~~Confidential~~

Helsinki, 24 June 2021

Addressees
Registrant(s) of Potassium Sodium Tartrate as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
30/05/2018

Registered substance subject to this decision ("the Substance")
Substance name: Potassium sodium tartrate
EC number: 206-156-8
CAS number: 304-59-6

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 in A.1., A.2., B.2., C.2. – C.6. below by ***29 September 2022*** and all other information listed below by ***2 April 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. Justification for an adaptation of short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.) based on the results of the Long-term toxicity testing on aquatic invertebrates requested below (Annex IX, Section 9.1.5.)

2. 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. 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

2. Justification for an adaptation of a Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.) based on the results of the Long-term toxicity testing on fish request below (Annex IX, Section 9.1.6.)

C. 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)

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

3. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

4. Long-term toxicity testing on terrestrial invertebrates (triggered by Annex IX, Section 9.4., column 2; test method: OECD TG 222 or 220 or 232)

5. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: EU C.21./OECD TG 216 and test method: EU C.22./ OECD TG 217)

6. Long-term toxicity to terrestrial plants (triggered by Annex IX, Section 9.4., column 2; test method: OECD TG 208 with at least six species or ISO 22030)

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". 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

0. Category and read-across proposed in the comment on the draft decision

For the aquatic toxicity and terrestrial toxicity information requirements requested in the present draft decision, in your comments you propose grouping the following substances in the "Tartaric acid and its salts" category and applying a read-across approach in accordance with Annex XI, Section 1.5 :
- tartaric acid (EC 201-766-0);
- sodium potassium tartrate (EC 206-156-8);
- potassium hydrogen tartrate (EC 212-769-1);
- dipotassium tartrate (EC 213-067-8); and
- calcium tartrate (EC 221-621-5).

You propose to report in the registration dossier results of the short-term toxicity study with aquatic invertebrates and of the growth inhibition study with aquatic plants with calcium tartrate which are available in the registration dossier of that substance.

Moreover, in your comments on the draft decision you propose to perform long-term toxicity testing on aquatic invertebrates and on fish with one of the category members, all three terrestrial toxicity tests with either sodium potassium tartrate or potassium hydrogen tartrate and to report this information in the registration dossier. You intend to use results of the long-term toxicity testing on fish as justification for an adaptation of short-term toxicity testing on fish.

ECHA considers that the proposed read-across approach for the aquatic toxicity and terrestrial toxicity information requests is plausible and could fulfil the information gaps as long as reliable studies with member(s) of the category will be reported in the registration dossier and for the aquatic and terrestrial toxicity studies the molecular weight of the counter-ion of the source substance(s) is considered:
- for the selection of the maximum test concentration, in order to ensure that the test concentration of the common tartaric acid anion relevant (i.e. expected to be present when maximum concentration of the target substance as required by the test guideline would be present in the test solution) for each of the target substance(s) (i.e. category members) has been reached in the test with the source substance(s); and
- for the estimation of aquatic and terrestrial toxicity effect concentration for the target substance(s).

The quality of the aquatic toxicity and terrestrial toxicity tests will be evaluated after the expiry of the deadline set out in the draft decision according to Article 42 of the REACH Regulation.

1. Assessment of your Weight of Evidence adaptation under Annex XI, Section 1.2.

You have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, section 1.2:

Information in your dossier
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

Annex XI adaptation in your comments on the initial draft decision

In your comments on the initial draft decision you provided the following information under your title "Comments on reproductive toxicity requests":

- "*Therefore, the Addressees invoke EFSA risk assessment as adaptation under Annex XI to claim that further toxicological testing for reproductive and developmental effects is scientifically unjustified for all the substances in the Category and ask ECHA to consider this issue. Therefore, the Addressees invoke adaptation of information requirements according to Annex XI and claim that further toxicological testing for reproductive and developmental effects is scientifically unjustified for all the substances in the Category, considering the results of the assessment performed by EFSA. The Addressees ask ECHA to consider this issue".*
- "*information requirements in this specific case can be deemed fulfilled*"; specifically you raised the following:
    - *"ADME data show lower internal exposure to tartaric acid in humans compared to rats"*
    - *"tartrate is not metabolised to oxalate"*
    - *"in available studies, no maternal or developmental effects were reported at the highest dose tested"*
    - *"according to EFSA Panel's review, no studies for reproductive toxicity were available; however, no histopathological findings were reported in testes, ovaries and uterus in various studies"*
    - *"in mice given up to 2150 mg/L (+) tartaric acid/kg bw per day by gavage for 5 days, no statistically significant differences in the frequency of 'cell aberration' in primary spermatocytes were observed in the treated groups compared to the negative control groups"*
    - *"the EFSA Panel considered that monosodium L(+)-tartrate was not carcinogenic and identified an NOAEL of 3100 mg monosodium tartrate/kg bw per day, the highest dose tested".*

Your weight of evidence adaptation raises the same decifiencies irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in the following appendices.

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

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 that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, Section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

However, for each relevant information requirement, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property.

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

The issue identified below is relevant for the information requirements in which you invoked a weight of evidence.

QSAR predictions rejected

Section 2 of the present Appendix identifies deficiencies of the information based on application of (quantitative) structure-activity relationships (QSAR) submitted under your weight of evidence adaptations.

Furthermore, in relation to information you submitted referring to risk assessment performed by EFSA, note that an EFSA finding that there is no risk incurred by the dietary exposure of consumers to a substance does not mean that an overall analysis of the intrinsic properties of the substance has taken place as required under the testing annexes of the REACH Regulation.

Besides the above common issues, your weight of evidence approach has deficiencies that that are specific for these information requirements individually. The specific deficiencies are set out under the information requirement concerned in the Appendices below.

2. Assessment of (quantitative) structure-activity relationships estimations

You have provided information based on application of (quantitative) structure-activity relationships (QSAR) as supporting studies for the following standard information requirements:

1. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
2. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

In your comments on the draft decision you have provided predictions by Organic Module Evaluation (ECHA understands by ECOSAR), Vega software and by Consensus method for the above listed aquatic toxicity information requirements. Furthermore, you have provided predictions for the long-term aquatic toxicity and for algae toxicity by Organic Module Evaluation and Vega software, and for short-term toxicity to terrestrial invertebrates by Organic Module Evaluation.

We understand that the information for human health, which you have provided in your comments on the initial draft decision, relates to the following standard information requirements:

1. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

We have evaluated the information provided and identified the following issues:

(i) Information on aquatic toxicity and terrestrial toxicity in your registration dossier and comments on the draft decision

Information generated by application of various QSARs applied by you raises the same deficiencies irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in the following appendices.

Annex XI, Section 1.3. states that results obtained from valid QSAR models may be used instead of testing when several cumulative conditions are met, in particular:

1. results are derived from a QSAR model whose scientific validity has been established;
2. the substance falls within the applicability domain of the QSAR model;
3. adequate and reliable documentation of the applied method is provided; and
4. the results are adequate for classification and labelling and/or risk assessment.

You have provided QSAR predictions by VegaNIC v.1.0.8 and by T.E.S.T. v.4.1 for the aquatic toxicity endpoints listed above in your registration dossier in order to comply with the REACH information requirements.

You have provided in the dossier documentation supporting applied models.

We have assessed this information and identified the following issues:

Applicability domain of the VegaNIC v.1.0.8 toxicity models for Daphnia and fish and adequacy for classification and labelling and/or risk assessment

ECHA Guidance R.6. explains that, in order for a QSAR result to be adequate for classification and labelling and/or risk assessment, the following conditions must be fulfilled:

- the estimate should be generated by a valid (relevant and reliable) model;
- the model should be applicable to the chemical of interest with the necessary level of reliability;
- the model endpoint should be relevant for the regulatory purpose.

The Guidance R.6 further notes that if a model is applied to a chemical outside its applicability domain, it is possible that the estimated result may be not sufficient reliable for the purpose. It is therefore important to determine the applicability of the model to the chemical of interest.

You have provided documentation of the *VegaNIC v.1.0.8 toxicity models for Daphnia and fish and documentation of the prediction by these models. However,* the compounds in the training set for both the fish and Daphnia VegaNIC v.1.0.8 toxicity models have significant differences to the predicted substance._E.g. there are no compounds which would include two carboxyl and two hydroxy functional groups, as the predicted substance or some compounds have elements (e.g. nitrogen, phosphorus) and functional groups (e.g. ester) which are not present in the structure of the predicted substance. Furthermore, the document provided for the fish model states: "*only moderately similar compounds with known experimental value in the training set have been found*".

You have not explained why the predicted substance would be within the applicability domain of the VegaNIC v.1.0.8 toxicity models for Daphnia and fish, and why the prediction can be considered adequate for the regulatory purpose, i.e. classification and labelling and/or risk assessment, despite the issue noted.

In absence of such information, you have not established that the model can be used to meet the above listed information requirements.

Inadequate documentation of the model (QMRF) for T.E.S.T. v.4.1

Under Appendix C of the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) and ECHA Guidance R.6.1.6.3., adequate and reliable documentation must include a (Q)SAR Model Reporting Format document (QMRF) which reports, among others, the following information:

- the predicted endpoint, including information on experimental protocol and data quality for the data used to develop the model;
- an unambiguous definition of the algorithm, the descriptor(s) of the model and its applicability domain,
- an estimate of the goodness-of-fit and of the predictivity of the model, including information on training set and validation statistics.

You have provided in the dossier document describing the toxicity models for Daphnia and fish applied without a definition of the applicability domain.

In absence of such information, ECHA cannot establish that the model can be used to meet above listed information requirements.

Inadequate documentation of the prediction (QPRF) for T.E.S.T. v.4.1

ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the model prediction(s), including the endpoint,
- a precise identification of the substance modelled,
- the relationship between the modelled substance and the defined applicability domain,
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You have provided in the dossier a QPRF document providing description of predictions of toxicity for Daphnia and fish without information about the relationship between the modelled substance and the defined applicability domain.

In absence of such information, ECHA cannot establish that the prediction can be used to meet above listed information requirement.

Lack of documentation of the model and of the prediction

Under Appendix C of the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) and ECHA Guidance R.6.1.6.3., adequate and reliable documentation must include a (Q)SAR Model Reporting Format document (QMRF) which reports, among others, the following information:

- the predicted endpoint, including information on experimental protocol and data quality for the data used to develop the model;
- an unambiguous definition of the algorithm, the descriptor(s) of the model and its applicability domain,
- an estimate of the goodness-of-fit and of the predictivity of the model, including information on training set and validation statistics.

Furthermore, ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the model prediction(s), including the endpoint,
- a precise identification of the substance modelled,
- the relationship between the modelled substance and the defined applicability domain,
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You have not included QMRFs and a QPRFs for the aquatic and terrestrial toxicity predictions by Organic Module Evaluation and Consensus method provided in your comments on the draft decision.

In absence of such information, ECHA cannot establish that the prediction can be used to meet these information requirements.

(ii) Adequacy of predictions for the purpose of risk assessment and/or classification and labelling

Under ECHA Guidance R.6.1.3.4 a prediction is adequate for the purpose of classification and labelling and/or risk assessment when the model is applicable to the chemical of interest with the necessary level of reliability. ECHA Guidance R.6.1.5.3. specifies that, among others, the following cumulative conditions must be met:

- the model predicts well substances that are similar to the substance of interest, and
- reliable input parameters are used, and
- the prediction is consistent with information available for other related endpoint(s).

In your comments on the draft decision you provided predictions by Vega software for the aquatic toxicity.

Based on the models' reports provided in your comments, these predictions for the Substance used as input are uncertain. More specifically, in the reports of the specific aquatic toxicity models provided in your comments the following issues are noted:

1) "*only moderately similar compounds*" in the training set have been found;

2) "*some similar molecules found […] have experimental values that disagree with the predicted value*";

3) the Substance cannot be classified according to the rules implemented in the model, so "*it is not possible to perform an assessment*";

4) the Substance could be out of the applicability domain of the model;

5) "*the maximum error in prediction of similar molecules[…] has a moderate value*";

6) the Substance is out of the applicability domain of the model;

7) "*no similar compounds*" in the training set have been found;

The following issues cause prediction(s) by the specific model to be uncertain:

- MOA toxicity classification by EPA T.E.S.T. 1.0.0: issues 1 and 2;

- Verhaar classification by TOXTREE 1.0.0: issue 3;
- Fish acute classification by SarPy/IRFMN 1.0.2: issue 1;
- Fish Acute Toxicity by KNN/Read-Across 1.0.0: issues 4 and 5;
- Fish Acute Toxicity by NIC 1.0.0: issues 1, 2 and 4;
- Fish Acute Toxicity by IRFMN 1.0.0: issues 1, 2 and 6;
- Fish Acute Toxicity by IRFMN/Combase 1.0.0: issues 1, 4 and 5 etc.;
- Fish Chronic Toxicity by IRFMN 1.0.0: issues 6 and 7 etc.;
- Fish (Fathead Minnow) Acute Toxicity by EPA 1.0.7: issues 1 and 4;
- Fish (Fathead Minnow) Acute Toxicity by KNN/IRFMN 1.1.0: the Substance has both, (double) carboxyl acid and (double) alcohol functional groups with no other functional groups present in the molecule, while the training set contains acids (without alcohols), alcohol (without acids), ester, and alcohols with ester functional group; thus, ECHA considers that there is a lack of sufficiently similar substances in the training set;
- Aquatic invertebrates (*Daphnia magna*) Acute Toxicity by EPA 1.0.7: issues 1 and 6 etc.;
- Aquatic invertebrates (*Daphnia magna*) Acute Toxicity by Demetra 1.0.4: issue 4;
- Aquatic invertebrates (*Daphnia magna*) Acute Toxicity by IRFMN 1.0.0: issues 1 and 4;
- *Daphnia magna* Acute Toxicity model: issues 1 and 6 etc.;
- Aquatic invertebrates (*Daphnia magna*) Chronic Toxicity by IRFMN 1.0.0: issues 1 and 4;
- Algae Acute Toxicity by IRFMN 1.0.0: issues 1 and 4;
- Algae Acute Toxicity by ProtoQSAR/Combase: issues 1 and 4;
- Algae Chronic Toxicity by IRFMN 1.0.0: issues 1, 2 and 4;
- Algae Classification Toxicity by ProtoQSAR/Combase: issue 1.

Furthermore, some of used models provide only qualitative information (e.g. MOA toxicity classification by EPA T.E.S.T. 1.0.0, Verhaar classification by TOXTREE 1.0.0, Algae Classification Toxicity by ProtoQSAR/Combase) and thus does not serve the purpose of filling data gap for an information requirement.

Finally, quantitative predictions of short-term effect concentration for fish by various models significantly differ (e.g. LC50 of 9.3 mg/l by NIC 1.0.0 and of 534.54 mg/l by IRFM/Combase 1.0.0). You have not further explained which value of short-term effect concentration for fish should be used for the purpose of classification and labelling and/or risk assessment.

Therefore, you have not demonstrated that the prediction for the Substance is adequate for the purpose of classification and labelling and/or risk assessment.

(iii) Information for human health in your comments on the initial draft decision

In your comments you do not refer to QSAR adaptations for human health. However, you provided documentation using VEGA reports on:

i. Developmental Toxicity model (CAESAR) 2.1.7
ii. Developmental/ Reproductive Toxicity library (PG) 1.1.0
iii. Estrogen Receptor Relative Binding Affinity model (IRFMN) 1.0.1
iv. Estrogen Receptor-mediated effect (IRFMN/CERAPP) 1.0.0
v. Androgen Receptor-mediated effect (IRFMN/COMPARA) 1.0.0
vi. Thyroid Receptor Alpha effect (NRMEA) 1.0.0, and
vii. Thyroid Receptor Beta effect (NRMEA) 1.0.0.

We have assessed the information provided and identified the following deficiencies:

Modelled endpoint not well defined

Under ECHA Guidance R.6.1.3., a (Q)SAR model must fulfil the principles described in the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) to be considered scientifically valid. The first OECD principle requires the endpoint of a (Q)SAR model to be well defined. ECHA Guidance R.6.5.1.2 specifies that for a well-defined endpoint:

- the training set must be obtained from experimental data generated with homogeneous experimental protocols, and

- the effect modelled being predicted by the (Q)SAR must be the same as the effect measured by a defined test protocol relevant to the information requirement, which in this case includes OECD TG 414 and 421/422.

You specify that the effect that is modelled is: (i-ii)developmental toxicity, (iii-iv) estrogen receptor related effects, (v) androgen receptor related effects, and (vi) receptor related effects.

It is not clear and it cannot be excluded that the endpoints predicted by the (Q)SAR are not the same as the endpoints measured by the relevant test protocols and the training set data is not from homogeneous test protocols.

More specifically,

- There is lack of specific information on the endpoints.
- There are no experimental data, or when there are experimental data it is aggregated and sources of original (raw) data are not available.
- Species and test protocols are not specified.
- Details on test results are missing.
- The model is based on qualitative data and thus does not serve the purpose of filling data gap for an information requirement.

Therefore the endpoint of the model is not well defined and you have not established that the use of this model is a scientifically valid approach to meet these information requirements.

Conclusion

Consequently, ECHA cannot verify and/or confirm that the cumulative conditions of Annex XI, Section 1.3 listed above are met for the provided QSAR predictions. Therefore, you have not demonstrated the reliability of the provided information and this information is rejected.

3. Assessment of your adaptation for effects on terrestrial organisms

You have provided the same Annex IX, Section 9.4., Column 2 adaptation for the following standard information requirements:

1. Long-term toxicity testing on terrestrial invertebrates (triggered by Annex IX, Section 9.4., column 2)
2. Effects on soil micro-organisms (Annex IX, Section 9.4.2)
3. Long-term toxicity to terrestrial plants (triggered by Annex IX, Section 9.4., column 2)

You based your adaptation on the reason that direct and indirect exposure of the soil compartment is unlikely. You provided the following justification of the adaptation: "*According to column 2 of REACH Annex IX, the study does not need to be conducted since the exposure to tartaric acid and its salts of the soil compartment is unlikely. Indeed, these substances have a low potential for adsorption (i.e. these substances have a low octanol water partition coefficient).*"

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

According to Annex IX, Section 9.4., Column 2 soil toxicity testing does not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.

Regarding direct and indirect exposure of the soil compartment:
In the registration dossier you identify professional use of the substance in the sector of use SU1: Agriculture, forestry and fishing. Furthermore, you identify professional use of the Substance in construction industry and consumer use of the Substance, both with widespread outdoor applications (e.g. non-industrial spaying for professionals). These indicate that the direct/indirect exposure of the soil is likely. Moreover, there is no exposure potential assessment and/or information on controls of exposure by the Substance provided in the CSR which would support your claim that direct and indirect exposure of the soil compartment is unlikely.

Thus, your adaptation is rejected.

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

1. Justification for an adaptation of short-term toxicity testing on aquatic invertebrates based on the results of the Long-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 adapted this information requirement by using a WoE adaptation in accordance with Annex XI, section 1.2.

You have provided the following information:

i. OECD TG 202 study with the analogue substance tartaric acid (EC 201-766-0).
ii. Study similar to OECD TG 202 with with the analogue substance tartaric acid (EC 201-766-0).
iii. Prediction of effect concentration to daphnids by VegaNIC v.1.0.8.
iv. Prediction of effect concentration to daphnids by T.E.S.T. v.4.1.

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

As explained under Appendix on Reasons common to several requests, Section 1, the weight of evidence 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.

To fulfil the information requirement, normally a study performed according to OECD TG 202 must be provided. OECD TG 202 requires the study to investigate the following key investigation:

- the concentration of the test material leading to the immobilisation of 50% of daphnids at the end of the test is estimated.

Coverage of key investigations

All provided sources of information may provide information on the immobilization of daphnids.

However, the reliability of these sources of information is significantly affected by the deficiencies identified under Appendix on Reasons common to several requests, Section 1.

In addition, the reliability of these sources of information is significantly affected by the following deficiencies:

Reliability of the experimental studies i. and ii. listed above

To fulfil the information requirement, normally a study according to OECD TG 202 must be provided. The specifications of this test include:

- the test duration is 48 hours or longer;
- the concentrations of the test material are measured at least at the highest and lowest test concentration, at the beginning and end of the test;
- the effect values can only be based on nominal or measured initial concentration if the

concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also ECHA Guidance R.7b, Section R.7.8.4.1);
- the test design (*e.g.* static or semi-static test, number of replicates) and the test procedure (*e.g.* composition of the test medium, loading in number of *Daphnia* per test vessel) are reported.

Your registration dossier provides the following information for the experimental studies i. and ii:
- the test duration was 24 hours for the study i. and 32 hours for the study ii.;
- no information about analytical monitoring of exposure concentrations throughout the test duration for the study i. and no analytical monitoring of exposure concentrations was conducted in the study ii.;
- information on the test design and procedure is missing from the registration dossier for the study i.

Based on the above, the listed above specifications are not met for neither of the provided experimental studies. Thus, there are critical methodological deficiencies significantly affecting their reliability.

As a conclusion, sources of information as indicated above, provide information on the immobilization of daphnids, but provided information is not reliable.

Based on the assessment above, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 202 study. Therefore, your adaptation is rejected.

In your comments on the draft decision, you provided study report for the hydrolysis study and for the short-term toxicity testing with invertebrates study with analogue substance tartaric acid (EC 201-766-0) which was not provided in the registration dossier. However, information neither on the analytical method nor on the results of the analytical determination of exposure concentrations throughout the test duration is reported in the study report. This is necessary to confirm that the concentration of the Substance being tested has been satisfactorily maintained and the effect concentrations can be based on nominal concentrations. It should be noted that hydrolysis is not the only possible mechanism of the losses of substances from the test solutions as well as the concentration of a substance in the prepared initial solution might differ from the expected nominal concentration. As the analytical determination of exposure concentrations throughout the test duration was not performed in the study, there are critical methodological deficiencies resulting in the rejection of the study results.

As explained above under Appendix on Reasons common to several requests provided information (in the registration dossier and in your comments on the draft decision) based on application of QSAR is rejected.

Therefore, the information requirement is not fulfilled.

The present decision requests the registrant(s) concerned to conduct and submit a long-term toxicity study on aquatic invertebrates (OECD TG 211; see Appendix C.2 for details). According Annex VII, Section 9.1.1., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study on aquatic invertebrates does not need to be provided.

Because you still must comply with the information requirement in Annex VII, Section 9.1.1., you are requested to submit a justification for the adaptation provided in Annex VII, Section 9.1.1., Column 2, second indent.

There is a parallel dossier evaluation process to request the joint submission registrants concerned to generate and submit a long-term toxicity study on aquatic invertebrates. Unnecessary animal testing must be avoided. Therefore, to fulfil the information requirement covered by this endpoint, a justification for an adaptation based on column 2 of the present information requirement should be considered instead of the standard test.

As explained in the Appendix on Reasons common to several requests, section 0 in your comments on the draft decision you propose grouping of the listed substances in the "Tartaric acid and its salts" category and applying a read-across approach in accordance with Annex XI, Section 1.5. You propose to report in the registration dossier results of the short-term toxicity study with aquatic invertebrates with calcium tartrate which is available in the registration dossier of calcium tartrate.

ECHA considers that the proposed read-across approach is plausible and could fulfil the information gap as long as you comply with the conditions specified in the Appendix on Reasons common to several requests, section 0 about reporting of reliable source study(-ies), selection of the maximum test concentration and estimation of effect concentration(s) for the target substance(s).

As the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

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 adapted this information requirement by using a WoE adaptation in accordance with Annex XI, section 1.2.

You have provided the following information:

i. Experimental study where "*tartaric acid solution was used as solvent and it was tested to assess its toxicity (negative control). A concentration of 0.06% tartaric acid was resulted in no or little growth inhibition among all the strains tested: the highest value for inhibition was 11.3% for I. galbana."*.

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

As explained under Appendix on Reasons common to several requests, Section 1, the weight of evidence 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.

You have provided information from the single source in the registration dossier. However, information from a single source alone is insufficient to support weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property.

In spite of these critical deficiencies, ECHA has nevertheless assessed the reliability and relevance of the source of information provided.

To fulfil the information requirement, normally a study performed according to OECD TG 201 must be provided. OECD TG 201 requires the study to investigate the following key investigation:

- the concentrations of the test material leading to a 50 % and 0% (or 10%) inhibition of growth at the end of the test are estimated.

Coverage of key investigations

The provided source of information may provide information on the inhibition of growth of algae.

However, the reliability of this source of information is significantly affected by the following deficiencies:

Reliability of experimental study

To fulfil the information requirement, normally a study according to OECD TG 201 must be provided. The specifications of this test include:

- the concentrations of the test material are measured at least at the beginning and end of the test:
  1) at the highest, and
  2) at the lowest test concentration, and
  3) at a concentration around the expected EC_{50}.
- the results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within 20 % of the nominal or measured initial concentration throughout the test;
- information on the test design (e.g., number of replicates etc.), test conditions (e.g., biomass density at the beginning of the test) and biological results are reported.

Your registration dossier indicates that no analytical monitoring of exposure concentrations throughout the test duration was conducted and does not provide information on the test design (e.g., number of replicates etc.), test conditions (e.g., biomass density at the beginning of the test) and biological results for the provided study.

Based on the above, the listed above specifications are not met for the provided experimental study. Thus, there are critical methodological deficiencies significantly affecting its reliability.

As a conclusion, source of information as indicated above, provide information on the inhibition of growth of algae, but information provided is not reliable.

Based on the assessment above, it is not possible to conclude, based on the source of information alone, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 201 study. Therefore, your adaptation is rejected.

In your comments on the draft decision, you provided study report for the hydrolysis study and for the algae growth inhibition study with analogue substance tartaric acid (EC 201-766-0) which was not provided in the registration dossier. However, information neither on the analytical method nor on the results of the analytical determination of exposure concentrations throughout the test duration is reported in the study report. This is necessary to confirm that the concentration of the Substance being tested has been satisfactorily

maintained and the effect concentrations can be based on nominal concentrations. As noted above, hydrolysis is not the only possible mechanism of the loss of substances from the test solutions as well as the concentration of a substance in the prepared initial solution might differ from the expected nominal concentration. Furthermore, data on the algal biomass determined daily for each treatment group and control are not reported and therefore, it is not possible to independently assess if validity criteria of OECD TG 201 are met. Thus, there are critical methodological deficiencies resulting in the rejection of the study results.

As explained above under Appendix on Reasons common to several requests provided information in your comments on the draft decision based on application of QSAR is rejected.

Therefore, the information requirement is not fulfilled.

As explained in the Appendix on Reasons common to several requests, section 0 in your comments on the draft decision you propose grouping of listed there substances in the "Tartaric acid and its salts" category and applying a read-across approach in accordance with Annex XI, Section 1.5. You propose to report in the registration dossier results of the Growth inhibition study aquatic plants with calcium tartrate which is available in the registration dossier of calcium tartrate.

ECHA considers that the proposed read-across approach is plausible and could fulfil the information gap as long as you comply with the conditions specified in the Appendix on Reasons common to several requests, section 0 about reporting of reliable source study(-ies), selection of the maximum test concentration and estimation of effect concentration(s) for the target substance(s).

As the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

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

1. Screening for reproductive/developmental toxicity

Screening for reproductive/developmental toxicity is a standard information requirement under Annex VIII to REACH. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII or a general adaptation rule under Annex XI.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence).

In support of your adaptation, you have provided the following study records:

(i) Four teratology studies (similar to OECD TG 414) performed with an analogue substance (tartaric acid, EC no 201-766-0) in rats, rabbits, mice and hamsters at doses < 300 mg/kg bw/day (1973)

(ii) One 150-day study performed with an analogue substance (sodium tartrate) in rabbits (1963) at a concentration of 7.7% in diet.

In your comments on the initial draft decision you provided

(iii) complementing information for your adaptation according to Annex XI, Section 1.2 (Weight of evidence);

(iv) (quantitative) structure-activity relationships estimations (Annex XI, Section 1.3)

We have assessed this information and identified the following issues:

Weight of evidence

As explained under Appendix on Reasons common to several requests, the weight of evidence 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.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.1 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.

Sexual function and fertility

Sexual function and fertility on both sexes must include information on mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, organ weights and histopathology of reproductive organs and tissues, litter sizes, nursing performance and other potential aspects of sexual function and fertility.

The sources of information (i) provide information on maintenance of pregnancy and litter sizes. However, they do not inform on mating, fertility, parturition, lactation, organ weights and histopathology of reproductive organs and tissues, or nursing performance.

The source of information (ii) provides information on organ weights and histopathology of testes.

The sources of information (i-ii) provide some relevant information on several aspects of the sexual function and fertility, but not on all aspects that have to be covered, as defined above.

The EFSA report, which you refer to in your comments (iii) and consider as a key source of information, describes the sources of information (i-ii). The additional repeated dose studies included in the EFSA report provide relevant information on organ weights and histopathology of reproductive organs in both sexes.

Furthermore, as explained in the Appendix on Reasons common to several requests (Section 1), an EFSA finding is limited to the evaluation of risk incurred by the dietary exposure to a substance and does mean that the evaluated substance has been subject to an overall analysis of the intrinsic properties of the substance as required by the testing annexes under the REACH Regulation.

The other arguments you raised in your comments (see the Appendix on Reasons common to several requests (Section 1)), do not provide relevant information on sexual function and fertility.

The reliability of the sources of information (i-ii) is significantly affected by the following deficiency:

To be considered compliant and to generate information concerning the effects of the Substance on male and female reproductive performance, the study has to meet the requirements of EU B.63/OECD TG 421 or EU B.64/OECD TG 422. The criteria of this test guideline specify for example that the highest dose level should aim to induce toxic effects.

The highest dose level in the sources of information (i and ii) did not induce any toxicity and you have not shown that the aim was to induce toxicity. Neither did they reach the limit dose level of 1000 mg/kg bw/day. Therefore, the dose level selection was too low, and the studies do not fulfil the criterion set in EU B.63/OECD TG 421 or EU B.64/OECD TG 422.

In conclusion, there are no reliable sources of information for sexual function and fertility.

Toxicity to offspring

Information on pre- and perinatal developmental toxicity reflected by litter sizes, postimplantation loss (resorptions and dead foetuses), stillborns, and external malformations, postnatal developmental toxicity reflected by survival, clinical signs and body weights of the pups (or litters), and other potential aspects related to pre-, peri- and postnatal developmental toxicity observed up to postnatal day 13.

The sources of information (i) provide information on pre-natal developmental toxicity (litter sizes, postimplantation loss) but not on peri- and postnatal toxicity up to postnatal day 13 (postnatal litter sizes, survival, stillborns, clinical signs and body weights of pups). The source of information (ii) and the EFSA report do not provide any information of toxicity to offspring.

Therefore, there is lack of significant amount of information on various aspects of toxicity to offspring similar to foreseen to be investigated in an EU B.63/OECD TG 421. Furthermore, as indicated above under sexual function and fertility, the sources (i) providing relevant information, are not reliable.

Systemic toxicity

Information on systemic toxicity include information on clinical signs with specific observations, survival, body weights, food consumption, haematology, clinical biochemistry, organ weights and histopathology of non-reproductive organs and other potential aspects of systemic toxicity in the parental generation up to postnatal day 13.

The sources of information (i and ii) and the repeated dose studies included in the EFSA report provide some information on systemic toxicity.

However, information on the following aspects are missing: haematology, clinical biochemistry, and maternal toxicity during lactational period. Furthermore, the arguments provided in your comments ("*ADME data show lower internal exposure to tartaric acid in humans compared to rats" and "tartrate is not metabolised to oxalate"*) do not bring proof on lack of systemic effects.

Therefore, there is lack of information on some aspects of systemic toxicity foreseen to be investigated in an EU B.63/OECD TG 421. Furthermore, as indicated above under sexual function and fertility, the sources (i and ii) providing relevant information, are not reliable.

Conclusion on weight of evidence

It is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in EU B.63/OECD TG 421 or EU B.64/OECD TG 422. Therefore, your adaptation is rejected.

b) Predictions by application of (quantitative) structure-activity relationships

As explained above under Appendix on Reasons common to several requests, the information provided in your comments on the draft decision, based on application of QSAR, is rejected.

Conclusion

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[2] administration of the Substance.

There is a parallel dossier evaluation process to request the joint submission registrants concerned to generate and submit an extended one-generation reproductive toxicity study (EOGRTS). Unnecessary animal testing must be avoided. Therefore, to fulfil the information requirement covered by this endpoint, a justification for an adaptation based on column 2 of the present information requirement should be considered instead of the standard test.

In your comments on the initial draft decision you propose that, if your weight of evidence adaptation is not accepted by ECHA, the studies requested in this decision are performed using the Substance or one of the members of the Category "Tartaric acid and its salts" [i.e. tartaric acid (EC 201-766-0), sodium potassium tartrate (EC 206-156-8), potassium hydrogen tartrate (EC 212-769-1), dipotassium tartrate (EC 213-067-8), and calcium tartrate (EC 221-621-5)]. You "*request ECHA to formally accept at Decision stage [..] that the studies will be performed with one substance representative of the Category (source substance) and used for all the members of the Category (target substances)*".

ECHA considers the proposed read-across approach plausible and could fulfil the information gaps. However, it is in your discretion to generate and provide the necessary supporting information in order to justify your proposed read-across adaptation to fulfil the information

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

requirement in accordance with the requirements of Section 1.5 of Annex XI to REACH.

2. Justification for an adaptation of a Short-term toxicity testing on fish based on the results of the Long-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 adapted this information requirement by using a WoE adaptation in accordance with Annex XI, section 1.2.

You have provided the following information:

i. Prediction of effect concentration to fish by VegaNIC v.1.0.8.
ii. Prediction of effect concentration to fish by T.E.S.T. v.4.1.

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

As explained under Appendix on Reasons common to several requests, Section 1, the weight of evidence 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.

To fulfil the information requirement, normally a study performed according to OECD TG 203 must be provided. OECD TG 203 requires the study to investigate the following key investigation:

- the concentration of the test material leading to the mortality of 50% of the juvenile fish at the end of the test is estimated.

Coverage of key investigations

All provided sources of information may provide information on the mortality of fish.

However, the reliability of these sources of information is significantly affected by the deficiencies identified under Appendix on Reasons common to several requests, Section 1.

As a conclusion, sources of information as indicated above, provide information on the mortality of fish, but provided information is not reliable.

Based on the assessment above, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated in an OECD TG 203 study. Therefore, your adaptation is rejected.

As explained above under Appendix on Reasons common to several requests provided information in your comments on the draft decision based on application of QSAR is rejected.

In your comments on the draft decision, you provided study report for the hydrolysis study and for the short-term toxicity testing with fish study with analogue substance tartaric acid (EC 201-766-0) which was not provided in the registration dossier. Study report of the short-term toxicity testing with fish provides information on mortalities and sub-lethal effects, a number of test animals per test concentration/control and fish loading. However, information neither on the analytical method nor on the results of the analytical determination of exposure

concentrations throughout the test duration is reported. This is necessary to confirm that the concentration of the Substance being tested has been satisfactorily maintained and the effect concentrations can be based on nominal concentrations. As noted above, hydrolysis is not the only possible mechanism of the loss of substances from the test solutions as well as the concentration of a substance in the prepared initial solution might differ from the expected nominal concentration. Furthermore, study report notes that '*tests were performed at test substance concentrations of 10 mg/l, 5 mg/l, 2.5 mg/l, 1 mg/l and 0.5 mg/l*", i.e. last specification of OECD TG 203 noted above is not fulfilled. Thus, there are critical methodological deficiencies resulting in the rejection of the study results.

Therefore, the information requirement is not fulfilled.

The present decision requests the registrants concerned to conduct and submit a long-term toxicity study on fish (OECD TG 210; see Appendix C.3 for details). According Annex VIII, Section 9.1.3., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study on fish does not need to be provided.

Because you still must comply with the information requirement in Annex VIII, Section 9.1.3., you are requested to submit a justification for the adaptation provided in Annex VIII, Section 9.1.3., Column 2, second indent.

There is a parallel dossier evaluation process to request the joint submission registrants concerned to generate and submit a long-term toxicity study on fish. Unnecessary animal testing must be avoided. Therefore, to fulfil the information requirement covered by this endpoint, a justification for an adaptation based on column 2 of the present information requirement should be considered instead of the standard test.

As explained in the Appendix on Reasons common to several requests, section 0 in your comments on the draft decision you propose grouping of listed there substances in the "Tartaric acid and its salts" category and applying a read-across approach in accordance with Annex XI, Section 1.5. You propose to perform long-term toxicity testing on fish with one of the category members and to report this information in the registration dossier. You intend to use results of the long-term toxicity testing on fish as justification for an adaptation of the short-term toxicity testing on fish.

ECHA considers that the proposed read-across approach is plausible and could fulfil the information gap as long as you comply with the conditions specified in the Appendix on Reasons common to several requests, section 0 about reporting of reliable source study(-ies), selection of the maximum test concentration and estimation of effect concentration(s) for the target substance(s).

As the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

Appendix C: 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 (Section 8.7.2.) to REACH.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence).

In support of your adaptation, you have provided the following study records in your dossier:

(i) Four teratology studies (similar to OECD TG 414) performed with an analogue substance (tartaric acid, EC no 201-766-0) in rats, rabbits, mice and hamsters at doses < 300 mg/kg bw/day (1973)

(ii) One study in which an analogue substance (L-tartaric acid) was injected into the air cell or yolk of chicken eggs (1973), dose 8 mg/kg.

In your comments on the initial draft decision you provided

(iii) complementing information for your adaptation according to Annex XI, Section 1.2 (Weight of evidence)

(iv) (quantitative) structure-activity relationships estimations (Annex XI, Section 1.3)

We have assessed this information and identified the following issues:

a) Weight of evidence

As explained under Appendix on Reasons common to several requests, the weight of evidence 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.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.2 at Annex IX includes similar information that is produced by the OECD TG 414 on one species. The following aspects are covered: 1) prenatal developmental toxicity, 2) maternal toxicity, and 3) maintenance of pregnancy.

Pre-natal developmental toxicity

Pre-natal developmental toxicity includes information after pre-natal exposure on embryonic/foetal survivial (number of live foetuses; number of resorptions and dead foetuses, postimplantation loss), growth (body weights and size) and structural malformations and variations (external, visceral and skeletal).

The sources of information (i and ii) provide relevant information on embryonic/foetal survival, growth and structural malformations and variations.

The EFSA report, which you refer to in your comments and consider as a key source of information, describes the sources of information (i) but does not provide further relevant information on embryonic/foetal survival, growth or structural malformations and variations.

The other arguments you raised in your comments (see the Appendix on Reasons common to several requests (Section 1.)), do not provide relevant information on embryonic/foetal survival, growth and structural malformations and variations.

The reliability of these sources of information is significantly affected by the following deficiencies:

To be considered compliant and to generate information concerning the effects of the Substance on pre-natal developmental toxicity, the study has to meet the requirements of OECD TG 414. The criteria of this test guideline specify for example that the highest dose level should aim to induce some developmental and/or maternal toxicity.

The highest dose level in the sources of information (i and ii) did not induce any developmental and/or maternal toxicity and you have not shown that the aim was to induce toxicity. Neither did they reach the limit dose level of 1000 mg/kg bw/day. Therefore, the dose level selection was too low, and the studies do not fulfil the criterion set in OECD TG 414.

Regarding the source of information (ii), the chicken eggs study, has not been accepted /validated as an international (OECD) test method to predict prenatal developmental toxicity for regulatory uses (hazard classification and risk assessment). Furthermore, it uses non-mammalian species without *in utero* development of embryos/foetuses, non-relevant route of administration (injection into the air cell or yolk), and unknown embryonic/foetal exposure period. Therefore, the limited information from the source (ii) is not reliable.

Taken together, the relevant information on prenatal developmental toxicity provided is not reliable.

Maternal toxicity

Maternal toxicity includes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in dams.

The sources of information (i) provide information on maternal toxicity. The study design of (ii) does not include maternal exposure.

However, as indicated under pre-natal developmental toxicity above, the sources of information (i) do not provide reliable information.

The EFSA report and the additional arguments in your comments do not provide further relevant information on maternal toxicity.

Maintenance of pregnancy

Maintenance of pregnancy includes information on abortions and/or early delivery as a consequence of gestational exposure and other potential aspects of maintenance of pregnancy.

The sources of information (i) provide information on maintenance of pregnancy. The study design of (ii) does not include pregnancy.

However, as indicated under prenatal developmental toxicity above, the sources of information (i) do not provide reliable information.

The EFSA report and the additional arguments in your comments do not provide further relevant information on maintenance of pregnancy.

Taken together, the sources of information (i-ii) provide relevant information on prenatal developmental toxicity, maternal toxicity, and maintenance of pregnancy. However, the provided sources of information (i-ii) are not reliable based on reasons indicated above.

Conclusion on weight of evidence

It is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in OECD TG 414. Therefore, your adaptation is rejected.

b) Predictions by application of (quantitative) structure-activity relationships

As explained above under Appendix on Reasons common to several requests, the information provided in your comments on the draft decision, based on application of QSAR, is rejected.

Conclusion

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[3] administration of the Substance.

In your comments on the initial draft decision you propose that, if your weight of evidence adaptation is not accepted by ECHA, the studies requested in this decision are performed using the Substance or one of the members of the Category "Tartaric acid and its salts" [i.e. tartaric acid (EC 201-766-0), sodium potassium tartrate (EC 206-156-8), potassium hydrogen tartrate (EC 212-769-1), dipotassium tartrate (EC 213-067-8), and calcium tartrate (EC 221-621-5)]. You "*request ECHA to formally accept at Decision stage [..] that the studies will be performed with one substance representative of the Category (source substance) and used for all the members of the Category (target substances)*".

ECHA considers the proposed read-across approach plausible and could fulfil the information gaps. However, it is in your discretion to generate and provide the necessary supporting information in order to justify your proposed read-across adaptation to fulfil the information requirement in accordance with the requirements of Section 1.5 of Annex XI to REACH.

2. Long-term toxicity testing on aquatic invertebrates

Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

You have provided the following information:

- a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification: "According to column 2 of REACH Annex IX, the study *does not need to be conducted since tartaric acid and its salts are not toxic to aquatic environment and they are all both biodegradable and non-bioaccumulable.*"

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. It must be understood as a trigger for providing further information on aquatic invertebrates if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

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

As explained above under Appendix on Reasons common to several requests provided information in your comments on the draft decision based on application of QSAR is rejected.

As explained in the Appendix on Reasons common to several requests, section 0 in your comments on the draft decision you propose grouping of listed there substances in the "Tartaric acid and its salts" category and applying a read-across approach in accordance with Annex XI, Section 1.5. You propose to perform long-term toxicity testing on aquatic invertebrates with one of the category members and to report this information in the registration dossier.

ECHA considers that the proposed read-across approach is plausible and could fulfil the information gap as long as you comply with the conditions specified in the Appendix on Reasons common to several requests, section 0 about reporting of reliable source study(-ies), selection of the maximum test concentration and estimation of effect concentration(s) for the target substance(s).

As the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

On this basis, the information requirement is not fulfilled.

3. Long-term toxicity testing on fish

Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

You have provided the following information:

- a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification: "*According to column 2 of REACH Annex IX, the study does not need to be conducted since tartaric acid and its salts are not toxic to aquatic environment and they are all both biodegradable and non-bioaccumulable.*".

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

As explained above under Appendix on Reasons common to several requests provided information in your comments on the draft decision based on application of QSAR is rejected.

As explained in the Appendix on Reasons common to several requests, section 0 in your comments on the draft decision you propose grouping of listed there substances in the "Tartaric acid and its salts" category and applying a read-across approach in accordance with Annex XI, Section 1.5. You propose to perform long-term toxicity testing on fish with one of the category members and to report this information in the registration dossier.

ECHA considers that the proposed read-across approach is plausible and could fulfil the information gap as long as you comply with the conditions specified in the Appendix on

Reasons common to several requests, section 0 about reporting of reliable source study(-ies), selection of the maximum test concentration and estimation of effect concentration(s) for the target substance(s).

As the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

4. Long-term toxicity on terrestrial invertebrates

Long-term toxicity testing on invertebrates must be considered (Annex IX, Section 9.4., Column 2) if the substance has a high potential to adsorb to soil or is very persistent.

You have adapted this information requirement according to Annex IX, Section 9.4., Column 2. You based your adaptation on the reason that direct and indirect exposure of the soil compartment is unlikely. You provided the following justification of the adaptation: "*According to column 2 of REACH Annex IX, the study does not need to be conducted since the exposure to tartaric acid and its salts of the soil compartment is unlikely. Indeed, these substances have a low potential for adsorption (i.e. these substances have a low octanol water partition coefficient).*"

We have assessed this information and identified the following issues:

a) Triggering of the long-term toxicity testing

According to ECHA Guidance R.7c, Section R.7.11.6.3. substances that are ionisable are considered highly adsorptive.

Based on the information provided in the registration dossier (the Substance is water soluble organic salt with dissociation constants reported app. 2.9-5.0) the Substance is considered to be present in the ionised form(s) at environmentally relevant pHs (4-9), i.e. considered as highly adsorptive.

Thus, the long-term toxicity testing on terrestrial organisms is required.

b) Rejection of adaptation

As explained in the Appendix on Reasons common to several requests, Section 3, your adaptation according to Annex IX, Section 9.4., Column 2 is rejected.

In your comments on the draft decision you have provided predictions for the short-term toxicity to terrestrial invertebrates by Organic Module Evaluation. Information on the short-term toxicity to terrestrial invertebrates cannot inform on the long-term toxicity to terrestial invertebrates, so is not relevant for the requested information. Furthermore, as explained above under Appendix on Reasons common to several requests provided information in your comments on the draft decision based on application of QSAR is rejected.

As explained in the Appendix on Reasons common to several requests, section 0 in your

comments on the draft decision you propose grouping of listed there substances in the "Tartaric acid and its salts" category and applying a read-across approach in accordance with Annex XI, Section 1.5. You propose to perform long-term toxicity testing with terrestrial invertebrates with either sodium potassium tartrate or potassium hydrogen tartrate and to report this information in the registration dossier.

ECHA considers that the proposed read-across approach is plausible and could fulfil the information gap as long as you comply with the conditions specified in the Appendix on Reasons common to several requests, section 0 about reporting of reliable source study(-ies), selection of the maximum test concentration and estimation of effect concentration(s) for the target substance(s).

As the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

On this basis, the information requirement is not fulfilled.

Study design

The earthworm reproduction test (OECD TG 222), Enchytraeid reproduction test (OECD TG 220), and Collembolan reproduction test (OECD TG 232) are each considered capable of generating information appropriate for the fulfilment of the information requirement for long-term toxicity testing on terrestrial invertebrates.

ECHA notes that when log Kow >5 or log Koc >4, the test OECD 232 is not appropriate as the dominant route of exposure for Collembolans is via pore water.

ECHA is not in a position to determine the most appropriate test protocol, since such determination is dependent upon species sensitivity and substance properties.

5. Effects on soil micro-organisms

Effects on soil micro-organisms is an information requirement under Annex IX to REACH (Section 9.4.2.).

You have adapted this information requirement according to Annex IX, Section 9.4., Column 2. You based your adaptation on the reason that direct and indirect exposure of the soil compartment is unlikely. You provided the following justification of the adaptation: "*According to column 2 of REACH Annex IX, the study does not need to be conducted since the exposure to tartaric acid and its salts of the soil compartment is unlikely. Indeed, these substances have a low potential for adsorption (i.e. these substances have a low octanol water partition coefficient).*"

We have assessed this information and identified the following issue:

As explained in the Appendix on Reasons common to several requests, Section 3, your adaptation according to Annex IX, Section 9.4., Column 2 is rejected.

As explained in the Appendix on Reasons common to several requests, section 0 in your comments on the draft decision you propose grouping of listed there substances in the "Tartaric acid and its salts" category and applying a read-across approach in accordance with Annex XI, Section 1.5. You propose to perform toxicity testing with soil micro-organisms with either sodium potassium tartrate or potassium hydrogen tartrate and to report this

information in the registration dossier.

ECHA considers that the proposed read-across approach is plausible and could fulfil the information gap as long as you comply with the conditions specified in the Appendix on Reasons common to several requests, section 0 about reporting of reliable source study(-ies), selection of the maximum test concentration and estimation of effect concentration(s) for the target substance(s).

As the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

On this basis, the information requirement is not fulfilled.

Study design

According to ECHA Guidance R.7c, Section R.7.11.3.1., the nitrogen transformation test is considered sufficient for most non-agrochemicals. However, as the substance has identified agrochemical uses, ECHA considers that both the nitrogen (EU C.21./OECD TG 216) and carbon transformation (EU C.22./OECD TG 217) tests should be performed simultaneously.

6. Long-term toxicity on terrestial plants

Long-term toxicity testing on plants must be considered (Section 9.4., Column 2) if the substance has a high potential to adsorb to soil or is very persistent.

You have adapted this information requirement according to Annex IX, Section 9.4., Column 2. You based your adaptation on the reason that direct and indirect exposure of the soil compartment is unlikely. You provided the following justification of the adaptation: "*According to column 2 of REACH Annex IX, the study does not need to be conducted since the exposure to tartaric acid and its salts of the soil compartment is unlikely. Indeed, these substances have a low potential for adsorption (i.e. these substances have a low octanol water partition coefficient).*"

We have assessed this information and identified the following issues:

a) Triggering of the long-term toxicity testing

As explained in the Appendix C, Section 4, the long-term toxicity testing on terrestrial organisms is required.

b) Rejection of adaptation

As explained in the Appendix on Reasons common to several requests, Section 3, your adaptations according to Annex IX, Section 9.4., Column 2 is rejected.

As explained in the Appendix on Reasons common to several requests, section 0 in your comments on the draft decision you propose grouping of listed there substances in the "Tartaric acid and its salts" category and applying a read-across approach in accordance with Annex XI, Section 1.5. You propose to perform long-term toxicity testing with terrestrial plants with either sodium potassium tartrate or potassium hydrogen tartrate and to report this information in the registration dossier.

ECHA considers that the proposed read-across approach is plausible and could fulfil the information gap as long as you comply with the conditions specified in the Appendix on Reasons common to several requests, section 0 about reporting of reliable source study(-ies),

selection of the maximum test concentration and estimation of effect concentration(s) for the target substance(s).

As the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

On this basis, the information requirement is not fulfilled.

Study design

OECD TG 208 (Terrestrial plants, growth test) considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing shall be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208 guideline. You should consider if testing on additional species is required to cover the information requirement.

Terrestrial plants, growth test (OECD TG 208 with at least six species) and Soil Quality – Biological Methods – Chronic toxicity in higher plants (ISO 22030) are each considered capable of generating information appropriate for the fulfilment of the information requirement for long-term toxicity testing on terrestrial plants.

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[4].

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 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[5].

[4] https://echa.europa.eu/practical-guides
[5] https://echa.europa.eu/manuals

Appendix E: General recommendations when conducting and reporting new tests for REACH purposes

A. Testing strategy for terrestrial toxicity testing

If results of the requested aquatic toxicity tests on fish, aquatic invertebrates and algae allow the subsequent derivation of a PNEC for aquatic organisms, you may consider the ITS as recommended in ECHA Guidance R.7c (Section R.7.11.6) and determine the need for further testing on terrestrial organisms. If you conclude that no further or only confirmatory investigation of effects on terrestrial organisms is required, you should update your technical dossier by clearly stating the reasons for adapting specific information requirements of Annex IX, Section 9.4. of the REACH Regulation.

ECHA emphasises that the intrinsic properties of soil microbial communities are not addressed through the EPM extrapolation method and therefore the potential adaptation possibility based on EPM outlined for the information requirement of Annex IX, Section 9.4. does not apply for the endpoint of Effects on soil micro-organisms.

Appendix F: 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 20 January 2020.

ECHA notified you of the draft decision and invited you to provide comments.

In your comments you asked ECHA to *"include in the final Decision a transitional period of 12 months in order to comprehensively update the dossiers, thus formally including in the dossiers data offered with these comments for satisfying ECHA requests with existing data"*.

The time necessary to perform the required tests and update the CSA/CSR is considered in the deadline(s) set in the draft decision. It is your responsibility to submit or improve adaptations to the standard information requirements covered by the requests within the above deadline(s).

You may update your dossier at any point of time and submit compliant information to fulfil the information requirements covered by the requests. ECHA will only evaluate the updated dossier after the deadline of the final decision.

ECHA took into account your comments and did not amend the request(s) or 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 G: List of references - ECHA Guidance[6] 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)[7]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[8]

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[9]

[6] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[7] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[8] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm
[9] 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 H: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]

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.