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Helsinki, 16 December 2019

Addressees
Registrants of Sepisol Fast Blue 85219 listed in the last Appendix of this decision (registrant(s)[1])

Decision/annotation number
Please refer to the REACH-IT message which delivered this communication (in format SEV-D-XXXXXXXXXX-XX-XX/F)

Substance subject to this decision, hereafter 'the Substance'
Substance name: Sepisol Fast Blue 85219
EC number: 700-579-6
CAS number: n.a.
Date of latest submission(s) considered: 03 August 2018

DECISION ON SUBSTANCE EVALUATION

In accordance with Article 46(1) of the REACH Regulation (Regulation (EC) No 1907/2006), you must submit the following information:

1. Water Solubility with the Substance; test method: OECD 105 column elution method. The test must be performed under relevant conditions with varying pH (i.e. 3, 7 and 10) and temperatures (i.e. 20 and 50°C). The test must include analytical determination of the Substance and the dissociation products.

You must provide an update of the registration dossier(s) containing the requested information, including robust study summaries and, where relevant, an update of the chemical safety report by the deadline as defined below:

Request 1: the information required according to point 1 above must be generated and provided by **16 June 2020**.

The reasons of this decision and any further test specifications of the requirements are set out in Appendix 1. The procedural history is described in Appendix 2. Further information, observations and technical guidance as appropriate are provided in Appendix 3. Appendix 4 contains information related to Appendix 1 (Reasons). Appendix 5 contains a list of registration numbers for the addressees of this decision. This appendix is confidential and not included in the public version of this decision.

[1] The terms registrant(s), dossier(s) or registration(s) are used throughout the decision, irrespective of the number of registrants addressed by the decision.

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Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has a suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals

Authorised[2] by Christel Schilliger-Musset, Director of Hazard Assessment

[2] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

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Appendix 1: Reasons

Based on the evaluation of all relevant information submitted on Sepisol Fast Blue 85219 and other relevant available information, ECHA concludes that further information is required to enable the evaluating Member State Competent Authority (MSCA) to complete the evaluation of whether the substance constitutes a risk to the environment.

The evaluating MSCA will subsequently review the information submitted by you and evaluate if further information should be requested to clarify the concern for PBT/vPvB properties in the follow up process.

The potential risk - environment

The identification of a potential risk is based on a combination of exposure and hazard information.

According to information in the registration dossier, the Substance is used as dye in ink and toners. Significant exposure to the environment can therefore not be excluded.

Based on information in the registration dossier and information from [redacted] as detailed below, there is a concern that the Substance may be a PBT or vPvB substance as defined in REACH Annex XIII.

The Substance is [redacted] complex that consists of the following starting materials: the [redacted] (EC number [redacted]) also known with the commercial name [redacted], hereafter referred to as dissociation product 1 and [redacted] (EC number [redacted]) also known with the commercial name of [redacted], hereafter referred to as dissociation product 2. For the complex itself there is no PBT/vPvB concern as the molecular weight and log Kow of the complex are too high to give a concern for bioaccumulative behaviour in the environment (see Appendix 4, Table 1). However, there is a potential PBT/vPvB concern for dissociation product 2 as it meets all PBT screening criteria (see Appendix 4, Table 1). As the Substance may dissociate into dissociation product 1 and 2, and the current solubility information in the dossier is not sufficient to exclude dissociation of the Substance into the starting materials/dissociation products, ECHA has a PBT/vPvB concern for the Substance.

Based on this exposure and hazard information, there is a potential risk for the environment. As the available information is not sufficient to conclude on potential PBT/vPvB properties, further information is needed, as explained below.

The possible risk management measures – environment

If the obtained data from Request 1 are sufficient to confirm the suspected PBT/vPvB properties as defined in REACH Annex XIII, the evaluating MSCA will assess the need for further regulatory risk management in the form of identification as a substance of very high concern (SVHC) under Article 57 of REACH and subsequent authorisation or restriction of the Substance.

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This would lead to stricter risk management measures than those currently in place because substances that are PBT/vPvB or contain PBT/vPvB like components >0.1%, or can release components that have PBT/vPvB like properties would require substitution when technically suitable and economically viable alternatives are available. Until the substitution is achieved, the releases of and exposures to PBT and vPvB substances would need to be minimised.

Explanation of the testing strategy – environment

Annex XIII to REACH provides that the identification of PBT/vPvB substances must also take account of the PBT/vPvB properties of relevant transformation and/or degradation products. If any one transformation and/or degradation product is confirmed as meeting the P, B and T or vP and vB criteria and therefore having PBT/vPvB properties, then the Substance itself, as the source of those transformation and/or degradation products, can be identified as a PBT/vPvB. In the decision for case number A-004-2017, ECHA's Board of Appeal has also confirmed that ECHA can under substance evaluation request a registrant to perform a study to determine the transformation and/or degradation products of the substance on the basis that these products may have potential PBT/vPvB properties. This is irrespective of the fact that the parent substance itself is not PBT/ vPvB.

The information requested constitutes the first tier in a testing strategy to clarify the concerns for PBT/vPvB. Hence, the evaluating MSCA will review the information submitted by the registrant(s) as an outcome of the first tier of the testing strategy, and evaluate if further information should be requested to clarify the concern for PBT/vPvB properties. ECHA currently requests information on the solubility and specifically the dissociation behaviour of the Substance.

If the results from requirement 1 above show that the Substance does not dissociate at all, no further testing seems necessary at this moment. If the results show that the Substance transforms to dissociation product 2, the evaluating MSCA may consider whether further information will be required to clarify concerns for the release of a potential PBT/vPvB constituent from the Substance. As there is a possibility that dissociation product 2 is formed as a transformation product in e.g. environmental (bio)degradation processes, it might become necessary to request further information on the potential release of dissociation product 2 from the Substance from you in the future, but this cannot be defined yet. Any future request for further information on the potential release of dissociation product 2, or on its PBT properties, will be in a new evaluation decision. Any such future decision would be based on all information available at that point in time, including any relevant information in the registration dossiers for dissociation product 2. The addressees of any future decision would be determined at that point in time.

1. **Water Solubility with the Substance; test method: OECD 105 column elution method. The test must be performed under relevant conditions with varying pH (i.e. 3, 7 and 10) and temperatures (i.e. 20 and 50°C). The test must include analytical determination of the Substance and the dissociation products.**

<u>The concern(s) identified</u>

ECHA has a potential PBT/vPvB concern for the dissociation product 2 as it meets all PBT screening criteria (see Appendix 4, Table 1). The current data are not adequate to conclude

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on the possible dissociation of the Substance which would potentially release dissociation product 2 in the environment. Moreover, some preliminary screening data on solubility and dissociation provided by you [[redacted], 2017] indicate that color changes were observed when the Substance was added to water at different pH values. Color changes were observed at pH=3 and pH=10 and these color changes were faster at higher temperatures (40-50°C). These color changes are seen as indicators of dissociation product 2 chromophore changes as the pH would not influence the chromophore if it were completely insoluble. Therefore there is a concern that dissociation product 2 will be released when the Substance dissociates under environmental relevant conditions (pH 4-9 and ambient temperature) or under conditions relevant to the life cycle of the Substance (i.e. recycling of paper and de-inking of paper in the paper life cycle).

Furthermore the current water solubility information in the dossier and the provided background information on the solubility testing showed that water fraction in the solubility test was coloured blue. This is attributed by you to very fine insoluble particles of the Substance that could not be filtered out. This is however not substantiated by evidence of particles in the water. The blue colour of the water fraction could be interpreted as (potential) dissociation product 2 in aqueous solution. The argument that [redacted] is needed for [redacted] to go into solution can not be an argument for insolubility of the Substance as the production of the Substance consists of [redacted] Such a [redacted] might well be reversible, especially under the more extreme environmental conditions that can be expected during the ink and dye life-cyle.

Why new information is needed

Based on the available non-guideline non-GLP water solubilty test as provided in the registration dossier, the evaluating MSCA cannot evaluate whether the Substance dissociates and thus whether dissociation product 2 is released. In this study, a certain amount of the Substance has been dissolved in water and filtrated twice over a cellulose membrane (with 0.45 µm and 0.20 µm porosity). The filtrates were analysed by UV-spectrophotometry. The ratio of dissociation product 1 to dissociation product 2 was measured to be (96-100%) to (0-4%) after the first filtration. After a second filtration no dissociation product 2 was identified anymore, i.e. the ratio was 100% dissociation product 1 to 0% dissociation product 2. Based on these results you conclude that the Substance contains [redacted] as an impurity which has been solubilised in water, and that the traces of dissociation product 2 may come from fine particles that have passed through the first filter. Based on this data you conclude that the Substance is not soluble in water at the limit of detection (0.0075 mg/L).

However, in ECHA's view this study is not adequate to conclude on the dissociation of the Substance. First, there is high probability that the Substance and dissociation product 2 will have a higher affinity to bind to the filter than being dissolved in water (see Appendix 4, Table 1). Therefore, this study set-up, with the application of cellulose membrane filters, may not provide a true reflection of the water solubility. Second, the Substance has the same UV-absorption spectrum as the dissociation product 2. As a consequence, in the filtrate no distinction can be made between dissociation product 2 and

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the undissociated Substance. Third, the limit of detection of the water solubility test provided is deemed inadequate.

In addition, this study was only conducted under one specific condition (i.e. 22°C, pH not determined), not covering all conditions relevant to the life cycle of the Substance. Elevated temperatures and pH might highly influence the dissociation of the Substance.

Considerations on the test method

As dissociation product 2 might be formed when the Substance is dissolved, a reliable water solubility study is required with analytical determination of the Substance, the [redacted] and the [redacted]. For this purpose the column elution water solubility test method according to the OECD test guideline 105 should be conducted. This method is considered applicable for substances with a water solubilty below 10^{-2} g/l.

As the Substance will not only encounter neutral pH and room temperature during its life cycle and as it is expected that pH and potentially temperature influence the water solubilty and dissociation of the Substance, you are requested to conduct the water solubility test under varying conditions. You are required to conduct the water solubility test under three different pH conditions: 3, 7 and 10. These pH values may sufficiently represent the conditions as encountered during the life cycle of the Substance (i.e. the paper life cycle, including paper recycling processes) [European Commission, 2015].

Furthermore, you are required to conduct the water solubility test under two different temperatures: 20 and 50°C. Based on preliminary dissociation information voluntarily provided by you [[redacted] 2017], the color changes observed at pH=3 and pH=10 were faster after heating at a temperature from 40 to 50°C. This may indicate that dissociation is faster and potentially higher at an increased temperature. As during the life cycle of the Substance (i.e. the paper recycling processes), the temperature is regularly around 40-50°C [European Commission, 2015], these conditions are also considered relevant for the Substance.

For the analytical determination, ECHA stresses that the Substance and dissociation product 2 have comparable (or even similar) UV-absorption spectra. An analytical method should be selected that is able to distinguish the complex (the Substance) from dissociation product 2 in solution and should have a limit of detection below 0.1 µg/L or as low as technically feasible.

For the interpretation of the results, ECHA notes that [redacted] and [redacted] (starting materials for the Substance) may be present in the Substance as impurities. The concentrations of the impurities should be considered separately from the dissociation of the Substance. The [redacted] impurity is considered relevant for PBT/vPvB assessment when it is present in a concentration ≥ 0.1% (w/w) (ECHA Guidance R.11, 2017). Dissociation product 2 is considered relevant for PBT/vPvB assessment at any concentration. By using the column elution method (OECD TG 105) it is ensured that the measured concentrations of dissociation product 2 are formed due to dissociation of the Substance, as the column is flushed several times to remove impurities and unbound substance before starting the solubility measurement (OECD TG 105, paragraph 15). Furthermore, ECHA notes that it should be ensured that

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the pH-buffer used for the water solubility test should have minimal influence on the water solubility and dissociation of the Substance.

Consideration of alternative approaches

The request is suitable and necessary to obtain information that will allow to clarify whether a concern for release of chemicals with PBT/vPvB properties is applicable to this substance. More explicitly, there are no equally suitable alternative ways available of obtaining this information. E.g. the hydrolysis test (OECD TG 111) is only applicable to substances with appreciable water solubility, and the OECD TG 112 "Dissociation constant in water" is less appropriate according to the Qualifying statements in the guideline (see section 1 of the guideline). ECHA notes that there is no other experimental study available at this stage that will generate the necessary information.

Consideration of your comments on the draft decision

You argue that the analytical methods available do not allow to make a distinction between dissolved and bound dissociation product 2, and the limit of detection of 0.1 µg/L will be difficult to attain. This is considered to be addressed by application of the OECD TG 105 generated column method, and possibly another analytical method, i.e. not spectrometry. If the Substance is completely retained on the generated column, anything blue eluting from the column has to be dissolved dissociation product 2 and should thus also be possible to detect and quantify using spectrometry.

The request in this decision is intended to elucidate the possible release of dissociation product 2 from the Substance and is not intended to conclude on the PBT-status of (salts of) dissociation product 2. You argued that you have no access to the details of the substance identity of the dissociation product 2 in a NONS dossier which was used to support the (potential) PBT concern identified by the evaluating MSCA to discuss their relevance and reliability. The information from the NONS dossier (including the [redacted]) is however considered confidential and the concern for the PBT-like properties of dissociation product 2 (irrespective of the [redacted]) is not depending on the (very limited) information in this dossier. The NONS dossier reference has therefore been removed. The screening criteria for PBT are fulfilled by the information on dissociation product 2 from the safety datasheet you supplied and confirmed by QSAR estimations (see Appendix 4). You are asked to generate further information on the dissociation behavior of the Substance, in order to evaluate whether a potentially PBT-like substance (dissociation product 2, with [redacted] hydroxide, or [redacted], both present under environmental conditions, or other [redacted] that are available under environmental conditions and might lead to [redacted] with the Substance) can be released during the life cycle of the Substance. You are not requested to generate information, or evaluate and discuss the (potential) PBT concern for dissociation product 2 but to give adequate information to support your claim that no dissociation product 2 will be released from the Substance during its life cycle.

Furthermore, you indicated that the feasibility of a more detailed water solubility study is, according to exchanges with the contract laboratory, uncertain. This is noted, however, currently, the given solubility/dissociation information is deemed insufficient to take away the concern that dissociation product 2, as a potential PBT/vPvB chemical is released as a transformation product during the life-cycle of the Substance, as the Substance (small particles) and dissociation product 2 can not be distinguished by the analytical method used (spectrometry), and the filtering step is claimed to be insufficient to retain all Substance particles. Using the OECD TG 105 generated column method it is thought that

there is no need to distinguish between dissociation product 2, dissolved or bound to the Substance (assuming complete insolubility of the Substance), as anything that is released from the generated column has to be considered dissolved dissociation product 2.

Two Proposals for Amendments (PfAs) were received regarding the responsibility for possible further testing needed to elucidate the PBT properties of dissociation product 2 potentially released from the Substance during its life time.
In a comment on the PfA, you stated that you can agree with the decision "only if the responsibility of [redacted] is not automatically engaged for any determination regarding the [redacted] status." The text under 'Explanation of the testing strategy – environment' has been modified to further clarify possible further testing.

It was noted in a PfA that Table 1 in Appendix 4 has been amended to refer to the Dissociation product 2 and to include QSAR predictions. You commented on the use of QSAR estimates as an indication of the biodegradability/persistence in Appendix 4 with the request for structural representations (SMILES) used for the log Kow estimates. All values used in Appendix 4 are now documented, the log Kow estimates are documented, and the rationale for the chosen representative log Kow value is given. The estimates for biodegradation use the same SMILES leading to what is thought the most representative value for log Kow (Table 2 and 3 in Appendix 4).

You commented on the modified information in Appendix 4 stating that in your opinion SMILES nr.3 is the best representation of dissociation product 2, without argumentation. You also indicate that SMILES nr.1 in Appendix 4 could be representative of dissociation product 2, again without argumentation. Both SMILES nr.1 and nr.3 are however the [redacted], which could represent the starting material ([redacted]) but not dissociation product 2. Removing the [redacted] in order to represent dissociation product 2 would give SMILES nr.2 and nr.5 respectively. SMILES nr. 2 and nr. 5 show a very large difference in log Kow estimation between the two models used (KowWIN and ClogP). In your further comment you state that "*Indeed, there is a free electron circulation between the nitrogens and the aromatic structures. It means that the electron circulation goes from a nitrogen thought an aromatic structure and the central carbon to another aromatic structure and finally to another nitrogen.*" This is in agreement with the arguments given in Appendix 4 leading to adaptation of SMILES nr. 5, and selection of SMILES nr.10 (for KowWIN) and SMILES nr. 11 (for ClogP) as best representations of chemical structure for dissociation product 2. All SMILES with the distributed aromatic character give log Kow estimates that are significantly above the screening criterion for Bioaccumulation (log Kow > 4.5) for both software models (KowWIN and ClogP). Furthermore, the estimates from the biodegradation QSARs do not depend on the choice of most appropriate SMILES as you also state in your comment "*The choice of the SMILE will not impact the results of the* BioWin predictions."

In a last remark you suggest to use [redacted] as a read across source substance for the log Kow for dissociation product 2. However, in the absence of arguments and evidence to support this read-across for log Kow estimation, ECHA can not assess the validity of such a read-across for that specific endpoint.

Consideration of the time needed to perform the requested study

In the draft decision communicated to you, the time indicated to provide the requested information was 12 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also requested an In Vitro Mammalian Cell Gene Mutation Test. This test is no longer requested, as it is deemed more appropriate

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to address this concern by the registrant of the impurity that raised the concerns. Therefore, ECHA has modified the deadline for provision of the required information.

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References

[redacted]. 2017. SEV [redacted] – Feedback (e-mail) to questions of evaluating MSCA. Materials safety datasheets for the starting materials [redacted] and [redacted] and the testing report for the preliminary solubility/dissociation testing already undertaken by the testing laboratory contracted by the registrant.

European Commission. 2015. Best Available Techniques (BAT) Reference Document for the Production of Pulp, Paper and Board. Report EUR 27235 EN (p.69).

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Appendix 2: Procedural history

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to suspected PBT/vPvB and wide dispersive use, Sepisol Fast Blue 85219 (EC No 700-579-6) was included in the Community rolling action plan (CoRAP) for substance evaluation to be evaluated in 2017. The updated CoRAP was published on the ECHA website on 21 March 2017. The competent authority of the Netherlands (hereafter the evaluating MSCA) was appointed to carry out the evaluation.

In accordance with Article 45(4) of the REACH Regulation, the evaluating MSCA carried out the evaluation of the above substance based on the information in your registration(s) and other relevant and available information.

The evaluating MSCA considered that further information was required to clarify the abovementioned concerns. Therefore, it prepared a draft decision under Article 46(1) of the REACH Regulation to request further information. It subsequently submitted the draft decision to ECHA on 21 March 2018.

ECHA notified you of the draft decision and invited you to provide comments.

ECHA received comments from you and forwarded them to the evaluating MSCA without delay.

The evaluating MSCA took the comments from you, which were sent within the commenting period, into account and they are reflected in the reasons (Appendix 1). The requests and the deadline were amended. The request for an in vitro gene mutation study in mammalian cells has been removed.

The evaluating MSCA notified the draft decision to the competent authorities of the other Member States and ECHA for proposal(s) for amendment.

Subsequently, the evaluating MSCA received proposals for amendment to the draft decision and modified the draft decision. They are reflected in the reasons (Appendix 1).

ECHA referred the draft decision, together with your comments, to the Member State Committee.

ECHA invited you to comment on the proposed amendment(s). Your comments on the proposed amendments were taken into account by the Member State Committee.

ECHA notified you of the modified part of Appendix 4 and invited you to provide comments on the draft text in that Appendix. This consultation was based on your earlier comments on the Draft Decision that had not been sufficiently addressed and which you reiterated in your comments on the proposals for amendment. Your comments on this part were taken into account by the Member State Committee.

MSC agreement seeking stage

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-67 meeting and ECHA took the decision according to Article 52(2) and 51(6) of the REACH Regulation.

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Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided by you in the registration(s) is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on your dossier(s) at a later stage, nor does it prevent a subsequent decision under the current substance evaluation or a new substance evaluation process once the present substance evaluation has been completed.

2. Failure to comply with the request(s) in this decision, or to otherwise fulfil the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

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Appendix 4: Information related to Appendix 1: Reasons

Table 1: *PBT/vPvB relevant properties of the Substance (Sepisol Fast Blue 85219) and its starting products for formulation / dissociation products* [redacted] *dissociation product 1) and* [redacted] *dissociation product 2)*

Properties	Sepisol Fast Blue 85219	Dissociation product 1	Dissociation product 2
Mol. weight	1454-1622	496-664 ([redacted])	514 (as [redacted]) 495 (as hydroxide)
Water solubility	<0.007 mg/L[1]	>1000 mg/L[1] (pH 8.3; OECD105)	20-25 g/L[4]
Log Kow	>7.54[1] (solubility octanol / solubility water) >20 (QSAR estimate KowWIN v1.68/ ClogP v1.5)	<-2.68[1] (pH 4.8; OECD107) 2.18 (1R); 7.84 (2R)[2]	7.00[2] (KowWIN v1.68) 7.67[2] (ClogP v1.5)
Biodegradation	45% ThCO2[1] (28d; OECD301B)	0% ThOD[1] (20d; OECD301D) 21% DOC[1] (28d; OECD302B)	QSAR[3]: - Biowin2: Does not biodegrade fast - BioWin3: Mineralization half life months to years - BioWin6: Not readily biodegradable
Toxicity	0.006 mg/L[1] (EC50-48h; daphnids) >12.6 mg/L[1] (NOEC-72h; algae)	0.65 mg/L[1] (NOEC-168h; daphnids) 3.85 mg/L[1] (LC50-96h; fish) 100 mg/L[1] (NOEC-3w; algae)	0.015 mg/L[4] (EC50-48h; daphnids) 0.03 mg/L[4] (LC50-96h; fish) 2.91 mg/L[4] (LC50-96h; algae)
PBT/vPvB concern	No (not B)	No (not B, not T)	Yes (potential P/vP, potential B/vB, T)

[1] = *Substance registration dossier*

[2] = *QSAR estimate (KowWin v1.68 as part of EPIWIN, US EPA. 2019. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.1. United States Environmental Protection Agency, Washington, DC, USA). Multiple values between log Kow 3.9 and 10.8 result from the QSAR estimations based on different structural representation (SMILES) and the software used (KowWin or ClogP). The list of SMILES and the corresponding estimations of Log Kow values ranging from 3.9 to 10.8 are given in Table 2 and 3 together with a rationale for selecting the best representations.*

[3] = *QSAR estimates (BIOWIN v4.10 (September 2010), as part of EPIWIN, US EPA. 2019. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.1. United States Environmental Protection Agency, Washington, DC, USA). SMILES nr. 9 and 10 – with and without the* [redacted] *– have been used as input BioWin2. BioWin2 result 0.0002; without* [redacted] *0.0003: Does not biodegrade fast, P-screening criterion <0.5. BioWin3 result with* [redacted] *1.5533, without* [redacted] *1.6295: P-screening criterion < 2.7. BioWin6 result with* [redacted] *0.0001, without* [redacted] *0.0001: Not readily biodegradable, P-screening criterion < 0.5. (REACH guidance R11).*

[4] = *safety data sheet for* [redacted] *(*[redacted]*) as supplied in the communication to evaluating MSCA and ECHA [*[redacted]*, 2017]*

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In Table 2 below, eleven different SMILES of the dissociation product 2 are given. These have been used as input for two QSAR models estimating the octanol/water partition coefficient (log Kow). The log Kow estimation is subsequently used as a screening criterion for potential Bioaccumulative properties of a substance (REACH guidance R11) in Table 1. When the log Kow is >4.5 a substance is considered potentially B or vB. Based on the structure representation (with or without chloride anion) and based on the interpretation of the substructure fragments recognised by the two estimation models the best SMILES for dissociation product 2 are nr. 10 for the KowWIN model, and nr. 11 for the ClogP model.

For estimation of the environmental persistence, the BioWIN v4.10 QSAR estimation program is used. The SMILES that are acceptable and used for the BioWIN v4.10 QSAR program (with and without the chloride anion) are nr. 9 and 10 in Table 2). The results are compared with the screening criteria for Persistence in REACH guidance R11 (see Table 1 and its footnote 3).

The two QSAR estimation softwares used to predict log Kow are KowWin v1.68 as part of EPIWIN, US EPA. 2019. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.1. United States Environmental Protection Agency, Washington, DC, USA, and BioLOOM ClogP, © 1993-2019 BioByte Corporation, http://www.biobyte.com/index.html. The software used to estimate the biodegradation potential of Dissociation product 2 is BioWIN v4.10 as part of EPIWIN, US EPA. 2019. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.1. United States Environmental Protection Agency, Washington, DC, USA.

The KowWIN program is freely available, however the commercial ClogP program is considered to give more reliable estimations. It should be noted that all ClogP estimations of the octanol/water partition coefficient for the 11 different SMILES are well above the Bioaccumulation screening criterion log Kow>4.5. The structure representations leading to a very large difference between the KowWIN and the ClogP estimation models are considered less reliable. The SMILES that is considered to be most representative of the dissociation product 2 gives log Kow estimates that are well in line with each other; log Kow is estimated to be 7.0 using the KowWin model and log Kow 7.67 using the ClogP model.

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Draft decision notified to the registrant(s) under Article 50(1) of REACH for comments

Table 2. *Different structure representations (SMILES) of dissociation product 2 with and without chloride anion.*

SMILE nr.	SMILES used as input to the estimation programs
1	[redacted]
2	[redacted]
3	[redacted]
4	[redacted]
5	[redacted]
6	[redacted]
7	[redacted]
8	[redacted]
9	[redacted]
10*	[redacted]
11*	[redacted]

**** Considered to be the most representative SMILES for dissociation product 2***

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Draft decision notified to the registrant(s) under Article 50(1) of REACH for comments

Table 3 *Estimates of the octanol/water partition coefficient (log Kow) as screening criterion for bioaccumulative behaviour, using the two best practice QSAR models.*

SMILE nr.	log Kow estimate KowWin v1.68	log Kow estimate ClogP v1.5	Remarks
1	4,06	10,40	SMILES from the SMILECASDB (belonging to CAS nr. 2390-60-5). A huge difference between KowWIN and ClogP estimates.
2	4,06	7,40	Chlorine removed from the SMILES, to represent Dissociation product 1. Still a large difference between KowWin and ClogP.
3	#N/A	9,51	SMILES from PubChem (Kekulé representation of aromaticity)
4	3,88	9,44	H removed from [NH+] to make SMILES acceptable to KowWin v1.68
5	6,08	9,51	chlorine ion removed from SMILES
6	10,58	8,50	If the charge is removed from the nitrogen to yield the neutral structure the calculated log Kow is 10.58. This would be incorrect as it gives an incorrect valence for the nitrogen atom. All nitrogens in the structure have a valence of three, where the structure requires one nitrogen atom to have a valence of 5.
7	8,98	9,30	Using aromatic bonds instead of Kekulé representation of the aromatic rings
8	9,43	8,30	Aromaticity can also be applied to the central carbon atom, which is more realistic, as the conjugated pi system is shared all over the structure. The log Kow estimate then becomes 9.43
9	7,00	8,67	The nitrogen atom is made 5-valent by including an explicit chloride as well as a hydrogen. This is thought to be the best log Kow estimate for Basic Blue 7.
10	**7,00**	8,60	With the chloride anion removed, and a positive charge on the nitrogen the ClogP estimate becomes log Kow = 8.60. KowWin does not change (7.00) **This is thought to be the best representation of dissociation product 2 for the KOWWIN v1.68 model**
11	#N/A	**7,67**	There is a specific fragment [NH+] in ClogP (but not in KowWIN), using fragment in the SMILES representation lowers the log Kow estimate from ClogP from 8.60 to 7.67. **This is thought to be the best representation of dissociation product 2 for the ClogP v1.5 model.**