EUROPEAN CHEMICALS AGENCY

Helsinki, 18 February 2020

Addressees
Registrants of [redacted] listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
08/03/2013

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Diisopropyl 3,3'-[(2,5-dichloro-1,4-phenylene)bis[iminocarbonyl(2-hydroxy-3,1-naphthylene)azo]]bis[4-methylbenzoate]
EC number: 275-639-3
CAS number: 71566-54-6

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

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***25 August 2022***.

A. Requirements applicable to all the Registrants subject to Annex VII of REACH

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method EU B.13/14. / OECD TG 471) with the Substance;

B. Requirements applicable to all the Registrants subject to Annex VIII of REACH

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487)

2. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method OECD TG 476 or TG 490)

3. Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.; test method OECD 412), in rats, inhalation route, with the Substance. The study must include measurements of lung burden and bronchoalveolar lavage fluid (BALF) analysis as described in the current version (25 June 2018) of the OECD TG 412;

4. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method OECD 421/422) in rats, oral route with the Substance

Conditions to comply with the requests

You are bound by the requests for information corresponding to the REACH Annexes applicable to your own registered tonnage of the Substance at the time of evaluation. Therefore you have to comply with the requirements of Annexes VII and VIII of REACH.

The Appendix on general considerations addresses common arguments that are applicable throughout the present decision while the other Appendices state the reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information. The timeline has been set to allow for sequential testing where relevant.

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] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[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 on general considerations

(i) Assessment of the Grouping of substances and read-across approach, in light of the requirements of Annex XI, Section 1.5.

You seek to adapt the information requirements for the following standard information requirements by grouping substances in the category and applying a read-across approach in accordance with Annex XI, Section 1.5:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.) if a negative result in Annex VIII, Section 8.4.2. is obtained.
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

ECHA has considered the scientific and regulatory validity of your grouping and read-across approach 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 (addressed under 'Scope of the grouping'). 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 R.6 and related documents.

A. Scope of the grouping

i. Description of the grouping

In your registration dossier you refer to a category of 'disazocondensation red pigments'. You have provided a read-across/category justification documentation in sections of the CSR (toxicokinetic, discrete endopints).

For the purpose of this decision, the following abbreviations are used for the group members:

	Abbreviation/Name	CAS number
1)	**PB23**/Pigment Brown 23	35869-64-8
2)	**PB41**/Pigment Brown 41	68516-75-6
3)	**PR144**/Pigment Red 144	5280-78-4
4)	**PR166**/Pigment Red 166	3905-19-9
5)	**PR214**/Pigment Red 214	40618-31-3
6)	**PR220**/Pigment Red 220	68259-05-2
7)	**PR221**/Pigment Red 221	71566-54-6
8)	**PR242**/Pigment Red 242	52238-92-3
9)	**PR262**/Pigment Red 262	79665-24-0

As reasons for grouping the substances you argue that they are not bioavailable and thus of no toxicological relevance due to their low solubility in different media and large molecular size.

You define the the structural basis for the grouping as "disazocondensation red pigments". ECHA understands that this is the applicability domain of the grouping and will assess your predictions on this basis.

In your comments to the draft decision you clarify that your intention is not to define a category but to use "*read-across approach*" to adapt individual information requirements. ECHA acknowledges your clarifications. On that basis, ECHA understands that you submitted an analogue approach. The basis for predictions, which apply to an analogue approach as part of a read-across adaptation, is discussed further below under B. *Predictions for properties*; these additional explanations do not change the outcome of ECHA's assessment.

B. Predictions for properties

You have provided the following reasoning for the prediction of toxicological properties: The *"category hypothesis is fundamentally based on the low bioavailability. None of the pigments are sufficiently soluble either in water or in octanol for systemic uptake or metabolism."* [...] You argue this based on the molecular weight [redacted] and modelled rigidity of the structures, low solubility (<0.1 mg/L) and *"no increased solubility or degradation in stomach acid is possible."* You further consider a potential metabolism of the analogue substances, which would lead to metabolites of higher toxicity.

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. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

You intend to predict the properties for the analogue substances from information obtained from valid studies[2] with the following analogue substances:

I. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.) similar or according to OECD TG 471:
   a. PR144 (CAS 5280-78-4), 2006
   b. PR166 (CAS 3905-19-9), 2006

II. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.) similar or according to OECD TG 473
   a. PR242 (CAS 52238-92-3), 1992

III. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.) similar or according to OECD TG 476.
   a. PR166 (CAS 3905-19-9), 1989

IV. Repeated dose toxicity (Annex VIII-IX, Section 8.6)
   a. PR166 (CAS 3905-19-9) according to OECD TG 407, 2009
   b. PR220 (CAS 68259-05-2), according to OECD TG 422, 2012

V. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1) and Pre-natal developmental toxicity (Annex IX, Section 8.7.2)

[2] You have provided further *in vivo* genotoxicity studies, which ECHA considers invalid or inappropriate for the relevant endpoints, for reasons explained in the the endpoint section, below.

a. PR220 (CAS 68259-05-2), according to OECD TG 422, 2012

ECHA notes the following shortcomings with regards to predictions of toxicological properties.

1. *Missing supporting information*

Annex XI, Section 1.5 of the REACH Regulation states that "*adequate and reliable documentation of the applied method shall be provided*". Within this documentation "*it is important to provide supporting information to strengthen the rationale for the read-across*"[3]. 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).

"*Adequate and reliable documentation*" must include

i. supporting information on the absence of bioavailability and
ii. bridging studies to compare such properties of the analogue substances.

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

Supporting information on the absence of bioavailability

In your read-across hypothesis, you state that the analogue substances have a molecular weight between [redacted] as well as low solubility in water and organic solvents, which results in a very low bioavailability and thus no or low toxicity. Furthermore, you have submitted short-term toxicity studies on two of nine analogue substances, PR166 and PR220, which demonstrate no effect levels at the limit dose of 1000 mg/kg bw/d.

This data set reported in the technical dossier does not include relevant, reliable and adequate information for the target and the source substances to support your read-across hypothesis.

In your comments to the draft decision:

- you consider the "*existing information is sufficient.*"
- you refer to "*structurally similar pigments*" and state "*any uptake would have resulted in either detection of the colored substance in tissues (non-metabolized) or in severe amine-related toxicity (destruction of the chromophore by metabolism).*" You also point to pigment red 53:1 (EC 225-935-3) and pigment red 48:2 (EC 230-303-5) as examples of pigments that have coordination bonds with a cation that will disintegrate in the acidic environment of the stomach and known to cause systemic toxicity. You did not provide the related data (e.g. robust study summaries of the relevant studies) in your documentation.
- you refer to the presence or absence of systemic or reproductive toxicity in numerous available repeated dose toxicity and reproductive toxicity studies on structurally variable types of pigments outside the scope of the category which are available in the ECHA database. You did not explain the relevance of the indicated supporting information specifically to disazocondensation red pigments. For instance, you did not explain how mechanisms other than solubilisation through ionisation would -or would

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

not- contribute to systemic toxicity, and how this allows a prediction of properties of the analogue substances. You also did not include a justification for the selection of the structurally similar pigments to exclude potential bias.

- you indicate your intention to perform static and dynamic dissolution assays to support the claims of poor absorption and low bioavailability, and to acquire the necessary supporting information with regard to your claims on bioavailability. You also state that, in absence of available guidance or fixed criteria for the assessment of lack of bioavailability, *"any toxicokinetic study potentially performed may be potentially considered as inadequate because the limit of detection or the investigated tissues are viewed as insufficient."*

First, the existing information gives some indications about low bioavailability based on molecular size and solubility. However, in the absence of data demonstrating absence of bioavailability (e.g. toxicokinetic studies), it is not possible to conclude on bioavailability for any of the analogue substances. Furthermore, the fact that the analogue substances PB 23 and PR 166 have been tested positive in ames tests only in presence of metabolic activation suggest that enzymatic metabolism can be relevant for the analogue substances tested. Your theoretical considerations on the absence of bioavailability have not been substantiated by experimental data such as studies on toxicity after repeated exposure (e.g. OECD TG 407/421/422), and are thus rejected.

Second, it is not possible to conduct an evaluation of the referred supporting information in absence of sufficient documentation and in the absence of an explanation of their relevance for your read-acros adaptation.

Third, it is in your discretion to generate and provide the necessary supporting information in order to justify your read-across adaptation. If you do so, you are responsible for demonstrating the fulfilment of the requirements of Section 1.5 of Annex XI to REACH.

Bridging studies to compare such properties of the analogue substances

You did not provide appropriate bridging studies (such as a screening study OECD TG 421 or 422) to compare the properties of the analogue substances with regard to repeated dose and reproductive/developmental toxicity. As also explained in the next section (data density), your hypothesis of low bioavailability is not supported by results from repeated dose toxicity studies with representative analogue substances across the category.

In the absence of such information, you have not established that the target and the source substances are likely to have similar properties. The allegation on potential metabolism is unsubstantiated, without further explanation on its impact on the prediction of hazardous effects by potentially bioavailable parent substance.

Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

2. *Data density to derive a regular pattern*

Annex XI, Section 1.5. provides that *"substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances.*

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[4] and related documents[5, 6]. To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the analogue substances needs to be available.

You have provided the following valid studies:

1. For *in vitro* genotoxicity with bacteria (Annex VII, Section 8.4.1), two out of nine analogue substances (PR144 and PR166) have been tested according to OECD TG 471 with modified metabolic activation for azo-substances, such as the analogue substances, whereas all other bacterial tests are invalid because they are without this relevant modification.

2. For *in vitro* chromosomal aberrations in mammalian cells (Annex VIII, Section 8.4.2 and 8.4.3), one out of nine analogue substances (PR242) has been tested (OECD TG 473).

3. For *in vitro* gene mutations in mammalian cells, one out of nine analogue substances (PR166) has been tested (OECD TG 476).

4. For repeated dose toxicity (Annex VIII, Section 8.6.1 and Annex IX, Section 8.6.2), one category member (PR166) has been tested in an oral short-term (28-day) toxicity study (OECD TG 407, 2009) and one of the analogue substances (PR220) in a combined repeated dose toxicity and screening for reproductive/developmental toxicity (OECD TG 422, 2012). No repeated dose toxicity studies by the inhalation route have been provided. No sub-chronic toxicity studies (90-day) have been provided.

5. For screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1) and pre-natal developmental toxicity (Annex IX, Section 8.7.2), one of nine analogue substances (PR220) has been tested in a combined repeated dose toxicity and screening for reproductive/developmental toxicity (OECD TG 422, 2012). No pre-natal developmental toxicity studies have been provided.

Based on these studies you claim that there are similar properties between the analogue substances.

The analogue substances have multiple structural differences, but no information has been provided to establish whether and to what extent any of the analogue substances are representative of the whole category or a subset of it. In addition, the available studies cover only a small subset of these structural differences for each endpoint. Information for two (1.+4., above) or one (2., 3.+5., above) analogue substances is not sufficient to conclude which substances are representative of the analogue substances for *in vitro* genotoxicity, repeated dose toxicity and toxicity to reproduction and pre-natal development in the absence of (lower tier) toxicity studies with all analogue substances for the relevant endpoint. Considering the distinct structural differences between the analogue substances, there are too few data points (i.e. low data density) in the current data matrix for demonstrating consistency and predicting properties for the listed toxicological endpoints as proposed by

[4] 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
[5] 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)
[6] 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

you. Therefore, the information provided is not sufficient to conclude that toxicological properties are likely to follow a regular pattern.

C. Conclusions on the grouping of substances and read-across approach

As explained above, you have not established that relevant properties of the registered substance can be predicted from data on the analogue substance. 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.

Appendix A: Reasons for the requests to comply with Annex VII of REACH

In accordance with Articles 10(a) and 12(1) of REACH, a technical dossier registered at 1 to 10 tonnes or more per year must contain, as a minimum, the information specified in Annex VII to REACH.

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

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

You have provided a key study in your dossier:

i. Key study: *In vitro* gene mutation study in bacteria (1994) according to OECD TG 471.

You have also provided an adaptation based on a grouping of substances and read-across approach.

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

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471 (1997). The key parameter(s) of this test guideline include:

a) If Substance is an azo-dye or a diazo-compound, the test in presence of metabolic activation must be performed following the Prival modification.

The reported data for the studies you have provided did not include the Prival modification, in spite of the fact that the tested substance is a diazo-compound.

Therefore, the information provided does not cover a key parameter required by OECD TG 471.

In addition, you have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the Appendix on general considerations your adaptation is rejected.

Therefore the information requirement is not fulfilled.

Appendix B: Reasons for the requests to comply with Annex VIII of REACH

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 10 to 100 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII and VIII to the REACH Regulation.

1. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)

An *In vitro* cytogenicity study in mammalian cells or an *In vitro* micronucleus study is a standard information requirement in Annex VIII to REACH.

You have provided the following studies in your dossier/as part of the category justification:

i. *in vivo* Mammalian Erythrocyte Micronucleus Test with the substances
   a. PB23 ([redacted] 2010)
   b. PR166 ([redacted] 1981)
   c. PR221 ([redacted] 1995)

You have also provided an adaptation based on a grouping of substances and read-across approach.

We have assessed this information and identified the following issue:

To adapt this information requirement, an *in vivo* cytogenicity study must be adequate for that particular information requirement. This is not the case, for example, if there are relevant uncertainties on whether the substance may reach, or may have reached, the bone marrow for various reasons (Guidance R.7a, section R.7.7.6.3).

The reported data for the *in vivo* study you submitted did not include a verification of systemic or target tissue (bone marrow) exposure to the Substance.

No information to conclude on bioavailability are provided either (see Appendix on general considerations).

You did not demonstrate that the testing material reached the bone marrow and the information available is insufficient to conclude that it did.

Furthermore, study b. (PR166, [redacted] 1981) is invalid because it is a non-GLP, non-OECD study not addressing the key parameters of the relevant OECD TG 474, such as reporting the proportion of immature erythrocytes among total erythrocytes, and the mean number of micronucleated immature erythrocytes for each group of animals.

Therefore, considering the uncertainties on the test material reaching the bone marrow or not, an *in vitro* study is still justified to assess the effects of the Substance, the provided *in vivo* test is not adequate, and the column 2 adaptation is rejected.

In addition, you have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the Appendix on general considerations your adaptation is rejected. Therefore, the information requirement is not fulfilled.

To fulfil the information requirement for the Substance, both *In vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) and *in vitro*

micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, in vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

An *in vitro* gene mutation study in mammalian cells is a standard information requirement in Annex VIII to REACH in case of a negative result in the *in vitro* gene mutation in bacteria and the *in vitro* cytogenicity test.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the Appendix on general considerations your adaptation is rejected. The valid *in vitro* gene mutation study in mammalian cells with PR166 and the *in vivo* genotoxicity studies with PB23 and PR166, which are considered inappropriate for this endpoint because they are only indicators of DNA lesions or non-guideline studies, cannot be used to adapt the information requirement for *in vitro* gene mutation in mammalian cells. Therefore, the information requirement is not fulfilled.

Your dossier contains data for an *in vitro* gene mutation study in bacteria, and an adaptation for an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study, which are rejected for the reasons provided in sections 1. of Appendices A. and B and the Appendix on general considerations.

The result of the requests for information in sections 1. of Appendices A. and B. will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

To fulfil the information requirement for the Substance, both the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) and the thymidine kinase gene (OECD TG 490) are considered suitable.

3. Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.);

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII to REACH.

You have adapted the standard information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained under Appendix General considerations, your adaptation according to Annex XI, Section 1.5 is rejected, and the information requirement is not fulfilled.

Test design

First, following the criteria provided in Annex VIII, Section 8.6.1., Column 2, the inhalation route is the most appropriate route of administration to investigate repeated dose toxicity[7]. The short-term repeated dose toxicity study (28 days) must be performed according to the OECD TG 412, in rats and with administration of the Substance by inhalation. The information

[7] ECHA Guidance R.7a, Section R.7.5.4.3.

provided in the technical dossier and the chemical safety report on properties of the Substance and its uses (industrial, professional and consumer uses, including PROCs 7 and 11 industrial and non-industrial spraying) indicate that human exposure to the Substance by the inhalation route is likely. More specifically, the Substance is reported to occur as a dust with a significant proportion of particles of inhalable size. Furthermore, the Substance is respirable [redacted] of low water solubility and consequently there is a potential for accumulation of the substance in the lungs.

Second, there is evidence that the lower respiratory tract is a site of deposition and retention of the Substance because of its poor solubility in water and respirable particle size.

In your comments on the initial draft decision you state that "*The request for information on sub-acute toxicity via the inhalation route and based on current discussions on respirable, inert dusts and their regulation, the need for a clear definition and assessment criteria became overt*" and "*We consider organic pigments to belong to the group of poorly soluble, low toxicity materials (PSLT)*".

You are reminded that several paragraphs of the OECD TG 412 address specific issues related to testing of poorly soluble solid aerosols. Details on measurement and evaluation of lung burden are also provided in the OECD GD 39.

Further, you have not provided any supporting evidence for your argument on any 'current discussions', PSLT nor a reason for how such grouping would affect this information requirement.

You are requested to perform measurements of lung burden and bronchoalveolar lavage fluid (BALF) which are specifically designed to address such situation. The latest guidance on how to perform such measurements are described in the revised version of the OECD 412 test guideline adopted on 25 June 2018. The measurements shall therefore be conducted as described in the guideline version adopted on 25 June 2018.

4. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.);

A Screening for reproductive/developmental toxicity study (OECD TG 421 or 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted the standard information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5

As explained under Appendix General considerations, your adaptation according to Annex XI, Section 1.5 is rejected, and the information requirement is not fulfilled.

A study according to the test method OECD TG 421/422 should be performed in rats with oral[8] administration of the Substance.

[8] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix C Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of the REACH Regulation.

The compliance check was initiated on 17 January 2019.

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

ECHA took into account your comments and did not amend the request(s) or the deadline.

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 Observations and technical guidance

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

2. 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 the Member States.

3. Test guidelines, GLP requirements and reporting

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

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

   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: 'How to report robust study summaries'[9].

4. Test material

   Selection of the test material(s)

   The registrants of the Substance are responsible for agreeing on the composition of the test material to be selected for carrying out the tests required by the present decision. The test material selected must be relevant for all the registrants of the Substance, i.e. it takes into account the variation in compositions reported by all members of the joint submission. The composition of the test material(s) must fall within the boundary composition(s) of the Substance.

   While selecting the test material you must take into account 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.

   Technical reporting of the test material

   The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

   Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"[10].

5. List of references of the ECHA Guidance and other guidance/ reference documents[11]

[9] https://echa.europa.eu/practical-guides
[10] https://echa.europa.eu/manuals
[11] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment

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 in this decision.

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 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)[12]

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.

OECD Guidance documents[13]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.
Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD43.

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

Appendix E List of the registrant to which the decision is addressed and the corresponding information requirements applicable

Registrant Name	Registration number	(Highest) Data requirements to be fufilled
[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.