~~Confidential~~

Helsinki, 16 January 2024

Addressee(s)
Registrant(s) of Reactive Red F01-0481 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
21/12/2018

Registered substance subject to this decision ("the Substance")
Substance name: Pentasodium 4-hydroxy-3-(2-methoxy-5-(2-sulfooxyethanesulfonyl)phenylazo)-7-(sulfomethylamino)-8-(2-sulfo-4-(2-sulfooxyethanesulfonyl)phenylazo)naphthalene-2-sulfonate
EC number/List number: 464-700-1

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 ***23 April 2026***.

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

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

1. Skin sensitisation (Annex VII, Section 8.3.)

    a) *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.); and

    b) only if the *in vitro/in chemico* test methods specified under point a) above are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429)

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

2. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111) – test under slightly alkaline conditions (i.e., covering only pH values between 7 and 8.5 and at least pH values of 8 and 8.5).

The reasons for the request(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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 requirements for testing and reporting new tests under REACH, see Appendix 4.

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

Appendix 1: Reasons for the request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 for the request(s)

Contents

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Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

1 Skin sensitisation is an information requirement under Annex VII, Section 8.3. Under Section 8.3., Column 1, the registrants must submit information allowing (1) a conclusion whether the substance is a skin sensitiser and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

1.1. Information provided

2 You have adapted this information requirement by using Annex VII, Section 8.3., Column 2. To support the adaptation, you have provided the following information:

(i) Justification: "*an in vitro skin sensitisation study does not need to be conducted because adequate data from an in vivo skin sensitisation study are available*";

(ii) Guinea pig maximisation test (2005) with the Substance.

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

1.2.1.1. The provided study does not meet the specifications of the test guideline(s)

3 To fulfil the information requirement, and to enable concluding whether the Substance causes skin sensitisation, a study must comply with the EU Method B.6/OECD TG 406 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the challenge dose is the highest non-irritation concentration.

4 In study (ii):

a) the challenge concentration selection (highest concentration tested) was not demonstrated to be the highest non-irritating concentration because the dose-range finder experiment results specifying the lowest irritating concentration were not included in the dossier, and conflicting indications of irritation at the highest tested concentration 25% have been reported.

5 The information provided in the dossier does not cover the specification(s) required by the EU Method B.6/OECD TG 406.

6 In your comments to the draft decision you clarify the interpretation of the pre-test results. You explained that "it is possible and reasonable that the same test concentration could be the highest concentration used causing mild-to-moderate skin irritation and well-tolerated systemically during the induction phase on pre-damaged skin and the highest non-irritant concentration during challenge in intact skin." You also clarified that 25% preparation was the highest concentration that could be formulated.

7 On the basis of the information included in your current registration dossier, it cannot be concluded whether the Substance causes skin sensitisation. However, the information regarding the pre-test provided in your comments to the draft decision justifies the dose-selection in the main study, and needs to be included in the dossier by the deadline of this decision.

1.2.2. No assessment of potency

8 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

9 As the currently available data in your registration dossier does not allow to conclude whether the Substance causes skin sensitisation (see section 1.2.1. above), this condition cannot be assessed. This is, however, remedied by the information in your comments.

10 Therefore, the information requirement is not fulfilled in your registration dossier. The information regarding the pre-test provided in your comments to the draft decision needs to be included in the dossier by the deadline of this decision.

1.3. Specification of the study design

11 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

12 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or newly generated data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

Reasons related to the information under Annex VIII of REACH

2. Hydrolysis as a function of pH

13 Hydrolysis as a function of pH is an information requirement under Annex VIII to REACH (Section 9.2.2.1.).

2.1. Information provided

14 You have provided:

(i) a hydrolysis study (2005) according to EU Method C.7 and OECD TG 111 with the Substance.

2.2. Assessment of the information provided

2.2.1. The provided study does not meet the specifications of the test guideline

15 To fulfil the information requirement, a study must comply with OECD TG 111 (Article 13(3) of REACH). This TG is designed as a tiered approach and each tier is triggered by the results of the previous tier. Therefore, the following specifications must be met:

16 Hydrolysis testing (Tier 2)

a) the test must be performed at the pH value(s) at which the test material was found unstable in the preliminary test (i.e. > 10 % hydrolysis in Tier 1 test);

17 Testing at pH values other than 4, 7, 9

b) additional tests at pH values other than 4, 7 and 9 may be required for a hydrolytically unstable test substance.

18 In the provided study (i):

19 Hydrolysis testing (Tier 2)

a) hydrolysing testing (Tier 2) was not performed at pH 7 and 9 while the test material was found unstable in the preliminary test (Tier 1) at pH 7 and 9 (the decomposition of the Substance after 2.4 h at 50°C was > 50% at pH 7 and >95% at pH 9);

20 Testing at pH values other than 4, 7, 9

b) The study provided indicates substantial hydrolytical degradation of the Substance in alkaline pH. The decomposition of the Substance in Tier 1 test was 53% at pH 7 and 95% at pH 9 after 2.4 hour. This indicates significant depletion of the Substance between pH 7 and 9 and implies hydrolytical instability of the Substance in alkaline pH. Based on this preliminary test you have estimated the hydrolysis half-life value to be < 1 day at 25°C for both pH 7 and 9. However, you have not considered testing hydrolysis at pH values other than 4, 7 and 9.

21 In your comments to the draft decision you explain the mechanism of the dyeing reaction according to the literature and knowledge of "common industrial dyeing process". You mention that the Substance is fully hydrolysed in this process and as such is released in the environment. Based on that, you mention that carrying out further testing of the hydrolysis

behaviour of the Substance would not lead to the new knowledge of the environmental hazard.

22 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results, specifically:

- The hydrolysis was not investigated at pH 7 and 9, as Tier 2 test was not performed for pH 7 and 9;
- You have not investigated the hydrolysis behaviour of the Substance between pH 7 and 9. An abrupt change of the hydrolytical behaviour is expected for the Substance between pH 7 and 9. This pH range is relevant both for the environmental assessment and for the interpretation of ecotoxicological tests. The pH of wastewater or sewage water is typically between 6–8 but can reach 8.5, implying that the Substance may be hydrolysed in the wastewater or sewage water before it reaches the environment[2]. Test guidelines for aquatic toxicity tests tolerate pH of up to 8.5 and even beyond for some of them. Therefore, investigating further the hydrolysis behaviour of the Substance between pH 7 and 8.5 is necessary for the environmental risk assessment of the Substance and for interpreting the results of the ecotoxicity tests.
- Regarding your claim in the comments on the draft decision that testing at such pH would not result in new knowledge, the OECD TG does not provide for any exception. Further, you refer to information on use, which is irrelevant for the investigation of intrinsic properties, as is the case here, except in the case of exposure-based adaptation under Annex XI, Section 3, which you have not submitted. In any case, your claim is based on generic considerations (literature and knowledge), rather than being substantiated on the basis of your registration dossier, in particular on the basis of a rigorous exposure assessment.
- The objective of this test is to investigate an intrinsic property, hydrolysis, in pH that may be relevant for the environment, including in waste treatment. It is in light of this objective that this decision discusses pH in sewage water, i.e. in light of the objective of the OECD TG for hydrolysis. However, your claim in the comments on the draft decision that testing at such pH would not result in new knowledge is a use consideration specific to your Substance which must be assessed on the basis of and rejected on the basis of the considerations set above.

23 On this basis, the specifications of OECD TG 111 are not met.

24 Therefore, the information requirement is not fulfilled.

2.3. Study design

25 As explained above, the hydrolysis test must be performed under slightly alkaline conditions at pH values between 7 and 8.5 and at least at pH values of 8 and 8.5.

[2] The pH of domestic wastewater is typically between 6–8 but is largely related to the alkalinity of the carriage water. In areas having soft water (alkalinity between 50 and 100 mg/L as $CaCO_3$), the pH of domestic wastewater is around 6.0 to 6.5. In areas having moderately hard water (alkalinity between 100 and 300 mg/L as $CaCO_3$) it is between 7.0 and 8.0. In areas having hard water (alkalinity higher than 300 mg/L as $CaCO_3$) it is between 7.5 and 9.0. Some industrial wastewaters can be quite acidic or alkaline. The optimum pH range for aerobic biodegradation lies between 6.5 and 8.5. Any wastewater beyond that range would need to be neutralised by the operator of the wastewater treatment system.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2012).
Guidance on intermediates; ECHA (2010).
All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017).
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs; ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: 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 08 August 2022.

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).

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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 3: Addressee(s) of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- 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;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

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

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

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. 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[3].

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2. Test material

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

(1) Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

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

(2) Information on the Test Material needed in the updated dossier

You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.

The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

[3] https://echa.europa.eu/practical-guides

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (https://echa.europa.eu/manuals).