity assays;

• it also does not predict mutagenicity *in vitro* (Ames) or carcinogenicity (mammalian) for the Substance (Michler's ethyl ketone).

Therefore, (i.) the negative prediction from the DEREK software for the Substance is of low reliability because DEREK also mispredicts (false negative) the mutagenicity and carcinogenicity of Michler's Ketone; (ii.) for the Derek QSAR prediction the change of the di-methyl substitution (Michlers base, Michler's ketone) to di-ethyl (present in the Substance, and in Michler's ethyl base) does not invalidate the mutagenicity and carcinogenicity alerts.

Conclusion: the predictions still lead to concern for (potential) mutagenicity and carcinogenicity of the Substance.

• Available test data on mutagenicity and carcinogenicity

A summary of available mutagenicity and carcinogenicity data can be found on the USEPA NIH website (NTP website; Dunkel et al., 1985; Mitchell et al., 1988; Myhr and Caspary, 1988; Zeiger et al., 1992). A brief overview of the weight of evidence conclusions is given below (Table 9) for the mutagenicity and carcinogenicity endpoints:

Table 9

Test	**Michler's ketone**	**Michler's base**
EC No. CAS RN	202-027-5 90-94-8	202-959-2 101-61-1
Ames test, OECD TG 471	+	+
In vitro chromosome aberration (CA) test, OECD TG 473	-	-
In vitro Mouse Lymphoma Assay (MLA), OECD TG 490	+	+
Carcinogenicity bioassay (rats and mice, male and female)	+ (both species and both sexes)	+ (male and female rats; female mice) Equivocal in male mice

For Michler's base and Michler's ketone, the experimental evidence allows to conclude that the substances are carcinogenic as well as mutagenic.

Conclusion on the available information

A negative Ames test is available indicating that the Substance is not a mutagen *in vitro* in bacteria. However, the two structurally analogue substances also showed some negative or equivocal results specifically for the TA100 strain (with and without rabbit and rat S9 mix) and the TA98 strain (without S9 mix) in the Ames test but with positive results for the TA98 strain with S9 mix leading to the overall conclusion that the substances are

positive in the Ames test[2]. The two structurally analogue substances also gave negative results for the chromosome aberration tests in vitro (Table 9). Nevertheless, for both analogues the positive results in the MLA test indicate that an Ames and/or chromosome aberration test alone is not sufficient to conclude on in vitro mutagenicity for these substances.

It is known that the mutagenicity of aromatic amines can give rise to false negative results in the Ames test (Burke et al., 1994). Aromatic amines are pro-mutagens and require metabolic activation. The use of S9 may be inadequate to mimic the metabolic capacity required for the Substance and may account for negative findings.

Therefore, overall, the available information is not sufficient to draw a conclusion on the potential hazard mutagenicity and/or carcinogenicity of the Substance. To establish whether such properties can be attributed to the substance, the eMSCA considered an MLA *in vitro* assay (in addition to the existing Ames test, in which the Substance tested negative) a necessary first step to elucidate the mutagenic potential of the Substance.

Developments during substance evaluation process

During the substance evaluation decision making process, all registrations have been revoked in accordance with article 50(3) of the REACH Regulation due to cease of manufacture and the substance evaluation was terminated. Therefore, as there were no longer any uses within the scope of substance evaluation, the risk-based concern for mutagenicity no longer exists.

At the time of finalising this report, there were no other active registrations.

The evaluating MSCA is of the opinion that the concern for Mutagenicity remains unresolved since no additional information was requested to further clarify the concern due to the termination of the substance evaluation decision making process.

The evaluating MSCA recommends that further assessment of the Mutagenicity hazard shall be undertaken in the event of new future registrations of the Substance.

7.9.2. Carcinogenicity

No carcinogenicity data are available for the Substance.

The potential hazard for mutagenicity is derived from mutagenicity data from two analogues of the Substance (see also section ‘Mutagenicity’).

The analogues (Michler’s Ketone and Michler’s Base) have a harmonized classification as Carcinogen Cat. 1B. Both analogous substances are identified as a Substance of Very High Concern (SVHC).

The two close structural analogues Michler’s ketone and Michler’s base, as well as the analogue Michler’s ethyl base show completely similar QSAR alert profiles as the Substance (see section ‘’Mutagenicity’).

The evaluating MSCA is of the opinion that the concern for Carcinogenicity remains unresolved since no additional information was requested to further clarify the concern due to the termination of the substance evaluation decision making process.

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[2]Reference to detailed NTP test results:

1) https://cebs.niehs.nih.gov/cebs/get_file/accno/12420_15827/file/635282_G06_Ames_Summary_Data.pdf
2) https://cebs.niehs.nih.gov/cebs/get_file/accno/12196_15603/file/716121_G06_Ames_Summary_Data.pdf.

The evaluating MSCA recommends that further assessment of the Carcinogenicity hazard shall be undertaken in the event of new future registrations of the Substance. The mutagenicity assessment would be the first step in this evaluation.

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.11. PBT and vPvB assessment

Not evaluated.

7.12. Exposure assessment

Not evaluated.

7.13. Risk characterisation

Not evaluated.

7.14. References

Burke, D.A., Wedd D.J., Herriott, D., Bayliss, M.K., Spalding, D.J., Wilcox, P.. Evaluation of pyrazole and ethanol induced S9 fraction in bacterial mutagenicity testing. Mutagenesis. 1994 Jan;9(1):23-9. doi: 10.1093/mutage/9.1.23.

NTP website. Michler's ketone (90-94-8). Chemical Effects in Biological Systems (CEBS). Research Triangle Park, NC (USA): National Toxicology Program (NTP). Accessed 2022-03-09. https://cebs.niehs.nih.gov/cebs/test_article/90-94-8.

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7.15. Abbreviations

AF	Assessment factor
CAS	Chemical abstracts service
C&L	Classification and labelling
CLP	Classification, labelling and packaging (Regulation (EC) No 1272/2008)
CMR	Carcinogenicity, mutagenicity and toxicity to reproduction
DNEL	Derived no effect level
MSCA	Member state competent authority
OECD	Organisation for Economic Co-operation and Development
PROC	Process category
TG	Test guideline
TPA	Tonnes per annum