~~Confidential~~

Helsinki, 24 November 2021

Addressees
Registrant(s) of JS_Manganese_TallOilFattyAcids as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
11/02/2021

Registered substance subject to this decision ("the Substance")
Substance name: Fatty acids, tall-oil, manganese salts
EC number: 232-445-3
CAS number: 8030-70-4

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 ***2 May 2024***.

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. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471)

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 tests performed for the information requirement of Annex VII, Section 8.4.1. and 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. 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

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

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats,

2. 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:

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VII 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, VIII and IX to REACH, for registration at 100-1000 tpa.

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

1. **Assessment of the Grouping of substances and read-across approach under Annex XI, Section 1.5.**

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 gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- 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.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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.

Grouping of substances and read-across approach

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)').

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].

A. Predictions for toxicological properties

You have provided a read-across justification document in IUCLID Section 13.

You read-across between the structurally similar substances, Manganese (II) sulfate **monohydrate**, EC No. 600-072-9, (CAS No. 10034-96-5), manganese sulphate **dihydrate**, EC No. 232-089-9, (CAS No. 15244-36-7), substance Manganese sulphate **heptahydrate**, EC No. 231-298-2, (CAS No. 10034-99-8), manganese **dichloride** EC No. 231-869-6, (CAS No. 7773-01-5), and manganese **sulphate**, EC No. 232-089-9, (CAS No. 7785-87-7), as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties: *"Since read-across includes two sub-categories (sub-category 1: manganese cations and sub-category 2: tallate anions), the hypothesis is that manganese salts release manganese cations, and fatty acids, tall-oil and similar fatty acids release tallate or structurally similar anions upon dissolution in (eco-)toxicological relevant conditions. The common characteristic of the target substance and the source substances is that all substances liberate the same (eco-)toxic moiety upon dissolution in aqueous media, as shown in the figure below. The*

[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

structural similarity is based on the fact that the (eco-)toxicological units "cation" (sub-category 1) and "anion" (subcategory 2) are formed upon dissolution under toxicological relevant conditions such as body fluids and in the environment. Two chemical entities are identified, a specific metal ion and a carboxylic acid ion."

ECHA understands that 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 Substance are predicted to be quantitatively equal to those of the source substance.

ECHA notes the following shortcoming(s) with regards to prediction(s) of toxicological properties.

- *Missing supporting information*

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*"[4]. 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 toxicokinetic information on the formation of the common compound and bridging studies to compare properties of the Substance and source substances.

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

As indicated above, 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 dissolution products and to assess the impact of the exposure to the parent compounds as well as the impact of non-common dissociation products.

You claim that "*The source substances have the similar or identical chemical structure as the target substance or share the same dissolution product. Most of the source substances are also mono-constituent substances or naturally occurring substances.*"

However, you have not provided experimental data to demonstrate similarity of the dissolution rates of these substances.

According to the information in your dossier, water solubility differs for several orders of magnitude between the target and sources substances. Finally, you have not addressed the effect of the counterion, i.e. fatty acids on the uptake, bioavailability and toxicity of manganese cation.

In the absence of this information, you have not provided supporting evidence establishing that the proposed common dissolution products are formed in a comparable rate as assumed in your read-across hypothesis: neither have you addressed the potential toxicological impact

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

of the non-common dissociation products. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

In your comments to the initial draft decision, you claim that "*the effect of the fatty acid tall oil on uptake, bioavailability of manganese is considered negligible compared to manganese salts"*. However, you have not provided any data to support that assumption. Specifically, you have not provided data that demonstrates an absence of potential carrier effects by the associated counter-anion. Therefore, we consider that in order to justify read-across between organic and inorganic metal compounds, the potential difference in toxicokinetics needs to be addressed. You point out that the Substance is an "organic metal salt", which leaves open the possibility of differences in toxicokinetics between the Substance and the inorganic source substances used in the read-across approach.

You also explain that you intend to "*strengthen the read-across justification and provide bioelution data focusing on the dissolution and dissociation behaviour of the substance resulting in the formation of common compounds*". However, this data e.g. on bioelution is not provided in your comments. The provided information on stability constants does not cover the Substance. Furthermore, the method of deriving the results is unclear. Please note that in cases of *in silico* predicted results ECHA requires documentation in analogy to adaptations according to Annex XI Section 1.3 (QSAR) to independently assess the reliability.

We acknowledge your intentions to improve the (eco)toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made.

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). Due to the deficiencies identified in the previous sub-section, 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).

You have provided an in vitro gene mutation studies in bacteria, in vitro cytogenicity studies, in vitro gene mutation study in mammalian cells, two-generation reproductive toxicity studies, chronic toxicity studies and a pre-natal developmental toxicity study, as below on the source substances, while you did not provide studies on these toxic effects of 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 and of the source substance(s) to support your read-across hypothesis.

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.

3. Adequacy and reliability of source study

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

- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

Related deficiencies are addressed under the corresponding Appendix below.

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. 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.

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

1. *In vitro* gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

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:

i) Bacterial Reverse Mutation Assay, OECD Guideline 471 (supporting study), with an analogue substance, manganese sulphate monohydrate, EC No. 600-072-9, (CAS No. 10034-96-5), reliability 2, GLP not specified, performed in 1985. Marzin

ii) Bacterial Reverse Mutation Assay, OECD Guideline 471 (supporting study), with an analogue substance, manganese sulphate, EC No. 232-089-9, (CAS No. 7785-87-7), reliability 2, GLP not specified, performed in 1986. Mortelmans

iii) Bacterial Reverse Mutation Assay, OECD Guideline 471 (key study), with an analogue substance, manganese dichloride, EC No. 231-869-6, (CAS No. 7773-01-5), reliability 2, according to GLP, performed in 2009.

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

The read-across that you propose is not acceptable as explained above in **Appendix on Reasons common to several requests.** In addition, we have identified the following shortcomings:

As provided in the Appendix on reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case OECD TG 471[5] (1997). One of the key parameters of this test guideline includes:

a) Two separate test conditions must be assessed: in absence of metabolic activation and in presence of metabolic activation.
b) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)

The reported data for the study i) you have provided did not include:

a) two separate test conditions, but only in absence of metabolic activation,
b) results for the appropriate 5 strains.

The information provided in study i) does not cover these key parameters required by OECD TG 471

In addition, study ii) does not correspond the requirements of OECD TG 471, because only four strains of bacteria were included.

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

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

[5] ECHA Guidance R.7a, Table R.7.7–2, p.557

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:

i) *In vitro* Mammalian Chromosome Aberration Test, equivalent or similar with OECD Guideline 473 (supporting study), with an analogue substance manganese sulphate monohydrate, EC No. 600-072-9, (CAS No. 10034-96-5), reliability 3, GLP not specified, performed in 1993.

ii) *In vitro* Mammalian Chromosome Aberration Test, OECD Guideline 473 (key study), with an analogue substance manganese dichloride, EC No. 231-869-6, (CAS No. 7773-01-5), reliability 2, according to GLP, performed in 2009.

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

The read-across that you propose is not acceptable as explained above in **Appendix on Reasons common to several requests.**

In addition, we have identified the following shortcomings:

As provided in the Appendix on reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case OECD TG 473 or OECD TG 487[6]. The key parameter(s) of these test guidelines include:

a) The maximum concentration tested must induce 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest,
b) The response for the concurrent negative control must be inside the historical control range of the laboratory.

The reported data for the study i) you have provided did not include:

a) Information on cytotoxicity,
b) a negative control with a response inside the historical control range of the laboratory.

Therefore, the information provided does not cover key parameters required by OECD TG 473/487.

Based on the above, the information you provided 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.

[6] ECHA Guidance R.7a, Table R.7.7–2, p.557

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 an adaptation for an *in vitro* gene mutation study in bacteria, and an adaptation for an in vitro cytogenicity study in mammalian cells or *in vitro* micronucleus study.

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:

i) Mouse Lymphoma Assay, OECD Guideline 476 (key study), with an analogue substance manganese dichloride, EC No. 231-869-6, (CAS No. 7773-01-5), reliability 2, according to GLP, performed in 2009.

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

The read-across that you propose is not acceptable as explained above in **Appendix on Reasons common to several requests.**

The results of the request for information in sections A.1 and 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* gene mutation study in bacteria and the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provide 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. 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:

i) a non-guideline study, "Assessment of aggression, sexual behaviour and fertility in adult male rat following long-term ingestion of four industrial metal salts" (supporting study), made with the analogue substance manganese sulphate dihydrate, EC No. 232-089-9, (CAS No. 15244-36-7), in rats, reliability 2, performed in 1998, GLP not specified.

ii) a non-guideline study, "Short-term exposure of female rats to industrial metal salts: effect on implantation and pregnancy" (supporting study), made with the analogue

substance manganese sulphate, EC No. 232-089-9, (CAS No. 7785-87-7), in rats, reliability 4, performed in 2007, GLP not specified.

iii) a non-guideline study, "NTP technical report on the toxicology and carcinogenesis of manganese(II) sulphate monohydrate in F344/N rats and B6C3F1 mice" (key study), made with the analogue substance manganese sulphate monohydrate, EC No. 600-072-9, (CAS No. 10034-96-5), reliability 2, performed in 1993, GLP not specified.

You have provided an adaptation according to Annex XI, Section 1.5. in your dossier to fulfil the conditions of Section 8.7.1, Column 2, fourth indent. In support of your adaptation you have provided the following information:

iv) A two-generation reproductive toxicity study according to OECD TG 416 with manganese dichloride EC No. 231-869-6, (CAS No. 7773-01-5), in rats, via inhalation, reliability 2, performed in 2017, according to GLP.

v) A two-generation reproductive toxicity study according to OECD TG 416 (key study) with manganese dichloride EC No. 231-869-6, (CAS No. 7773-01-5), in rats, via inhalation, reliability 1, performed in 2016, GLP not specified.

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

The read-across that you propose is not acceptable as explained above in **Appendix on Reasons common to several requests.** In addition, the following shortcomings have been identified:

As provided in the Appendix on reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case EU B.63/OECD TG 421 or EU B.64/OECD TG 422. The key parameters of these test guidelines include for example

- Testing of at least three dose levels and a concurrent control
- Dosing of the Substance for a minimum of four weeks for males and approx. 63 days for females to cover premating, conception, pregnancy and at least 13 days of lactation
- Examination of parameters for sexual function and fertility such as /those for mating and fertility/duration of gestation, parturition, lactation and weight and histopathology of reproductive organs and tissues
- Monitoring of oestrus cycles
- Haematological examinations
- Clinical biochemistry
- Weights and histopathology of organs and tissues

The study ii) you have provided was conducted with one dose level.

In study i) females were not exposured to the test substance.

The study iii) does not have a required exposure according to OECD TG 421 because the exposure does not cover pregnancy and at least 13 days of lactation, investigations for parameters for sexual function and fertility such as those for mating and fertility, duration of gestation, parturition, and lactation have not been performed, oestrus cycles have not been monitored and investigations for duration of gestation, number and sex of pups, stillbirths and live births, gross abnormalities, pup body weight, litter weight, anogenital distance, number of nipples and areolae in male pups have not been performed.

In the study i) you have provided, haematological examinations, clinical biochemistry determinations and histopathology of organs have not been performed.

Therefore the studies do not fulfil the criteria set in EU B.63/OECD TG 421 or EU B.64/OECD TG 422.

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

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[7] administration of the Substance.

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

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

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

A Sub-chronic toxicity study (90 day) is a standard information requirement under Annex IX 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:

i.) A non-guideline study with the analogue substance Manganese sulphate, EC number: 232-089-9, (CAS number: 7785-87-7) with pigs, reliability 3, no GLP, performed in 2000

ii.) A study equivalent or similar to OECD Guideline 453, NTP technical report on the toxicology and carcinogenesis of manganese(II) sulphate monohydrate in F344/N rats and B6C3F1 mice (feed studies) with the analogue substance Manganese (II) sulfate monohydrate, EC No. 600-072-9, (CAS No. 10034-96-5) reliability 2, no GLP, performed in 1993

iii.) A study equivalent or similar to OECD Guideline 408, NTP technical report on the toxicology and carcinogenesis of manganese(II) sulphate monohydrate in F344/N rats and B6C3F1 mice (feed studies)with the analogue substance Manganese (II) sulfate monohydrate EC No. 600-072-9, (CAS No. 10034-96-5), reliability 2, no GLP, performed in 1993

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

Your read-across adaptation is not concisdered acceptable, as explained above in **Appendix on Reasons common to several requests.** In addition, the following shortcomings have been identified:

As provided in the Appendix on reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case OECD TG 408. The following key parameter(s) of this test guideline include, among others

1. At least 10 female and 10 male animals should be used at each dose level (including control group)
2. dosing of the Substance daily for a period of 90 days until the scheduled termination of the study
3. histopathology of the organs specified in OECD TG 408, recording of hematology and clinical biochemistry.

The study i) does not fulfil the criterion set in OECD TG 408, because only 5-8 animals per dose group were used, examination of histopathology, hematology and clinical biochemistry were missing. Furthermore, this study does not have the required exposure duration of 90 days as required in OECD TG 408, because you indicated an exposure duration of 5 weeks that does not fulfil the criterion set in OECD TG 408.

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

Information on the design of the study to be performed
Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the Substance is solid and according to the granulometry information it is without a significant proportion (>1% on weight basis) of particles of inhalable size.

Therefore the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) 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 provided an adaptation according to Annex XI, Section 1.5. in your dossier. In support of your adaptation you have provided the following information:

i) A non-guideline study with the analogue substance Manganese sulphate heptahydrate, EC No. 231-298-2, (CAS No. 10034-99-8) with rats, reliability 2, no GLP, performed in 1975,
ii) A non-guideline study with the analogue substance Manganese sulphate, EC No. 232-089-9, (CAS No. 7785-87-7) with mice, reliability 4, no GLP, performed in 1987,
iii) Pre-natal developmental toxicity study, according to OECD TG 414, with manganese dichloride, EC No. 231-869-6, (CAS No. 7773-01-5), reliability 2, according to GLP, in rats, performed in 2016.

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

Your read-across adaptation is not concisdered acceptable, as explained above in chapter **Appendix on Reasons common to several requests.** In addition, the following shortcomings have been identified:

As provided in the Appendix on reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case OECD TG 414. The criteria of this test guideline include e.g.

- 20 female animals with implantation sites for each test and control group
- dosing of the Substance from implantation until the day prior to scheduled caesarean section
- examination of the dams for weight and histopathology of the thyroid gland/thyroid hormone measurements/gravid uterus weight/uterine content/body weight of the dams/clinical signs of the dams

The study i) you have provided, was conducted with 10 or 11 pregnant females for each test group. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of 20 pregnant females for each test group set in OECD TG 414.

In the study ii) you have provided, the animals were exposed during GD 8, 9 or 10. The study does not have a required exposure duration because the exposure duration is not from implantation until the day prior to scheduled caesarean section as required in OECD TG 414.

In the studies i) and ii) you have provided, the weight and histopathology of the thyroid gland has not been examined in dams, thyroid hormone measurements have not been conducted in dams, gravid uterus weight has not been measured, and uterine content has not been examined as required in OECD TG 414.

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

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[8] administration of the Substance.

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

Appendix D: 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[9].

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:

a) 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

a) 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.

b) The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods,

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[10].

[9] https://echa.europa.eu/practical-guides
[10] https://echa.europa.eu/manuals

Appendix E: 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.

In your comments on the initial draft decision you requested an extension of the deadline to provide information from 24 to 29 months from the date of adoption of the decision.

The CRO that you have contacted explained that "*The test item, "fatty acids, tall-oil, manganese salts" is an inorganic, highly viscous, sticky, UVCB substance which will require extra research time to ensure that formulation analytics is robust and compliant to OECD guidelines and GLP requirements*." Furthermore, the CRO refers to their limited capacity.

ECHA took into account your comments and amended the deadline.

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 F: List of references - ECHA Guidance[11] 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)[12]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[13]

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[14]

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