ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 9 April 2018

Addressee: [redacted]

Decision number: CCH-D-2114394289-32-01/F
Substance name: barium bis[2-chloro-5-[(2-hydroxy-1-naphthyl)azo]toluene-4-sulphonate]
EC number: 225-935-3
CAS number: 5160-02-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 17/03/2016
Registered tonnage band: 100-1000

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. **Spectral data (Annex VI, Section 2.3.5) and High-pressure liquid chromatogram, gas chromatogram (Annex VI, Section 2.3.6.) of the registered substance;**

2. **Description of the analytical methods (Annex VI, Section 2.3.7.)**

3. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance;**

4. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: Alga, growth inhibition test, EU C.3./OECD TG 201 or Aquatic plant Lemna sp growth inhibition test OECD TG 221) with the registered substance ;**

5. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**

6. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) 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 to the REACH Regulation. 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 adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by ***16 October 2019***. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and 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, has to 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

INFORMATION ON THE IDENTITY OF THE SUBSTANCE

In accordance with Article 10(a)(ii) of the REACH Regulation, the technical dossier must contain information on the identity of the substance as specified in Annex VI, Section 2 to the REACH Regulation. In accordance with Annex VI, Section 2 the information provided has to be sufficient to enable the identification of the registered substance.

1. **Spectral data (Annex VI, Section 2.3.5.) and High-pressure liquid chromatogram, gas chromatogram (Annex VI, Section 2.3.6.)**

According to the Annex VI.2.3.5 and 2.3.6, the spectral and chromatographic data reported in the registration dossier are required to be generated on the substance registered by your legal entity.

In the reports attached to section 1.4 of your dossier, you have stated that the data reported has been generated on a sample synthetized in a laboratory and not a sample extracted from the manufacturing process: *"[...]* [redacted] *".*
You have not included data generated on the substance as manufactured/imported by your legal entity.

The lab synthesis parameters (e.g. temperature, time etc.) influence the composition of the lab sample and may differ from the manufactured substance in terms of main constituent and impurity concentrations. Therefore spectral and analytical data generated on a lab sample does not enable the identity and compositional information of the substance registered by your legal entity to be verified.

You are accordingly requested to submit spectral and chromatographic data generated on a representative sample of the substance as manufactured/imported by you. This information needs to be sufficient to enable information reported on identity and composition in section 1.1 and 1.2 of your dossier to be verified.

The spectral and chromatographic data will be attached to section 1.4.

ECHA notes that in your comments on the draft decision, you agreed to provide the requested information.

2. **Description of the analytical methods (Annex VI, Section 2.3.7.)**

According to Annex VI, section 2.3.7 of the REACH Regulation, a registration dossier shall report a description of the analytical methods or the appropriate bibliographic references for the identification of the substance and where appropriate for the identification of impurities and additives. The reporting shall be given in sufficient detail that the methods may be reproduced.

You have stated in the reports "[redacted]" and "[redacted]" attached to section 1.4 that the method used to quantify the main constituent concentration was by subtraction: *"[...] The purity was calculated by subtracting the concentrations of the impurities from 100%.*
Purity = 100 – [redacted]

Purity = 100 – [redacted]
Purity [redacted]

You have not included a description of methods used for the direct quantification of the main constituent.

A method that solely describes the quantification of impurities does not enable the determination of the main constituent concentration values. As your substance identity is based on the contribution the main constituent to the substance composition, the description of the methods used need to describe how this main constituent was quantified.

You are accordingly requested to include a description of the methods used to quantify the main constituent of the substance manufactured/imported by your legal entity. The description of the method(s) will be reported in such detail that the method may be reproduced and will include details of the experimental protocol(s), any calculations made and the results obtained.

The documentation will be attached in section 1.4 of your dossier.

ECHA notes that in your comments on the draft decision, you agreed to provide the requested information.

TOXICOLOGICAL INFORMATION

3. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. 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 the technical dossier you have provided two study records for a pre-natal developmental toxicity study:

1) Pre-natal developmental toxicity study, in rats, according to a guideline equivalent or similar to OECD TG 414, [redacted] 1972 D&C Red No 9 - Teratology in rats performed at dose levels of 0, 1.5, 5, and 15 mg/kg/bw.
2) Pre-natal developmental toxicity study, in rabbits, according to a guideline equivalent or similar to OECD TG 414, [redacted] 1972, D&C Red No 9 - teratology study in rabbits performed at dose levels of 1.5, 5, and 15 mg/kg/bw

However, neither of these studies provides the information required by Annex IX, Section 8.7.2., because both studies were performed using very low doses without any justification. ECHA notes that the OECD TG 414 states the following regarding the dosing of the animals: *"At least three dose levels and a concurrent control should be used. Healthy animals should be assigned in an unbiased manner to the control and treatment groups. The dose levels should be spaced to produce a gradation of toxic effects. Unless limited by the*

physical/chemical nature or biological properties of the test substance, the highest dose should be chosen with the aim to induce some developmental and/or maternal toxicity (clinical signs or a decrease in body weight) but not death or severe suffering".

ECHA notes that according to the study summary provided in your dossier, no maternally toxic effects or embryotoxic/teratogenic effects were observed in either study, and the NOAEL for both developmental toxicity and maternal toxicity was set at 15mg/kg/bw/day (the highest dose tested). No justification has been provided for the low doses, and no indication was given either that higher doses are not possible. Therefore, ECHA considers that the provided studies do not meet the criteria of the OECD TG 414, and are not adequate to cover the endpoint.

In your comments on the draft decision, you indicated that the available studies were performed using the most appropriate route of exposure as described above, and that in the absence of maternal toxicity, no compound related effect on any foetal parameter was observed in either study. As a result, you consider that it is not justified to perform any new studies due to animal welfare considerations.

However, your comments do not address the identified deficiency with both studies, namely the low doses used, and you have not provided any justification for the use of these doses in your comments.

Therefore, 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 the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 5.0, December 2016) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.

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: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a first species (rat or rabbit) by the oral route.

ECOTOXICOLOGICAL INFORMATION

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Your registration dossier contains for the endpoints on Algal growth inhibition, Acute aquatic toxicity tests to Daphnia and to Fish (sections 6.1.5, 6.1.1, 6.1.3) adaptation arguments in form of a grouping and read-across approach according to Annex XI, 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 4., 5. and 6.).

Grouping and read-across approach for ecotoxicological information

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. 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 (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances[2]. This hypothesis explains why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration. Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests. Similarly, biotic and abiotic degradation may alter the fate and bioavailability of compounds as well as be themselves hazardous, bioaccumulative and/or persistent. Thus, physicochemical and degradation properties influence the human health and environmental properties of a substance and should be considered in read-across assessments. However, the information on physicochemical and degradation properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis[3]- (1) (Bio)transformation to common compound(s)- the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s)- the read-across hypothesis is that the organism is exposed to different compounds which have similar (eco)toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common compounds).

Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

You consider to achieve compliance with the REACH information requirements for the registered substance barium bis[2-chloro-5-[(2-hydroxy-1-naphthyl)azo]toluene-4-sulphonate] using data of structurally similar substances or analogue approach of Naphthol

[2] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.
[3] Please see ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

Metal Lakes and BONA Metal Lakes for Ecological properties. The following analogues were used for the eco-toxicological endpoints : Pigment Red 53:1 (your registered substance in this dossier) and 53:3 (PR53:3, CAS 73263-40-8/EC 277-335-6) from the Naphtol Metall Lake pigment category, as well as from BONA Metal Lake Pigment category: Pigment Red 57:1 (PR 57:1, CAS: 5281-04-9/EC: 226-109-5), Pigment Red 57:Sr PR 57:Sr (CAS: 73612-29-0/EC 277-552-6) and Pigment Red 48:2 (PR 48:2 , CAS: 7023-61-2/EC: 230-303-5) (hereafter the 'source substances').

You have provided a read-across documentation in the CSR. You use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group: on the basis of the similarity in physico-chemical and ecotoxicological effects and fate in the environment which you provided as follows: "*Both naphthol Metal Lakes and BONA Metal Lakes are of low solubility in water and octanol. In either highly acidic (pH < 3; e.g. stomach) or highly basic environments (pH > 12), disintegration of the salt complex occurs which results in increased solubility. The compounds have a divalent metal ion of low toxicity such as Ca2+, Ba2+ and Sr2+, so that the hazard profile is determined by the organic anion. The pigments do not contain any functional groups that are susceptible to pH-dependent hydrolysis at environmentally relevant pH values (pH 4 to pH 9). They are not readily biodegradable and do not show any potential to bioaccumulate.* "

So your hypothesis is relying on similar low solubility and the absence of functional groups. As an integral part of this prediction, you propose that the sources or category members and registered substance have similar properties for the above-mentioned information requirements. ECHA considers that this information is your read-across hypothesis.

ECHA's evaluation and conclusion

Your proposed adaptation argument is that the similarity in chemical structure and in some of the physico-chemical/ ecotoxicological properties between the sources and registered substance is a sufficient basis for predicting the properties of the registered substance for other endpoints.

ECHA acknowledges that your justification document contains the hypothesis for the analogue or grouping approach and information on the source chemicals including CAS/EC numbers names and chemical structure, or on their purity profile and a data matrix.

However, ECHA notes that structural similarity is only a prerequisite for applying the grouping and read-across approach. So, similarity in chemical structure and similarity of some of the physico-chemical and therefore ecotoxicological properties does not necessarily lead to predictable or similar environmental properties in other endpoints. Therefore your justification based on structural similarity, similar physico-chemical, ecotoxicological properties has not established why the prediction is reliable for the environmental end-points for which the read across is claimed.

Additionally, ECHA has taken into account all of your arguments together.
ECHA firstly notes that you did not explain nor justify sufficiently the difference in solubility between the Naphtol metal Lakes and BONA lake pigments with the registered substance. Furthermore, you did not justify the discrepancies observed between the known water solubility of the different analogues and of your registered substance, or between the solubility in test media of the analogues and of your substance.

Furthermore, you did not provide reliable water solubility data for your registered substance and for the analogues, as further explained under the following environmental endpoints requests provided below.

Secondly, the defects of each individual argument are not mitigated by the other arguments you have provided, and so ECHA considers that the arguments when taken all together do not provide a sufficient and reliable basis for predicting the properties of the registered substance.

Therefore, ECHA considers that this grouping and read-across approach does not provide a reliable basis whereby the environmental effects of the registered substance may be predicted from data for reference substances within the group. Hence, this approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation. 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 under the endpoint concerned.

As described above, further elements are needed to establish a reliable prediction for ecotoxicological properties, based on recognition of the structural similarities and differences between the source and registered substances. This could be achieved (if it is possible) by a well-founded hypothesis of (bio)transformation to a common compounds, or that the registered and source substances have the same type of effects, together with sufficient supporting information to allow a prediction of environmental properties.

General comments and testing strategy on aquatic toxicity

After reception of the draft decision you provided comments for each of the requested environmental studies, where you said: *"ECHA pointed out that in case the substance is a nanomaterial, several nano-specific guidance documents shall be consulted to choose an adequate test design for the above-mentioned studies."* You provided further the following comment: *"Applying the all-embracing, very broad EU Commission Recommendation on the Definition of Nanomaterial of 18 October 2011 to powdered materials, most of them can be considered as nanomaterials. Even though EU-funded projects like NanoDefine which have been initiated to develop methods for the implementation of the European definition of nanomaterials, no standardized and certified methods are available yet to prove if a powdered material falls under the definition or more specifically to prove that this is not the case. Generally organic pigments like barium bis[2-chloro-5-[(2-hydroxy-1-naphthyl)azo]toluene-4-sulphonate], CAS No 5160-02-1 (EC No 225-935-3) are powdered materials which are almost insoluble in water and most solvents. Pigments in general have a broad particle size distribution, are strongly agglomerated or aggregated and are only poorly dispersible at least in aqueous media. The registered substance was synthesized for the first time already in 1902, has thus been marketed for more than 100 years mainly for printing applications and has not been "invented" just recently as an engineered nanomaterial or something similar. Based on this situation, any requirements just based on the assumption that the registered material could be a nanomaterial are seen as not proportionate and cannot be accepted, also in view of the fact that the revision of the EU nano definition is still pending and not yet in place."*

With regard to your comment, ECHA notes that whether the substance meets the EU recommendation for the definition of a nanomaterial or not, has no impact on ECHA's conclusion regarding these identified incompliances. ECHA has identified data gaps for these endpoints based on the information included in the dossier. Therefore, ECHA considers that your comments on the EC recommendation for the definition of a nanomaterial are

irrelevant to the conclusion as to whether or not the dossier is incompliant for these endpoints. Furthermore, ECHA has not made any requests "*based on the assumption that the registered material could be a nanomaterial*".

It is a fact that your substance consist of small particles poorly soluble in water. However, in the note below, ECHA eludes explicitly the question as to whether your substance is to be considered as a nanomaterial or not. It is a question to be addressed by the registrant under its exclusive responsibility and your dossier does not contain any information allowing ECHA to take position on this question. Accordingly, the above paragraph aims at specifying the best methods and guidance to be followed in case the substance to be tested is poorly water soluble and remain potentially in particles of very small sizes, whether such substance meets the definition of nanomaterial or not. Consequently, the instructions to follow Appendices for ECHA Guidance chapter R7a and R7b were provided to you. While the substance may or may not be a nanomaterial, it consists in any event of small particles poorly soluble in water. The instruction to follow the appropriate ECHA Guidance is therefore relevant for you to adapt your testing strategy, as needed. Indeed, ECHA notes that you have used the guidance in order to develop a specific testing strategy that takes into account your existing knowledge regarding the properties of the substance.

As such, ECHA acknowledges your proposal for the sequential testing using information gained of the results once the dispersion stability behaviour of the substance will have been measured (using the OECD TG *318: Dispersion Stability of Nanomaterials in Simulated Environmental Media*).
Depending on the result you proposed to assess aquatic toxicity (aquatic plants, aquatic invertebrates, but not fish) or sediment toxicity. However, you did not specify in which level of aggregation and/or agglomeration you consider to favour sediment toxicity testing over aquatic organisms toxicity tests.

ECHA considers that the test material may be considered to have high potential for agglomeration and/or aggregation when the test material, according to the OECD TG 318, can be assigned to have low dispersion stability (≤ 10%). If the results of this test demonstrate the low stability of the substance, then the testing strategy proposed by you will be justified only in relation to aquatic invertebrates toxicity test. However, for the reasons explained below, the proposed testing strategy will not be acceptable in any case with regard to the primary producers or toxicity to aquatic vertebrates.

In your comments on the draft decision, you justify the choice of OECD TG 225 as a relevant study as it uses endobenthic organisms as test organism. Endobenthic species, in contrast to epibenthic organisms, burrow in the sediment and ingest sediment particles below the sediment surface. According to you, this would ensure exposure of the test organisms to the test substance via all possible uptake routes (e.g. contact with, and ingestion of contaminated sediment particles, but also via pore-water and overlying water). Especially as the test material is expected to agglomerate and deposit, a test organism ingesting sediment particles would represent worst-case exposure conditions. You further point out that this would be in line with ECHA's recommendation for nanomaterials in Appendix R7-1 for nanomaterials applicable to Chapter R7b and scientifically reasonable, as aquatic exposure is negligible.

If, according to OECD TG 318, the test material has a low dispersion stability (≤ 10%), ECHA agrees that the proposed OECD TG 225 (Sediment-Water Lumbriculus Toxicity Test Using Spiked Sediment) could be used as a weight of evidence, to fulfil the standard information requirement set in Annex IX, 9.1.5 for long term toxicity testing on aquatic invertebrates, provided that relevant and reliable test is performed.

However, ECHA notes that currently there is no relevant information in the dossier on primary producers (algae) and aquatic vertebrates (fish). Therefore, ECHA considers that you should perform testing on both algae and fish, as described in sections 4 and 6 of this decision.

ECHA acknowledges that, regardless of the proposed testing strategy, you disagreed to conduct a long-term toxicity study to fish according to OECD TG 210 as it is, in your view, scientifically not justified. You argued that even if the difference in the species sensitivity cannot be established in absence of valid acute data, the registered substance is not bioaccumulative. ECHA notes that regardless of the bioaccumulative properties of the substance, information on toxicity to fish is needed to be valid and adequate for the purpose of classification and labelling and/or risk assessment.

Note for consideration on aquatic toxicity testing (sections 4 to 6)

If your substance is a nanomaterial and, in any case, taking into account its nature of small particles poorly water soluble, ECHA recommends you to consult the OECD document ENV/JM/MONO (2014)40/1 as it would apply better to your substance with regard to its specific properties rather than the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6. Besides the OECD Guidance Documents, ECHA would further recommend that you consult Appendix R7-1 for nanomaterials applicable to the ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R7b, (Version 4.0 - June 2017) and specifically in the 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.

4. 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.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing key study records for growth inhibition test on Algae (OECD TG 201) with the following analogue substances PR 48:2 (CAS: 7023-61-2/EC: 230-303-5, GLP, 2007), then with PR 57:1 (CAS: 5281-04-9/EC: 226-109-5, non GLP, 1992) and PR 57:Sr (CAS: 73612-29-0/EC 277-552-6, GLP, 2005).

However, as explained above in Appendix 1, under Grouping and read-across approach for ecotoxicological information section of this decision, your adaptation of the information requirement cannot be accepted.

Notwithstanding the above considerations on the read-across and grouping approach, ECHA further notes the following deficiencies with regards to the individual studies on the source substances:

For PR 48:2 (CAS: 7023-61-2/EC: 230-303-5)

- Insufficient reporting in the robust study summary with no raw data and no information on the validity criteria.
- The measured concentration is not maintained within [redacted]% of the nominal measured concentration and,
- Results are reported on nominal concentration and not on measured concentration, so there is no information on the monitoring and measurement of the tested material.

For PR 57:1 (CAS: 5281-04-9/EC: 226-109-5)

- A non-GLP study was provided,
- The WAF method was reported to be used used but without analytical monitoring concentrations used and the results reported are much higher than the water solubility reported for the substance (1250 µg/L).
- The purity of the test substance used was reported to be 87% but no information on impurity was reported.
- The results are reported only based on the biomass and no result is based on yield measurements
- Similar reporting deficiencies as stated above were observed: no information on the validity criteria, no raw data and insufficent reporting in the robust study summary

For PR 57:Sr (CAS: 73612-29-0/EC 277-552-6)

- The saturation solubility determined during the test (0.6-1 mg/L) is much lower than the reported water solublity (38000 µg/L) for the source substance.

Furthermore, none of the results obtained in these three studies was used to derive a $PNEC_{aquatic}$ value based on measured concentration of the registered substance.

In light of the deficiencies listed in the studies afore mentioned, ECHA cannot verify whether (i) the study design is adequate and reliable for the purpose of the prediction, or (ii) the results are adequate for the purpose of classification and labelling and/or risk assessment.

Consequently, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex XI, Section 1.5., because no valid information on short- or long-term toxicity to aquatic plant or Algae on the registered substance is available in the registration dossier.

Therefore, your adaptation of the information requirement cannot be accepted.

Hence 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.

In your comments you proposed an alternative testing stategy for aquatic toxicity endpoints. As explained above in this Appendix under "General comments and testing strategy on aquatic toxicity", ECHA considers that the proposed testing strategy is not

adequate as there is a need for information on growth inhibition study for aquatic plants (Algae). This information is needed for the purpose of classification and labelling and/or risk assessment.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) 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.

In your comments on the draft decision you also proposed that, due to the colour of the registered substance, the OECD TG 221 on *Lemna* sp. Growth Inhibition Test could be performed as an alternative test for Algae growth inhibition test. ECHA notes that the aquatic plant test, *Lemna sp.* Growth Inhibition Test (OECD TG 221), may be used as an alternative method when the color of the test material may lead to technical difficulties in performing test with algae.

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) or *Lemna* sp. Growth Inhibition Test (OECD TG 221).

5. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.
"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. 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.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation: "*In Annex IX of Regulation (EC) No 1907/2006, it is laid down that long-term toxicity tests shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on fish. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB. The hazard assessment of the present substance reveals neither a need to classify the substance as dangerous to the environment, nor is it a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment.*
Therefore, a long-term toxicity testing in Daphnia magna is not provided."

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.5., column 2 for the two reasons explained below:

1) You did not provide adequate and reliable coverage, addressed in the corresponding test method referred to in Article 13(3) for any of the acute aquatic toxicity tests on Daphnia, on the registered substance as on the category members.

Indeed, under IUCLID endpoint 6.1.1., you provided five studies on the Short-term test/ acute aquatic toxicity tests on Daphnia, with two key studies and three supporting studies. All studies were performed as follows:

- using OECD TG 202, on the registered substance (1993, GLP, Key study)
- using WAF approach in the second key study, with an analogue substance PR53:3 (CAS 73263-40-8/EC 277-335-6, GLP, 2002); and
- using WAF approach in the three supporting studies performed on analogues 48:2 (CAS: 7023-61-2/EC 230-303-5, GLP, 2007), PR 57:1 (CAS: 5281-04-9/ EC: 226-109-5, non GLP, 2202) and PR57:Sr (CAS: 73612-29-0/ EC: 277-552-6,GLP).

However, as explained above in Appendix 1, under Grouping and read-across approach for ecotoxicological information section of this decision, your adaptation of the information requirement cannot be accepted.

Notwithstanding the above considerations on the read-across and grouping approach, ECHA further notes the following deficiencies regarding specifically the quality of the individual acute toxicity studies on the registered and source substances:

For the registered substance PR53:1, key study, ECHA has identified the following deficiencies:

- The measured concentrations (2.39-5.14 mg/L) are above the reported water solubility (10-2986 µg/L).
- Test concentrations used are not mentioned (only initial concentration and concentrations at the end of the test are reported). It is thus not clear how many test concentrations were used.
- The test concentration was not maintained within [redacted]% of the initial concentration of the test substance. According to the Test Guideline, geometric mean of measured concentration should be used for reporting, but it seems that arithmetic means were used. Geometric mean would be 3.5 mg/L (arithmetic mean: 3.8 mg/L).

For the analogues studies (used as key or supporting) provided under this endpoint, ECHA has identified the following deficiencies:

- Pigment Red 53:3 (CAS: 73263-40-8/ EC: 277-335-6, Key study)
  - The test concentrations (12.5, 25, 50, 100 mg/L) are much higher than the reported water solubility of the substance (20 µg/L according to the read-across justification document).
  - WAF approach was applied but no analytical monitoring was performed or reported.
  - The results are reported in nominal concentrations, which are much higher than the water solubility.
  - Media containing chelating agent (M4 media) should be avoided for testing substance containing metals (i.e. Sr).
  - Validity criteria is not verified (the DOC at the end of the test, as well as the % immobilization in control are not reported).

- Pigment Red 48:2 (CAS: 7023-61-2/EC 230-303-5, supporting study)
  - Results are reported only in nominal concentration (100 mg/L) although the measured concentration was much lower (0.0086 mg/L) and nominal

concentration much higher than the reported substance water solubility (260 µg/L).
- Validity criteria are not verified (the DOC at the end of the test, as well as the % immobilization in control are not reported).
- At least five concentrations should be tested according to the Test Guideline, but only one concentration (100 mg/L) used as limit test was applied, without proper justification.

- Pigment Red 57:1 (CAS: 5281-04-9/ EC: 226-109-5, supporting study)
  - The test concentrations (12.5, 25, 50, 100 mg/L) are much higher than the reported substance water solubility (1250 µg/L)
  - WAF approach was applied but no analytical monitoring was performed.
  - The results are reported in nominal concentrations and are much higher than the water solubility reported.
  - Media containing chelating agent (M4 media) should be avoided for testing substance containing metals (i.e. Sr), and
  - The validity criteria are not verified (the DOC at the end of the test, as well as the % immobilization in control are not reported).

- Pigment Red 57:Sr (CAS: 73612-29-0/ EC: 277-552-6, supporting study)
  - Saturation concentration in test solution (0.1-1 mg/L) is much lower than that the reported water solubility (38000 µg/L) in the read-across justification document.
  - The validity criteria are not verified, for the same criteria, as mentioned in the supporting studies above.
  - Results are reported on nominal concentration and not on measured concentration, so there is no information on the monitoring and measurement of the tested material.

ECHA further considers that all the analogue substances, regardless if used as key study or supporting studies, do not fulfil the requirement of Annex XI, Section 1.5 of the REACH Regulation as cannot verify whether (i) the study design is adequate and reliable for the purpose of the prediction, or (ii) the results are adequate for the purpose of classification and labelling and/or risk assessment.

2) Your substance and the used Azo pigment lakes and BONA metal lakes category members are poorly water soluble.

In cases where substances are poorly water soluble, REACH Section 9.1.1 Annex VII column 2 clearly indicates that long term aquatic toxicity test shall be considered, consequently the integrated or tier-testing strategy from acute to long term toxicity tests does not apply to your substance or its analogues.

As a consequence of the deficiencies observed in the testing performed on the analogues and source substances and of their poor solubility, it is not acceptable nor reliable to perform only tests to assess the acute aquatic toxicity for the source substances or analogues of this category.

In addition, the study results provided for the aquatic invertebrates acute testing are not assessed as reliable and valid to be considered as an acceptable adaptation, as per Annex XI Section 1.5 and due to the poor reporting quality and the issues with the relevance of the testing for all studies reported.

Hence, your justification that Chemical Safety Assessment does not indicate a need for further investigation, as stated in your adaptation for not performing long term toxicity testing on aquatic invertebrates, is not acceptable as no exposure assessment was provided nor a valid $PNEC_{aquatic}$ value.

Therefore, your adaptation of the information requirement cannot be accepted.

In your comments on the draft decision, you proposed a testing strategy on aquatic toxicity depending on the outcome of the OECD TG 318 Dispersion stability test. The proposed testing strategy is described and discussed above in this Appendix. ECHA aknowledges that if, based on the results on the OECD TG 318, the registered substance can be considered as having a low dispersion stability (≤10%), the proposed testing strategy would be plausible regarding the toxicity to aquatic invertebrates. In this case you could, instead of performing a long-term toxicity test on Daphnia, consider applying a weight of evidence approach according to Annex XI by providing data from an OECD TG 225 on sediment invertebrates. While ECHA considers that an adaptation to this information requirement may be possible, provided that results on the OECD TG 318 demonstrate that the registered substance has a low dispersion stability (≤10%), the information contained in the dossier is currently not compliant with the information requirement. Accordingly, the present decision requests you to provide the study specifically required under this endpoint. You may decide to adapt the requested information according to the rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, it is your responsibility to provide a scientific justification, referring and conforming to the appropriate rules set in Annex XI, and adequate and reliable documentation.

As explained above, 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 4.0, June 2017) *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

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: *Daphnia magna* reproduction test (test method: EU C.20./OECD TG 211).

Note for consideration for aquatic testing

Once results of the test on long-term toxicity to aquatic invertebrates are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation.

6. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex IX, Section 9.1.6., column 2. You provided the following justification for the adaptation: "*In Annex IX of Regulation (EC) No 1907/2006, it is laid down that long-term toxicity tests shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on fish. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or is assessed to be a PBT or vPvB.*
The hazard assessment of the present substance reveals neither a need to classify the substance as dangerous to the environment, nor is it a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Therefore, and for reasons of animal welfare a long-term toxicity test in fish is not provided."

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.1.6., column 2, because of the following considerations:

1) You did not provide adequate and reliable coverage, addressed in the corresponding test method referred to in Article 13(3) for any of the study acute aquatic toxicity tests on Fish, on the registered substance as on the category members.

Indeed, under IUCLID endpoint 6.1.3., you provided four studies for the Short-term test/ acute aquatic toxicity tests on fish, with two key studies and two supporting studies.
All studies were performed as follows:

- as per OECD TG 203 on fish (1982, GLP), with the registered substance
- in the second key study, with an analogue substance PR53:3 (CAS 73263-40-8/EC 277-335-6, non TG, non GLP, 2001); and
- in the two supporting studies performed on analogues PR48:2 (CAS: 7023-61-2/EC 230-303-5, OECD TG 203, GLP, 2002) and PR57:Sr (CAS: 73612-29-0/ EC: 277-552-6, non OECD TG, non GLP).

You also provided two disregarded studies with the analogue substance PR 57:1 (CAS 5281-04-9/ EC: 226-109-5) which were not assessed further

However, as explained above in Appendix 1, under Grouping and read-across approach for ecotoxicological information section of this decision, your adaptation of the information requirement cannot be accepted.

Notwithstanding the above considerations on the read-across and grouping approach, ECHA further notes the following deficiencies with regards to the individual studies on the registered and source substances:

For the registered substance PR 53:1 key study (OECD 203, GLP, 1982):

- No data on the control was provided.
- Biomass loading rate was not provided and it cannot be derived because the weight of the fish is also not provided.

- Static system testing without analytical monitoring was applied. According to the validity criteria, there should be evidence that the test concentration of the test substance has been satisfactorily maintained throughout the test.
- The concentrations used are significantly higher than the water solubility of the substance (10-2986 µg/L).
- The dissolved oxygen dropped below 60% of the air saturation after 24 hr. However, the vessels were then subsequently aerated.

For the analogue studies used either as key or supporting studies:
- PR 53:3 (CAS 73263-40-8/EC 277-335-6, key study)
  - Non-OECD TG study was performed although conditions applied would be similar to OECD TG 203.
  - No information on the validity criteria were provided (no information on control, dissolved oxygen, and measured concentrations).
  - Static system with WAF approach was applied but no analytical monitoring was specified.
  - The results are reported in nominal concentration (100 mg/L) which is much higher than the water solubility (20 µg/L).
  - Only one test concentration tested whereas the test guideline requires that at least five concentrations are used, and no justification was provided.

- Pigment Red 48:2 (CAS: 7023-61-2/EC 230-303-5, supporting study, OECD TG 203, GLP)
  - WAF approach was applied and measured concentration is much lower than the initial nominal concentration, however the results are reported in nominal concentration (100 mg/L), rather than the measured concentration (0.01 mg/L).
  - Only one test concentration was tested whereas the test guideline requires that at least five concentrations are used, and no justification was provided.
  - No information on validity criteria was provided (no information on control, dissolved oxygen, nor on measured concentrations).

- Pigment Red 57:Sr (CAS: 73612-29-0/EC: 277-552-6, supporting study, non OECD TG, non GLP)
  - Non-OECD TG study was provided with poor reporting
  - The reliability of the study could not be assessed as you provided a reliability score 4.
  - No information about analytical monitoring was provided in the robust study summary.
  - The result given is much higher than the reported water solubility of the substance (38000µg/L).
  - No sufficient information was reported on test parameters and the validity criteria provided (no information on dissolved oxygen, vessels, fish size etc.).

ECHA, further considers that the three studies on analogue substances (key and supporting ones) do not fulfil the requirement of Annex XI, Section 1.5 of the REACH Regulation as ECHA cannot verify whether (i) the study design is adequate and reliable for the purpose of the prediction, or (ii) the results are adequate for the purpose of classification and labelling and/or risk assessment.

2) Besides these deficiencies, ECHA also notes that your substance and the used Azo pigment lakes and BONA metal lakes category members are poorly water soluble.

In such case where substances are poorly water soluble, REACH Section 9.1.3 Annex VIII column 2 clearly indicates that long term aquatic toxicity test shall be considered. Consequently the integrated or tier-testing strategy from acute to long term toxicity tests does not apply to your substance or its analogues.

As a consequence of the deficiencies observed and listed above, in the testing performed on the analogues and source substances and of their poor water solubility, it is not acceptable nor reliable to perform only tests to assess the acute aquatic toxicity for the source substances or analogues of this category.

In addition, the study results provided for the Fish acute testing are not assessed as reliable and valid to be considered as an acceptable adaptation, as per Annex XI Section 1.5 due to the poor reporting quality and the issues with the relevance of the testing for all studies reported.

Hence, your justification that Chemical Safety Assessment does not indicate a need for further investigation, as stated in your adaptation for not performing long term toxicity testing on aquatic invertebrates, is not acceptable as no exposure assessment was provided nor a valid $PNEC_{aquatic}$ value.

Therefore, your adaptation of the information requirement cannot be accepted and ECHA considers that there is a need to further investigations.

In your comments on the draft decision, you proposed a testing strategy on aquatic toxicity depending on the outcome of the OECD TG 318 Dispersion stability test. The proposed testing strategy is described and discussed above in this Appendix.

ECHA acknowledges that regardless of the proposed testing strategy, relying on the dispersion stability test, you disagreed to the need to conduct a long-term toxicity study to fish according to OECD TG 210, as it is scientifically not justified, in your view. You argued that even if the difference in the species sensitivity cannot be established in absence of valid acute data, the registered substance is not bioaccumulative. ECHA notes that regardless of the bioaccumulative properties of the substance, information on toxicity to fish is needed to be valid and adequate for the purpose of classification and labelling and/or risk assessment. Therefore, as there is no reliable information provided on the toxicity to fish and as the substance has a low water solubility the need to perform a long-term toxicity tests to Fish remains. In addition, results provided by the aquatic plants test and the invertebrate toxicity test will not suffice to cover the toxicity to aquatic vertebrates.

Therefore, according to ECHA *Guidance on information requirements and chemical safety assessment*, Chapter R.7b (version 4.0, June 2017), the fish early-life stage (FELS) toxicity test (test method OECD TG 210), the fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15/ OECD TG 212) and the fish juvenile growth test (test method EU C.14/ OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

However, the FELS toxicity test, performed according to OECD TG 210, is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15/ OECD TG 212), or the fish, juvenile growth test (test method EU C.14/ OECD TG 215), as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth (see ECHA Guidance on information requirements and chemical safety assessment (version 4.0, June 2017), Chapter R7b, Figure R.7.8-4). Moreover, the FELS

toxicity test is preferred for the examination of the potential toxic effects of substances, which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA Guidance Chapter R7b, version 4.0, June 2017).

For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as most appropriate and suitable.

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: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

Note for consideration for aquatic testing

ECHA notes that due to lack of effects and reliable short-term studies it is not possible to determine the sensitivity of species. Therefore, the Integrated testing strategy (ITS) outlined in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), 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.

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.

The compliance check was initiated on 21 March 2017.

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.

ECHA took into account your comments and amended the request(s).

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 the 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 requests in this decision, or to otherwise fulfil the information requirements 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 in relation to Annex VII-XI data requirements, 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 tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the substance as actually manufactured or imported by each registrant.

   Finally there must be adequate information on substance identity for the sample tested and the substance registered to enable the relevance of the tests to be assessed. For each study record reported, adequate information on the test material used to generate the data needs to be documented in the test material record linked to the EndPoint Study Record. The test material record will document as a minimum the constituent concentration values and any other parameter that is relevant (for instance the size, the shape and the surface chemistry of the particles). The registrants' rationale for the choice of each representative test material will be given in sufficient detail so that its relevance and representativeness for the registered substance can be independently verified. Technical instructions are available in the Manual "How to prepare registration and PPORD dossiers" on the ECHA website https://echa.europa.eu/documents/10162/22308542/manual_regis_and_ppord_en.pdf.