EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 12 May 2021

Addressees
Registrant(s) of JS_467-63-0_[redacted] as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
14/08/2019

Registered substance subject to this decision ("the Substance")
Substance name: p,p',p''-tris(dimethylamino)trityl alcohol
EC number: 207-396-6
CAS number: 467-63-0

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***17 August 2022***.

Requested information must be generated using the Substance unless otherwise specified.

Many of this type of organic substances are listed in various national inventories of nanomaterials, such as the French nano-particulate substances reporting system.[1] In the case where the Substance is manufactured and/or imported in the European Union in nanoforms by any addressee of the present decision, the REACH Regulation (as amended by Regulation Commission Regulation (EU) 2018/1881) sets out explicit information requirements for nanoforms of substances. Manufacturers and/or importers of nanoforms must have fulfilled these specific information requirements by 1st January 2020. As far as the registration dossiers currently submitted on the Substance by any addressee of the present decision they do not cover any nanoform. Any incompliances identified in the present decision on the Substance relate only to information required on non-nanoforms.

Based on the above, the requested information in this present decision must be generated using exclusively non-nanoforms of the Substance.

A. Information required from all the Registrants subject to Annex VII of REACH

1. Water solubility (Annex VII, Section 7.7.; test method: EU A.6./OECD TG 105)
2. Partition coefficient n-octanol/water (Annex VII, Section 7.8.; using an appropriate test method)
3. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471)
4. Only if study under section A.1 shows the substance is poorly water soluble, Long-term toxicity testing on aquatic invertebrates (triggered by Annex VII, Section 9.1.1., column 2; test method: EU C.20./OECD TG 211)
5. Only if study under section A.1. shows the substance is not poorly soluble, Short-term

[1] "*Dispositif de déclaration des substances à l'état nanoparticulaire* », Decree 2012-232 of French *Conseil d'Etat* of 17 February 2012.

toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202)

6. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)
7. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301A/B/C/D/E/F or OECD TG 310)

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendix entitled "Reasons to request information required under Annex VII of REACH".

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[2] under the authority of 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.

Appendix on Reasons common to several requests

1. Assessment of your read-across approach under Annex XI, Section 1.5.

You seek to adapt in the dossier the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

In your dossier:
- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2)
- Ready biodegradability (Annex VII, Section 9.2.1.1)

In your comments on the initial draft decision:
- Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2)

ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[3] and related documents[4, 5].

A. Predictions for (eco)toxicological properties

You have not provided a read-across justification document in your dossier. However, you have provided a read-across justification document with your comments on the initial draft decision.

For the endpoints listed above, you used data from the following source substances:

In your dossier:
i) Crystal Violet Lactone (EC 216-293-5)
ii) Pigment Violet 27 (EC 235-468-7)
iii) [4-[[4-anilino-1-naphthyl][4-(dimethylamino)phenyl]methylene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium acetate (280-898-0)

[3] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9
[4] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)
[5] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

iv) [4-[[4-(dimethylamino)phenyl][4-(methylamino)phenyl]methylene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium acetate (282-246-2)
v) Basic violet 1 (EC 616-846-4)

Additionally, in your comments on the initial draft decision:
vi) [4-[α-[4-(dimethylamino)phenyl]benzylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium acetate (EC 255-288-2).

For the environmental endpoints, you have mentioned the following an additional source substance in the comments on the initial draft decision, however the read-across justification document doesn't include it:
vii) α,α-bis[4-(dimethylamino)phenyl]-4-(phenylamino)naphthalene-1-methanol (EC 229-851-8)

In your comments to the initial draft decision, you have provided the following reasoning for the prediction of toxicological properties: *" The following assessment intends to demonstrate that the target and read-across substances covered in this justification have common properties and present comparable environmental fate and toxicological behavior".*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects, and that the properties of your Substance are predicted to be quantitatively equal to those of the source substance.

Attached to your comments on the initial draft decision you submitted a read-across justification document. In your justification document you have indicated that 'Scenario 2' was selected for the analogue approach. You provided the following reasoning for the prediction of (eco)toxicological properties: *"read-across of environmental fate, ecotoxicological and toxicological data from an analogue may be justified on the basis of:*

- *Identifying the read across substances based on common functional groups and further filled with relate mechanistic approaches and finally fine-tuned with structural similarity using the QSAR Toolbox Version 3.4*
- *Common structural alerts or reactivity*
- *Common physico-chemical properties*
- *Likelihood of common breakdown products via biological/degradation processes"*

You conclude that *"the descriptors, various alerts and scenario (for analogue approach) which were taken into consideration for ecotoxicological and toxicological assessment as reported in this RA justification document obtained by using OECD QSAR toolbox v.3.4 of the target substance and source substances (i.e., read across analogues) were evaluated to be similar and therefore justified and appropriate".*

As the analogues are used as source substances to predict the property of the Substance, we understand that you have adapted the standard information requirements under Annex XI, Section 1.5 to REACH (grouping and read-across). Based on the above, you used the QSAR Toolbox for the identification of analogues and use information on these analogues to predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance(s).

ECHA notes the following shortcomings with regards to prediction of (eco)toxicological properties.

Read-across documentation

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summary(ies) of the source study(ies).[6]

You have provided studies conducted with other substances than your Substance in order to comply with the REACH information requirements. In your dossier, you have not provided documentation as to why this information is relevant for your Substance.

The (further) documentation of the studies provided in your comments to the draft decision for biodegradability endpoint does not cover sufficient information to make an independent assessment of the study as indicated under the endpoint.

In the absence of such documentation, ECHA cannot verify that the properties of your Substance can be predicted from the data on the source substance(s).

In your comments on the initial draft decision you provided a read across justification but with shortcomings identified in this Appendix.

Characterisation of the source substance(s)

Annex XI, Section 1.5 states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*".

According to the ECHA Guidance, "*the purity and impurity profiles of the substance and the structural analogue need to be assessed*", and "*the extent to which differences in the purity and impurities are likely to influence the overall toxicity needs to be addressed, and where technically possible, excluded*". The purity profile and composition can influence the overall toxicity/properties of the potential source substances, including test materials.[7] Therefore, qualitative and quantitative information on the compositions of the test materials should be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities.

The provided information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on source substances.

You do not provide any description of the source substances introduced in your dossier. Furthermore, for all the studies provided in the technical dossier that were conducted with these substances, as listed above, no information on the composition of the test material used to generate the source data is provided.

The read-across justification document attached to your comments to the draft decision specify the type of the additional source substances (mono-constituent or UVCB) without further characterisation on purity profile and composition.

Regarding your consolidated comments to the draft decision for the sources substances for the environment, you have indicated these substances can be considered as potential read-across due to the presence of a common organic moiety "triphenyl methane, despite the %

[6] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.6.1
[7] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.4.1

of similarity being low. You state further that this similarity is based on the presence of inorganic moiety "copper ferrocyanide" in one of the source substances, CAS 12237-62-6. However, you have not provided any further characterisation on purity profile and compositional information that could support your comments.

Without such information, no qualitative or quantitative comparative assessment of the compositions of the different test materials can be completed. Therefore, is not possible to assess whether the attempted predictions are compromised by the composition of the test materials and their relation to source and target substances.

Missing supporting information to compare properties of the substances

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[8]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s). Supporting information must include bridging studies to compare properties of the Substance and source substances.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both types of substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

You have provided studies in the dossier and in the comments on the draft decision which have been conducted with source substances. You have not provided studies that were conducted with the Substance on the endpoints for which you have submitted a read-across adaptation.

Therefore, there is no endpoint-specific information (bridging studies) available to compare properties of the source substances with those of the target substance. The data set reported in the technical dossier and with the comments on the draft decision does not include relevant, reliable and adequate information for the Substance and of the source substance(s) to support your read-across hypothesis.

In the absence of such information, you have not established that the Substance and of the source substance(s) are likely to have similar properties. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substances. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

[8] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

2. Assessment of your weight of evidence adaptation under Annex XI, Section 1.2.

ECHA understands that you have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2:

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
2. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
3. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2)
4. Ready biodegradability (Annex VII, Section 9.2.1.1)

Your weight of evidence adaptation raises the same deficiencies irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in the following appendices.

Annex XI, Section 1.2 states that there may be sufficient weight of evidence weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, Section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

However, for each relevant information requirement, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property.

In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation.

The issue identified below is essential for all the information requirements in which you invoked a weight of evidence.

Reliability of the read across approach

Section 1. of the present Appendix identifies deficiencies of the grouping and read across approach used in your dossier. These finding apply equally to the sources of information relating to analogue substances submitted under your weight of evidence adaptations.

Therefore the studies cannot be regarded as reliable.

Reliability of (Q)SAR adaptation

Section 3. of the present Appendix identifies deficiencies of the (Q)SAR adaptations used in your dossier. These finding apply equally to the related sources of information submitted under your weight of evidence adaptations.

Therefore the (Q)SAR predictions cannot be regarded as reliable.

Further, specific considerations are addressed under the individual information requirements.

3. Assessment of your Qualitative and Quantitative structure-activity relationship ((Q)SAR) under Annex XI section 1.3

You have adapted the following standard information requirements by applying Qualitative and Quantitative structure-activity relationship ((Q)SAR) adaptation in accordance with Annex XI, section 1.3:

- Water solubility (Annex VII, Section 7.7.)
- Partition coefficient n-octanol/water (Annex VII, Section 7.8.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

While an adaptation was not specifically indicated by you, ECHA has evaluated the provided information under the rules set in Annex XI, Section 1.3. Qualitative or quantitative structure-activity relationship (QSAR).

Rule for Annex XI, Section 1.3 adaptation

Annex XI, Section 1.3. states that results obtained from valid QSAR models may be used instead of testing when the following cumulative conditions are met, in particular:

1. results are derived from a QSAR model whose scientific validity has been established;
2. the substance falls within the applicability domain of the QSAR model;
3. adequate and reliable documentation of the applied method is provided; and
4. the results are adequate for classification and labelling and/or risk assessment.

According to ECHA's Practical guide "How to use and report (Q)SARs", section 3.4, a QSAR Model Reporting Format (QMRF) and a QSAR Prediction Reporting Format (QPRF) are required to establish the scientific validity of the model, to verify that the Substance falls within the applicability domain of the model, and to assess the adequacy of the prediction for the purposes of classification and labelling.

The Substance is outside the applicability domain

ECHA Guidance R.6.1.5.3 specifies that a substance must fall within the applicability domain specified by the model developer.

For ecotoxicological information requirements, the applicability domain of the model you used is defined for Neutral Organics and Benzyl Alcohols.

The Substance used as input for the prediction is not a Neutral organic (since it dissociates) nor a benzene alcohol.

Therefore, you have not demonstrated that the Substance falls within the applicability domain of the model.

Missing supporting information, in particular QMRF/QPRF

- For physico-chemical information requirements, you have provided i) a reference to the estimation Programs Interface Suite™ QSAR predictions V4.11, ii) a reference to SRC PhysProp Database, iii) a reference to the Danish QSAR predictions database and iv) a reference to ACD (Advance Chemistry Development)/I-Lab.

  You did not provide QMRFs and QPRFs in the dossier for the predictions applied.

- For ecotoxicological information requirements, you have provided estimated toxicity values for the endpoints derived with ECOSAR program version 1.11. You have provided summaries of the predictions and the outcome of the predictions. However, you have not provided documentation establishing the scientific validity of the model for the QSAR predictions (i.e. QMRF and QPRF are not provided in the technical dossier, including identity of the compounds used during the parameterisation of the models, defined descriptor and structural fragment domains).

- For environmental fate and pathways information requirements, you have provided estimated toxicity values for the endpoints derived with, Estimation Programs Interface Suite™ V4.11 (2019), OECD QSAR tool box version 3.3 and BIOWIN, version 4.10. You have provided summaries of the predictions and the outcome of the predictions. However, you have not provided documentation establishing the scientific validity of the model for the QSAR predictions (i.e. QMRF and QPRF are not complete in the technical dossier)

  In your comments to the initial draft decision you agree to update the dossier with a QSAR Model Reporting Format (QMRF). The information in your comments is not sufficient for ECHA to make an assessment. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). Please note that, in case of QSAR adaptation, a QSAR Prediction Reporting Format (QPRF) must be submitted.

Inadequacy for the purpose of classification and labelling and risk assessment

QSAR results must be adequate for classification and labelling/risk assessment and thus be reliable.

For the physico-chemical information requirements, you have used a QSAR model lacking data in its training set for dyes, or substances mostly dissociated and highly ionisable at pH 5-8.

The Substance is a dye that in environmental pH (5-8) will be mostly dissociated and highly ionisable.

By not taking into account the specific properties of the Substance provided above, you have not demonstrated that the prediction is reliable and adequate for the purpose of classification and labelling and risk assessment.

Further, specific considerations are addressed under the individual information requirements.

Therefore, your adaptations do not comply with the general rules of adaptation as set out in Annex XI, Section 1.3. and your (Q)SAR adaptations are rejected.

Appendix A: Reasons to request information required under Annex VII of REACH

1. Water solubility

Water solubility is an information requirement under Annex VII to REACH (Section 7.7). ECHA understands that you have provided QSAR adaptations based on Annex XI, Section 1.3 of REACH, using the following information:

i) Water Solubility using Estimation Programs Interface Suite™ QSAR predictions V4.11
ii) SRC PhysProp Database (2018)
iii) DANISH Q(S)AR predictions database for water solubility (2017):

We have assessed this information and identified the following issue:

As explained in the Appendix on Reasons common to several requests, Section 3, your adaptation under Annex XI, Section 1.3. is rejected. In addition, ECHA has identified additional deficiencies presented below.

Water solubility was estimated using WSKOWIN module of EPI Suite™ v.4.11., the WSKOWIN model is LogKOW based. Therefore, for the reasons mentioned in section A.2., ECHA could not assess the reliability of the QSAR prediction.

In your comments to the draft decision you indicated that you have conducted a new water solubility study according to OECD TG 105. As no further details have been indicated in your comments on the initial draft decision, ECHA cannot assess the new study. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation).

On the basis of the above, the information requirement is not fulfilled.

Study design

Considering the properties of the Substance (solubility < 10 mg/L), the column elution described in EU A.6/OECD TG 105 is the most appropriate method to fulfil the information requirement for the Substance.

2. Partition coefficient n-octanol/water

Partition coefficient in n-octanol/water is an information requirement under Annex VII to REACH (Section 7.8).

ECHA understands that you have provided QSAR adaptations based on Annex XI, Section 1.3 of REACH, using the following information:

i) Partition coefficient using Estimation Programs Interface Suite™ QSAR predictions V4.11
ii) DANISH Q(S)AR predictions database
iii) Partition coefficient by ACD (Advanced Chemistry Development)/I-Lab

We have assessed this information and identified the following issues:

As explained in the Appendix on Reasons common to several requests, Section 3, your adaptation under Annex XI, Section 1.3. is rejected. In your comments on the draft decision, you agree to perform the requested study.

On the basis of the above, the information requirement is not fulfilled.

Study design

Considering the properties of the Substance (sparingly soluble particles), the Partition Coefficient (n-octanol/water), HPLC Method (test method: OECD TG 117) or alternatively the Partition Coefficient (1-Octanol/Water): Slow-Stirring Method (test method: OECD TG 123) are the most appropriate method to fulfil the information requirement for the Substance.

3. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is a standard information requirement in Annex VII to REACH.

You have adapted this information requirement by using Grouping of substances and read-across approaches under Annex XI, Section 1.5., and Weight of Evidence under Annex XI, Section 1.2. of REACH.

You have provided the following sources of information to support your adaptations:

Studies in your dossier:

i) *In vitro* gene mutation study in bacteria (2018) with analogue substance Pigment Violet 27 (EC 235-468-7)
ii) *In vitro* gene mutation study in bacteria (1981) with analogue substance Basic Violet 1 (EC 616-846-4).

Studies described in your comments:

iii) *In vitro* gene mutation study in bacteria (2002) with analogue substance dimethylamino-3,3-bis(4-dimethylaminophenyl)phthalide (Crystal Violet Lactone, EC 216-293-5)
iv) *In vitro* gene mutation study in bacteria (2020) with analogue substance [4-[α-[4-(dimethylamino)phenyl]benzylidene]cyclohexa-2,5-dien-1-ylidene]dimethylammonium acetate (EC 255-288-2).

ECHA assessed this information and identified the following issues:

A. Read-across

As explained in the Appendix on Reasons common to several requests your adaptation under Annex XI, Section 1.5. is rejected.

B. Weight of evidence

As explained in Section 2 of the Appendix common to several requests, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

To fulfil the information requirement, normally a study according to OECD TG 471 must be provided. The key elements investigated by this test are:

- Detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies; and

- Data provided on 5 bacterial strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

The provided studies (i) to (iv) detect and quantify mutations in bacteria. However, the provided studies (i and ii) do not include data on the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101).

Therefore, the provided studies provide relevant information, although for studies (i) and (ii), only partly relevant.

Furthermore, the reliability of these sources of information is significantly affected by the deficiencies identified in Section 2 of the Appendix on Reasons common to several requests.

In addition, the reliability of the source of information (ii) is for this information requirement affected by the following issue:

Testing in accordance with OECD TG 471, requires that the following specifications/ conditions have to be met:

- The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose must correspond to 5 mg/plate or 5 ml/plate.
- The evaluation of at least 5 doses in each test condition.

In study (ii) the highest tested dose was 10 µg/plate *("Maximum non-toxic dose")* but no information on cytotoxicity investigations is included and there is no information on other doses used in the test.

Therefore, the provided studies cannot be considered a reliable source of information.

As a conclusion, the sources of information as indicated above provide information on mutations in bacteria which is only partly relevant, and the information provided is not reliable.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated by the required study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

4. Long-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex VII of REACH. However, pursuant to Annex VII, section 9.1.1, column 2, for poorly water soluble substances (e.g. water solubility below 1 mg/L or below the detection limit of the analytical method of the test substance) long-term toxicity study on aquatic invertebrates (Annex IX, Section 9.1.5) must be considered instead of an acute test.

You have not provided any data on long-term toxicity to aquatic invertebrates.

Poorly water soluble substances require longer time to reach steady-state conditions. Hence, the short-term tests may not give a true measure of toxicity for this type of substances. Therefore, if the information requested on water solubility (request A.1) confirms that the substance is poorly water soluble (<1 mg/L), a long-term toxicity test on aquatic invertebrates must be conducted.

In your comments on the initial draft decision, you agree to perform the requested study on two analogue substance EC 235-468-7 / CAS no. 12237-62-6 and EC 229-851-8 / CAS no. 6786-83-0 for long-term study on Daphnia by following the OECD test 211 from a GLP certified laboratory. We understand that you are proposing an adaptation according to Annex XI, section 1.5.

ECHA notes that the read-across justification document attached to your comments on the initial draft decision does not include information on the analogue substance EC 235-468-7 / CAS no: 12237-62-6. However, notwithstanding that as explained in the Appendix on Reasons common to several requests your adaptation under Annex XI, Section 1.5. is rejected.

Only one valid study is required to fulfil the standard information requirement.

Study design

The Substance is difficult to test due to the indicated low water solubility (below 1 mg/L) depending on the results of requests A.1, its ionic character and the use of the Substance as a dye indicating adsorptive properties. OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 211. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solutions.

5. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex VII of REACH.

You have adapted this information requirement by using Weight of Evidence under Annex XI, Section 1.2., Qualitative or Quantitative structure-activity relationship ((Q)SAR) under Annex XI, Section 1.3 and Grouping of substances and read-across approaches under Annex XI, Section 1.5. of REACH.

You have provided the following sources of information to support your adaptations:

i) Data derived from Qualitative or quantitative structure-activity relationship (QSAR) in accordance with Annex XI, Section 1.3 for the Substance (Key study).
ii) OECD TG 202 study with the analogue substance EC 282-246-2 / CAS 84434-47-9 (2017).
iii) OECD TG 202 study with the analogue substance EC 280-898-0/ CAS 83803-79-6. Guideline OECD 202.

We have assessed this information and identified the following issue(s):

A. Read-across

As explained in the Appendix on Reasons common to several requests your adaptation under Annex XI, Section 1.5. is rejected.

B. Weight of evidence

As explained in Section 2 of the Appendix on Reasons common to several requests, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

To fulfil the information requirement, normally a study according to OECD TG 202 must be provided. The key element investigated by this test is the concentration of the test material leading to the immobilisation of 50% of daphnids at the end of the test is estimated. All the sources of information you provided investigate this key element. Therefore, they provide information that would contribute to the conclusion on this key element.

However, the reliability of these sources of information is significantly affected by the deficiencies identified in Section 2 of the Appendix common to several requests.

Taken together, even if these sources of information provide information on the key element, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated by in an OECD TG 202 study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

C. QSAR calculation

As explained in the Appendix on Reasons common to several requests your adaptation under Annex XI, Section 1.3. is rejected.

In your comments on the initial draft decision, you indicated that you will be adapting this information requirement based on the results of the long term toxicity testing data on aquatic invertebrates. Under this decision, it is, however, either the short invertebrates or the long term invertebrates, depending exclusively on whether the Substance is poorly soluble.

Based on the above, the information you provided do not fulfil the information requirement.

However, Annex VII, section 9.1.1, column 2, requires to perform a long-term toxicity study on aquatic invertebrates (Annex IX, Section 9.1.5) instead of an acute test when the substance concerned is poorly water soluble. In that respect, as explained under request A.1, your dossier currently does not include a reliable value on the water solubility of the substance. However, based on the information currently contained in the dossier it might be poorly water soluble. Therefore, a short-term toxicity testing on aquatic invertebrates must only be conducted if the data generated under request A.1 do not confirm that the substance is poorly water soluble (i.e. water solubility below 1 mg/L).

The Substance is difficult to test due to its ionic character, and the substance is a coloured dye. OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations.

Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

6. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2).

You have adapted this information requirement by using Weight of Evidence under Annex XI, Section 1.2., Qualitative or Quantitative structure-activity relationship ((Q)SAR) under Annex XI, Section 1.3 and Grouping of substances and read-across approaches under Annex XI, Section 1.5. of REACH.

You have provided the following sources of information to support your adaptations:

i) Data derived from Qualitative or quantitative structure-activity relationship (QSAR) in accordance with Annex XI, Section 1.3 for the Substance (Key study).
ii) OECD TG 201 study with the analogue substance EC 282-246-2 / CAS 84434-47-9 (2019).
iii) OECD TG 202 study with the analogue substance EC 235-468-7/ CAS 2237-62-6 EC 235-468-7/ CAS 2237-62-6 (2018)

We have assessed this information and identified the following issues:

A. Read-across

As explained in the Appendix on Reasons common to several requests your adaptation under Annex XI, Section 1.5. is rejected.

B. *Weight of evidence*

As explained in Section 2 of the Appendix on Reasons common to several requests, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

To fulfil the information requirement, normally a study according to OECD TG 201[9] must be provided. The key element investigated by this test is growth rate of algal cultures.

All the sources of information you provided investigate this key element. Therefore, they provide information that would contribute to the conclusion on this key element.

[9] ECHA Guidance R.7b, Section R.7.8.4.1

However, the reliability of these sources of information is significantly affected by the deficiencies identified in Section 2 of the Appendix common to several requests.

Taken together, even if these sources of information provide information on the key element, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated by in an OECD TG 201 study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

C. QSAR calculation

As explained in the Appendix on Reasons common to several requests your adaptation under Annex XI, Section 1.3. is rejected.

In your comments to the draft decision you agree to perform the requested study.

Based on the above, the information you provided do not fulfil the information requirement.

Study design

OECD TG 201 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.5.

7. Ready biodegradability

Ready biodegradability is an information requirement under Annex VII to REACH (Section 9.2.1.1.).

You have adapted this information requirement by using Weight of Evidence under Annex XI, Section 1.2., Qualitative or Quantitative structure-activity relationship ((Q)SAR) under Annex XI, Section 1.3 and Grouping of substances and read-across approaches under Annex XI, Section 1.5. of REACH.

You have provided the following sources of information to support your adaptations:

i) Data derived from Qualitative or quantitative structure-activity relationship (QSAR) in accordance with Annex XI, Section 1.3 for the Substance (Key study): BioWin EPIsuite v4.10 US EPA (2019).
ii) OECD TG 301 study with the analogue substance EC 216-293-5 / CAS 1552-42-7 (2017)
iii) Modified Sturm test (EPA OTS 7963206) with the analogue substance Pigment Violet27 (EC 235-468-7) (1989)

In your comments on the initial draft decision you have provided the following additional source of information to support your adaptation

iv) OECD TG 301-D study with the analogue substance EC 282-846-2 / CAS 84434-47-9

We assessed this information and identified the following issue(s):

A. Read-across

As explained in the Appendix on Reasons common to several requests your adaptation under Annex XI, Section 1.5. is rejected.

B. Weight of evidence

As explained in Section 2 of the Appendix on Reasons common to several requests, the weight of evidence must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

To fulfil the information requirement, normally a study according to OECD TG 301A/B/C/D/E/F or OECD TG 310 study must be provided. The key element investigated by these tests is the ultimate aerobic biodegradation (as measured by parameters such as DOC removal, CO_2 production and oxygen uptake) of the test material under low inoculum concentration is measured at sufficiently frequent intervals to allow the identification of the beginning and end of biodegradation.
All the sources of information you provided in the dossier and in your comments to the draft decision investigate this key element. Therefore, they provide information that would contribute to the conclusion on this key element.

However, the reliability of these sources of information is significantly affected by the deficiencies identified in Section 2 of the Appendix common to several requests.

In addition, the reliability of source of information iv) is significantly affected by the following issue:

The OECD TG 301 includes the following specifications:

- the ultimate aerobic biodegradation (as measured by parameters such as DOC removal, CO2 production and oxygen uptake) of the test material under low inoculum concentration is measured at sufficiently frequent intervals to allow the identification of the beginning and end of biodegradation;
- The difference of extremes of replicate values of the removal of the test material at the plateau, at the end of the test or, if appropriate, at the end of the 10-d window is ≤ 20%;
- In the toxicity control, the degradation of the reference substance has reached ≥ 35% (based on DOC) or ≥ 25% (based on ThOD or ThCO2) by day 14;
- Oxygen depletion in the inoculum blank is ≤ 1.5 mg dissolved O2/L after 28 days;
- The residual concentration of oxygen in the test bottles is ≥ 0.5 mg O2/L at any time;

As you have not provided information on the parameters listed above, an independent assessment of the study reliability is not possible.

Taken together, even if these sources of information provide information on the key element, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated by in an OECD TG 301A/B/C/D/E/F or OECD TG 310 study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

C. QSAR calculation

As explained in the Appendix on Reasons common to several requests, Section 3, your adaptation under Annex XI, Section 1.3. is rejected. In addition, ECHA has identified additional deficiencies presented below.

QSAR results must be adequate for classification and labelling/risk assessment and thus be reliable.

You have used 'prediction approach by read-across from category members which takes average value from the 13 nearest neighbours' with QSAR Toolbox. You have not provided category hypothesis and it was unclear how you came up with those 13 nearest substances as category members. Furthermore you have not justified how the QSAR value obtained by taking the average from those nearest 13 neighbours is reliable and scientifically valid. You have not provided any relevant documentation on external validity, goodness-of-fit, statistic power of this methodology to justify it is capable of predicting a reliable value for this endpoint.

Therefore, you have not demonstrated that the predicted value is reliable and therefore adequate for regulatory purposes.

On this basis, the information requirement is not fulfilled.

Appendix B: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

1. Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

2. Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[10].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[11].

C. Analytical monitoring

[10] https://echa.europa.eu/practical-guides
[11] https://echa.europa.eu/manuals

For ecotoxicological information requirements (requests 4, 5 and 6):

- You must select an analytical method that is able to distinguish to the extent technically feasible the Substance and the dissociation products in solution. Otherwise, it is not possible to relate the observed effects to the Substance itself considering that the Substance in environmental pH (5-8), will be mostly dissociated and highly ionisable.
- For the same reason, you must provide a description on the analytical method used, monitor the test concentration(s) to the extent technically feasible, indicate what has been monitored and on which chemical species the effect concentrations are based.

Appendix C: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 12 February 2020.

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

ECHA took into account your comments and did not amend the requests.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix D: List of references - ECHA Guidance[12] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[13]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[13]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[14]

[12] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[13] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[14] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix E: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.