~~Confidential~~

Helsinki, 11 September 2023

Addressee(s)
Registrant(s) of JS_280-57-9_TEDA as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
07 June 2022

Registered substance subject to this decision ("the Substance")
Substance name: 1,4-diazabicyclooctane
EC/List number: 205-999-9

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)

Under Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***16 June 2026***.

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

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

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats

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

2. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rabbit)

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 addressee(s) 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 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 IX of REACH

1. Sub-chronic toxicity study (90-days)

1 A sub-chronic toxicity study (90 day) is an information requirement under Annex IX, Section 8.6.2.

1.1. Information provided to fulfil the information requirement

2 You have submitted a testing proposal for a Sub-chronic toxicity study (90 day) according to OECD TG 408 with the Substance.

3 ECHA requested your considerations for alternative methods to fulfil the information requirement for Repeated dose 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.

4 ECHA agrees that a 90-day study is necessary.

1.2. Specification of the study design

1.2.1. Species and route of exposure

5 You proposed testing in the rat. ECHA agrees with your proposal because the rat is the preferred species according to the OECD TG 408. Therefore, the study must be conducted in the rat.

6 You proposed testing by the oral route. ECHA agrees with your proposal because this route of administration is appropriate to investigate systemic toxicity; Guidance on IRs and CSA, Section R.7.5.4.3.2.

1.2.2. Additional parameters

7 You have initially proposed to include the following investigations parameters related to reproductive toxicity:

- Sperm analysis (in the first instance all main phase males)
- Staging of the spermatogenic cycle (in the first instance, control and high dose main phase males)
- Oestrus cycle evaluation (in the first instance, control and high dose main phase females)

8 You have not provided any data that indicate effects in reproductive organs. You may include additional investigations at your own discretion as long as their inclusion do not compromise the integrity of the OECD TG 408 study design. Should you choose to include additional investigations, the following parameters should be considered:

- At termination, testis and epididymis weights are recorded for all males. At least one epididymis from each male should be reserved for histopathological examination. The remaining epididymis may be used for enumeration of cauda epididymis sperm reserves sperm morphology or motility (for further specifications see OECD TG 408, para. 39-40). The testis should be preserved for histopathology by immersion in Bouin's or Davidson's fixative. The histopathological examinations must include staging of seminiferous tubule cross sections (for specifications see OECD TG 408, para. 45);

- Oestrous cycles must be monitored for a period of two weeks, commencing around treatment day 75. During this time vaginal smears should be examined daily to determine the length of the oestrus cycle;
- At necropsy, the oestrus cycle of all females should be determined by taking vaginal smears. These observations will provide information regarding the stage of oestrus cycle at the time of sacrifice and assist in histological evaluation of oestrogen sensitive tissues (for specifications see OECD TG 408, para. 45); and
- At termination, ovarian histopathological examinations should follow the specification in the Extended one-generation reproductive toxicity study (for specifications see OECD TG 443, para. 73).

9 In the comments to the draft decision, you agree to perform the requested study. You indicate that you no longer plan to investigate additional parameters related to reproductive toxicity. ECHA reiterates that inclusion of these additional parameters is at your own discretion. Therefore, ECHA has no objection if you decide not to conduct these additional investigations.

1.2.3. Satellite groups

10 You have proposed to perform a '13-week oral toxicity study in rats followed by a 4-week recovery period', thereby including two additional satellite groups (high-dose group + control group)

11 According to OECD TG 408, para. 22, 'The observation period should be at least 90 days. If a satellite group is included in the study, animals in the satellite recovery group scheduled for follow-up observations should be kept for an appropriate period without treatment to detect persistence of, or recovery from toxic effects'.

12 Your proposal is in line with OECD TG 408. Therefore, you may include the additional satellite groups at your own discretion as long as their inclusion does not compromise the integrity of the OECD TG 408 study design.

13 In the comments to the draft decision, you indicate that you no longer plan to include a 4-week recovery period, requiring additional satellite groups. ECHA notes that inclusion of satellite recovery groups in the sub-chronic toxicity study is at your own discretion. Therefore, ECHA has no objection if you decide not to include them.

1.3. Outcome

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

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

2. Pre-natal developmental toxicity study

15 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in two species is a standard information requirement under Annex X, Section 8.7.2.

2.1. Information provided to fulfil the information requirement

16 Your dossier contains a PNDT study in a first species.

17 You have submitted a testing proposal for a PNDT study in a second species according to the OECD TG 414 with the Substance.

18 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.

19 ECHA agrees that a PNDT study in a second species is necessary.

2.2. Specification of the study design

20 You proposed testing in the rabbit as a second species.

21 The study in the first species was conducted in the rat. The rat or the rabbit are the preferred species under the OECD TG 414 (ECHA Guidance R.7a, Section R.7.6.2.3.2.). Therefore, the study in the second species must be conducted in the rabbit.

22 You did not specify the route for testing. As the Substance is a solid, the study must be conducted with oral administration of the Substance (Annex X, Section 8.7.2., Column 1).

2.3. Outcome

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

24 In your comments, you agree to perform the requested study.

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

The information requirement for an Extended One-Generation Reproductive Toxicity Study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study are needed for the design of the EOGRTS.

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 26 August 2022.

ECHA held a third-party consultation for the testing proposal(s) from 26 October 2022 until 12 December 2022. ECHA did not receive information from third parties.

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

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

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

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA 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 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]
[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.

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

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 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