SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Octabenzone

EC No 217-421-2

CAS No 1843-05-6

Evaluating Member State(s): Italy

Dated: 02 August 2018

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2013

Before concluding the substance evaluation a Decision to request further information was issued on: 17 June 2015.

Further information on registered substances here:

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

DISCLAIMER

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

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Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Octabenzone was originally selected for substance evaluation in order to clarify concerns about:

- human health/sensitiser
- potential endocrine disruptor
- consumer use
- exposure/wide dispersive use
- high aggregated tonnage

During the evaluation also other concerns were identified. The additional concerns were:

- potential risk for environmental compartments (sediment, soil)
- potential human exposure via the environment
- reproductive toxicity

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

None.

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	X
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

4. FOLLOW-UP AT EU LEVEL

On the basis of the available information, a harmonized classification of the substance is envisaged by eMSCA, as a follow-up at EU level by adding the following hazard category: Skin Sens. 1, H317.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

Not applicable.

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

The eMSCA has the intention to prepare an Annex XV dossier with a proposal for harmonized classification and labelling tentatively in 2020.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Octabenzone was originally selected for substance evaluation in order to clarify concerns about:

- Human health/Sensitiser
- potential endocrine disruptor
- Exposure/Wide dispersive use
- Consumer use
- High aggregated tonnage

During the evaluation also other concerns were identified. The additional concerns were:

- Potential risk for environmental compartments (sediment, soil)
- Potential human exposure via environment
- Reproductive toxicity

Table 2

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Endpoint 1 Sensistisation	No further information was required to clarify the concern for sensitisation.
Endpoint 2 Endocrine disruption	The available studies provide no indication of endocrine disrupting potential.
Enpoint 3 Reproductive toxicity	Requests fulfilled by the registrants. No further action is needed.
Endpoint 4 Long-term toxicity testing to sediment organisms	Request fulfilled by the Registrants. Submitted data are sufficient and suitable for Chemical Safety Assessment (CSA) as well as for a definitive assessment of this endpoint. No further action is needed.
Endpoint 5 Effects on terrestrial organisms	Requests fulfilled by the Registrants. Submitted data are sufficient and suitable for CSA as well as for a definitive assessment of this endpoint. No further action is needed.
Endpoint 6 Environmental exposure assessment	Requests fulfilled by the registrants. No further action is needed.

Endpoint 7 Clarification of the adopted risk management measures (RMMs)	Requests fulfilled by the registrants. No further action is needed.
Endpoint 8 Environmental regional assessment: regional Predicted environmental concentrations (PECs)	Requests fulfilled by the registrants. No further action is needed.
Endpoint 9 Proper characterisation of the risk for soil compartment	Requests fulfilled by the registrants. No further action is needed.

7.2. Procedure

The Substance evaluation of the Octabenzone started on March 2013.
The initial grounds for concern were relating to: human health/sensitiser; suspected endocrine disruptor; exposure/wide dispersive use; consumer use; aggregated tonnage.
In the course of the evaluation, the evaluating MSCA noted additional concern regarding potential risk for environmental compartments (sediment, soil), potential human exposure via the environment and reproductive toxicity.
The evaluating MSCA considered that no further information was required to clarify the concern for sensitisation. The evaluating MSCA considered that further information was required to clarify the other abovementioned concerns.
Therefore, it prepared a draft decision pursuant to Article 46(1) of the REACH Regulation to request further information. On 20 March 2014 the evaluating MSCA sent the draft decision to ECHA.
After discussion in the Member State Committee meeting on 20 to 23 April 2015, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 22 April 2015. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.
Subsequently the Registrants provided the requested information in the updated dossier.

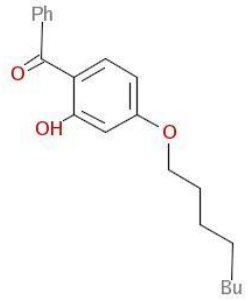
7.3. Identity of the substance

Table 3

SUBSTANCE IDENTITY	
Public name:	octabenzone
EC number:	217-421-2
CAS number:	1843-05-6
Index number in Annex VI of the CLP Regulation:	--
Molecular formula:	C21H26O3
Molecular weight:	326.429 g/mol
Synonyms:	2-benzoyl-5-(octyloxy)phenol CAS name: methanone, [2-hydroxy-4-(octyloxy)phenyl]phenyl- IUPAC name: [2-hydroxy-4-(octyloxy)phenyl](phenyl)methanone

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

Structural formula:



7.4. Physico-chemical properties

Table 4

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Solid
Vapour pressure	4.5E-6 Pa at 20°C
Water solubility	<0.001 mg/L at 20°C at approx. pH 6
Partition coefficient n-octanol/water (Log Kow)	Log Kow= 7.6 at 25°C
Flammability	- Not a flammable solid - No pyrophoric properties based on experience in manufacture or handling - Does not emit flammable gases in contact with water, based on the chemical structure and experience in handling and use
Explosive properties	No explosive properties
Oxidising properties	No oxidising properties
Granulometry	MMD= 112 µm D10= 28 µm D90= 41 µm
Stability in organic solvents and identity of relevant degradation products	The stability of the substance in organic solvents is not considered to be critical
Dissociation constant	pKa= 10.2 at 25°C

7.5. Manufacture and uses

7.5.1. Quantities

Table 5

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☐ 100 – 1000 t	☒ 1000- 10,000 t	☐ 10,000-50,000 t
☐ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

This substance is manufactured and/or imported in the European Economic Area in 1000+ tonnes per year. This substance is used by consumers, in articles, by professional workers (widespread uses), in formulation or re-packing, at industrial sites and in manufacturing.

Table 6

USES	Use(s)
Formulation	This substance is used in the following products: polymers, coating products and adhesives and sealants. Release to the environment of this substance can occur from industrial use: formulation in materials and formulation of mixtures.
Uses at industrial sites	This substance is used in the following products: polymers, adhesives and sealants and coating products. This substance is used for the manufacture of: plastic products and chemicals. Release to the environment of this substance can occur from industrial use: in the production of articles.
Uses by professional workers	This substance is used in the following products: coating products, adhesives and sealants and polymers. This substance is used for the manufacture of: chemicals and machinery and vehicles.
Consumer Uses	This substance is used in the following products: adhesives and sealants, coating products and polymers.
Article service life	Release to the environment of this substance can occur from industrial use: in the production of articles and formulation in materials.

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

The substance is not currently listed on Annex VI of CLP Regulation ((EC) No 1272/2008).

7.6.2. Self-classification

- In the registration(s):

Skin Sens. 1B	H317

- The following hazard classes are in addition notified among the aggregated self-classifications in the C&L Inventory:

Skin Sens. 1	H317
Skin Irrit. 2	H315
Eye Irrit. 2	H319
Aquatic Chronic 1	H410
Aquatic Chronic 3	H412
Aquatic Chronic 4	H413
Flam. Liq. 3	H226

7.7. Environmental fate properties

7.7.1. Degradation

Hydrolysis

In the registration dossier there is a key study with reliability 1 (unpublished study report 1, 2001) where the hydrolysis was based on OECD 111/EU Method C.7.

According to the guideline, a preliminary test was performed on the substance at 50°C at each of pH 4.0, 7.0 and 9.0. For this substance, less than 10% of the reaction of hydrolysis was observed after 5 days at 50°C; this result is equivalent to a half-life > 1 year at 25°C for each of the buffers solutions tested.

The registrants concluded the substance is hydrolytically stable and based on the available information, the eMSCA can support this conclusion.

Phototransformation in air

The Registrants provided a calculation according to AOPWIN v1.92 (EPISUITE), according to which the tested substance is indirectly photodegraded by reaction with hydroxyl radicals in the atmosphere with a half-life (t1/2) of about 0.588 hours.

Regarding phototransformation in air, eMSCA noted some information deficiencies, but considered more related to a compliance check for standard information requirement than to a Substance Evaluation process (e.g.: the appropriate QSAR Reporting Formats was not provided). Moreover, eMSCA noted that in the last updated CSR, the Registrants revised this endpoint reporting the sentence: "No relevant information available".

Indeed under substance evaluation procedure, this endpoint is not considered relevant by eMSCA for concern clarification. Therefore no need for further request is foreseen for this endpoint.

Summary and discussion on degradation

Abiotic degradation

According to OECD 111, hydrolysis is not expected.

After evaporation or exposure to the air, the test substance will be rapidly degraded by photochemical processes with a half life of 0.59 hours.

Biotic degradation

The Registrants concluded that the substance is not readily biodegradable according to OECD criteria (OECD 301B, unpublished study report 2, 1989) and based on the available information, the eMSCA can support this conclusion. No data on the biodegradation in simulation tests is available.

7.7.2. Environmental distribution

In the registration dossier, logkoc is calculated using the software SRC PCKOCWIN v.2.0. EPISuite v4.11, (unpublished study report 3, 2016). The estimated value is logkoc =4.8 (KOC=63750).

The Registrants concluded that the substance is likely to bind to soil and sediments and, based on the available information, the eMSCA can support this conclusion.

Summary and discussion of environmental distribution

Based upon a determined log Koc of 4.8 an adsorption to the solid soil phase is expected. The test substance will not evaporate from the water surface into the atmosphere. According to the substance properties, the compound will preferentially be distributed into the compartments soil and sediment.

The Registrants concluded that the substance has a greater distribution in the soil and sediment compartments and, based on the available information, the eMSCA can support this conclusion.

7.7.3. Bioaccumulation

Two studies were provided by the Registrants:

Aquatic bioaccumulation of octabenzone was investigated in two flow-through system carried out in 1992, according to OECD guideline 305C. Both the studies use as test organism *Cyprinus carpio*.
It is noted that OECD guideline 305C was replaced, but in this case it can still be used for assessment because it is not used for new tests after the time when it was replaced, as foreseen by OECD.
For the key study with reliability 1 the BCF values obtained are ≥89-≤190 and 99 (2 µg/l and 0,2 µg/l concentrations); for the supporting study with reliability 2 the BCF values are ≥18-≤140 and ≥1,5-≤35 (0,05 mg/l and 0,6 mg/l concentrations).
According to OECD 305 (page 2-3): "*The aqueous exposure test is most appropriately applied to stable organic chemicals with log KOW values between 1.5 and 6.0 but may still be applied to strongly hydrophobic substances (having log KOW > 6.0), if a stable and fully dissolved concentration of the test substance in water can be demonstrated*". In the IUCLID dossier submitted by the Registrants, it is shown that the substance is fully dissolved in water (*see measured concentrations*).

Moreover, a predicted value BCF of 209.5 (BCFWIN v.2.15, EPISUITE) is in the same range as the BCF (about 200) derived experimentally according to OECD 305.

The Registrants concluded that the substance has a low potential of bioaccumulation and, based on the available information, the eMSCA can support this conclusion.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

Short term toxicity tests for three trophic levels were performed to examine the aquatic toxicity of the test substance. The L(E)C50 values for fish, algae and activated sludge were found to be greater than 100 mg/L (nominal).

Given the low water solubility (value used for CSA: <0.73 µg/L) and the high log Kow (calculated logKow 7.6 at 25°C), the substance is expected to partition strongly to sediment and suspended solids. In such cases, it seems both impractical and uninformative to test pelagic species via the water phase. Moreover, exposure data provided by the Registrants indicate that a concern for aquatic compartment is unlikely. Therefore, based on the available information, the eMSCA can support the conclusion and no action is required concerning the toxicity to aquatic organisms.

7.8.1.1. Fish

For short term toxicity on fish, the Registrants provided a key study, and two supporting studies. No acute toxic effects occur within the range of solubility. The Registrants concluded that the substance with high probability is not acutely toxic to fish. eMSCA noted some uncertainties on the real value of the concentration, (e.g. no evidence that the concentration of the substance has been satisfactorily maintained throughout the static test). Despite this, eMSCA agrees that no acute toxic effects occur within the range of solubility.

The Registrants provide a justification for waiving the long-term toxicity to fish, according to the results of the exposure assessment. Based on the available information, the eMSCA can support the above conclusion.

7.8.1.2. Aquatic invertebrates

Two short-term studies were provided by the Registrants on *Daphnia magna*: a key study with reliability 1 (unpublished study report 4, 2008) and a supporting study with reliability 2 (unpublished study report 5, 1988). Due to the low solubility of the test substance (water solubility <0.001 mg/L at 20°C at approx. pH 6), a solvent and an emulsifier has been used in the key and in the supporting study, respectively.

For the key study, after 48h no acute toxicity within the range of solubility could be observed. The water solubility was tested in a preliminary study to guarantee that the main test will be conducted up to the maximum solubility within the test media. Therefore, DMF was additionally used as solubilizer and a limit test was conducted.The 48-hour EC50 obtained from the limit test study was > 0.0052 mg/L (based on nominal concentrations) and > 0.0038 mg/L (based on Time Weighted Average).

Regarding the supporting study, a 24-hours EC50 of the test item was calculated to be 52 mg/L (based on nominal concentrations). Initially the test substance appeared homogeneously distributed in the test vessels. A slight deposit was observed at conc. of 1.8-58 mg/L (nominal) after 24 h exposure.

The Registrants concluded that the substance is not acutely toxic to aquatic invertebrates. Despite some deficiencies in the study descriptions and the difficulties for the very low water solubility, (the test substance was rather dispersed than dissolved) the eMSCA can support this conclusion. Moreover, exposure data provided by the Registrants, indicate that a concern for aquatic compartment is unlikely. Therefore, based on the available

information, the eMSCA can support the conclusion and no action is required concerning the long-term toxicity to invertebrates.

7.8.1.3. Algae and aquatic plants

Two studies were provided by the Registrants: a key study and a supporting study. Deficiencies in the information provided were noted by eMSCA, however no acute toxic effects resulted within the range of solubility. The Registrants concluded that the test item is with high probability acutely not harmful to aquatic algae. Based on the available information, the eMSCA can support the above conclusion.

7.8.1.4. Sediment organisms

In the Substance Evaluation Decision the Registrants were required to carried out a long term toxicity testing to sediment organisms (test method :OECD 218, Sediment-Water Chironomid Toxicity using Spiked Sediment) in order to definitively clarify the effects of Octabenzone on sediment-dwelling organisms, including the related risk characterization for sediment compartment. Given the low water solubility and the high adsorption properties, the registered substance is expected to strongly partition into sediment and soil. Therefore, this information request was considered relevant to clarify the identified additional concern relating to potential risk for sediment compartment.

The Registrants submitted a reliable sediment organisms toxicity study (Unpublished study report 6, *2016*), a limit test performed with the registered substance according to OECD 218 and in compliance with GLP criteria.

A 28d No Observed Effect Concentration (NOEC) value of 10000 mg/Kg sediment dw (concentration expressed as nominal) has been determinated for both endpoints of the study: emergence and development rates in sediment-dwelling organisms (*Chironomus riparius*). No toxicity effects have been observed in the study at the highest test concentration. All validity criteria of the test were met.

These submitted data were used for derivation of Predicted No Effect Concentration (PNEC) sediment values as well as for definitive assessment of the toxicity on sediment organisms.

Therefore, following the assessment, eMSCA concludes that the newly submitted data provided by the Registrants meet the request specified in the Decision. No further information is needed as the concern for this endpoint has been clarified.

7.8.2. Terrestrial compartment

As requested in the Substance Evaluation Decision, the Registrants submitted studies on long term toxicity testing on soil macro-organisms, terrestrial plants and soil micro-organisms in order to clarify the identified additional concern for soil compartment and accordingly to derive a robust and conclusive PNEC soil and related risk characterization.

Toxicity to soil macro-organisms

As requested, the Registrants provided a reliable toxicity study on soil macro-organisms (unpublished study report 7, 2016) using *Eisenia fetida* according to OECD guideline 222 (test method: Earthworm reproduction test) and in compliance with GLP criteria. All validity criteria of the test were met. Mortality, body weight development (28 days after application) and reproduction (56 days after application) have been tested.

After 28 days of exposure, no mortality of adult worms was observed in the controls and at all replicates with the test substance. The 28d NOEC (mortality) has been determined to be ≥ 1000 mg/Kg soil dw.

The EC10 on reproduction (by count of juvenile worms) after 56 days resulted to be 668 mg/kg soil dw. This most sensitive value was used for derivation of PNEC soil.

eMSCA concludes that soil macro-organisms toxicity data can be considered suitable and definitive for this endpoint. Consequently, the concern is clarified and no additional information is required.

Toxicity to soil micro-organisms

In accordance with the information request under Substance Evaluation Decision, the Registrants submitted a reliable toxicity study on soil micro-organisms (unpublished study report 8, 2016) carried out according to OECD guideline 216 (Soil Microorganisms: Nitrogen Transformation Test) and in compliance with GLP criteria.

No toxicity effects have been observed with soil micro-organisms at any of the concentrations tested. A 28d EC10 for soil microorganisms was determined to be at >1000 mg/Kg soil dw based on nitrate formation rate.

These study results are considered consistent with all relevant validity criteria according to the guidelines and the submitted data meet the information requested under SEV Decision.

eMSCA supports these findings, considering that no further information is needed on this endpoint.

Toxicity to Terrestrial Plants

Following the information requested in Substance Evaluation Decision, the Registrants provided a reliable long term toxicity testing on terrestrial plants (unpublished study report 9, 2016) according to OECD guideline 208 (Terrestrial Plants, Growth Test) and GLP criteria, performed with six plants species tested (two monocotyledonae and four dicotyledonae species, respectively).

After 21-28 days of exposure, no effects on seedling emergence and growth conditions were observed. A NOEC value resulted to be ≥ 1000 mg/Kg soil dw for all endpoints and species. No toxicity effects have been observed at the highest test concentration.

All validity criteria of the test were met.

Following the assessment, eMSCA concludes that terrestrial plants data can be considered acceptable; no further information is needed to clarify this endpoint and related concern.

7.8.3. Microbiological activity in sewage treatment systems

The Registrants provided a study, static, as limit test, (unpublished study report 10, 1988), according to OECD Guideline n. 209 Activated Sludge, Respiration Inhibition Test. The Registrants assign a reliability of 2 to the study. An EC50 > 100 mg/L (nominal) was reported.

Based on the available information, the eMSCA can support the above results.

7.8.4. PNEC derivation and other hazard conclusions

Table 7

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	PNEC (freshwater): 0.052 mg/l Intermittent releases: 0.52 mg/l	Assessment factor: 1000 Only acute tests for all three trophic levels are available. The justification was based on an EC50 value of 52 mg/L (Daphnia magna) taken from the only study in which any effects were observable. The test substance was rather dispersed than dissolved in this test and the NOEC is high above the water solubility due to the use of an emulsifier. However, this EC50 was taken as worst case consideration. PNEC intermittent release assessment factor: 100
Marine water	PNEC (marine water): 0.005mg/L Intermittent releases: 0.052mg/L Intermittent releases: 0.052mg/L	Assessment factor: 10000 Extrapolation method: assessment factor No marine data are available. The justification was based on the freshwater data
Sediments (freshwater)	PNEC sediment (freshwater): 100 mg/Kg sediment dw	Assessment factor: 100 Extrapolation method: Assessment factor A 28d NOEC value of 10000 mg/Kg sediment dw was used to derive this PNEC sediment value, with a specific assessment factor of 100 in accordance with ECHA Guidance R.10
Sediments (marine water)	PNEC sediment (marine water): 10 mg/Kg sediment dw	Assessment factor: 1000 Extrapolation method: Assessment factor A 28d NOEC value of 10000 mg/Kg sediment dw was used to derive this PNEC sediment value, with a specific assessment factor of 1000 in accordance with ECHA Guidance R.10
Sewage treatment plant (STP)	PNEC (STP): 1mg/L	Assessment factor: 100 Extrapolation method: assessment factor

		Justification was based on the EC50 of > 100 mg/L derived from the activated sludge respiration inhibition test according to OECD 209. To note that it is a screening PNECstp
Soil	PNEC soil = 66.8 mg/Kg soil dw	Assessment factor: 10 Extrapolation method: assessment factor PNEC soil value was derived from the lowest result determined in the toxicity study on soil macroorganisms (EC10 of 668 mg/kg soil dw) and an assessment factor of 10, according to ECHA Guidance R.10

PNEC water

Based on available data, the Registrants provided a PNECwater derived from the EC50 value of the supporting study (unpublished study report 5, 1988) equal to 52mg/L (*Daphnia magna*) taken as worst case consideration. As specified above in the previous sections, the tests provided by the Registrants showed some deficiencies. Nevertheless, given the low water solubility (value used for CSA: <0.73 µg/L) and the high log Kow (calculated logKow 7.6 at 25°C), the substance is expected to partition strongly to sediment and suspended solids. In such cases, it is likely both impractical and uninformative to test pelagic species via the water phase. Moreover, currently, exposure data provided by the Registrants, seem to indicate that a concern for aquatic compartment is not expected. Therefore, no action is required concerning the aquatic compartment.

PNEC sediment (freshwater and marine water)

Based on the reliable sediment toxicity study results, PNEC sediment (freshwater and marine water) values were derived from a 28d NOEC value of 10000 mg/Kg sediment dw with a specific assessment factor in accordance with ECHA Guidance R.10. eMSCA considers the resulting PNEC sediment values as valid and suitable as well as sufficient to conclude on sediment hazard assessment.

PNEC STP

The PNEC was calculated using EC50 value of >100 mg/L (above the water solubility), derived from micro-organisms respiration inhibition test in a sewage treatment plant (STP). The Assessment Factor used is 100 and valid according to ECHA Guidance R.10. The experimentally derived results are higher than the aqueous solubility, but can still be used as valid information to derive a PNECstp, because it is a conservative estimate unlikely to occur in practice. This respiration inhibition test is generally a screening test. Moreover, the substance was tested in a limit test, using one concentration (100 mg/L, nominal) only. The limit test is not sufficient to predict a PNECstp estimation, but only a screening PNECstp.

PNEC soil

Based on the reliable results from terrestrial toxicity studies, PNEC soil value was derived using the lowest result determined in the toxicity study on soil macroorganisms (EC10 of 668 mg/kg soil dw) and an assessment factor of 10, according to ECHA Guidance R.10.

eMSCA considers the resulting PNEC soil value as valid and considers that the information is suitable to conclude on terrestrial hazard assessment.

7.8.5. Conclusions for classification and labelling

The data provided by the Registrants to assess the aquatic toxicity is based on short-term studies. The aquatic organisms (algae, crustacea, fish) do not show any toxicity up to the limit of the water solubility of the substance.

eMSCA concludes that, based on the available information, there are no indication to propose a classification for the environment according to Regulation (EC) No. 1272/2008.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

Not relevant for this evaluation.

7.9.2. Acute toxicity and Corrosion/Irritation

Not relevant for this evaluation.

7.9.3. Sensitisation

Three Guinea Pig Maximization (GPMT) tests (following test guideline OECD 406, EU method B.6) are available and presented in the IUCLID dossier. The tests are conducted with commercial material from two different suppliers.

In a study conducted in 1991 with the registered substance (CAS 1843-05-6) the test material from a supplier was found sensitizing in a GPMT performed under GLP and following the procedure of OECD testing guideline 406 (EU method B.6) without deviations. In this study Pirbright White guinea pigs were used (10/sex). Negative and positive controls were included in the study. The tested sample was a commercial product with a purity of >99.5%. Applied concentrations were 5% in arachis oil for intradermal induction, 30% in vaseline for epicutaneous (occlusive) induction and 20% in vaseline for epicutaneous (occlusive) challenge. After challenge, 13 and 12 of 20 animals showed skin reactions after 24 and 48h, respectively.

The test item was reported to be sensitizing in a second GPMT performed in 2001 under GLP and following the procedure of OECD testing guideline 406 (EU method B.6) with a deviation regarding the number of animals,.Male and female Himalayan spotted guinea pigs were used (10 instead of 20 test animals). The tested sample was a commercial product and details on purity were not given in the report: this study was conducted with test material provided by the same supplier of the study conducted in 1991 with Pirbright White guinea pigs illustrated above. Concentrations were 15% in PEG 300 for intradermal induction, 40% in PEG for epicoutaneous induction and 40% in PEG 300 for epicoutaneuos (occlusive) challenge. Prior to epidermal induction, the skin was treated with 10% sodium lauryl sulphate to induce irritation. After challenge, 7 and 7 of 9 animals showed skin reactions after 24 and 48h, respectively (one animal of the test group was found dead on test day 14 - i.e. 2 days after the 48-hour reading of the epidermal induction).

In a further GPMT study conducted in 2000 and performed following the procedure of OECD testing guideline 406 male Dunkin Hartley guinea pigs were used. In this study, the tested sample was a commercial product with a purity of > 98.5%. Concentrations were 5% in arachis oil for intradermal and epicutaneous induction and 50% in arachis oil for epicutaneous (occlusive) induction. The epidermal induction treatment caused mostly grade 2 erythema at the 1h reading and mostly grade 1 erythema at the 24h reading. After epicutaneous (occlusive) challenge with either 25% or 50% in arachis oil, none of the twenty animals showed skin reactions at the 24h or 48h reading.

Octabenzone is confirmed as skin sensitizer on the basis of positive results on two Guinea pig maximization tests. Although the criteria for classification to subcategory 1B are fulfilled, the classification for subcategory 1A cannot be excluded due to the high concentrations used for topical induction in the two GMPT tests with positive results. Thus, on the basis of the available information the eMSCA envisages an harmonized classification as Skin sensitiser (H317), Category 1 of the substance as a follow-up at EU level.

7.9.4. Repeated dose toxicity

Not relevant for this evaluation.

7.9.5. Mutagenicity

Not relevant for this evaluation.

7.9.6. Carcinogenicity

Not relevant for this evaluation.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

During the evaluation eMSCA noted that the IUCLID dossier was not conclusive for fertility. However a Prenatal Developmental Toxicity Study (OECD Guideline 414) and Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test (OECD Guideline 422) were performed by the Registrant and the results were provided in the updated dossier.

The OECD 414 test was carried out by gavage and it was adequately performed and reported. Octabenzone was administered to pregnant Wistar rats on gestation days 6-19, at the dose levels of 100, 300 and 1000 mg/kg bw/day, to evaluate its potential maternal and prenatal developmental toxicity. There was no evidence for maternal toxicity or treatment-related effects on prenatal viability, growth or morphology at any dose. Therefore, the NOAEL for both maternal and developmental toxicity was 1000 mg/kg bw/day (max dose tested), thus a LOAEL was not identified.

The OECD TG 422 was performed according to the updated TG (adopted on 2016). The study was carried out by gavage and it was adequately performed and reported. The dose levels were 100, 300 and 1000 mg/kg bw/day. No treatment-related effects were observed concerning parental and litter toxicity, including neurobehavioral testing and histopathology of organs and tissues, as well as male and female fertility parameters.
At Post-Natal Day (PND) 13 in male pups of top dose level (1000 mg/kg bw/d), T4 levels were significantly lower compared to controls; since this finding was not persistent at the last sampling time (around PND 30), was not accompanied by an increase in TSH (indicative of functional thyroid imbalance) nor by histological findings, it is considered as treatment-related but it does not meet the requirement for being identified as adverse. Overall, the NOAEL and LOAEL for all effects were, respectively, 1000 and > 1000 mg/kg bw/day; for transient T4 changes the NOEL and LOEL were, respectively, 300 and 1000 mg/kg bw/day. The study findings do not trigger the need for a OECD TG 443, which will represent an unnecessary use of laboratory animals.
Moreover, the transient modulation of T4 levels cannot indicate, *per se*, the presence of endocrine disruption. It is widely recognized that many substances may transiently change the levels of a few hormones at high dose levels, whereas endocrine disruption is a potentially serious health concern, occurring when changes in the endocrine signalling network lead to identifiable adverse effects (Solecki et al., 2017).
The lack of endocrine activity, which might lead to endocrine disruption, by octabenzone is supported by a robust ensemble of eight non-standard studies using different approaches and protocols (*in silico* and/or *in vitro*) and also assessing octabenzone in comparison to benzophenone. Contrary to benzophenone, octabenzone did not show any relevant

endocrine activity, including binding to and transactivation of estrogen receptors beta and alpha, modulation of prostaglandin synthesis, etc.

Conclusion. Octabenzone showed no effects on fertility and on offspring in an updated GLP-compliant OECD TG 422 study on rats up to the dose level of 1000 mg/kg bw/day; a previous, old four-generation feeding study in rats was considered inconclusive, but it was superseded by the evidence provided by the new and adequate TG 422 study.

Octabenzone did not elicit maternal nor developmental toxicity in OECD 414 study up to the up to the dose level of 1000 mg/kg bw/day.

The available *in vitro* and *in vivo* studies did not indicate any endocrine disrupting potential.

7.9.8. Hazard assessment of physico-chemical properties

None impacting human health.

7.9.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

Table 8

CRITICAL DNELS/DMELS					
Endpoint of concern	**Type of effect**	**Critical study(ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL/ DMEL**	**Justification/ Remarks**
Workers Inhalation	Systemic effects - Long-term	Repeated dose toxicity (Oral)	NOAEC 66.1 mg/m^3	DNEL 6.61 mg/m^3	**AF** for dose response relationship: 1 **AF** for difference in duration of exposure: 2 **AF** for interspecies differences (allometric scaling): 1 **AF** for other interspecies differences**:** 1 **AF** for intraspecies differences: 5 **AF** for the quality of the whole database: 1 **AF** for remaining uncertainties: 1 **Overall Assessment Factor:** 20

Workers Dermal	Systemic effects - Long-term	Repeated dose toxicity (Oral)	NOAEL 75mg/kg bw/day	DNEL 1.88mg/kg bw/day	**AF** for dose response relationship: 1 **AF** for difference in duration of exposure: 2 **AF** for interspecies differences (allometric scaling): 4 **AF** for other interspecies differences**:** 1 **AF** for intraspecies differences: 5 **AF** for the quality of the whole database: 1 **AF** for remaining uncertainties: 1 **Overall Assessment Factor:** 40
General population Inhalation	Systemic effects - Long-term	Repeated dose toxicity (Oral)	NOAEC 32.6 mg/m^3	DNEL 1.63 mg/m^3	**AF** for dose response relationship: 1 **AF** for difference in duration of exposure: 2 **AF** for interspecies differences (allometric scaling): 1 **AF** for other interspecies differences**:** 1 **AF** for intraspecies differences: 10 **AF** for the quality of the whole database: 1 **AF** for remaining uncertainties: 1

					Overall Assessment Factor: 20
General population Dermal	Systemic effects - Long-term	Repeated dose toxicity (Oral)	NOAEL 75mg/kg bw/day	DNEL 0.94 mg/kg bw/day	**AF** for dose response relationship: 1 **AF** for difference in duration of exposure: 2 **AF** for interspecies differences (allometric scaling): 4 **AF** for other interspecies differences**:** 1 **AF** for intraspecies differences: 10 **AF** for the quality of the whole database: 1 **AF** for remaining uncertainties: 1 **Overall Assessment Factor:** 80
General population Oral	Systemic effects - Long-term	Repeated dose toxicity (Oral)		DNEL 0.94 mg/kg bw/day	**AF** for dose response relationship: 1 **AF** for difference in duration of exposure: 2 **AF** for interspecies differences (allometric scaling): 4 **AF** for other interspecies differences**:** 1 **AF** for intraspecies differences: 10 **AF** for the quality of the whole database: 1 **AF** for remaining

					uncertainties: 1 **Overall Assessment Factor:** 80

7.9.10. Conclusions of the human health hazard assessment and related classification and labelling

On the basis of the available information, an harmonized classification of the substance is envisaged by eMSCA, as a follow-up at EU level by adding the following hazard category: Skin Sens. Cat. 1, H317.

7.10. Assessment of endocrine disrupting (ED) properties

7.10.1. Endocrine disruption – Environment

Not evaluated.

7.10.2. Endocrine disruption - Human health

In silico and in vitro studies on the potential endocrine disrupting properties of Octabenzone including assays in comparison with other substances, are available in the open literature. In these studies, Octabenzone was shown to display no estrogenic, androgenic or anti-androgenic activity. Available in vivo studies (subchronic studies and a 4-generation study in rats) showed no relevant endocrine disrupting effects and/or activity. Furthermore, the new study performed following the updated TG 422, discussed in section 7.9.7., is considered a valuable test for screening assessment about the potential reproductive and/or developmental (including thyroid-disrupting) effects and, eventually, to decide on the Extended One-Generation (OECD TG 443) need. In such an updated TG 422 study, it was observed that at PND 13, male pups treated with the top dose level (1000 mg/kg bw/d) showed significantly lower T4 levels in comparison to controls. Despite this, such an effect was neither persistent at the last sampling time (around PND 30), nor accompanied by an increase in TSH (indicative of functional thyroid imbalance), nor by histological findings: hence, it is considered as treatment-related but without to meet the requirement for being identified as adverse. Indeed, it is widely recognized that the transient modulation of T4 levels cannot indicate, *per se*, the presence of endocrine disruption.

7.10.3. Conclusion on endocrine disrupting properties (combined/separate)

Overall, *in vitro* and *in vivo* assessment provide no indication of endocrine disrupting potential at the estrogen, androgen and thyroid level.

7.11. PBT and VPVB assessment

1) Persistence,
A study according to OECD 301B -Ready Biodegradability: CO_2 Evolution test (unpublished study report 2, 1989) was performed. A biodegradation of 6% within 28 d was reached (with a initial test substance concentration of 10.7 mg/l), and when an initial test substance concentration of 20.2 mg/l was used, a biodegradation of 5% within 28d was reached. Therefore, the substance should be considered not readily biodegradable, and a Modified MITI Test (I) supports this result.

Hence, the substance has to be regarded as potentially persistent (P) or even very persistent (vP) in the environment according to annex XIII for screening criteria of P/vP of the REACH.

2) Bioaccumulation

Calculated BCF values of 90 - 190 from a japanese MITI (1992) study equivalent to OECD Guideline 305 C using carp point to the fact that the test compound is not bioaccumulative according to the B criterion. Those results are supported by a second MITI study revealing a BCF <= 140.
Furthermore, the PBT working group decided in 2008 that the test substance has a low to moderate bioaccumulation potential and does not meet the B criterion (ECB, 2008).

2) Toxicity

The data used by the Registrants to assess the T criterion is based on short-term aquatic toxicity studies. The Registrants state that aquatic organisms (algae, crustacea, fish) do not show any toxicity up to the limit of the water solubility of the substance.

Based on the available information on the environmental toxicity there are no indications on fulfilling toxicity criteria for the environment.

4) Overall conclusion

Octabenzone does not meet the B or T criteria. It is considered to meet the screening P/vP criteria. Therefore, it is concluded that octabenzone is not considered as a PBT/vPvB substance.

7.12. Exposure assessment

The substance is produced in a range between 1000 - 10,000t per year with small fluctuations over the years (2009-2017). Many uses are identified for this substance: formulation, uses at industrial sites, uses by professional workers, consumer uses and article service life. Therefore, it is considered as a substance with wide dispersive use.

7.12.1. Human health

Not evaluated.

7.12.2. Environment

In order to clarify the possible impact on the environment, pursuant to Article 46(1) of the REACH Regulation, the Registrants were requested to provide justification about missing elements regarding environmental exposure assessment needed to conclude on the concern for the environment.
In particular the Registrants were requested to provide missing or not justified assumptions regarding use descriptors and Operational Conditions (OCs) and Risk Management Measures (RMMs) as well as local and regional PEC values for all compartments and, consequently, providing an updated proper characterization of the risk for all compartment and in particular for soils.
The Registrants provided all the requested elements about environmental exposure. Although a descriptive text for each adopted refinement on environmental exposure for all scenarios is still missing, attachments in tabular format were provided.

In the contributing scenarios controlling environmental exposure, the Registrants applied default values for release fraction to all compartmens by Environmental Release Concentrations (ERCs) or refinements according to available Specific Environmental Release Concentrations (SpERCs) (CEPE, FEICA and ISOPA), and according to the OECD

Emission Scenario Document Number 3 on Plastic Additives. Therefore, the input values of the exposure assessment can be considered acceptable.

7.13. Risk characterisation

Environment

In response to the Substance Evaluation decision, the Registrants provided a refined risk assessment for all compartments, particularly for the terrestrial one. Furthermore, regarding the environmental regional assessment, the Registrants provided a declaration that the regional background (PECregional) is included in the given PEC values, unless stated otherwise. In conclusion, eMSCA support the conclusion that all RCR values are less than 1 and the risk is considered to be controlled in each environmental compartment.

7.14. References

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7.15. Abbreviations

AF	Assessment Factor
BW	Body Weight
CAS	Chemical Abstracts Service
C&L	Classification and Labelling
CLP	Classification, Labelling and Packaging (Regulation (EC) No1272/2008)

CMR	Carcinogenicity, Mutagenicity and Toxicity to Reproduction
CSR	Chemical Safety Report
DNEL	Derived No Effect Level
DW	Dry Weight
eMSCA	Evaluating Member State Competent Authority
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
PBT	Persistent, Bioaccumulative, Toxic
PEC	Predicted Environmental Concentration
PNEC	Predicted No Effect Concentration
RCR	Risk Characterization Ratio
vPvB	Very Persistent and very Bioaccumulative