~~Confidential~~

Helsinki, 24 November 2021

Addressees
Registrant(s) of JS_IP34_242-520-2 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
16/07/2015

Registered substance subject to this decision ("the Substance")
Substance name: Manganese bis(dihydrogen phosphate)
EC number: 242-520-2
CAS number: 18718-07-5

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 ***29 August 2023***.

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

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

1. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats

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

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

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.

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, 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

For the information addressed in this decision, you did not propose read-across adaptation in your registration dossier. In your comments to the draft decision, you suggest read-across from Mn dichloride to the Substance and justify it with the following:

"*Manganese cation (Mn2+) was likely to have the greatest influence on the toxicity of manganese phosphates and as such read-across with other metal cation phosphates would not be advisable. Chloride or phosphate anions are naturally occurring components of all biological fluids and as such are not considered to have any influence on the effective toxicity of Mn2+ nor any toxicity in their own right and can be disregarded when assessing the toxicity of these materials. Any toxicological effects will be as a result of the presence of Mn2+ and therefore an assessment of the relative toxicity of soluble inorganic manganese salts with non-toxic anions can be made on the basis of data from similar substances."*

Furthermore, you claim that "*Read-across to source substances with higher water solubility are considered to enable a worst-case assumption for hazard assessment due to higher bioavailability of the manganese cation as compared to insoluble compounds*."

You also provided a comparison of physico-chemical properties of the source and target substances.

We have assessed the information and identified the following issues:

Annex XI, Section 1.5. specifies two general 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. But, secondly, it is further required that the relevant properties of a substance within the group can be predicted from data for reference substance(s) within the group. Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6. and related documents[2,3].

For the following reasons the available information does not demonstrate a possible prediction of data.

1. *Information on the formation of common compounds and impact of non-common compounds*

We understand that your read-across hypothesis is based on the transformation 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 dissociation of the Substance and of the source substances is necessary to confirm the formation of the proposed common dissociation products and to assess the impact of the exposure to the parent compounds as well as the impact of non-common dissociation products.

However, you have not provided experimental data on rate and extent of the dissociation of the Substance and of the source substance. Furthermore, you have not addressed the potential effect of the phosphate counterion on the kinetics of the manganese cation.

[2] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

[3] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

In the absence of this information, you have not provided supporting evidence establishing that the proposed common dissociation products are formed in a comparable rate as assumed in your read-across hypothesis

2. *Missing supporting information to compare toxic properties of the substances*

As indicated above, your read-across hypothesis is based on the assumption that the target and source substances dissociate to common compounds, which cause same type of effect(s). 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. Such information can be obtained, for example, from **bridging studies** of comparable design and duration for the Substance and of the source substance(s).

However, you have not provided study summaries of the experimental data on the source substance of those toxic endpoints that are addressed in the draft decision, i.e. reproductive and pre-natal developmental toxicity. Moreover, concerning the information requirements addressed in this decision, you have provided no studies on the Substance that would enable comparison with the studies made with the source substance.

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, and neither have you demonstrated that the source substance could serve as a "worst-case". Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

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

1. 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. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have not provided any study on reproductive toxicity.

You have provided the following adaptation "*Manganese bis(dihydrogen phosphate) is considered to be classified as STOT RE2 (target organ brain) in accordance with Regulation (EC) No. 1272/2008 (EU CLP) and on the basis of neurological symptoms (neurotoxicity) observed after inhalation of manganese. Neurotoxicity is considered to be the leading health effect and as such an IOELV has been proposed and adopted by the European Commission1. This value is considered to be sufficiently protective so that the required risk management measures will defend against any unidentified health risks. Further, in a 2-year carcinogenicity study of manganese sulphate, no evidence of any effects on the reproductive system was observed.*"

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

You have justified the adaptation by stating that the Substance meets the classification criteria to STOT RE 2 and that there are no effects on the reproductive system observed in a 2-year carcinogenicity study. However, this is not a valid adaptation possibility according to Annex VIII, 8.7., Column 2 or the general rules for adaptation under Annex XI.

In any case, in the carcinogenicity study you refer to, investigations for parameters for sexual function and fertility such as, those for mating and fertility/duration of gestation, parturition, lactation, oestrus cycles, duration of gestation, number and sex of pups, stillbirths and live births, gross abnormalities, pup body weight, litter weight, anogenital distance, and number of nipples/areolae in male pups have not been performed as required in EU B.63/OECD TG 421.

Based on the above, the information you provided does not fulfil the information requirement.

In your comments on the draft decision you suggest an adaptation of the information. However, as explained above in the **Appendix on Reasons common to several requests**, the information submitted does not meet the requirements for the adaptation.

Information on study design

A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats with oral[4] administration of the Substance.

[4] ECHA Guidance R.7a, Section R.7.6.2.3.2.

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

1. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

You have not provided any study on developmental toxicity.

You have provided the following adaptation "*Manganese bis(dihydrogen phosphate) is considered to be classified as STOT RE2 (target organ brain) in accordance with Regulation (EC) No. 1272/2008 (EU CLP) and on the basis of neurological symptoms (neurotoxicity) observed after inhalation of manganese. Neurotoxicity is considered to be the leading health effect and as such an IOELV has been proposed and adopted by the European Commission1. This value is considered to be sufficiently protective so that the required risk management measures will defend against any unidentified health risks. Further, in a 2-year carcinogenicity study of manganese sulphate, no evidence of any effects on the reproductive system was observed.*"

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

You have justified the adaptation by stating that the Substance meets the classification criteria to STOT RE 2 and that there is no effects on the reproductive system observed in a 2-year carcinogenicity study. However, this is not a valid adaptation possibility according to Annex IX, 8.7., Column 2 or the general rules for adaptation under Annex XI.

In any case, the carcinogenicity study you refer to, does not have a required exposure during pregnancy as provided under OECD TG 414, because the exposure duration is not from implantation until the day prior to scheduled caesarean section. Furthermore, in that study gravid uterus weight has not been measured, and uterine content has not been examined. Finally, in the study you have provided the sex and body weight of the foetuses has not been examined, external, skeletal and soft tissue alterations (variations and malformations) have not been examined, the number of resorptions and or dead foetuses have not been recorded and anogenital distance has not been measured in live foetuses as required in OECD TG 414.

Based on the above, the information you provided do not fulfil the information requirement.

In your comments on the draft decision you suggest an adaptation of the information. However, as explained above in the **Appendix on Reasons common to several requests**, the information submitted does not meet the requirements for the adaptation.

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[5] administration of the Substance.

[5] ECHA Guidance R.7a, Section R.7.6.2.3.2.

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

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[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 18 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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.