~~Confidential~~

Helsinki, 22 February 2024

Addressees

Registrants of JointS_PBTC as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
06 May 2022

Registered substance subject to this decision ("the Substance")
Substance name: 2-phosphonobutane-1,2,4-tricarboxylic acid
EC/List number: 253-733-5

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-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 ***27 November 2026***.

Requested information must be generated using the **analogue substance tetrasodium hydrogen 2-phosphonatobutane-1,2,4-tricarboxylate, EC number 266-442-3**.

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

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

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 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 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.

~~Confidential~~

Appendix 1: Reasons for the request(s)

Contents

Reasons common to several requests

0.1. Read-across adaptation accepted

1 You have submitted testing proposals for the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5.:

- Pre-natal developmental toxicity study in a second species (Annex X, Section 8.7.2.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

2 You provide a read-across justification document in IUCLID Section 13.

0.1.1. Identification of source substances and read-across hypothesis

3 You predict the properties of the Substance from information obtained from the following source substance:

- tetrasodium hydrogen 2-phosphonatobutane-1,2,4-tricarboxylate, EC number 266-442-3 (source substance 1);

4 You provide the following reasoning for the prediction of toxicological properties: ”In aqueous conditions, both compounds dissociate to form the common compound for read-across purposes”.

5 ECHA understands that your read-across hypothesis is based on the formation of common (bio)transformation products. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

0.1.2. Assessment of the read-across hypothesis

6 The evaluation by ECHA of testing proposals submitted by registrants aims at ensuring that generation of information is tailored to real information needs. To this end, it is necessary to consider whether programmes of testing proposed by you are appropriate to fulfil the relevant information requirements and to guarantee the identification of health and environmental hazards of substances. In that respect, the REACH Regulation aims at promoting, wherever possible, the use of alternative means, where equivalent results to the prescribed test are provided on health and environmental hazards.

7 Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated whenever possible by means other than vertebrate animal tests, including information from structurally related substances (grouping of substances and read-across), "provided that the conditions set out in Annex XI are met".

8 The first Recital and the first Article of the REACH Regulation establish the "promotion of alternative methods for assessment of hazards of substances" as an objective pursued by the Regulation. In accordance with that objective, ECHA considers whether a prediction of the relevant properties of the substance subject to the present decision by using the results of the proposed tests is plausible based on the information currently available.

9 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 sections.

10 ECHA agrees that:

- The Substance and source substance 1 are structurally similar substances as they differ only in counter ions. This is because the Substance is the non-charged parent compound containing three carboxylic acid functionalities and a phosphonate

moiety, while source substance 1 is a tetrasodium salt of the Substance in which the carboxylic acid functional groups and one OH-functionality of the phosphonate moiety, are deprotonated.

- The transformation process (i.e. the deprotonation) taking place in aqueous solution can be described by the dissociation constants of the two compounds: pKa_1: 1.08; pKa_2: 3.99; pKa_3: 4.44; pKa_4: 4.99, pKa_5 8.59. The dissociation is expected to take place upon contact with water.
- The non-common compounds are counter ions (protons H^+ and sodium cations Na^+), that are not expected to have relevant (eco)toxicological effects.

0.1.3. Conclusion

11 ECHA agrees that based on the read-across justification provided and the other information available in the dossier there is a basis for considering the hypothesis of your read across approach plausible. Therefore, you have plausibly demonstrated that relevant properties of the Substance may be predicted from data on the analogue substance (i.e. source substance 1). However, ECHA emphasises that any final determination on the validity of your read-across approach will only be possible when the information on the requested study will be available in the updated registration dossier.

Reasons related to the information under Annex IX of REACH

1. Long-term toxicity testing on fish

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

1.1. Information provided to fulfil the information requirement

13 You have submitted a testing proposal for a Fish, Early-Life Stage Toxicity Test (test method: OECD TG 210).

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

15 ECHA requested your considerations for alternative methods to fulfil the information requirement for long-term toxicity on fish. You provided your considerations and you applied read-across to fulfil the respective information requirement, and no other alternative methods were available. ECHA has taken these considerations into account.

16 ECHA agrees that an appropriate study on long-term toxicity on fish is needed.

1.2. Assessment of the read-across approach

17 As explained in Section 0 of the present Decision, ECHA agrees that on the basis of the currently available information, the read-across approach presented in your testing proposal is plausible and the test material selection is justified.

1.3. Study design

18 The proposed 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.).

19 The source substance 1 is difficult to test due to being ionisable in the environmentally relevant pH range of 4-9 (pKa_1: 1.08; pKa_2: 3.99; pKa_3: 4.44; pKa_4: 4.99, pKa_5 8.59). OECD TG 210 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 210. 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.

1.4. Outcome

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

21 In the comments to the draft decision, you agree to perform the requested test.

Reasons related to the information under Annex X of REACH

2. Pre-natal developmental toxicity study

22 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

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

24 You have submitted a testing proposal for a PNDT study in a second species according to the OECD TG 414 by the oral route with the analogue substance tetrasodium hydrogen 2-phosphonatobutane-1,2,4-tricarboxylate (EC No. 266-442-3).

25 ECHA requested your considerations for alternative methods to fulfil the information requirement for Developmental toxicity. You provided your considerations and you applied read-across to fulfil the respective information requirement, and no other alternative methods were available. ECHA has taken these considerations into account.

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

2.1. Assessment of the read-across approach

27 As explained in Section 0 of the present Decision, ECHA agrees that on the basis of the currently available information, the read-across approach presented in your testing proposal is plausible and the test material selection is justified.

2.2. Specification of the study design

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

29 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 (Guidance on IRs and CSA, Section R.7.6.2.3.2.). Therefore, the study must be conducted in the rabbit.

30 You proposed testing by oral route. ECHA agrees with your proposal.

2.3. Outcome

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

32 In your comments on the draft decision, you question the necessity to perform a PNDT study in a second species in light of the upcoming REACH revision. You refer to CARACAL-48 meeting where '*it was proposed to delete the information requirement of the pre-natal developmental toxicity study 2nd species (Annex X and trigger in Annex IX; OECD TG 414'*. Therefore, you suggest '*to postpone the decision of the Pre-natal developmental toxicity study in a second species (OECD TG 414) with the above mentioned substance until the future of this information requirement is clarified*.'

33 ECHA points out that you refer to ongoing discussions. Under the currently applicable legislation a PNDT study in a second species is standard information requirement under Annex X, Section 8.7.2.

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 (2023).
Guidance on intermediates; ECHA (2010).
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 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.

In the testing proposal you have submitted for the long-term toxicity testing on fish information requirement, you mention an ongoing court case (Symrise v ECHA - Case T-656/20). In relation to this, you ask ECHA to suspend the decision making on the submitted testing proposal. However, the ongoing proceedings of this court case have no suspensive effect on the present decision.

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, with the corresponding requests in this decision provided within parenthesis:

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

(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:

- its representativeness towards the specified analogue substance,
- it supports the read-across prediction as presented in the read-across justification document,
- the impact of each constituent/impurity on the test results for the endpoint to be assessed. For example, if a constituent/impurity of the analogue 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.

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 Practical Guide on How to use alternatives to animal testing to fulfil your information requirements (Chapter 4.4., https://echa.europa.eu/practical-guides).