ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 21 December 2017

Addressee: [redacted]

Decision number: CCH-D-2114381690-46-01/F
Substance name: 1-[(2,4-dinitrophenyl)azo]-2-naphthol
EC number: 222-429-4
CAS number: 3468-63-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 13.06.2013
Registered tonnage band: 10-100 tonnes per year (based on submission number: [redacted] - latest tonnage band)

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA requests you to submit information on

1. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG with the registered substance**
2. **Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**
3. **Long-term toxicity testing on fish (Annex VIII, Section 9.1.3., column 2; test method: Fish, early-life stage (FELS) toxic with the registered substance;**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **28 June 2019**. You shall also update the chemical safety report, where relevant.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Advice and further observations are provided in Appendix 3.

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, shall be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under http://echa.europa.eu/regulations/appeals.

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2

[1] 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 1: Reasons

ECOTOXICOLOGICAL INFORMATION

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 10 to 100 tonnes per year must contain, as a minimum, the information specified in Annexes VII to VIII to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

The information requested in this decision is needed to meet the respective requirements of members of the joint submission registered at tonnages of 10 to 100 tonnes per annum (Annex VIII) as part of the jointly submitted registration dossier.

Your registration dossier contains for the endpoints : Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.), Long term toxicity test on aquatic invertebrates (Annex VII, Section 9.1.1., column 2) and Long term toxicity test on Fish (Annex VIII, Section 9.1.3., column 2), adaptation arguments in form of a grouping and read-across approach according to Annex XI, Section 1.5. of the REACH Regulation. ECHA has assessed first the scientific and regulatory validity of your Grouping and read-across approach in general before the individual endpoints (sections 1, 2 and 3).

Grouping and read-across approach

Article 13(1) of the REACH Regulation requires information on intrinsic properties of substances on human toxicity to be generated whenever possible by means other than vertebrate animal tests, including from information from structurally related substances (grouping or read-across), "*provided that the conditions set out in Annex XI are met*". According to Annex XI, Section 1.5. there needs to be structural similarity among the substances within a group or a category and furthermore, it is required that the relevant properties of a substance within the group can be predicted from the data from the source substance within the group, by interpolation.

You consider to achieve compliance with the REACH information requirements for the registered substance C.I. PIGMENT ORANGE 5, i.e. 1-[(2,4-dinitrophenyl)azo]-2-naphthol (acronyms: PO5, Pigment Orange 5), using data of a structurally similar substance C.I. PIGMENT RED 3, i.e. 1-(4-methyl-2-nitrophenylazo)-2-naphthol (acronyms: PR3, Pigment Red 3) (EC number 219-372-2) (hereafter the 'source substance').

You have provided a read-across justification as part of the CSR (section 1.2) containing the following arguments to support the prediction of properties of the registered substance from data of a source substance: the substances show similarity in their structure, their physico-chemical properties and environmental fate as well as similar toxicological and eco-toxicological properties, as you mentioned "*Lacking bioavailability is probably the reason for the absence of any relevant mammalian toxicity. None of the category members showed a toxic effect after single oral or inhalational exposure [...]. Furthermore, Monoazo Red Pigments do not exert toxic effects to aquatic, terrestrial and sediment organisms as well as bacteria. [...]" and* concluded: "*structural similarities with very similar physical-chemical properties, environmental fate, ecotoxicity and mammalian toxicity enable the treatment of these Monoazo Red Pigments as a category and fulfilment of data requirements by read across from one category members to all other category members is justified.*"

To support the proposed read-across hypothesis, you have provided experimental data mainly on PR3 (EC number 219-372-2).

Furthermore, you also provided together with this justification document, a data matrix summarizing the findings and properties of the 3 members of this Monoazo Red Pigments category (section 1.3 of the CSR).

ECHA considers that this information is your read-across hypothesis, which provides the basis whereby you predict the properties of the registered substance from the source substance, according to Annex XI, Section 1.5.

1. You have proposed that structural similarity is a basis for predicting the properties of the registered substance. For this, you provided the following argument: the pigments grouped in this category are structurally similar and contain a substituted phenyl moiety, an azo moiety, and a 2-hydroxynaphthalene (β-naphthol). Differences between the various Monoazo Red Pigments are due to the different identity of the substituents of the phenyl ring. Structural similarity is a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or in this specific case that structural similarity *per se* – as you argue – is sufficient to enable the prediction of environmental fate or ecotoxicology properties of a substance, since structural similarity does not always lead to predictable or similar fate and ecotoxicological properties. Hence, further elements are needed but were not provided by you, such as a well-founded hypothesis of (bio)transformation to a common compound(s), or that different compounds have the same type of effect(s), to allow a prediction of ecotoxicological and fate properties that does not underestimate risks.

2. Similarly, you have proposed that the physicochemical properties of the substances are similar and follow a regular pattern, and that this is a basis for predicting the properties of the registered substance. For prediction of environmental fate, ecotoxicological properties you stated further in your justification document that: "*All members of this category are solids, which decompose at high temperatures. The solubility of these red and orange pigments in water and n-octanol is limited, […] resulting in a low partition coefficient in n-octanol/water (log P_{ow} < 3.7), which is below the limit of concern considered to be critical for bioaccumulative properties. All category members tested showed very limited biodegradability, which is assumed to be due to their unavailability for microorganisms. Monoazo Red Pigments do not hydrolyse in aqueous solutions, i.e. no hazardous substances are liberated from these pigments.*"

   Similarity or a regular pattern of physicochemical properties are a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or in this specific case that physicochemical similarity or regular properties *per se* – as you argue – are sufficient to enable the prediction of ecotoxicological properties of a substance (and in particular for the endpoints Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.), Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2), Long-term toxicity testing on fish (Annex VIII, Section 9.1.3., column 2), since physicochemical similarity or regular properties does not always lead to predictable or similar ecotoxicological properties.

   To the specific arguments that there are low bioaccumulative properties, limited biodegradability, or that these substances do not hydrolyse, ECHA considers that these physicochemical properties do not provide a valid scientific explanation to predict the properties of the substance for fate and ecotoxicological endpoints as these are based on few experimental data with high uncertainty, or on the absence of data that were applied across the category.

As such the waiver for hydrolysis or the absence of data is not considered a valid argument of similar behaviour, nor is a calculation made for one substance and applied to the target substance.

Hence ECHA considers that such physicochemical properties of the substance cannot be predicted and therefore used for, in particular for the endpoints of Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.), Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2) and Long-term toxicity testing on fish (Annex VIII, Section 9.1.3., column 2).

3. Similarly, you have proposed that the ecotoxicological properties of the substances are similar and follow a regular pattern, and that this is a basis for predicting the properties of the registered substance.
   Similarity or a regular pattern of ecotoxicological properties are a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or in this specific case that ecotoxicological similarity or regular properties *per se* – as you argue – are sufficient to enable the prediction of environmental properties of a substance, since ecotoxicological similarity or regular properties in one ecotoxicological endpoint does not always lead to predictable or similar environmental properties in other ecotoxicological endpoints. In your case the absence of found eco-toxicological effects does not suffice to support a prediction from one category member to the others. Especially when considering the very limited number of studies which allow comparison between the two substances (i.e. one study for both substances was submitted only for the respiration inhibition test on microbial sludge endpoint). Hence it is not possible to conclude that this provides a well-founded basis to predict that the fate and ecotoxicological properties of the two substances are indeed similar or follow a regular pattern for the endpoints you attempt to cover, namely Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1. column 2), Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.) and Long-term toxicity test on aquatic invertebrates (Annex VII, Section 9.1.1., column 2).

4. Similarly, you have proposed that the environmental fate properties of the substances are similar and follow a regular pattern, and that this is a basis for predicting the properties of the registered substance. Your arguments on environmental fate properties mention the water solubility, octanol-water partition coefficients, persistence and bioavailability.

   Similarity or a regular pattern of environmental fate properties are a prerequisite for applying the grouping and read-across approach, but ECHA does not accept in general or in this specific case that environmental fate similarity or regular properties *per se* – as you argue – are sufficient to enable the prediction of environmental properties of a substance, since environmental fate similarity or regular properties in one environmental fate endpoint does not always lead to predictable or similar environmental properties in other environmental fate and behavioural endpoints.

Finally, ECHA has taken into account all of your arguments together. ECHA firstly notes that you have not provided a reasoning as to why these arguments add to one another to provide an improved justification for the read-across. Secondly, ECHA considers that the arguments when taken all together do not provide a basis for predicting the properties of the registered substance.

ECHA considers that this grouping and read-across approach does not provide a robust basis whereby the environmental effects and environmental fate may be predicted from data for reference substance within the group by interpolation to other substances in the

group (read-across approach). ECHA notes that there are specific considerations for the individual endpoints which also result in a failure to meet the requirement of Annex XI, Section 1.5, and these are set out below under the endpoint concerned.

In your comments on the draft decision, you commented on the scientific and regulatory validity of the category approach. Regarding the ecotoxicological and environmental fate properties and the related justifications provided for the read-across approach, ECHA notes your commitment to update the read-across argumentation in each dossier of the Monoazo red Pigments category. You also indicate that "*for all three substances measured partition coefficients octanol/water are available*" and that these "*may serve as basis for calculation/prediction of other endpoints*". ECHA notes that, as already indicated above, in the similarity of physicochemical properties of the substances or that they follow a regular pattern, is a prerequisite, but not sufficient to enable the prediction of ecotoxicological properties of the registered substance by a read-across approach. Nevertheless they can be used as part of an argumentation for a read-across approach. ECHA notes that no new data to support the read-across approach has been provided in your comments on the draft decision.

With regard to your indication to update the robust study summary of the bioaccumulation study on the analogue substance C.I. Pigment Red 3 (included as supporting study in the technical dossier used to prepare the draft decision, submission number [redacted], submission date 13 June 2013) to show that the substances are not bioaccumulative, ECHA emphasises that it is your responsibility to provide all relevant information and argumentation to be used to support the read-across approach proposed.

In conclusion, for the reasons as set out above, and taking into account all of your arguments, ECHA considers that your grouping and read-across approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation. Therefore, this adaptation cannot be accepted and there is a data gap for the endpoints covered by your read-across approach.

1. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In addition, column 2 of Annex VII, Section 9.1.2. specifies that the study does not need to be conducted if there are mitigating factors indicating that aquatic toxicity is unlikely to occur for instance if the substance is highly insoluble in water or the substance is unlikely to cross biological membranes.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record from a Key study (reliability 1, GLP) for an Algae growth inhibition test (OECD TG 201) with the source substance PR3 (EC number 219-372-2). The results showed no toxicity, with a 72-hour NOEC > 6µg/L growth rate.
However, as also explained, above in the "Grouping and read-across approach" section of this decision, your adaptation of the information requirement is not accepted, and testing of the registered substance is indicated.

In your comments to the draft decision, you proposed the following adaptation according to Column 2 of Annex VII, Section 9.1.2.: "*The study does not need to be conducted if there*

are mitigating factors indicating that aquatic toxicity is unlikely to occur for instance if the substance is highly insoluble in water or the substance is unlikely to cross biological membranes" Additionally, you stated that "*No aquatic toxicity was seen in an OECD 201 study with substance analogue C.I. Pigment Red 3. The draft evaluation by ECHA resulted in rejection of this study to fill the endpoint for C.I. Pigment Red 3. This conclusion is questioned by the registrant, who concludes that this study is valid both from a scientific and regulatory point of view. The evaluation is included as Appendix 1".*

You further clarified your choice of the preparation of the test solution for the alga study on the source substance PR3. You also indicated that analytical monitoring took place during the study and that the test substance concentrations were analytically confirmed. ECHA acknowledges your comments and notes that the study on the source substance, as such, can be considered acceptable.

However, as also explained above, your read-across adaptation for the ecotoxicological information requirements, including the present endpoint, is not accepted. Consequently it is also not possible to waive the present standard information requirement for the registered substance by referring to absence of effects on the (rejected) source substance.

Furthermore, ECHA notes that the registered substance has a reported water solubility of 6.3 µg/L. ECHA does hence not consider that the substance is "highly insoluble in water".

In the initial draft decision ECHA considered that it was necessary to extend the test duration to five days to obtain results relevant for classification purposes (Annex I of CLP Regulation, Section 4.1.2.6, notes 2 and 3 which are explanatory and applicable for poorly soluble substance). In your comments to the draft decision you reasoned that extending the test is not a requirement in the CLP regulation and is also not recommended in the endpoint specific guidance. You also consider that extending the study may cause problems in fulfilling the validity criteria. ECHA agrees with your explanation and has removed the specific requirement of extending the study to five days.

In conclusion, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 3.0, February 2016) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Algae growth inhibition test, EU C.3./OECD TG 201).

2. Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.51., column 2) and 3. Long-term toxicity testing on fish (Annex VIII, Section 9.1.3., column 2)

"Short-term toxicity testing on invertebrates" is a standard information requirement as laid down in Annex VII, Section 9.1.1. of the REACH Regulation, whereas "Short-term toxicity testing on fish" is a standard information requirement as laid down in Annex VIII, Section 9.1.3. of the REACH Regulation. Furthermore, pursuant to Annex VII, Section 9.1.1, Column 2 the long-term aquatic toxicity testing on invertebrates (Annex IX, section 9.1.5.) and pursuant to Annex VIII, Section 9.1.3, Column 2, the long-term aquatic toxicity study

on fish shall be considered if the substance is poorly water soluble. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement. The choice of the appropriate test(s) will depend on the results of the chemical safety assessment.

ECHA considers that substances that are poorly soluble in water require longer time to be significantly taken up by the test organisms and so steady state conditions are likely not to be reached within the duration of a short-term toxicity test. For this reason, short-term tests may not give a true measure of toxicity for such substances and toxicity may actually not even occur at the water solubility limit of the substance if the test duration is too short. ECHA notes that the registered substance is poorly water soluble (WS<1mg/l), but not highly insoluble in water (water solubility of the registered substance reported to be 3.3 µg/L).

Therefore, long-term toxicity needs to be investigated already at the tonnage band currently applicable for the substance subject to the present decision.

ECHA observes that no information on long-term aquatic invertebrate and fish toxicity is reported in the registration dossier. ECHA acknowledges that there is short-term toxicity study with fish and with aquatic invertebrates on the read-across substance, PR3. In these studies no toxicity was observed at the water solubility limit of the analogue substance. In addition, ECHA acknowledges that there is a long-term aquatic invertebrate study available on the read-across substance, PR3. However, as addressed above in the "Grouping and read-across approach" section of this decision, your read-across adaptation for the ecotoxicological endpoints, including the current endpoint is rejected. Additionally, ECHA considers that short-term toxicity test with fish is not sufficient for the registered substance as the lack of toxicity at the short-term test cannot exclude long-term toxicity on aquatic invertebrate and fish due to poor water solubility of the registered substance.

Moreover, ECHA notes that the information on aquatic invertebrates and fish toxicity is needed for the proper Chemical Safety Assessment of the substance. As noted in the Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7b (ECHA, version 4.0, June 2017) standard information on aquatic toxicity (on aquatic invertebrates, fish and aquatic plants) is necessary to enable the environmental hazard assessment, i.e. for use in classification and labelling and derivation of the PNECwater (Predicted No Effect Concentration for water), and for determination of the toxicity (T) criterion in the PBT assessment.

Hence, in the absence of valid information on short-term toxicity to invertebrates and fish, it cannot be concluded if fish or invertebrates or aquatic plants are shown to be substantially more sensitive.

In conclusion, the information provided on the two endpoints for the registered substance in the technical dossier does not meet the information requirement. Consequently there are information gaps and it is necessary to provide information for these endpoints.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) the *Daphnia magna* reproduction test (test method: EU C.20/ OECD TG 211) is the preferred test.

Regarding the long-term toxicity testing on fish, ECHA considers that the FELS toxicity test according to OECD TG 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early

stages of growth and should therefore be used (see ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R7b, Figure R.7.8-4). The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance Chapter R7b, version 2.0, November 2014). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as appropriate and suitable.

ECHA notes that you did not comment the draft decision on these requests, Long-term toxicity testing on aquatic invertebrates and/or Fish, early-life stage (FELS) toxicity test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Long-term toxicity testing on aquatic invertebrates (Annex VII, 9.1.1., column 2.; test method: Daphnia *magna* reproduction test, EU C.20/ OECD TG 211) **and/or** Fish, early-life stage (FELS) toxicity test (Annex VIII, 9.1.3., column 2; test method: Fish, early-life stage toxicity test, OECD TG 210).

Note for consideration for aquatic testing

Due to the low solubility and particulate nature of your substance, you should consult the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity tests and for calculation and expression of the result of the tests. Alternatively you can also consult the OECD document ENV/JM/MONO (2014)40/1 as it could apply better to your substance with regard to its specific properties (particles, poorly water soluble and pigment).

ECHA notes that there are no reliable short-term studies available on aquatic invertebrates or on fish for the registered substance. Therefore the Integrated testing strategy (ITS) outlined in ECHA Guidance on information requirements and chemical safety assessment (version 3.0, February 2016), Chapter R7b (Section R.7.8.5, including Figure R.7.8-4), is not applicable in this case and the long-term studies on both invertebrates and fish are requested to be conducted. As the registered substance has a reported low water solubility, long-term study of fish is indicated. A long-term study on invertebrates is available.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation. Exceptionally, following your comments on the draft decision indicating a tonnage band downgrade, ECHA has however taken into account the updated tonnage band (submission number: [redacted] on 16 March 2017).
Based on the average production or import volumes for the three preceding calendar years, the tonnage band has been changed from 100-1000 tonnes per year (submission number: [redacted] to 10-100 tonnes per year (submission number: [redacted]).

ECHA notes that your own tonnage band is 1-10 tonnes per year but the tonnage band for several members of the joint submission is 10-100 tonnes per year.

The compliance check was initiated on 2 June 2016.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

Given the exceptional circumstances, ECHA has taken into account the dossier update when processing this decision, as well as your comments. This has resulted in the removal of the following decision requests: sub-chronic toxicity (90-day) study and pre-natal developmental toxicity study, and the amendment of the following decision requests in Appendix I: long-term toxicity testing on aquatic invertebrates, long-term toxicity testing in fish and growth inhibition study aquatic plants.
If a tonnage band increase occurs after ECHA has issued this decision, the requests which were removed may be requested in a future decision.

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

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for start of substance evaluation in 2019.

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

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

4. In relation to the information required by the present decision, the sample of the substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new test(s) is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.