Annex XV report

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name: 2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one

EC Number: 438-340-0

CAS Number: 119344-86-4

Submitted by: Austria

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ABBREVIATIONS

AAAPs	Alkylaminoacetophenones
AC	Article category
ATP	Adaptation to technical progress
C&L	Classification & Labelling
CLP	Classification, Labelling and Packaging
EuPIA	European Printing Ink Association
FCM	Food Contact Material
NONS	Notification of New Substances (preceding REACH)
PC	Product category
PI	Photoinitiator
PROC	Process category
RAC	Risk Assessment Committee
SU	Sector of use
SVHC	Substance of very high concern
UV	ultraviolet

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EC number: 438-340-0

CAS number: 119344-86-4

- The substance is proposed to be identified as a substance meeting the criteria of Article 57 (c) of Regulation (EC) No 1907/2006 (REACH) owing to its classification in the hazard class toxic for reproduction category 1B[1].

Summary of how the substance meets the criteria set out in Article 57 of the REACH Regulation

2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one will be covered by index number 606-158-00-2 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3 (the list of harmonised classification and labelling of hazardous substances) and it will be classified in the hazard class toxic for reproduction category 1B (H360Df "May damage the unborn child. Suspected of damaging fertility"), anticipated to be included in the 22nd ATP to CLP.

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification in the hazard class:

- Toxic for reproduction category 1B in accordance with Article 57 (c) of REACH.

Registration dossiers submitted for the substance: Yes

[1] Classification in accordance with section 3.7 of Annex I to Regulation (EC) No 1272/2008.

PART I

Justification

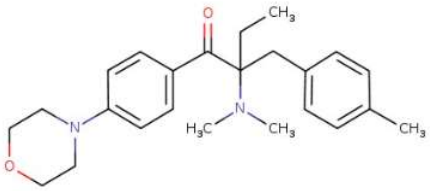
1. Identity of the substance and physical and chemical properties

1.1 Name and other identifiers of the substance

Table 1: Substance identity

EC number:	438-340-0
EC name:	2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one
CAS number (in the EC inventory):	119344-86-4
CAS number:	119344-86-4
IUPAC name:	2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one
Index number in Annex VI of the CLP Regulation	606-158-00-2[2]
Molecular formula:	C24H32N2O2
Molecular weight range:	380.5
Synonyms:	Omnirad 379 CGI 113 JRCure 379 Keycure 8179 Irgacure 379

Structural formula:



(source: European Chemicals Agency, http://echa.europa.eu/)

[2] 2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one will be covered with this Index No. in the next upcoming ATP

1.2 Composition of the substance

Name: 2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one

Description: solid (powder)

Substance type: multi-constituent (racemate)

Table 2: Constituents other than impurities/additives

Constituents	Typical concentration	Concentration range	Remarks
(R)-2-(4-methyl-benzyl)-2-(dimethylamino)-1-[4-(morpholin-4-yl)phenyl]butan-1-one	-	≥ 10% and < 80% (w/w)*	-
(S)-2-(4-methyl-benzyl)-2-(dimethylamino)-1-[4-(morpholin-4-yl)phenyl]butan-1-one	-	-≥ 10% and < 80% (w/w)*	-

* Multi constituent substance according to the Guidance for identification and naming of substances under REACH and CLP new format draft (europa.eu)

There are no impurities relevant for the identification of the substances as SVHC.

1.3 Identity and composition of degradation products/metabolites relevant for the SVHC assessment

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

1.4 Identity and composition of structurally related substances (used in a grouping or read-across approach)

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

1.5 Physicochemical properties

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

2. Harmonised classification and labelling

2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one does not yet have a harmonised classification, but according to an adopted opinion from RAC (ECHA, 2022), the substance meets the criteria in the hazard class toxic for reproduction, category 1B. The substance will be covered by Index number 606-158-00-2 in part 3 of Annex VI with the next upcoming 22nd ATP of the CLP Regulation as follows:

Table 3: Classification according to Annex VI, Table 3 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008

Index No	Chemical name	EC No	CAS No	Classification		Labelling			Spec. Conc. Limits, M-factors and ATEs[3]	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)		
606-158-00-2	2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one	438-340-0	119344-86-4	Repr. 1B Aquatic Acute 1 Aquatic Chronic 1	H360Df H400 H410	GHS08 GHS09 Dgr	H360Df H410		M = 1 M = 1	

[3] Acute Toxicity Estimate

3. Environmental fate properties

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

4. Human health hazard assessment

2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one does not yet have a harmonised classification, but according to an adopted opinion from RAC (ECHA, 2022), the substance meets the criteria in the hazard class toxic for reproduction, category 1B. The substance will be covered by Index number 606-158-00-2 in part 3 of Annex VI with the next upcoming 22nd ATP of the CLP Regulation.

5. Environmental hazard assessment

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

6. Conclusions on the SVHC Properties

6.1 CMR assessment

2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one will be covered by index number 606-158-00-2 of Regulation (EC) No 1272/2008 in Annex VI, part 3, Table 3 (the list of harmonised classification and labelling of hazardous substances) and it will be classified in the hazard class toxic for reproduction category 1B (H360Df "May damage the unborn child. Suspected of damaging fertility") with the next upcoming 22nd ATP to CLP.

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification in the hazard class:

- Toxic for reproduction category 1B in accordance with Article 57 (c) of REACH.

Part II

7. Registration and C&L notification status

7.1 Registration status

Table 4: Registration status

From the ECHA dissemination site[4]	
Registrations	☒ Full registration(s) (Art. 10) ☐ Intermediate registration(s) (Art. 17 and/or 18)

7.2 CLP notification status

Table 5: CLP notifications

	CLP Notifications[5]
Number of aggregated notifications	10
Total number of notifiers	107

8. Total tonnage of the substance

Table 6: Tonnage status

Total tonnage band for the registered substance (excluding the volume registered under Art 17 or Art 18)[6]	≥ 100 – < 1000 t/pa
Tonnage information from public sources other than registration dossiers (if available)	-

[4] Substance Information - ECHA (europa.eu) (accessed 05. July 2023)
[5] C&L Inventory database, http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database (accessed 05. July 2023)
[6] Registered substances - ECHA (europa.eu) (accessed 05. July 2023)

9. Information on uses of the substance

Table 7: Uses

	Use(s)	**Registered use** *(If not, specify the source of the information)*	**Use <u>likely</u> to be in the scope of Authorisation**
Uses as intermediate	-	No	-
Formulation or repacking	Formulation of UV inks for digital printing PC 18: Ink and toners PROC 5, 8b, 9, 28 Industrial formulation of preparations containing the photoinitiator PC 18: Ink and toners PC 21: Laboratory chemicals PROC 1, 2, 3, 5, 8a, 8b, 9, 15 Industrial manufacture of coatings and inks PC 18: Ink and toners PROC 1, 2, 3, 5, 8a, 8b, 9, 15	Yes	Yes
Uses at industrial sites	Industrial application of coatings and inks PC 18: Ink and toners PROC 7, 10, 13 Industrial use of the photoinitiator in UV-inks PC 18: Ink and toners PROC 1, 2, 3, 5, 8a, 8b, 10, 21, 24 Industrial use of UV-inks for digital printing PC 18: Ink and toners PROC 3, 4, 8b, 28 Use at industrial site (not further specified) PROC 1, 2, 3, 5, 8a, 8b, 10, 13, 15	Yes	Yes
Uses by professional workers	Wide dispersive indoor use (professional) of photoinitiator in UV-inks PC 18: Ink and toners PROC 2, 3, 5, 8a, 8b, 10, 21, 24	Yes	Yes

	Widespread use by professional workers: UV inks for digital printing PC 18: Ink and toners PROC 3, 4, 8a, 8b, 28 Professional application of coatings and inks PC 18: Ink and toners PROC 10, 13		
Consumer uses	-	No	-
Article service life	Use of printed or coated article (plastic and paper) PROC 21 Photoinitiator in UV-inks AC 1: Vehicles AC 7: Metal articles AC 10: Rubber articles AC 13: Plastic articles PROC 2, 3, 5, 8a, 8b, 10, 21 24	Yes	No

For explanation of PROCs see Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.12: Use description (R_12_CARACAL_cross_check_TC (europa.eu)).

Consumer use is not supported by the registration, however, there is consumer use of printed and coated articles, which are produced with the help of the substance as photoinitiator.

EC 438-340-0 belongs to the group of alkylaminoacetophenones (AAAPs). AAAPs are very reactive type I - photoinitiators[7]. The free radicals produced initiate a polymerisation process depending on the chemistry of the monomers and oligomers that are used.

AAAPs in general are very efficient in producing radicals and lead to very fast curing. They have become almost high-volume commodity chemicals. According to literature they are used in high-speed offset and flexo inks, UV ink-jet, etch resists, printing plates and solder masks. Due to their yellowing effect, they have only limited use in very clear coatings (Green, 2010).

10. Information on structure of the supply chain

According to ECHA dissemination site (brief profile, accessed July 2023) 2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one has seven active registrants under REACH (1 joint submission) and an aggregated medium tonnage band of ≥ 100 – < 1000 tpa. Active registrants are located in four different Member States.

[7] After light absorption the photoinitiator undergoes unimolecular bond cleavage to generate free radicals.

The substance is not registered for manufacture. Hence, it is imported into the EU, formulated and used in industrial and professional applications. The number of industrial and professional sites using the substance is unknown.

The substance has 10 aggregated notifications to ECHA's classification and labelling inventory with a total number of 107 notifiers (accessed July 2023).

The substance is used as photoinitiator for UV-inks and coatings and registered article categories are vehicles, metal articles, rubber articles and plastic articles; paper is also indicated. For some scenarios sector of end use SU 7 (Printing and reproduction of recorded media) is indicated. The main product category is PC 18: Ink and toners; also PC 21: Laboratory chemicals is registered (see Chapter 9).

11. Additional information

11.1 Substances with similar hazard and use profiles on the Candidate List

The structurally similar photoinitiators EC 400-600-6 and EC 404-360-3 are already identified as SVHCs and included in the Candidate List and in ECHA's draft 11th recommendation of priority substances to be included in REACH, Annex XIV. All three substances belong to the chemical group of alkylaminoacetophenones (AAAPs) and have similar properties, uses and risk patterns.

11.2 Alternatives

EC 438-340-0 belongs to the group of alkylaminoacetophenones (AAAPs) which includes the structurally similar photoinitiators EC 400-600-6 and EC 404-360-3 that are already included in the Candidate List. According to the registrant(s) there are several potential alternatives available[8] and the harmonised classification of EC 400-600-6 and EC 404-360-3 as Repr 1B has already led to a move towards alternative substances especially in printing inks, with EC 438-430-0 most likely one of them. For EC 438-340-0 the upcoming harmonised classification as Repr. 1B is expected to lead to a similar substitution effect.
The most obvious chemical alternatives may be the structurally similar alpha amino ketones Omnirad 264/389 (EC 827-771-3[9]) and Omnipol 910 (polymer, EC 806-887-8[9]), both are not registered under REACH.

In addition, there are dimeric alpha hydroxy ketones (Esacure KIP 160, EC 472-110-0; Omnirad 127, EC 444-860-9; Esacure ONE, EC 402-990-3) available; their UV-absorption is quite similar to those of AAAPs and, therefore, they may be used as an alternative if medium-pressure mercury-lamps are used as light sources. Unlike the alpha amino ketones, the hydroxyl compounds do not function optimally at 365 nm output LED source but rather at lower wavelengths. It is noted that the classification of alternative substances varies widely and the information for some substances is rather limited. While some are not registered others have a full registration under REACH. For further details it is referred to ECHA's assessment of regulatory needs on photoinitiators (ECHA, 2023).

There are also more expensive acyl phosphine oxides such as Omnirad 819 (EC 423-340-5). These photoinitiators, in contrast to the alpha hydroxy ketones, function satisfactorily

[8] email correspondence July, 2018
[9] Explanation on the role of LIST numbers is provided in the ECHA website at: https://echa.europa.eu/information-on-chemicals/registered-substances/information

with both medium pressure mercury and 365 nm LED sources. However, they have a poorer surface-cure.

Blended products may also be an option to obtain the best total cure under defined conditions. Specific alternatives need to be determined on a case-by-case basis under consideration of the specific properties needed (wavelength, moisture sensitivity, O_2-inhibition, yellowing, etc.).

Another possibility is the chemical modification of available photoinitiators to reduce their migration rate. Liao & Jin (2023) investigated the possibility to modify the photoinitiator EC 400-600-6 by creating a polymerisable or macromolecular photoinitiator to increase the migration stability. According to the study authors, especially the macromolecular strategy is an efficient way and has a great potential to be used in UV-vis curing systems. Publications show that there is continuous research for low migration photoinitiators (e.g., Ren, 2022) as well as the development of innovative, intrinsically less-hazardous systems (e.g., Pierau, 2022).

As shown for the similar photoinitiators EC 400-600-6 and EC 404-360-3, alternatives are available for many uses (van Gelder, 2018), and substitution is already taking place supported also by the recommendations of the EuPIA exclusion list[10]. A similar substitution potential for substance EC 438-340-0 can be expected to exist.

11.3 Existing EU legislation

EC 438-340-0 will be included into Annex VI of Regulation (EC) No 1272/2008 (Index number 606-158-00-2) with a harmonised classified as Repr. 1B, H360Df with the 22nd ATP to CLP.

In the EU no occupational exposure limits have been established for the substance. However, the substance meets the criteria for classification within a hazard class as laid down in the CLP regulation (Article 3) and thereby is regarded as a *hazardous chemical agent* as defined in Directive 2004/37/EC Carcinogens, Mutagens or Reprotoxic Substances at Work[11], Directive 98/24/EC Chemical Agents at work[12] and Directive 92/85/EEC on the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding[13].

No other existing EU legislation directly applies to the substance in question. However, printing inks must fulfil the general requirements according to EC No 1935/2004 (framework regulation on materials and articles intended to come into contact with food). According to Article 3 of this regulation, materials and articles shall be manufactured in compliance with good manufacturing practice[14] so that, under normal or foreseeable conditions of use, they do not transfer their constituents to food in quantities that could endanger human health (Lago et al., 2015; EFSA, 2020). Currently a comprehensive review of EU food-contact legislation is ongoing, including also printed FCMs[15].

[10] EuPIA Exclusion Policy for printing inks and related products - Eupia
[11] EUR-Lex - 02004L0037-20220405 - EN - EUR-Lex (europa.eu)
[12] EUR-Lex - 01998L0024-20190726 - EN - EUR-Lex (europa.eu)
[13] EUR-Lex - 31992L0085 - EN - EUR-Lex (europa.eu)
[14] Regulation (EC) No. 2023/2006
[15] Revision of EU rules on food contact materials (europa.eu)

11.4 Previous assessments by other authorities/ongoing regulatory activities

The substances EC 400-600-6 and EC 404-360-3, two similar alpha-amino acetophenones, have already been identified as SVHC (reproductive toxicity), are on the candidate list for Authorisation and have been added to the opinion of the MSC on the draft 11th recommendation of the priority substances to be included in Annex XIV. Consequently, authorisation may also be proposed for EC 438-340-0 in order to follow a group approach and to avoid regrettable substitution.

ECHA's assessment of regulatory needs for the photoinitiators group indicates a need for further EU regulatory risk management for reproductive toxicity hazard due to the potential for release/exposure of photoinitiator substances, including 2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one (ECHA, 2023).

REFERENCES

References for Part I

ECHA (2022): RAC Opinion proposing harmonised classification and labelling at EU level of 2-(dimethylamino)-2-[(4-methylphenyl)methyl]-1-[4-(morpholin-4-yl)phenyl]butan-1-one, EC 438-340-0, CAS 119344-86-4. Adopted 2 June 2022. [04.01-ML-014.03] (europa.eu).

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Ren X., Liu W., Yao Q., Wang S., Liu W., Gu H., Wang D., Fan J., Peng X. (2022): A UV-LED excited photoinitiator with low toxicity and low migration for photocurable inks. Dyes and Pigments Vol 200, 11, 110133.

Van Gelder S., Bellotti E., Bailey SE., Postle SR. (2018): Transcending regulatory issues: alternates to Omnirad 369. Postle-Stephen Transcending-regulatory-issues--alternates-to-Omnirad-369.pdf (radtech.org).