~~Confidential~~

Helsinki, 12 October 2022

Addressees
Registrants of JS_402-130-7 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
26/04/2022

Registered substance subject to this decision ("the Substance")
Substance name: 4,4'-Methylene-bis-(3-chloro-2,6-diethylaniline)
EC number: 402-130-7

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

DECISION ON TESTING PROPOSAL(S)

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***17 January 2025***.

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

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

1. Long-term toxicity testing on aquatic invertebrates (triggered by Annex VII, Section 9.1.1., column 2), same as below under Annex IX

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

2. Long-term toxicity testing on fish (triggered by Annex VIII, Section 9.1.3., column 2), same as below under Annex IX

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

3. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit).

4. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

5. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210)

The reasons for the decision(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.

In the list of requests above, the same information requirement is mentioned under different headings. This is because some information requirements may be triggered at different tonnage band(s) under different conditions. In such cases, only the reasons why the information requirement is triggered are provided in the pertinent section of Appendix 1 for the lower tonnage band. The reasons why the standard information requirement is actually not met as well as the specification of the study design are then provided in the pertinent section for the highest tonnage band. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

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 decision
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 decision

Contents

Reasons for the decision(s) related to the information under Annex VII of REACH

1. Long-term toxicity testing on aquatic invertebrates

1 Short-term toxicity testing on aquatic invertebrates is an information requirement under Column 1 of Annex VII to REACH (Section 9.1.1.). However, long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

2 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (Guidance on IRs and CSA, Section R.7.8.5).

3 Under Section 4.8 of your technical dossier, you have provided an EU Method A.6 study (column eluation). The water solubility of the Substance in water was determined to be 0.02 mg/L at 20°C.

4 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

5 The examination of the information provided as well as the selection of the requested test and the test design are addressed under Request 4.

6 In your comments to the draft decision, you agree to conduct the requested OECD TG 211 study on the Substance.

Reasons for the decision(s) related to the information under Annex VIII of REACH

2. Long-term toxicity testing on fish

7 Short-term toxicity testing on fish is an information requirement under Column 1 of Annex VIII to REACH (Section 9.1.3.). However, long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

8 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (Guidance on IRs and CSA, Section R.7.8.5).

9 As already explained under Request 1, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

10 The examination of the information provided, your considerations of alternative methods, of third party comments (if applicable), as well as the selection of the requested test and the test design are addressed under Request 5.

11 In your comments to the draft decision you repeat your intention to adapt the standard information requirement for this endpoint. The examination of the information provided is addressed under Request 5.

Reasons for the decision(s) related to the information under Annex IX of REACH

3. Pre-natal developmental toxicity study

12 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX to REACH (Section 8.7.2.).

3.1. Information provided to fulfil the information requirement

13 You have submitted a testing proposal for a PNDT study according to the OECD TG 414 by the oral route with the Substance.

14 ECHA requested your considerations for alternative methods to fulfil the information requirement for Developmental toxicity. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

15 ECHA agrees that a PNDT study in a first species is necessary.

3.2. Specification of the study design

16 You proposed testing in the rat as a first species. You may select between the rat or the rabbit because both are preferred species under the OECD TG 414 (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

17 You did not specify the route for testing. The oral route of administration is the most appropriate to investigate reproductive toxicity (ECHA Guidance R.7a, Section R.7.6.2.3.2.).

3.3. Outcome

18 Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the test, as specified above.

19 In your comments to the draft decision, you agree to conduct the requested OECD TG 414 study on the Substance.

4. Long-term toxicity testing on aquatic invertebrates

20 Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

4.1. Information provided to fulfil the information requirement

21 You have submitted a testing proposal for a Daphnia magna reproduction test (test method: EU C.20/OECD TG 211).

22 Your registration dossier does not include any information on long-term toxicity on aquatic invertebrates.

23 ECHA agrees that an appropriate study on long-term toxicity on aquatic invertebrates is needed.

4.2. Test selection and study specifications

24 The proposed Daphnia magna reproduction test (test method: EU C.20/OECD TG 211) is appropriate to cover the information requirement for long-term toxicity on aquatic invertebrates (Guidance on IRs and CSA, Section R.7.8.4.1.).

25 The Substance is difficult to test due to the low water solubility (0.02 mg/L) and high adsorption potential (log kow 6.5 and calculated log Koc 4.29). OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 211. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solutions.

4.3. Outcome

26 Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the test with the Substance, as specified above.

27 In your comments to the draft decision, you agree to conduct the requested OECD TG 211 study on the Substance.

5. Long-term toxicity testing on fish

28 Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

29 Under Article 40(3)(c) of REACH, ECHA may require a registrant to carry out one or more additional tests in case of non-compliance of the testing proposal with Annexes IX, X or XI of the REACH Regulation. The information requirement on Aquatic toxicity at Annex IX covers both long-term toxicity on invertebrates (Section 9.1.5.) and on fish (Section 9.1.6.). However, you have provided a testing proposal for long-term testing on aquatic invertebrates only. In case of a data gap for long-term toxicity testing on fish, it is necessary to request this information as an additional test to ensure compliance with the endpoint.

5.1. Information provided to fulfil the information requirement

30 Your registration dossier does not include any information on long-term toxicity on fish.

31 Instead, you have provided the following justification to omit the study: "*substance was found to be non-toxic at the solubility limit in the three acute aquatic toxicity studies on fish, Daphnia and algae; due to the poor water solubility, high log Pow and the lack of biodegradability, we propose to conduct a long-term toxicity study on an aquatic species;*

however as none of the three tested species showed effects in the acute tests, for animal welfare reasons we suggest to perform a reproduction test over 21 days on Daphnia magna."

32 We have assessed this information and identified the following issue:

5.2. Your justification to omit the study has no legal basis

33 A registrant may only adapt information requirements based on a specific adaptation rule or the general rules set out in Annex XI.

34 Your justification to omit this information does not refer to any such legal ground for adaptation.

35 Therefore, you have not demonstrated that this information can be omitted. Minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

36 Therefore, your adaptation is rejected and the information requirement is not fulfilled.

37 In your comments to the draft decision you repeat your intention to adapt the standard information requirement for this endpoint and carry out the long-term fish study only if effects are observed in the long-term Daphnia study or below the limit of water solubility.

38 As already explained above, Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. A registrant may only adapt this information requirement based on the general rules set out in Annex XI. The minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

39 In the comments to the draft decision, you also indicate your intention to adapt this information requirement by means of read across according to Annex XI, Section 1.5 of REACH Regulation.

40 You propose to predict the properties of the Substance from a source study on the analogue substance, M-DEA (4,4'-Methylenbis[2,6-diethylaniline, EC 237-185-4).

41 We have assessed the provided information and identified the following issues:

42 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.

43 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

44 We have identified the following issue(s) with the prediction of ecotoxicological properties:

45 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include an explanation why the properties of the Substance may be predicted from information on the source substance(s).

46 In your comments you refer to a study conducted with another substance than the Substance in order to comply with the REACH information requirements. However, you

have not provided documentation as to why this information is relevant for the Substance and thus why the properties of the Substance may be predicted from information on the source substance(s).

47 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substance(s).

48 Therefore, your adaptation is rejected and the information requirement is not fulfilled.

5.3. Test selection and study specifications

49 The Fish, Early-Life Stage Toxicity Test (test method: OECD TG 210) is appropriate to cover the information requirement for long-term toxicity on fish (Guidance on IRs and CSA, Section R.7.8.4.1.).

50 OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained under Request 1, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Request 4.

5.4. Outcome

51 Under Article 40(3)(c) of REACH, you are requested to carry out the additional test with the Substance, as specified above.

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).

All Guidance on REACH is 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

ECHA received your testing proposals on 7 December 2021 and started the testing proposal evaluation in accordance with Article 40(1).

ECHA held a third party consultation for the testing proposal(s) from 1 April 2022 until 16 May 2022. ECHA did not receive information from third parties.

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

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

ECHA took into account your comments and amended the deadline but not the requests.

> In your comments on the draft decision, you requested an extension of the deadline to provide information from 12 to 18 or 24 months from the date of adoption of the decision. You refer to laboratory capacity issues, however you did not provide any documentary evidence.
>
> Nevertheless, ECHA has exceptionally extended the standard deadline by 12 months to take into account currently longer lead times in contract research organisations. ECHA has therefore extended the deadline to 24 months.

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: Addressees 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, VIII and IX to REACH, for registration at 100-1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[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[2].

(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.

This information is needed to assess 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

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

prepare registration and PPORD dossiers[3].

2. General recommendations for conducting and reporting new tests

References to Guidance on REACH and other supporting documents can be found in Appendix 1.

[3] https://echa.europa.eu/manuals