~~Confidential~~

Helsinki, 11 March 2022

Addressees
Registrants of CAS_14689-29-3_JointSubmission listed in the last Appendix of this decision

Date of submission of the dossier subject of a decision
27/03/2020
Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Dipotassium [[N,N'-ethylenebis[N-(carboxylatomethyl)glycinato]](4-)-N,N',O,O',ON,ON']zincate(2-)
EC number: 238-729-3
CAS number: 14689-29-3

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 ***20 March 2023***.

The requested information must be generated using the Substance unless otherwise specified.

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

1. Long-term toxicity testing on aquatic invertebrates also requested below (triggered by Annex I, Section 0.5.; test method: EU C.20./OECD TG 211)

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

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

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

- Appendices entitled "Reasons to request information required under Annexes VIII to IX 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 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;

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

For certain endpoints, ECHA requests the same study from registrants at different tonnages.

In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given. Only one study is to be conducted; the registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants under Article 53 of REACH.

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 can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: https://echa.europa.eu/regulations/appeals.

Approved[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 A: Reasons to request information required under Annex VIII of REACH

This decision is based on the examination of the testing proposal you submitted.

1. Long-term toxicity testing on aquatic invertebrates

Pursuant to Article 12(1) and Annex VI of the REACH Regulation the standard information requirements listed in Annex VII to X of the REACH Regulation are considered minimum requirements. Annex VI, step 4 of the 'Guidance note on fulfilling the requirements of Annexes VI to XI' provides that the rules set out in Annexes VII to XI may require certain tests to be undertaken earlier than or in addition to the standard requirements. Furthermore, in accordance with Annex I of the REACH Regulation, certain additional information may have to be generated if it is necessary for producing the chemical safety report (CSR). According to the last subparagraph of Section 0.5. of Annex I of REACH, if the manufacturer or importer considers that further information is necessary for producing his CSR and that this information can only be obtained by performing tests in accordance with Annex IX and X, he shall submit a proposal for a testing strategy, explaining why he considers that additional information is necessary.

This means that when justified, higher tier/further studies may be conducted for substances where the tonnage level would not normally require this as a standard requirement. In order to understand the ecotoxicological properties of the registered substance in light of the adverse effects observed, it is necessary to investigate further so that appropriate risk management measures can be put in place and safe use of the substance can be ensured.

1.1. Information provided to fulfil the information requirement

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

In your testing proposal justification, you state the following for the Substance:

A. Testing on the Substance

1. "is to be tested with the intention of being used as the source substance for the grouping of substances and read-across approaches aimed at fulfilling the information requirements of Annex IX, Section 9.1.5 for other closely-related metal-EDTA complexes".

2. In your testing proposal, you further state that experimental data about the long-term toxicity of EDTA zinc complexes to aquatic invertebrates is needed for the hazard assessment due to the environmental behaviour (persistent) and the intrinsic toxicity of zinc.

B. You have adapted the standard information requirement according to Annex XI, Section 1.5. Grouping of substances and read-across approach of REACH Regulation.

In support of this adaptation of the information requirement, you have provided the following information for this endpoint:

i) A key study (1998) performed according to EEC Guideline XI/681/86, Draft 4: "Prolonged toxicity study with Daphnia magna: Effects on reproduction" on the analogue substance disodium dihydrogen ethylenediaminetetraacetate (CAS 139-33-3).

ii) A Key study (2010) performed according to OECD guideline 211 on the analogue substance, Disodium;2-[2-(bis(carboxylatomethyl)amino)ethyl-(carboxylatomethyl)amino]acetate (CAS 15375-84-5 / EC no 239-407-5)

We have assessed this information and identified the following issues:

A. Testing of the substance

You have provided no read across justification in your dossier, therefore ECHA cannot assess if the adaptation complies with the general rules of adaptation as set out in Annex XI, Section 1.5. Furthermore, it is the responsibility of the registrants of the other closely related metal-EDTA complexes to comply with Annex XI Section 1.5 in the technical dossier for the target substance(s).

Concerning your statement on the intrinsic toxicity of zinc, you have provided mechanistic evidence to justify your hypothesis that the metal ions will (partly) be released from the chelating agent, leaving them free to associate with other negatively charged ions and/or affect the test organisms.

ECHA agrees with your conclusion that there is a concern for long-term toxicity on aquatic invertebrates for the Substance and thus a need for further investigation on aquatic invertebrates.

In addition, consequently, there is a need for further information for producing a CSR (Annex 1. Section 0.5 – applicable to registrants from Annex VIII, onwards). Therefore, ECHA considers that testing of the Substance for a *Daphnia magna* reproduction test (test method: EU C.20/OECD TG 211) is acceptable.

B. Additional information provided in your dossier

Read across adaptation under Annex XI, Section 1.5

As per Appendix B., your read-across approach is rejected.

As per Appendix B., ECHA has taken your considerations into account.

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

Consequently, ECHA considers that testing of the Substance for a *Daphnia magna* reproduction test (test method: EU C.20/OECD TG 211) is acceptable.

Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the test with the Substance, as specified under Appendix C.1., below.

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

This decision is based on the examination of the testing proposal you submitted.

1. Long-term toxicity testing on aquatic invertebrates

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation.

1.1. Information provided to fulfil the information requirement

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

As per Appendix A.1., you provide a justification for the Substance:

In addition, you have adapted the standard information requirement according to Annex XI, Section 1.5. Grouping of substances and read-across approach of REACH Regulation.

As per Appendix A.1., you have provided supporting information of this adaptation.

We have assessed this information and identified the following issues:

A. Testing of the substance

The study is a standard information requirement at Annex IX.

B. Additional information provided in your dossier

Read across adaptation under Annex XI, Section 1.5

In addition, you have adapted the standard information requirement according to Annex XI, Section 1.5. Grouping of substances and read-across approach of REACH Regulation.

In support of this adaptation of the information requirement, you have provided the following information for this endpoint:

i) A key study (1998) performed according to EEC Guideline XI/681/86, Draft 4: "Prolonged toxicity study with Daphnia magna: Effects on reproduction" on the analogue substance disodium dihydrogen ethylenediaminetetraacetate (CAS 139-33-3).
ii) A Key study (2010) performed according to OECD guideline 211 on the analogue substance Disodium;2-[2-(bis(carboxylatomethyl)amino)ethyl-(carboxylatomethyl)amino]acetate (CAS 15375-84-5 / EC no 239-407-5)

We have assessed this additional information and identified the following issues:

In your testing proposal, you propose to replace the read across adaptation by experimental data from the registered substance itself and covered by the current testing proposal. Further, no read-across justification was provided for the analogue substances used for the two studies provided in the technical dossier. Such justification is required to strengthen the rationale for the read-across and, in the absence, you have not demonstrated that your adaptation

complies with the general rules of adaptation as set out in Annex XI, Section 1.5. Therefore, your read-across approach is rejected.

Within the dossier assessed for this draft decision, you provided your consideration(s) 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.

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

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

1.2. Test selection and study specifications

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 (ECHA Guidance R.7.8.4.1.).

The Substance is difficult to test due to the complexation properties of the Substance. 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 the 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 solution.

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[2].

B. 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 prepare registration and PPORD dossiers[3].

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

Appendix D: Procedure

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 15 January 2019.

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 did not receive any comments within the commenting period.

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[4] 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)[5]

RAAF - considerations on multi-constituent substances and UVCBs (RAAF UVCB, March 2017)[6]

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.

[4] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[5] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[6] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316

OECD Guidance documents[7]
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.

[7] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix F: Addressees of this decision and the corresponding information requirements applicable to them

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]
[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.