ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 21 January 2021

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

Date of submission of the dossier subject to this decision
30/07/2019

Registered substance subject to this decision ("the Substance")
Substance name: Potassium benzoate
EC number: 209-481-3
CAS number: 582-25-2

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 ***28 April 2022***.

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

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

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

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. In vivo mammalian erythrocyte micronucleus test; or In vivo mammalian bone marrow chromosomal aberration test; or In vivo mammalian alkaline comet assay (triggered by Annex VIII, Section 8.4., column 2);

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

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

4. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

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

- Appendix/Appendices entitled "Reasons to request information required under Annexes VII to VIII of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

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

1. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Section 9.1.1. of Annex VII to REACH.

You have provided a read-across adaptation using the following two studies:

- A Key study (1996) conducted according to the OECD TG 202 with an analogue substance sodium benzoate
- A supporting study (1996) conducted according to the EPA OPP 72-2 with an analogue substance potassium chloride.

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

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3). In this case, the applicable test method is OECD TG 202 which includes the following :

- The dissolved oxygen concentration at the end of the test should be ≥3 mg/l in control and test vessels,
- Analytical monitoring to verify initial concentrations and maintenance of these concentrations throughout the test as required in guideline,
- If test concentrations are not maintained within 20% of initial measured concentrations throughout testing, effect concentrations must be reported based on measured values (see ECHA Guidance R7b, section R.7.8.4.1),
- Young daphnids, aged less than 24 hours at the start of the test used.

You have provided studies showing the following:

- Dissolved oxygen is not specified for both key and supporting study,
- You indicated that the effect concentrations are based on nominal concentrations. However, for key study, analytical monitoring was not specified, and neither nominal or measured concentrations are provided. For supporting study, you did not specify the reported test concentrations as nominal or measured concentrations.
- For both studies, age of daphnid is not provided and culture condition and pre-conditioning of the test organisms are not provided.

With regards to the analytical monitoring, you did not provide any analytical monitoring of exposure concentrations and did not demonstrate that the test substance concentration during the test was maintained within the required 20% of the measured initial concentrations. Despite this, effect concentration is reported based on nominal concentration.

Therefore, the key parameters are not covered adequately and reliably for both key and supporting studies.

In the absence of adequate and reliable coverage of the key parameters of the corresponding test for the benzoate cation, your adaptation must be rejected.

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

Consequently, your adaptation is rejected.

In your comments to the draft decision, you state that you will commission a study to fulfil this information criteria if there are no suitable existing studies with the Substance or with an

analogue substance for which read-across can be justified. It is in your discretion to generate and provide the necessary supporting information in order to justify your read-across adaptation. If you do so, you are responsible for demonstrating the fulfilment of the requirements of Section 1.5 of Annex XI to REACH. If it fails and the resulting data does not support, or even contradict, your read-across hypothesis, you remain responsible for complying with this decision by the set deadline.

2. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is a standard information requirement in Section 9.1.2. of Annex VII to REACH.

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

In support of your adaptation, you have provided the following source of information:

(i) Results from experimental study on algae (OECD TG 201, 2017, GLP) conducted on an analogue substance, lithium benzoate.
(ii) Results from experimental study on algae (no guideline followed, 1980, no GLP) conducted on an analogue substance, benzoic acid.

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

Annex XI, Section 1.2 states that there may be sufficient weight of evidence 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.4.4, 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 of the information for the given regulatory information requirement. Subsequently, relevance, reliability, 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 this 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 sources of information must provide sufficient weight of evidence to conclude that the information requirement for growth inhibition study aquatic plant, as specified in the available test guideline OECD TG 201, is fulfilled by integrating and weighing the evidence, e.g. the following key investigations are covered:

- the concentration in the test substance leading to a 50 % inhibition of growth at the end of the test.

- Growth must be expressed as the logarithmic increase in biomass (average specific growth rate) during the exposure period.

ECHA has assessed to what extent the information submitted enables a conclusion of this property as investigated in the information requirement proposed to be adapted and identified the following deficiencies:

Concerning key investigations
While the sources of information (i) and (ii) provide relevant information on both key investigations, these sources of information have the following deficiencies affecting their reliability.

To comply with this information requirement, an OECD TG 201 study must fulfil the validity criteria and have adequate and reliable coverage of the key parameters of the corresponding OECD test guidelines (Article 13(3) of REACH), which include:

- The mean coefficient of variation for section-by-section specific growth rate in the control cultures not exceeding 35%
- The biomass in the control cultures should increase exponentially by a factor of at least 16 within the 72-hour test period
- The coefficient of variation of average specific growth rates during the whole test period in replicate control cultures must not exceed 7% in tests with *Desmodesmus subspicatus*, for other less frequently tested species, the value must be < 10%;
- Analytical monitoring to verify initial concentrations and maintenance of these concentrations throughout the test,
- If test concentrations are not maintained within 20% of initial measured concentrations throughout testing, effect concentrations must be reported based on measured values (see ECHA Guidance R7b, section R.7.8.4.1)
- The pH of the control medium must not increase by more than 1.5 units during the test,
- The initial biomass concentration must be compliant with the technical guideline recommendations.

The source information (i) provides some information on the analytical monitoring of the test concentrations and that measured concentrations are below limit of detection. However, the information on the limit of detection and limit of quantification are not provided in the the technical dossier. You indicate that validity criteria were fulfilled but you did not provide any information to verify them. In addition you did not report initial biomass concentration.

The source information (ii) does not specify whether the analytical monitoring of the test concentrations were performed. In addition, the result was reported as EC10 based on biomass. However, you did not specify wether reported effect concentration is based on nominal or measured concentration. Furthemore, no information on nominal and measured concentrations, as well as information in the test conditions (e.g. pH measurements and dissolved oxygen in the test solution) are provided. You did not specify weather the validity criteria were fulfilled and did not provide any raw data to verify them.

In both studies, algal biomass at the beginning and at the end of the study are not provided.

Based on above, the information provided does not demonstrate the fulfilment of the validity criteria and adequate and reliable coverage of the key parameters, and therefore are unreliable.

Taken together, the provided sources of information cannot be considered reliable due to lack of information on the essential key parameters as outlined above.

Therefore, it is not possible to conclude 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 and the information requirement is not fulfilled.

In your comments to the draft decision, you state that you will commission a study to fulfil this information criteria if there are no suitable existing studies with the Substance or with an analogue substance for which read-across can be justified. It is in your discretion to generate and provide the necessary supporting information in order to justify your read-across adaptation. If you do so, you are responsible for demonstrating the fulfilment of the requirements of Section 1.5 of Annex XI to REACH. If it fails and the resulting data does not support, or even contradict, your read-across hypothesis, you remain responsible for complying with this decision by the set deadline.

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

1. In vivo mammalian erythrocyte micronucleus test; or In vivo mammalian bone marrow chromosomal aberration test or In vivo mammalian alkaline comet assay

Under Annex VIII to REACH, the performance of an appropriate *in vivo* somatic cell genotoxicity study must be considered if there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII.

Your dossier contains a positive result for the *in vitro* cytogenicity test (OECD TG 473) which raises the concern for chromosomal aberration (experiments conducted only without metabolic activation).

Your dossier contains also a positive result for an In Vitro Sister Chromatid Exchange Assay in Mammalian Cells. The study is not relevant information for *in vitro* cytogenicity because the study does not identify agents that cause structural chromosome aberrations or detect micronuclei in the cytoplasm of interphase cells. The study has not been considered further in this evaluation.

The ECHA guidance R.*7a*[2] states that following a positive result in an *in vitro* test, "*adequately conducted somatic cell in vivo testing is required to ascertain if this potential can be expressed in vivo. In cases where it can be sufficiently deduced that a positive in vitro finding is not relevant for in vivo situations (e.g. due to the effect of the test substances on pH or cell viability, in vitro-specific metabolism: see also Section R.7.7.4.1), or where a clear threshold mechanism coming into play only at high concentrations that will not be reached in vivo has been identified (e.g. damage to non-DNA targets at high concentrations), in vivo testing will not be necessary*.".

However, no data from an *in vivo* somatic cell genotoxicity study is available in the dossier. Moreover, you did not provide any considerations explaining that the genotoxic potential of the substance cannot be expressed *in vivo*, based e.g. on lack of relevance for *in vivo* situations or the existence of threshold mechanism.

ECHA considers that an appropriate *in vivo* follow up mutagenicity study is necessary to address the concern identified *in vitro*.

In your comments to the draft decision, you state that "the biological properties of the benzoic acid its salts would be the same" and you will commission a study to fulfil this information criteria if there are no suitable existing studies with the Substance or with an analogue substance for which read-across can be justified. ECHA considers read-across between benzoic acid and simple salts (Na, K) to be plausible in principle. Nonetheless, you are responsible for demonstrating the fulfilment of the requirements of Section 1.5 of Annex XI to REACH, especially regarding the quality and documentation of the source study. You remain responsible for complying with this decision by the set deadline.

According to the ECHA Guidance Chapter R.7a[3], the mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) or the mammalian bone marrow chromosomal aberration test ("CA test", OECD TG 475) are suitable to follow-up a positive *in vitro* result on chromosomal aberration if the Substance or its metabolite(s) will reach the target tissue. Alternatively, the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) is a suitable test to

[2] ECHA Guidance R.7a, section R.7.7.6.3, p.570.
[3] ECHA Guidance Chapter R.7a, Section R.7.7.6.3

be performed. Therefore, the MN test, the CA test and the comet assay are suitable tests to follow up the chromosomal aberration concern identified for the Substance.

In case you decide to perform a MN or CA assay, according to the test method OECD TG 474 / OECD TG 475, the test must be performed in mice or rats. Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

Regarding the exposure of the target tissue, the applicable test guidelines states "If there is evidence that the test substance(s), or its metabolite(s), will not reach the target tissue, it may not be appropriate to use this test". Additionally, a negative test result can be considered reliable if "Bone marrow exposure to the test substance(s) occurred". Accordingly, if the Substance is negative in this test, but it is not possible to demonstrate that bone marrow exposure to the Substance occurred, then ECHA will consider any remaining uncertainty concerning the mutagenic potential of the Substance and whether to request any further information.

In case you decide to perform the comet assay according to the test method OECD TG 489, the test must be performed in rats. Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

Germ cells

> In case you decide to perform the comet assay, you may consider to collect the male gonadal cells collected from the seminiferous tubules (as described by e.g. O'Brien *et al.*[4]) in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells.

This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

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

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

You have adapted this information requirement according to Annex VIII, Section 8.6.1. Column 2, and Annex XI, Section 1.5. You provided the following study to support your

[4] O'Brien, J.M., Beal, M.A., Gingerich, J.D., Soper, L., Douglas, G.R., Yauk, C.L., Marchetti, F. (2014) Transgenic Rodent Assay for Quantifying Male Germ Cell Mutant Frequency. J. Vis. Exp. (90), e51576, doi:10.3791/51576

adaptation:

a) Multi-generation reproductive toxicity in rat, with analogue substance benzoic acid (EC 200-618-2). No guideline (1960)

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

As provided in Annex VIII, Section 8.6.1, Column 2, you may adapt the information requirement, provided you fulfil one of the identified criteria:

- a reliable sub-chronic toxicity study (90-day) is available

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3). In this case the study has to cover the key parameters of OECD TG 408, which include:

- testing of at least three dose levels and a concurrent control
- highest dose level should aim to induce some systemic toxicity, but not death or severe suffering
- examination of the animals for weight and histopathology (including, among others, brain heart, liver, kideney, ovaries, accessory sex organs, thymus, spleen, lymph nodes, and thyroid gland), ophthalmological examination, haematology, clinical biochemistry (including thyroid hormone measurements), urinalysis

For the provided study, you have reported that the study was conducted

- using less than three dose levels
- without inducing systemic toxicity in any dose groups
- with incomplete pathological examinations following sacrifice histopathology was performed only on males, and covering only brain, heart, liver, kidney, testis and spleen. You did not report that adrenals, thyroid, ovaries, accessory sex organs, thymus, or lymph nodes were subject to histopathological examinations.
- without haematology, clinical biochemistry, assessments of sensory reactivity or motor activity.

On this basis, you have not demonstrated that the study covered the required key parameters of OECD TG 408 and your adaptation is therefore rejected.

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

In your comments to the draft decision, you state that "the biological properties of the benzoic acid its salts would be the same" and you will commission a study to fulfil this information criteria if there are no suitable existing studies with the Substance or with an analogue substance for which read-across can be justified. ECHA considers read-across between benzoic acid and simple salts (Na, K) to be plausible in principle. Nonetheless, you are responsible for demonstrating the fulfilment of the requirements of Section 1.5 of Annex XI to REACH, especially regarding the quality and documentation of the source study. You remain responsible for complying with this decision by the set deadline.

Study design

Further information on the study design is provided under Section B.3. below.

3. Screening for reproductive/developmental toxicity

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

You have adapted this information requirement according to Annex XI 1.5 (grouping of substances and read-across) of REACH.

You have submitting the following study:

b) Multi-generation reproductive toxicity in rat, with analogue substance benzoic acid (EC 200-618-2). No guideline (1960)

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

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

In this case the study has to cover the key parameters of OECD TG 421 or 422, which include at least three dose levels, mating and fertility/duration of gestation or information on parturition, investigations for thyroid hormone assessment (P0 and F1), investigations for stillbirths and live births, gross abnormalities, anogenital distance, number of nipples, and areolae in male pups, monitoring of oestrus cycles.

The study you have provided deviated from the OECD TG 421 or 422 in that:

- it was conducted with two dose levels instead of three;
- it did not include investigations for thyroid hormone assessment (P0 and F1);
- it did not report the duration of gestation or give information on parturition;
- oestrus cycles were not monitored;
- investigations for stillbirths and live births, gross abnormalities, anogenital distance, number of nipples, and areolae in male pups were not reported.

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

In your comments to the draft decision, you state that "the biological properties of the benzoic acid its salts would be the same" and you will commission a study to fulfil this information criteria if there are no suitable existing studies with the Substance or with an analogue substance for which read-across can be justified. ECHA considers read-across between benzoic acid and simple salts (Na, K) to be plausible in principle. Nonetheless, you are responsible for demonstrating the fulfilment of the requirements of Section 1.5 of Annex XI to REACH, especially regarding the quality and documentation of the source study. You remain responsible for complying with this decision by the set deadline.

Study design

In a proposal for amendment (PfA), submitted by one of the Member States competent authorities, it was indicated that when there is no information available neither for the 28-day repeated dose toxicity endpoint (EU B.7, OECD TG 407) (as explained above under section B.2.), nor for the screening study for reproductive/ developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the

reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. Such an approach offers the possibility to avoid carrying out a 28-day study according to OECD TG 407, because the OECD TG 422 can at the same time fulfil the information requirement of REACH Annex VIII, 8.6.1 and that of REACH Annex VIII, 8.7.1.[5] ECHA agrees with this approach.

In your comments you agree with the PfA.

Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral[6] administration of the Substance.

4. Short-term toxicity testing on fish

Short-term toxicity testing on fish is a standard information requirement in Section 9.1.3 of Annex VIII to REACH.

You have provided following two studies for this endpoint.

- A Key study (1996) conducted according to the EPA OPP 72-1 with an analogue substance Benzoic acid.
- A supporting study (1996) conducted according to the EPA OPP 72-1 with an analogue substance potassium chloride.

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

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3). In this case, the applicable test method is OECD TG 203 which include the following:

- At least 7 fish must be used at each test concentrations and in the controls,
- The dissolved oxygen concentration must be at least 60 % of the air saturation value throughout the test,
- Analytical monitoring to verify initial concentrations and maintenance of these concentrations throughout the test as required in guideline,
- If test concentrations are not maintained within 20% of initial measured concentrations throughout testing, effect concentrations must be reported based on measured values (see ECHA Guidance R7b, section R.7.8.4.1),
- The test must be conducted on juveniles of similar age (or size);
- All fish must be held in the laboratory for at least 9 days before they are used for testing (including a 48 hours settling-in period and a 7 days acclimation period).

You have provided a key and supporting study showing the following:

- *Pimephales promelas* was the test organism used for both studies,
- no information on the number of fish used or size of the fish,
- no information on the conditions under which the organisms were maintained,
- no information on dissolved oxygen for the key study was provided and a single measured value (7) without any unit was provided for the supporting study,
- no information on measured concentrations and did not thus demonstrate that the concentrations were maintained throughout the study, no information on the analytical method used (including e.g. calibration, recovery and sensitivity

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

determination) and of the preparation of the test samples for analysis (including the description of filtration and/or extraction steps, if any)
- for the supporting study, effect concentrations were reported based on measured concentrations,
- no information was provided on the age and size of the fish, the pre-conditioning and conditions under which fish were hold for the key study. For supporting study, only the 16 hr of photo period was provided.

Therefore, you have not demonstrated that the key parameters are covered adequately and reliably for both key and supporting studies.

In the absence of adequate and reliable coverage of the key parameters of the corresponding test for the benzoate cation, your adaptation must be rejected.

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

Consequently, your adaptation is rejected.

In your comments to the draft decision, you state that you will commission a study to fulfil this information criteria if there are no suitable existing studies with the Substance or with an analogue substance for which read-across can be justified. It is in your discretion to generate and provide the necessary supporting information in order to justify your read-across adaptation. If you do so, you are responsible for demonstrating the fulfilment of the requirements of Section 1.5 of Annex XI to REACH. If it fails and the resulting data does not support, or even contradict, your read-across hypothesis, you remain responsible for complying with this decision by the set deadline

Appendix C: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

1. Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

2. Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[7].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[8].

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

Appendix D: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 9 July 2019.

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

ECHA took into account your comments and did not amend the request(s).

You indicate that you would like to reserve the right to request a deadline extension in order to facilitate in-vivo vertebrate testing, if needed. For the remaining part of the Dossier Evaluation decision making process, there is no further formal step for a registrant to comment on the draft decision, so your reservation is not possible.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s) and referred the modified draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

In addition, you provided comments on the draft decision. These comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-72 meeting and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix E: List of references - ECHA Guidance[9] 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)[10]

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

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

[9] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[10] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

OECD Guidance documents[11]
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.

[11] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix F: 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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

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