~~Confidential~~

Helsinki, 24 November 2021

Addressees
Registrant(s) of JS_945-591-4 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
03/11/2020

Registered substance subject to this decision ("the Substance")
Substance name: Manganese glycinate, reaction product of manganese sulphate with glycine
EC number: 945-591-4
CAS number: NS

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 the deadline of ***1 December 2022***.

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

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

1. Water solubility (Annex VII, Section 7.7.; test method: OECD GD 29);

2. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202);

3. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201).

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487);

2. If negative results are obtained in test performed for the information requirement of Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490);

3. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below (request B.3);

4. Combined repeated dose toxicity study with the Reproduction/developmental toxicity screening test (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats;

5. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD

TG 203) .

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

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VII to VIII 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;

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations 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, 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 Christel Schilliger-Musset, 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 on Reasons common to several requests

1. Assessment of your read-across adaptation under Annex XI, Section 1.5

Grouping of substances and read-across approach

You seek to adapt the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.);
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.);
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.);
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.);
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.);
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.).

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 appendices.

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 (addressed under 'Assessment of prediction(s)').

In your registration dossier you have provided information derived from experimental data from analogues using the OECD QSAR Toolbox and flagged the information as QSAR for the endpoints specified above. As the analogues are used as source substances to predict the property of the Substance, we understand that you have adapted the standard information requirements under Annex XI, Section 1.5 to REACH (grouping and read-across).

Additional information on what is necessary, when justifying a read-across approach can be found in the ECHA Guidance[2].

1.1. Predictions for (eco)toxicological properties

You provided the following justification: "*The computational simulation was performed based on the read-across approach. The read-across is one of the so-called alternative test methods recommended by REACH, where the predictions are based on the experimental data available for the most similar compounds*." You state that the OECD QSAR Toolbox, version 4.3 was used to predict the relevant toxicological and ecotoxicological properties.

ECHA understands that you read-across from $MnSO_4$ for genotoxicity and aquatic toxicity (short-term toxicity to fish and invertebrates), from $CuSO_4$ for repeated dose toxicity and from potassium N,N-dimethylglycinate for reproductive toxicity as source substances and the Substance as target substance.

You predict the properties of the Substance using a read-across hypothesis, which is based on the formation of common (bio)transformation/dissociation products. The properties of your

[2] ECHA Guidance R.6

Substance are predicted to be quantitatively equal to those of the source substance(s).

ECHA notes the following shortcomings with regards to predictions of (eco)toxicological properties based on analogue approach.

The common deficiencies are set out here, while the specific ones, which also add to the overall conclusion, are set out under Appendix A. sections 2 and 3 and Appendix B. sections 1 to 4.

i. Adequacy and reliability of source studies

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3);
- cover an exposure duration comparable to or longer than the corresponding test method referred to in Article 13(3) if exposure duration is a relevant parameter.

- *Lack of robust study summaries*

Under Annex XI, Section 1.5., the results to be read across must have a reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3). For independently assessing and establishing this for a key study, a robust study summary must be provided (Guidance on IRs and CSA, Section R.6.2.6; Art. 3(28) and 10(a)(vii) and Annex I, Section 1.1.4/3.1.5 of REACH).

A robust study summary must provide a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

In your technical dossier and Chemical Safety Report (CSR), you have identified the source study(ies) used as a key study but provided only the effect estimate, for all information requirements for which a read-across adaptation is proposed.

You have not provided detailed information on the methods, results and conclusions, allowing for an independent assessment of the study. In the absence of such information, the study cannot be considered to provide a reliable coverage of the key parameters foreseen to be investigated in a study according to the corresponding OECD TG.

- *Additional issues*

Specific reasons why your source studies do not meet these criteria are explained further below under the relevant information requirement sections A.2, B.1, B.2, B.3 and B.4. Therefore, no reliable predictions can be made for these information requirements.

ii. Missing supporting information to support predictions for (eco)toxicological properties

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting*

information to strengthen the rationale for the read-across"[3]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include information on the formation of common compounds and bridging studies to compare properties of the Substance and source substances.

A. Missing information on the formation of common compound

As indicated above, your read-across hypothesis is based on the (bio)transformation/dissociation of the Substance and of the source substance(s) to a common compound(s). In this context, information characterising the rate and extent of the hydrolysis/transformation of the Substance and of the source substance(s) is necessary to confirm the formation of the proposed common hydrolysis/transformation product and to assess the impact of the exposure to the parent compounds.

Specifically with regards to the prediction for aquatic toxicity, and genotoxicity you have described that the Substance is an organometallic compound where manganese metallic centres are linked by oxygen coordination bonds of the glycine ligands. You indicate that the weak bonds between metallic centres and the oxygen atoms in the compound structure will break easily and favour dissociation of the substance into its basic products (Gly, H2SO4 and Mn(OH)2). You have noted that glycine is an amino acid which is not considered as toxic compound.

You have merely explained how your Substance may behave in an aquatic environment but you have not provided any reliable information neither about the transformation/dissociation of your Substance nor of the source substance for aquatic toxicity (MnSO4). For metals or sparingly soluble metal compounds, the Transformation/Dissolution study in aqueous media (Annex 10 of UN-GHS and OECD GD 29) is the recommended method (ECHA Guidance R7.a, Section R.7.1.1.1) to provide this information.

Concerning the human health endpoints addressed in sections B.1, B.2, B.3 and B.4 below, you have not provided any experimental data or other adequate and reliable information, neither about the dissociation of your Substance nor about the dissociation of the source substances. Furthemore, you have not provided experimental data to demonstrate similarity of the dissolution rates of these substances.

In the absence of this information, you have not provided supporting evidence establishing that the proposed common transformation/dissolution product is formed as assumed in your read-across hypothesis. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

B. Missing information on the impact of non-common compounds

As indicated above, your read-across hypothesis is based on the (bio)transformation/dissociation of the Substance and of the source substance(s) to a common compound(s). In this context, exposure to the Substance and of the source substance(s) may also lead to exposure to other compounds than the common compound of interest. The impact of exposure to these non-common compounds on the prediction of properties of the target needs to be assessed to ensure that a reliable prediction can be made.

[3] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

The structure of the Substance (manganese glycinate) differs from that of the source substances, which are either inorganic compounds of manganese or glycinates with another metal cation than manganese. If the Substance and source substances dissociate, these structural differences will also lead to the formation of structurally different dissociation products. These non-common compounds are:

- structurally different glycinate moieties formed from the Substance and the source substance potassium N,N-dimethylglycinate;
- the sulfate ions formed from the source substances $MnSO_4$ and $CuSO_4$
- the copper ions formed from the source substance $CuSO_4$.

Some of the non-common compounds formed from the source substances such as copper ions and N,N-dimethylglycinate may have different (eco)toxicological properties than the dissociation products formed from the Substance. You have not provided information characterising the exposure to the non-common compounds resulting from exposure to the Substance and of the source substance(s). No experimental data or other adequate and reliable information addressing the impact of exposure to these non-common compounds is included in the documentation of your read-across approach. In the absence of such information, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

C. Missing supporting information to compare toxic properties of the substances

As indicated above, your read-across hypothesis is based on the (bio)transformation/dissociation of the Substance and of the source substance(s) to a common compound(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substance cause the same type of effects as a result of exposure to this common compound. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

You have provided studies conducted with source substances, but not with the Substance. The data set reported in the technical dossier does not include relevant, reliable and adequate toxicological information on the relevant toxicological endpoints for the Substance to support your read-across hypothesis. Such data is necessary to determine a potential effect of the glycinate moiety from the Substance on the availability and toxicity of the common compound, the manganese cation.

In the absence of such information, you have not established that the Substance and of the source substance(s) are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

Conclusions on the read-across approach

As explained above, based on the information in the dossier you have not established that relevant properties of the Substance can be predicted from data on the analogue substances. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

In the comments on the draft decision you outline how you intend to improve your read-across approaches for all the above-mentioned standard information requirements to address the deficiencies identified by ECHA in this decision. You indicate that you will update your

dossier to discuss the "*Substance behavior in aquatic environment related to solubility in water, bioaccumulation and biodegradation potential*" and that you will provide information "*on the formation of common compounds"* as well as "*on the reactions to which target, and source compounds are exposed"*. You indicate you will "*analyze series of available experimental studies on (eco)toxic properties of the substances (source, target, common and non-common compounds)*" and to provide further toxicological information on the Substance. You also indicate that you "*decided to base our prediction not on the data for CuSO4 and potassium N,N-dimethylglycinate but on the experimental measurements for MnCl2 and/or MnSO4*" and that "*justification regarding the selection of the new source compounds will be provided in the amended dossier documentation*".

ECHA acknowledges your intentions to improve the (eco)toxicological profile of the Substance and your plans to refine your read-across approach also with regards to the selection of the source substances. As you merely provide intentions and no concrete plans nor further experimental data to fulfil the shortcomings identified above, no conclusion on the compliance can currently be made. Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

In the comments on the draft decision you also indicate that "*In line with our company's policy of not using vertebrate animals, we wish to demonstrate that alternative research can be successfully used in our case*".

ECHA notes that minimisation of vertebrate animal testing is not on its own a legal ground for adaptation of standard information requirements under the general rules of Annex XI.

Appendix A: Reasons to request information required under Annex VII of REACH

1. Water solubility

Water solubility is a standard information requirement in Annex VII to REACH.

You have provided a key study (2018).

ECHA assessed this information and identified the following issues:

i. EU test method A.6 and OECD TG 105 describe two methods (the column elution method and the flask method) for conducting the study. The test method must be selected based on a water solubility estimate obtained in a preliminary study. For substances with preliminary water solubility below 10 mg/L the column elution method must be used.

You have provided in the registration dossier a study performed with the column elution method and you report a water solubility 175,3 mg/l.

The reported result falls outside of the applicability domain of the column elution.

i. In the comments to the draft decision, you have mentioned that there was an error in the registration dossier, the test was carried out using the flask method.

Your comments indicate that the correct test method was selected for carrying out the test. However, this information is not available in your registration dossier.

ii. You have also clarified in your comments that the organic carbon determination method was used as the analytical method.

ECHA Guidance R.7a and OECD TG 105 state that the solubility levels of the test substance should be determined analytically using a specific analytical method. The organic carbon determination method is an unspecific method based on an estimation, rather than using detections methods which identify and quantify the exact test substance.

Therefore, the provided information does not fulfil the information requirement.

Study selection

The Substance is an organometallic compound, and therefore, as suggested in the OECD series on Testing and Assessment Number 212 - Guidance on Selecting a Strategy for Assessing the Ecological risk of Organometallic and Organic Metal Salt Substances based on their Environmental Fate, water solubility shall be tested according to the test method described in OECD series on Testing and Assessment Number 29 - Guidance Document on Transformation/Dissolution of Metals and Metal Compounds in Aqueous media with adequate analytical techniques (examples of these are provided in OECD 212).

2. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

You have provided an adaptation according to Annex XI, Section 1.5. in your dossier. In support of your adaptation you have provided the following information: "*This read-across is based on the fact that target compound undergoes dissociation reaction, it is expected that*

this will be one of the first reactions to which our target chemical is exposed. As it was described within the Appendix A, the target substance dissociates completely into Mn2+, SO42- and Gly±. Thus, the prediction is based on toxicological data of the dissociation products of the target chemical. The target substance is an organometallic compound containing manganese (Mn) centres, glycine (Gly) ligands. The metallic centres of the substance are linked by oxygen coordination bonds of the Gly ligands. The weak bonds between metallic centres and the oxygen atoms in the compound structure break easily and favour rapid dissociation of the substance into its basic products (Gly, H2SO4 and Mn(OH)2). Glycine is an amino acid, which is not considered as toxic compound."

We have assessed this information and identified the following issue(s):

For the reasons detailed in Section 1 (in points 1.1. ii) A and B) of the Appendix on Reasons common to several requests, your read-across adaptation in accordance with Annex XI, Section 1.5. is rejected.

In the comments to the draft decision, you indicate your intention to adapt this information requirement based on a revised read-across adaptation in accordance with Annex XI, Section 1.5. As indicated in the Appendix on Reasons common to several requests, based on the information provided in the comments, there is currently no information to assess whether your adaptation fulfils the requirements of Annex XI, Section 1.5. You remain responsible for complying with this decision by the set deadline.

On this basis, the information requirement is not fulfilled.

3. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

You have provided the following information:

i. OECD TG 201 key study

We have assessed this information and identified the following issue[s]:

Missing robust study summaries

To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH). For independently assessing and establishing this for a key study, a robust study summary must be provided (Guidance on IRs and CSA, Section R.6.2.6; Art. 3(28) and 10(a)(vii) And Annex I, Section 1.1.4/3.1.5 of REACH).

Robust study summary must provide a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

In the robust study summary of this study you provided only the reference to the test method used and the effect values and indicated that the study is GLP compliant.

Therefore, you have not provided detailed information on the methods, results and conclusions, allowing for an independent assessment of the study. In the absence of such information, the study cannot be considered to provide a reliable coverage of the key parameters foreseen to be investigated in a study according to OECD TG 201.

In the comments to the draft decision, you have attached a copy of the study report. The study report includes the information required for an independent assessment of the study to verify that the study provides reliable coverage of they key parameters of an OECD TG 201 study. You have proposed to update your dossier with the information.

The information provided as part of your comments addresses the incompliances identified above. However, as the information is currently not available in your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

On this basis, the information requirement is not fulfilled.

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

1. *In vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

You have provided an adaptation according to Annex XI, Section 1.5. in your dossier. In support of your adaptation you have provided the following information:

In IUCLID section 7.6.1. you explain that "*The target compound undergoes dissociation reaction into its basic products: Gly, H2SO4 and Mn(OH)2. Due to the glycine is an amino acid which is not considered as toxic compound, the analogues search was performed assuming 100% ("exact match") structural similarity between dissociation products of source and target substances besides glycine. The toxicity prediction was performed based on the experimental data included in the OECD QSAR Toolbox. Manganese (II) sulphate would have the same dissociation products (H2SO4 and Mn(OH)2) as well as the experimental data related to its in vitro cytogenicity was available. Therefore, the prediction is based only on the MnSO4.*"

We have assessed this information and identified the following issue(s):

For the reasons detailed in Section 1 of the Appendix on Reasons common to several requests (in points 1.1. ii) A, B and C), your read-across adaptation in accordance with Annex XI, Section 1.5. is rejected.

In the comments to the draft decision, you indicate your intention to adapt this information requirement based on a revised read-across adaptation in accordance with Annex XI, Section 1.5. As indicated in the Appendix on Reasons common to several requests, based on the information provided in the comments, there is currently no information to assess whether your adaptation fulfils the requirements of Annex XI, Section 1.5. You remain responsible for complying with this decision by the set deadline.

On this basis, the information you provided in your dossier and in your comments do not fulfil the information requirement.

Study design

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. *In vitro* gene mutation study in mammalian cells;

An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

i. Triggering of the study

Your dossier contains (i) a negative result for *in vitro* gene mutation study in bacteria, and (ii) inadequate data for the other study (*in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study) (see Section B.1 above).

You have provided an adaptation according to Annex XI, Section 1.5. in your dossier. In support of your adaptation you have provided the following information:

In IUCLID section 7.6.1. you explained that "*The target compound undergoes dissociation reaction into its basic products: Gly, H2SO4 and Mn(OH)2. Due to the glycine is an amino acid which is not considered as toxic compound, the analogues search was performed assuming 100% ("exact match") structural similarity between dissociation products of source and target substances besides glycine. The toxicity prediction was performed based on the experimental data included in the OECD QSAR Toolbox. Manganese (II) sulphate would have the same dissociation products (H2SO4 and Mn(OH)2) as well as the experimental data related to its in vitro cytogenicity was available. Therefore, the prediction is based only on the MnSO4.*"

We have assessed this information and identified the following issue(s):

For the reasons detailed in Section 1 of the Appendix on Reasons common to several requests, (in points 1.1. ii) A, B and C) your read-across adaptation in accordance with Annex XI, Section 1.5. is rejected.

In the comments to the draft decision, you indicate your intention to adapt this information requirement based on a revised read-across adaptation in accordance with Annex XI, Section 1.5. As indicated in the Appendix on Reasons common to several requests, based on the information provided in the comments, there is currently no information to assess whether your adaptation fulfils the requirements of Annex XI, Section 1.5. You remain responsible for complying with this decision by the set deadline.

On this basis, the information you provided in your dossier and in your comments do not fulfil the information requirement.

The result of the request for information in section B.1 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

Consequently, you are required to provide information for this endpoint, if the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provides a negative result.

Study design

To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

3. Short-term repeated dose toxicity study (28 day), oral route (Annex VIII, Section 8.6.1.)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII to REACH.

You have provided an adaptation according to Annex XI, Section 1.5. in your dossier. In support of your adaptation you have provided the following information:

In IUCLID section 7.5.2. you explained that "*the target substance is an organometallic compound containing manganese (Mn) centres, glycine (Gly) and manganese (II) sulphate*

(MnSO4) ligands. The metallic centres of the substance are linked by oxygen coordination bonds of the Gly ligands. This read-across is based on the hypothesis that source and target substances have similar toxicological properties due to their dissociation into basic products (Gly, H2SO4 and Mn(OH)2). Glycine is an amino acid, which is not considered as toxic compound. Manganese (II) sulphate (MnSO4) would have the same dissociation products (H2SO4 and Mn(OH)2). However, since there were no data available for the MnSO4, the prediction was performed basing on a transformation analogue search assuming at least 50% similarity between dissociation products of source and target substances (besides glycine). CuSO4 analogue has been found as the most similar chemical, therefore it was used as the source compound."

We have assessed this information and identified the following issue(s):

For the reasons detailed in Section 1 of the Appendix on Reasons common to several requests (in points 1.1. ii) A, B and C), your read-across adaptation in accordance with Annex XI, Section 1.5. is rejected.

In the comments to the draft decision, you indicate your intention to adapt this information requirement based on a revised read-across adaptation in accordance with Annex XI, Section 1.5. As indicated in the Appendix on Reasons common to several requests, based on the information provided in the comments, there is currently no information to assess whether your adaptation fulfils the requirements of Annex XI, Section 1.5. You remain responsible for complying with this decision by the set deadline.

On this basis, the information you provided in your dossier and in your comments do not fulfil the information requirement.

Study design

Further information on the study design is provided under Section B.4. below.

4. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant.

You have provided an adaptation according to Annex XI, Section 1.5. in your dossier. In support of your adaptation you have provided the following information:

In IUCLID section 7.8.1. you explained that *"The target substance is an organometallic compound containing manganese (Mn) centres, glycine (Gly) and manganese (II) sulphate (MnSO4) ligands. The metallic centres of the substance are linked by oxygen coordination bonds of the Gly ligands. This read-across is based on the hypothesis that source and target substances have similar toxicological properties due to common underlying mechanism after administration. The prediction was performed basing on the source compound, which is classified as "Non-binder, non-cyclic" as well as "Aliphatic amines" and its structural similarity to the target compound is higher than 20%. Potassium N,N-dimethylglycinate was used as the source compound. The screening reproductive toxicity for the source compound was performed according to OECD 422."* You also indicate that "*the structural similarity between the source (potassium N,N-dimethylglycinate) and the target compound (Mn(Gly)SO4) equals to 21.1% ."*

We have assessed this information and identified the following issue(s):

For the reasons detailed in Section 1 of the Appendix on Reasons common to several requests (in points 1.1. ii) A, B and C), your read-across adaptation in accordance with Annex XI, Section 1.5. is rejected.

In the comments to the draft decision, you indicate your intention to adapt this information requirement based on a revised read-across adaptation in accordance with Annex XI, Section 1.5. As indicated in the Appendix on Reasons common to several requests, based on the information provided in the comments, there is currently no information to assess whether your adaptation fulfils the requirements of Annex XI, Section 1.5. You remain responsible for complying with this decision by the set deadline.

On this basis, the information you provided in your dossier and in your comments do not fulfil the information requirement.

Study design

When there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407) (as explained above under section B.2.), nor for the screening study for reproductive/ developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1.[4]

Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral[5] administration of the Substance.

2. Short-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

You have provided an adaptation according to Annex XI, Section 1.5. in your dossier. In support of your adaptation you have provided the following information: "*This read-across is based on the fact that target compound undergoes dissociation reaction, it is expected that this will be one of the first reactions to which our target chemical is exposed. Thus, the prediction is based on toxicological data of the dissociation products of the target chemical. The target substance is an organometallic compound containing manganese (Mn) centres, glycine (Gly) ligands. The metallic centres of the substance are linked by oxygen coordination bonds of the Gly ligands. The weak bonds between metallic centres and the oxygen atoms in the compound structure will break easily and favour dissociation of the substance into its basic products (Gly, H2SO4 and Mn(OH)2). Glycine is an amino acid which is not considered as toxic compound. Manganese (II) sulphate would have similar dissociation products H2SO4 and Mn(OH)2). Therefore, the prediction is based only on the MnSO4.*"

We have assessed this information and identified the following issue(s):

[4] ECHA Guidance R.7a, Section R.7.6.2.3.2., pages 484 to 485 of version 6.0 – July 2017. (https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf)
[5] ECHA Guidance R.7a, Section R.7.6.2.3.2.

For the reasons detailed in Section 1 (in points 1.1. ii) A and B) of the Appendix on Reasons common to several requests, your read-across adaptation in accordance with Annex XI, Section 1.5. is rejected.

In the comments to the draft decision, you indicate your intention to adapt this information requirement based on a revised read-across adaptation in accordance with Annex XI, Section 1.5. As indicated in the Appendix on Reasons common to several requests, based on the information provided in the comments, there is currently no information to assess whether your adaptation fulfils the requirements of Annex XI, Section 1.5. You remain responsible for complying with this decision by the set deadline.

On this basis, the information requirement is not fulfilled.

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[6].

B. Test material

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 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

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[7].

[6] https://echa.europa.eu/practical-guides
[7] https://echa.europa.eu/manuals

Appendix D: 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 03 November 2020.

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 E: List of references - ECHA Guidance[8] 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)[9]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[10]

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.

OECD Guidance documents[11]

[8] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[9] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[10] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[11] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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.

Appendix F: Addressees of this decision and their corresponding information requirements

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]

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.