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Helsinki, 14 November 2023

Addressee(s)
Registrant(s) of IP33_Trimanganesebis(orthoP) as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
10 August 2020

Registered substance subject to this decision ("the Substance")
Substance name: Trimanganese bis(orthophosphate)
EC/List number: 237-997-9

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 ***19 February 2026***.

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

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

1. Transformation/dissolution in aqueous media (triggered by Annex VII, Section 7.7., Column 2; test method: OECD GD 29).
   The screening test must be conducted and, if dissolution is < acute $ERV_{metal\ ion}$ as a result of the screening test, the full test must also be conducted.

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

2. Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.) by oral route, in rats, to be combined with the screening for reproductive/developmental toxicity requested below

3. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats

The reasons for the request(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 request(s)
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.

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Appendix 1: Reasons for the request(s)

Contents

Reasons common to several requests

0.1. Weight of evidence adaptation rejected

1 You have adapted the following standard information requirements by using Annex XI, Section 1.2. (weight of evidence). You have provided experimental data on Manganese (II) sulfate monohydrate (CAS 10034-96-5) for the following standard information requirements:

- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

2 The test material used is different than the Substance for the above-mentioned studies. Therefore, the studies conducted with these substances (hereafter referred to as the "source substances") will be evaluated as a read-across approach as part of the weight of evidence assessment.

3 Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

4 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

5 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency, and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

0.1.1. Lack of documentation justifying the weight of evidence adaptation

6 Annex XI, Section 1.2. requires that adequate and reliable documentation is provided to describe a weight of evidence approach. This documentation must include robust study summaries of the studies used as sources of information and a justification explaining why the sources of information together provide a conclusion on the information requirement.

7 You have not included a justification for your weight of evidence adaptation for each of the relevant information requirement, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

8 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation.

9 Your weight of evidence approach has deficiencies that are common to all information requirements under consideration and also deficiencies that are specific for these information requirements individually.

10 The common deficiencies are set out here, while specific deficiencies are set out under the information requirement concerned in request 3 below.

0.1.2. Read-across approach rejected for toxicological standard information requirements

11 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.

12 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.

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

14 You provide a read-across justification document in the respective endpoint summaries.

0.1.2.1. Scope of the grouping of substances – identification of source substances

15 You predict the properties of the Substance from information obtained from the following source substance(s):

(i) In your registration dossier: Manganese (II) sulfate monohydrate CAS 10034-96-5;

(ii) In your comments on the draft decision: Manganese bis(dihydrogen phosphate), CAS 18718-07-5.

16 You provide the following reasoning for the prediction of toxicological properties: ”Selected endpoints for the human health hazard assessment are addressed by read-across, using a combination of data on the phosphate moiety and the manganese moiety (or one of its readily soluble salts). This way forward is acceptable, since trimanganese bis(orthophosphate) dissociates to the phosphate anion and the manganese cation upon dissolution in aqueous media”.

17 ECHA understands that your read-across hypothesis is based on the formation of common (bio)transformation products, namely manganese and its counter-ions. You furthermore predict that the toxicological properties of the manganese ion from your Substance are qualitatively similar and quantitatively equal to those of the source substance.

0.1.2.2. Predictions for toxicological properties

18 We have identified the following issue(s) with the prediction(s) of toxicological properties:

0.1.2.2.1. Missing supporting information to compare the properties of the substances

19 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

20 Supporting information must include bridging studies to compare properties of the source substances and the Substance.

21 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar source substance(s) cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the source substance(s) is necessary to confirm that the substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration with the Substance and the source substance(s).

22 For repeated dose toxicity you provide studies used in the prediction for the source substance (i). Apart from those studies, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the source substance (ii) or the Substance that would confirm that the substances cause the same type of effects.

23 For reprotoxicity there are not any relevant studies, neither with the source substance(s) nor with the Substance. Specific reasons why the submitted studies cannot be considered relevant are explained further below under request 3. Thus, the data set reported in the technical dossier does not include relevant, reliable and adequate information for the source substance(s) to support your read-across hypothesis.

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

0.1.2.3. Conclusion on the read-across approach

25 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). You have not demonstrated that the sources of information relying on a read-across approach have any reliability.

Reasons related to the information under Annex VII of REACH

1. Transformation/dissolution in aqueous media

26 Water solubility is an information requirement under Annex VII to REACH (Section 7.7). However, under Column 2, information on transformation/dissolution in aqueous media must be provided if the substance is a metal or sparingly soluble metal compound.

1.1. Triggering of the information required

27 First, the Substance contains a metal, manganese, and is thus a metal compound.

28 Second, in the case of inorganic metal compound, that compound is sparingly soluble if a solubility product can be calculated for that compound and that compound yields a small amount of the available form by dissolution (OECD TG 29, para. 3(2)). In general, the solubility product of a compound is the product of molar concentrations of ions raised to the power of their respective stoichiometric coefficients in the equilibrium reaction.

29 The Substance does not contain carbon and is thus an inorganic metal compound.

30 In the provided OECD TG 105 studies (2018a, 2018b, 2018c, 2010), the water solubility of the Substance is $3.89*10^{-5}$ in mol/L, this amount is the available form and is significantly lower than the undissolved metal compound (around 100 times lower in the preliminary test). The solubility product of the Substance can be calculated and is $9.6*10^{-21}$. Therefore, the Substance is considered a sparingly soluble metal compound and information on transformation/dissolution in aqueous media is required.

1.2. Information requirement not fulfilled

31 You have provided water solubility studies according to OECD TG 105, but no information on the transformation/dissolution in aqueous media of the Substance.

32 In the absence of information on transformation/dissolution in aqueous media, the information requirement is not fulfilled.

33 In the comments to the draft decision, you agree to perform the requested study.

1.3. Study design and test specifications

34 Guidance on IRs and CSA, Section R.7.1.7.3. specifies that, for metals or sparingly soluble metal compounds, water solubility must be determined according to the OECD GD 29 Transformation/Dissolution of metals and metal compounds in aqueous media.

35 Depending on the results obtained with the screening test, i.e. if dissolution is < acute $ERV_{metal\ ion}$, you must conduct the full test according to OECD GD 29 in order to assess appropriately the hazard of the Substance in accordance with CLP guidance Annex IV Section 5.3.

Reasons related to the information under Annex VIII of REACH

2. Short-term repeated dose toxicity (28 days)

36 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1.

2.1. Information provided in your registration dossier

37 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) a chronic toxicity study (1993) in rat with the source substance Manganese (II) sulfate monohydrate (CAS 10034-96-5);

(ii) a chronic toxicity study (1993) in mouse with the source substance Manganese (II) sulfate monohydrate (CAS 10034-96-5).

2.1.2. Assessment of the information provided

38 As explained under Reasons common to several requests the weight of evidence adaptation already has critical deficiencies.

39 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

40 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.1 at Annex VIII includes, at general level, information on systemic toxicity in intact, non-pregnant and young adult males and females from: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity. Information should address effects on the following physiological systems: circulatory system, digestive/excretory system, endocrine system, immune system, integumentary system, musculoskeletal system, nervous system, renal/urinary system, reproductive system, and respiratory system.

41 Both sources of information (i) and (ii) provide such information.

2.1.2.1. Reliability of the provided information

42 Information from source substance(s) can be used as part of weight of evidence adaptation if the read-across is accepted.

43 The information from (i) and (ii) with read across source substances is rejected under Reasons common to several requests. Therefore, it cannot be used as part of the weight of evidence adaptation.

2.1.3. Conclusion

44 In summary, the sources of information (i) and (ii) provide relevant information on short-term repeated dose toxicity. However, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement.

45 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for short-term repeated dose toxicity.

46 Based on the above, your adaptation is rejected.

47 Therefore, the information requirement is not fulfilled.

2.2. Information provided in your comments to the draft decision

48 In your comments to the draft decision, you indicate your intention to adapt this information requirement using Annex XI, section 1.2 (weight of evidence) and section 1.5 (grouping and read-across approach).

49 You propose to predict the properties of the Substance for short-term repeated dose toxicity study (28 days) from a source study (OECD TG 422) yet to be conducted on the analogue substance manganese bis(dihydrogen phosphate) (CAS 18718-07-5). You provide a justification document to support your planned adaptation.

2.2.1. Assessment of the information provided

50 As your strategy relies on data which is yet to be generated, no assessment or conclusions on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

2.3. Specification of the study design

51 When there is no information available neither for the 28-day repeated dose toxicity (EU B.7, OECD TG 407), 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 (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

52 The study design is addressed in request 3.

3. Screening study for reproductive/developmental toxicity

53 A screening study for reproductive/developmental toxicity (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1., if there is no evidence from analogue substances, QSAR or in vitro methods that the substance may be a developmental toxicant.

3.1. Information provided in your registration dossier

54 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on experimental data from the following substances:

(i) a chronic toxicity study (1993) in rat with the source substance Manganese (II) sulfate monohydrate (CAS 10034-96-5);

(ii) a chronic toxicity study (1993) in mouse with the source substance Manganese (II) sulfate monohydrate (CAS 10034-96-5).

3.1.2. Assessment of the information provided

55 As explained in under Reasons common to several requests the weight of evidence adaptation has critical deficiencies.

56 In addition, as explained under Reasons common to several request, the adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

57 Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.3 at Annex VIII includes similar information that is produced by the EU B.63/OECD TG 421 or EU B.64/OECD TG 422. At general level, it includes information on the following key elements: 1) sexual function and fertility, 2) toxicity to offspring, and 3) systemic toxicity.

58 Source studies (i) and (ii) contain information on systemic toxicity. They do not contain information on sexual function and fertility or toxicity to offspring as the animals were not mated.

3.1.2.1. Reliability of the provided information

59 Information from source substance(s) can be used as part of weight of evidence adaptation if the read-across is accepted.

60 The information from (i) and (ii) with read across source substances is rejected under Reasons common to several requests. Therefore, they cannot be used as part of the weight of evidence adaptation.

3.1.3. Conclusion

61 In summary, the sources of information (i) and (ii) provide relevant information on systemic toxicity, but not on sexual function and fertility or toxicity to offspring. Furthermore, these sources of information have significant reliability issues as described above and cannot contribute to the conclusion on the information requirement screening study for reproductive/developmental toxicity.

62 It is not possible to conclude, based on any source of information alone or considered together, on the information requirement for a screening study for reproductive/developmental toxicity.

63 Based on the above, your adaptation is rejected.

64 Therefore, the information requirement is not fulfilled.

3.2. Information provided in your comments to the draft decision

65 In your comments to the draft decision, you indicate your intention to adapt this information requirement using Annex XI, section 1.2 (weight of evidence) and section 1.5 (grouping and read-across approach).

66 You propose to predict the properties of the Substance for screening study for reproductive/developmental toxicity from a source study (OECD TG 422) yet to be conducted on the analogue substance manganese bis(dihydrogen phosphate) (CAS 18718-07-5). You provide a justification document to support your planned adaptation.

3.2.1. Assessment of the information provided

67 As your strategy relies on data which is yet to be generated, no assessment or conclusions on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

3.3. Specification of the study design

68 A study according to the test method EU B.64/OECD TG 422 must be performed in rats.

69 As the Substance is a solid, the study must be conducted with oral administration of the Substance (Annex VIII, Section 8.7.1, Column 1).

70 Therefore, the study must be conducted in rats with oral administration of the Substance.

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

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 16 November 2022.

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).

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 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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII 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;
- 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]

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.

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

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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 manual on How to prepare registration and PPORD dossiers (https://echa.europa.eu/manuals).