~~Confidential~~

Helsinki, 25 April 2022

Addressees
Registrant(s) of Reaktiv-Orange DYPR 1410 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
31/03/2016

Registered substance subject to this decision ("the Substance")
Substance name: Alkali salt of substituted amino alkyl sulfonyl aryl diazo naphthalene sulfonate
EC number: 432-080-1
CAS number: NS

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***2 May 2023***.

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

A. Information required from 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)

B. Information required from all the Registrants subject to Annex VIII of REACH

1. If negative results are obtained in test performed for the information requirement of Annex VII, Section 8.4.1. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

2. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats

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

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VII to VIII of REACH", respectively.

Information required depends on your tonnage band

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

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100

tpa.

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

Authorised[1] under the authority of Mike Rasenberg, 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 Reasons common to several requests

Assessment of the Grouping of substances and read-across approach under Annex XI, Section 1.5.

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

- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1)

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

Grouping of substances and read-across approach

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

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6. and related documents[2,3].

A. Predictions for toxicological properties

You have provided a read-across justification document in IUCLID Section 13.

You read-across between the structurally similar substance Reactive Blau FC 05717**,** EC No. 401-560-2 as source substances and the Substance as target substance.

As your reasoning for the prediction of toxicological properties you claim that *"Given that the metabolism of dyestuffs is understood, and due to the similarities in the structures, the physico-chemical and (eco)toxicological properties of the molecules, and the common "skeleton" and degradation products of the structures, it is considered a viable conclusion to state that the expected (eco)toxicological effects for Reactive Orange DYPR 1410 and the read-across substances are likely to be similar*." You also refer to similarities in metabolism by "azo reductase enzymes."

The toxicokinetic studies, which you have provided, concern Reactive Black which is not a source substance for the read-across of the toxicological endpoints addressed in this decision. 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.

[2] 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)

[3] 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

ECHA notes the following shortcoming(s) with regards to prediction(s) of toxicological properties.

- *1. Missing supporting information*

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[4]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s). Supporting information must include bridging studies to compare properties of the Substance and source substances.

Missing information on the formation of common compounds

As indicated above, your read-across hypothesis is based on the transformation of the Substance and of the source substance(s) to a common compound(s). In this context, information characterising the rate and extent of the transformation of the Substance and of the source substances is necessary to confirm the formation of the proposed common transformation products and to assess the impact of the exposure to the parent compounds as well as the impact of non-common dissociation products.

In your dossier, you make reference to "*common skeleton and degradation products of the structures"* and to azo reductase enzymes. However, you have not provided experimental data to demonstrate similarity of the transformation products and rates of the cleavage of these substances with your dossier.

The read-across justification document in your dossier gives only generic information on hydrolysis and cleavage of azo substances. No experimental data on the transformation and cleavage of the Substance or that of the source substances has been provided.

In the comments to the initial draft decision, you provide an updated justification document with additional experimental information on the toxicokinetic behaviour of a representative source substance, which is a close analogue with high structural similarity. In addition, you provide a comparison of physicochemical and (bio)degradation properties of the Substance and the source substances, which were obtained by modelling (*in silico*).

The results of the toxicokinetic studies are in agreement with the modelled information which is available for the source substances and the Substance. Therefore, the information provided as part of your comments addresses the above issue regarding the supporting information. However, as the information is currently not available in your registration dossier, the data gap remains. You should submit a robust study summary for the toxicokinetic study with the source study and the updated justification document in an updated registration dossier by the deadline set in the decision.

2. *Adequacy and reliability of source study*

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across should:

- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

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

Related deficiencies are addressed under the individual information requirement specific reasons in Appendices A and B below.

B. Conclusions on the read-across approach

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

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

1. *In vitro* gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

You have provided a key study in your dossier:

i. A study according to OECD Guideline 471, Bacterial Reverse Mutation Test, with the Substance, EC No. 432-080-1, GLP, performed in 1999, without Prival modification.

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[5] (1997). One of the key parameters of this test guideline includes:

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 study you have provided did not include:

a) the Prival modification, in spite of the fact that the tested substance is an azo-dye/a diazo-compound.

The information provided does not cover one of the key parameters required by OECD TG 471.

Therefore, the information requirement is not fulfilled.

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

Study design

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

[5] ECHA Guidance R.7a, Table R.7.7–2, p.557

Appendix B: Reasons to request information required under Annex VIII of REACH

1. *In vitro* gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

Your dossier contains (i) a negative result for an *in vivo* micronucleus test used to adapt the information requirement for the *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study, and (ii) inadequate data for the other study (*in vitro* gene mutation study in bacteria).

The *in vitro* gene mutation study in bacteria provided in the dossier is rejected for the reasons provided in section A.1.

The result of the request for information in section A.1 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.

Your dossier contains an *in vitro* UDS test performed on the analogue substance Reactive Blau FC 05717**,** EC No. 401-560-2 according to OECD TG 482.

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

Your read-across adaptation in your dossier is not considered acceptable, as explained above in the Appendix on Reasons common to several requests.

In addition, the following deficiencies have been identified in that study.

As explained under the Appendix on reasons common to several requests, read-across results must have an adequate and reliable coverage of the key parameters of the corresponding test methods, in this case OECD TG 476 or 490 (ECHA Guidance R.7, Table R.7.7-2).

Your dossier contains an *in vitro* UDS test performed on the analogue substance Reactive Blau FC 05717**,** EC No. 401-560-2 according to OECD TG 482.

Please note that the OECD TG 482 was made obsolete by the OECD in 2014 and is not considered a standard test anymore. This test provides an indication of induced damage to DNA followed by DNA repair (measured as unscheduled DNA synthesis in liver cells), but does not provide direct evidence of mutation as the OECD TG 476 or 490. A negative result in a UDS assay alone is not a proof that a substance does not induce gene mutations in the conditions of the test. The information provided is not an *in vitro gene mutation study in mammalian cells*. The information provided does not provide adequate and reliable coverage of the key parameters required by the OECD TG 476 or 490.

Therefore, the information requirement is not fulfilled.

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

Study design

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

2. Screening study for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 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.

ECHA understands that you have provided a read-across adaptation using a key study in your dossier:

- A study according to OECD Guideline 415, One-Generation Reproduction Toxicity Study, in rats, with an analogue substance Reactive Blau FC 05717, EC No. 401-560-2, performed in 2002.

Your read-across adaptation in your dossier is not considered acceptable, as explained above in the *Appendix on Reasons common to several requests*.

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

Information on study design

A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats with oral[6] administration of the Substance.

Your comments on the initial draft decision are addressed in the *Appendix on Reasons common to several requests.* In conclusion, the information provided as part of your comments addresses the incompliance relating to this endpoint. However, as the information is currently not available in your registration dossier, the data gap remains. You should submit a robust study summary for the toxicokinetic study with the source substance and the updated justification document in an updated registration dossier by the deadline set in the decision.

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

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

A. Test methods, GLP requirements and reporting

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

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

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[7].

B. Test material

1. Selection of the Test material(s)

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

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

This information is needed to assess whether the Test Material is relevant for the Substance.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[8].

[7] https://echa.europa.eu/practical-guides
[8] https://echa.europa.eu/manuals

Appendix D: Procedure

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

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

The compliance check was initiated on 21 April 2021.

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

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

In your comments on the initial draft decision, you requested an extension of the deadline to provide information from 12 to 24 months from the date of adoption of the decision. You justified this by the time indicated by the testing laboratory for performance of an OECD TG 421 study. In addition you require additional time due to challenges related to sample preparation. However, ECHA notes that performance of an OECD 421 study may no longer be needed, provided that you submit the missing supporting information in a dossier update (for the details see the *Appendix on Reasons common to several requests*).

On this basis, ECHA does not consider it adequate to change 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 E: List of references - ECHA Guidance[9] and other supporting documents

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

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

Read-across assessment framework (RAAF, March 2017)[10]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[11]

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

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

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

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

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

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

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

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

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

OECD Guidance documents[12]

[9] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[10] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[11] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[12] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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

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

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

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

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

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

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

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.