~~Confidential~~

Helsinki, 03 May 2022

Addressees
Registrants of JS_alpha_HCA as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
11/02/2015

Registered substance subject to this decision ("the Substance")
Substance name: Octanal, 2-(phenylmethylene)-, (2E)-
EC number: 639-566-4
CAS number: 165184-98-5

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***10 February 2025***.

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

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

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

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)

3. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301B/C/D/F or OECD TG 310)

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

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

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

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

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

4. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: EU

C.21./OECD TG 216)

5. Long-term toxicity testing on terrestrial invertebrates also requested below (triggered by Annex IX, Section 9.4.1, column 2)

6. Long-term toxicity to terrestrial plants also requested below (triggered by Annex IX, Section 9.4.3., column 2)

D. Information required from all the Registrants subject to Annex X of REACH

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

2. Long-term toxicity testing on terrestrial invertebrates (Annex X, Section 9.4.4.; test method: OECD TG 222 or 220)

3. Long-term toxicity to terrestrial plants (Annex X, Section 9.4.6.; test method: OECD TG 208 with at least six species tested 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 X 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;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

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

For certain endpoints, ECHA requests the same study from registrants at different tonnages. In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given. Only one study is to be conducted; the registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants under Article 53 of REACH.

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 Mike Rasenberg, Director of Hazard Assessment

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

Appendix on Reasons common to several requests

1. **Assessment of the weight of evidence adaptations under the requirements of 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:

- Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

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 nevertheless assessed the validity of your adaptation. Your weight of evidence approach has deficiencies that are common to all information requirements under consideration and also deficiencies that are specific for these information requirements individually.

The following deficiency is common to all information requirements for which you invoked a weight of evidence adaptation. Deficiencies specific to certain information requirements are addressed under the respective sections in the Appendices below.

- <u>Reliability of the read across approach</u>

A. Assessment of your read-across approach

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category (addressed under 'Scope of the grouping'). Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within

the group (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6 and related documents.

B. Scope of the grouping

i. Description of the grouping

In your registration dossier you have formed a group (category) of 'Cinnamyl derivatives'. You have provided a read-across justification document in IUCLID Section 13.

For the purpose of this decision, the following abbreviations are used for the group members:
[1] Cinnamaldehyde (CAS No. 104-55-2, EC No. 203-213-9);
[2] Alpha-hexyl-cinnamaldehyde (CAS No. 165184-98-5, EC No. 639-566-4);
[3] Alpha-amyl-cinnamaldehyde (CAS No. 122-40-7, EC No. 204-541-5);
[4] Cinnamic acid (CAS No. 621-82-9, EC No. 210-708-3); and
[5] Cinnamic alcohol (CAS No. 104-54-1, EC No. 203-212-3);

You provide the following reasoning for the grouping the substances:

- You claim that group members [1], [2] and [3] share structural relationships and the resulting similarities of their physico-chemical and toxicological properties. These three group members are naturally occurring and are used in foods as flavouring substances, and in fragranced consumer products (e.g. soaps and cosmetics). You state that these group members are generally recognized as safe (GRAS) as flavouring substances by the U.S. Food and Drug Administration (US FDA) and as food additives by the World Health Organization (WHO). Based on the above, you conclude that studies using group members [1], [4] and [5] are reliable to assess the toxicological profile of the Substance.
- You provide a table showing the CAS No., molecular formula, molecular weight, partition coefficient, water solubility and vapor pressure of the following group members: [1], [2], [4] and [5].

On the basis of the above, we understand that you define the structural basis for the grouping as follows: the group members share structural relationships and in turn exhibit comparable physicochemical and toxicological properties. ECHA understands that this is the applicability domain of the grouping and will assess your predictions on this basis.

ii. Assessment of the grouping

ECHA notes the following shortcomings with regards to your grouping approach:

A. Applicability domain of the category

According to the ECHA Guidance, a category (grouping) hypothesis should address "*the set of inclusion and/or exclusion rules that identify the ranges of values within which reliable estimations can be made for category members for the given endpoint"* (Guidance on IRs and CSA, Section R.6.2.4.1.). Particularly, "*the applicability domain of a (sub)category would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members*" (Guidance on IRs and CSA, Section R.6.2.1.2.). Therefore, to reliably predict properties within a category the applicability domain should be described

including the borders of the category, for which chemicals the category does not hold and a justification for the inclusion and/or exclusion rules.

In your dossier, you describe the applicability domain of the substances covered by the grouping as: "*The grouping of Cinnamaldehyde, HCA and alpha-Amylcinnamaldehyde (ACA), into the* "Cinnamyl derivatives" *category is based on their structural relationships and the resulting similarities of their physico-chemical (as described in Table 7.1/1) and toxicological properties (see* [redacted]*, 2005)".*

This applicability domain does not introduce unambiguous inclusion/exclusion criteria which would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members.

In your comments on the draft decision, you state that you "*do not accept the ECHA conclusion that the category is not well defined*" and you argue that:

- "*The inclusion/exclusion criteria are identified, in that the five substances in the category define the criteria for inclusion and exclusion, no other substances are needed to be in the category*";
- "*the dossier in question was prepared and submitted many years before the RAAF document was published and therefore it is not surprising that the category has not been defined according to the latest guidance*";
- "*the US FDA and WHO consider these substances suitable for evaluation as a group, but also EFSA evaluated these 5 substances within a group approach*".

Finally, you claim that "*an improved and stronger category or grouping case according to the RAAF document of 2017 can be developed*".

ECHA notes that your comments on the draft decision does not provide the missing information identified above. ECHA acknowledges your intentions to improve the read-across approach. As indicated in your comments, this strategy relies essentially on information which is yet to be provided, therefore no conclusion on the compliance can currently be made. Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

C. Predictions for toxicological properties

You have provided the following reasoning for the prediction of toxicological properties: "*The grouping of Cinnamaldehyde, HCA and alpha-Amylcinnamaldehyde (ACA), into the* "Cinnamyl derivatives*" category is based on their structural relationships and the resulting similarities of their physico-chemical (as described in Table 7.1/1) and toxicological properties (see* [redacted]*, 2005)"* and *"Based on this grouping approach, studies on Cinnamaldehyde, its tautomer alcohol (Cinnamic alcohol) and their corresponding acid (cinnamic acid) were considered reliable to assess the toxicological profile of HCA (see attached figure* "Metabolism of cinnamaldehyde derivatives" *in §7.1.1)."*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

You intend to predict the properties for the Substance from information obtained from the following source substances:

Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Alpha-amylcinnamaldehyde (EC No. 204-541-5);

Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- cinnamaldehyde (EC No. 203-213-9);
- cinnamic acid (EC No. 210-708-3)
- cinnamic alcohol (EC No. 203-212-3)

ECHA notes the following shortcomings with regards to predictions of toxicological properties:

A. Composition of the substances within the group

Annex XI, Section 1.5 of the REACH Regulation provides that "*substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as group.*"

According to the Guidance on IRs and CSA Section R.6, "*in identifying a category, it is important that all potential category members are described as comprehensively as possible*", because the purity profile and composition can influence the overall toxicity/properties of the potential category members (Guidance on IRs and CSA, Section R.6.2.4.1.). Therefore, qualitative and quantitative information on the compositions of the category members must be provided to allow assessing whether the attempted predictions are compromised by the composition and/or impurities.

The Substance is a mono-constituent substance. You do not describe the composition of any category member. Furthermore, for the source studies provided in the technical dossier, no information on the composition of the test material is provided (see below under 'Adequacy and reliability of source studies').

Without this information, no qualitative or quantitative comparative assessment of the compositions of the different category members can be completed. Therefore, it is not possible to assess whether the attempted predictions are compromised by the composition of the category members.

B. Supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)". For this purpose "it is important to provide supporting information to strengthen the rationale for the read-across" (Guidance on IRs and CSA, Section R.6.2.2.1.f.). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on other category members.

Supporting information must include information to compare toxicokinetic properties of the category members and bridging studies to compare other properties of the category members.

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

You have not provided a read-across justification document in IUCLID Section 13 or your CSR. However, you have provided some explanation of the proposed approach for the prediction of toxicological properties in the summary of Section 5 of your CSR and for in the Section 7.1 of your technical dossier.

You have provided a data matrix containing limited information on structure and physicochemical properties of the Substance, cinnamaldehyde (EC No. 203-213-9), cinnamic acid (EC No. 210-708-3) and cinnamic alcohol (EC No. 203-212-3). The data matrix did not provide information on Alpha-amyl-cinnamaldehyde (EC No. 204-541-5). Furthermore, none of the data listed in the data matrix are supported by robust study summaries.

You argue on similar toxicokinetic properties for the group members. You have provided toxicokinetic data generated with the source substances cinnamaldehyde and cinnamic acid. However, you have not provided any toxicokinetic information generated with the other group members (including the Substance).

You have provided data for sub-chronic toxicity (90-day) and pre-natal developmental toxicity using several source substances. Apart from these studies, you have provided no bridging studies to compare the properties of the Substance and of the other members. Furthermore, the studies you have provided are not reliable for reasons addressed in the respective endpoints described below.

In the absence of such information, you have not established that the category members are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

In your comments on the draft decision, you state your "*opinion is that the read-across argument can be improved to include such information in order to avoid the performance of new studies on vertebrate animals*". You have provided no further information to address the issue identified above.

ECHA acknowledges your intentions to improve the read-across approach. As indicated in your comments, this strategy relies essentially on information which is yet to be provided, therefore no conclusion on the compliance can currently be made. Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

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

1. In vitro gene mutation study in bacteria

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

You have provided a key study in your dossier:

i. a study according to OECD TG 471 on the Substance with the following strains: TA 98, TA 100, TA 1535, TA 1537, and TA 1538, which all gave negative results.

We have assessed this information and identified the following issue:

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[2] (1997). Therefore, the following specifications must be met:

a) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).
b) The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose must correspond to 5 mg/plate.
c) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
d) The number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory.
e) The mean number of revertant colonies per plate must be reported for the treated doses and the controls.

The provided study shows the following:

a) The reported data does not include results for the appropriate *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).
b) The reported data does not include a maximum dose of 5 mg/plate or that induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance.
c) The reported data does not include a positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
d) The reported data does not include a negative control with a number of revertant colonies per plate inside the historical control range of the laboratory.
e) The reported data does not include data on the number of revertant colonies per plate for the treated doses and the controls

Therefore, study (i) above does not meet the specifications of the OECD TG 471.

On this basis, the information requirement is not fulfilled.

In your comments you have agreed to provide the information.

Study design

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

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

2. 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 provided the following information:

i. a study according to OECD TG 201 on the Substance

We have assessed this information and identified the following issue:

To fulfil the information requirement, a study must comply with OECD TG 201 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Validity criteria

- exponential growth in the control cultures is observed over the entire duration of the test;
- at least 16-fold increase in biomass is observed in the control cultures by the end of the test;
- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;
- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with *Desmodesmus subspicatus*.

Characterisation of exposure

a) the test media prepared specifically for analysis of exposure concentrations during the test is treated identically to those used for testing (*i.e.* inoculated with algae and incubated under identical conditions);

Reporting of the methodology and results

b) the test procedure is reported (*i.e.* composition of the test medium, nature and concentration of auxiliary solvent);
c) the methods used to prepare stock and test solutions are reported;
d) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

Your registration dossier provides an OECD TG 201 showing the following:

Characterisation of exposure

a) it is not specified, in your dossier, if the test media prepared specifically for analysis of exposure concentrations was inoculated with algae.

   However, in your comments on the draft decision, you clarified that "[t]*he test did not include parallels containing test substance without algae.* […] *Therefore, the analysis is from test solutions containing both test substance and algae*".

Reporting of the methodology and results

b) on the test procedure, you have not specified, in your registration dossier, the composition of the test medium, the identity and concentration of the auxiliary solvent;

   However, in your comments on the draft decision, you clarified that DMF was used as solvent at a concentration of 100 µg/L. You also provided the test medium composition.

This information indicates compliance with the corresponding requirements of the OECD TG 201.

c) the methods used to prepare stock and test solutions is not reported in your dossier.

However, you provided this information as part of your comments on the draft decision. This additional information was found to be acceptable.

d) tabulated data on the algal biomass determined daily for each treatment group and control are not reported in your registration dossier. However, you provided this information as part of your comments on the draft decision. This additional information indicates that the validity criteria of the test method listed above were met.

ECHA has assessed the additional information provided as part of your comments on the draft decision against the requirement in OECD TG 201. The information addresses the incompliances identified above. However, as the information is currently not available in your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

3. Ready biodegradability

Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

You have provided the following studies on the Substance:

i. a study according to OECD TG 301F on the Substance
ii. an inherent biodegradability test according to Ecotox SSOP N158 on the Substance
iii. a study according to OECD TG 301 B with sealed vessels on the Substance

We have assessed this information and identified the following issue:

A. The studies provided are not reliable

To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301, the following requirements must be met:

Validity criteria

a) The degradation of the reference compound has reached the pass level by day 14;
b) The difference of extremes of replicate values of the removal of the test material at the plateau, at the end of the test or, if appropriate, at the end of the 10-d window is ≤ 20%;
c) In the toxicity control, the degradation of the reference substance has reached ≥ 35% (based on DOC) or ≥ 25% (based on ThOD or $ThCO_2$) by day 14;
d) The inorganic carbon content (IC) of the test material suspension in the mineral medium at the beginning of the test is < 5% of the total carbon (TC);
e) The total CO_2 evolution in the inoculum blank at the end of the test does not normally exceed 40 mg CO_2/L for OECD TG 301B. The oxygen uptake of the inoculum blank does normally not exceed 20-30 mg O_2/L for OECD TG 301F;

Technical specifications impacting the sensitivity/reliability of the test

f) The inoculum is not be pre-adapted to the test material;

However, for study ii., you report that the inoculum was pre-adapted.

In your comments to the draft decision, you confirmed that, for study ii., the inoculum was pre-adapted. You state that "*this test was already considered K3, disregarded study, in the IUCLID*".

g) The concentration of the test material is in the range of 10-20 mg DOC (or TOC)/L;

However for study iii., you have reported in your dossier a nominal test concentration of 1.2 mg/L based on nominal Carbon.

In your comments to the draft decision, you indicate that study iii. "*is considered a supporting study and is not the key study and therefore does not change the overall conclusion from study i that HCA is readily biodegradable meeting the 10 day window*". ECHA understands that you agree study iii. is not adequate to meet the information requirement.

Reporting of the methodology and results

h) The source of the inoculum, its concentration in the test and any pre-conditioning treatment are reported;

This information is not available in your dossier for studies i. and iii.

In your comments to the draft decision, you specified that, for study i., the concentration fo the inoculum was "*30 mg/L in each of the bottles*". You state that "*the laboratory that performed the study has confirmed that the inoculum was obtained from a WWTP treating predominantly municipal waste. The identity and address of the WWTP will be included in the dossier*"

i) The results of measurements at each sampling point in each replicate is reported in a tabular form;

This information is not available in your dossier for studies i. and iii.

In your comments to the draft decision, you specify that for study i., only tabulated data at T0 and T 28 day are available. However, you also provided a graph showing measured values at various time points. You consider that the available tabulated values in combination to the graph provides sufficient information to conclude that the validity criteria specified under a) to b) and e) above were met. You specify that the validity criteria under c) does not apply to OECD TG 301F.

j) The test procedure is reported (e.g. number of replicates).

This information is not available in your dossier for studies i. and iii.

In your comments to the draft decision, you consider that the additional information provided on study i. allows concluding that an appropriate test procedure was used.

ECHA has assessed the additional information provided as part of your comments on the draft decision for study i. against the requirement in OECD TG 301F. The information addresses the incompliances identified above. However, as the information is currently not available in

your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

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

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

You have provided a key study in your dossier:

i. a study according to OECD TG 474 on the Substance

We have assessed this information and identified the following issue:

Under Section 8.4.2., Column 2, first indent, Annex VIII to REACH, the study may be omitted "if *adequate data from an in vivo cytogenicity test are available*". ECHA Guidance[3] clarifies that the *in vivo* study must be either a micronucleus test or a chromosomal aberration test, performed according to OECD TG 474 or 475, respectively[4].

For the data from an *in vivo* cytogenicity test to be considered adequate, the *in vivo* study you submitted has to meet the requirements of OECD TG 474, and the specifications/conditions of this test guideline include:

a) The study must include a negative control group with a response inside the historical control range of the laboratory and a positive control group.
b) The highest dose studied must be the maximum tolerated dose (MTD), i.e. the highest dose that is tolerated without evidence of toxicity (e.g. body weight depression or hematopoietic system cytotoxicity, but not death or evidence of pain, suffering or distress necessitating humane euthanasia). The highest dose can also be a dose that produces toxicity in the bone marrow (e.g. a reduction in the proportion of immature erythrocytes among total erythrocytes in the bone marrow or peripheral blood).
c) The proportion of immature among total (immature + mature) erythrocytes must be determined for each animal (by counting a total of at least 500 erythrocytes for bone marrow and 2000 erythrocytes for peripheral blood).
d) At least 4000 immature erythrocytes per animal must be scored for the incidence of micronucleated immature erythrocytes.

The reported data for the *in vivo* study you submitted did not include:

a) a negative control with a response inside the historical control range of the laboratory and a positive control group (or scoring control).
b) a maximum studied dose that is a MTD or induces toxicity. More specifically, you have not justified the selection of the maximum studied dose.
c) data on the proportion of immature erythrocytes among total erythrocytes and the mean number of micronucleated immature erythrocytes for each group of animals.
d) the analysis of the adequate number of cells

The information provided does not cover specifications/conditions required by OECD TG 474.

Therefore, the requirements of Section 8.4.2., Column 2, first indent, Annex VIII to REACH are not met.

[3] ECHA Guidance R.7a, R.7.7.6.3, p.568
[4] ECHA Guidance R.7a, Table R.7.7–3, p.558

On this basis, the information requirement is not fulfilled.

In your comments on the draft decision, you state that "*Since the dossier was submitted new data have been published ([redacted]; 2014) that provide the data that fulfil the data requirement for this endpoint. These data (negative for in vitro micronucleus induction) will be included in the updated dossier*".

However, you have not provided this information as part of your comments and therefore no conclusion on the compliance can currently be made. Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

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

1. Sub-chronic toxicity study (90-day)

Sub-chronic toxicity study (90-day) is an information requirement in Annex IX to the REACH Regulation (Section 8.6.2.)

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 sources of information:

i. a study according to OECD TG 421 on the Substance (2011)
ii. a preliminary 14-days study on the Substance used as range-finder experiment for study i. above (2010)
iii. a non-guideline 14-days short-term repeated dose toxicity study on the Substance (1980)
iv. a study similar to OECD TG 408 on the analogue substance alpha-amylcinnamaldehyde, EC No. 204-541-5 (1973)
v. a non-guideline 90 days repeated dose toxicity study on the analogue substance alpha-amylcinnamaldehyde, EC No. 204-541-5 (1965)

As explained in the Appendix on Reasons common to several requests, it would be sufficient to reject your weight-of-evidence adaptation based on the fact that you have not submitted any justification of your adaptation.

Nevertheless, ECHA has further assessed the information submitted in support of your weight of evidence adaptation and identified the following issue:

Relevant information (or key elements) that can be used to support weight of evidence adaptation for information requirement from Section 8.6.2 of Annex IX includes, at general level, information on systemic toxicity in intact, non-pregnant and young adult males and females from: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity. Information should address effects on the following physiological systems: circulatory system, digestive/excretory system, endocrine system, immune system, integumentary system, musculoskeletal system, nervous system, renal/urinary system, reproductive system, and respiratory system.

In-life observations

In-life observations must include information on survival, body weight development, clinical signs, functional observations, food/water consumption and other potential aspects of in life observations on the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory).

The sources of information provide information on survival (i, ii, iii, and iv), body weight development (i, ii, iii, iv, and v), clinical signs (i, ii, and iv), functional observations (ii), food/water consumption (i, ii, iv, and v) and other potential aspects of in life observations on the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory) as foreseen to be investigated in OECD TG 408.

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

1) Your read-across adaptation is rejected

Information from source substance(s) can contribute to weight of evidence adaptation only if the read-across is acceptable. Studies (iv and v) are performed with analogue substances. However, for the reasons explained under section 1 of the Appendix on Reasons common to several requests, the provided studies performed on source substances cannot be considered reliable sources of information that could contribute to the conclusion on the key parameters investigated by the required OECD TG 408.

In addition, the reliability of the sources of information is also affected by the following issues:

2) *The sources of information i.-iii. and v. are not reliable*

The specifications of OECD TG 408, include the following:

a. testing of at least three dose levels and a concurrent control
b. highest dose level should aim to induce some systemic toxicity, but not death or severe suffering
c. At least 10 female and 10 male animals should be used at each dose level (including control group)
d. dosing of the Substance daily for a period of 90 days until the scheduled termination of the study

The reported data for the studies you have provided include the following:

a. The study v. was conducted with less than three dose levels.
b. The highest dose level in the study v. did not induce any systemic toxicity. Therefore, the dose level selection was too low.
c. The studies i., ii. and iii. were conducted with less than 10 animals per sex per test dose group.
d. The studies i., ii. and iii. do not have the required exposure duration of 90 days as required in OECD TG 408, because you indicated an exposure duration of no more than 46 days, 14 days, and 14 days, respectively.

Therefore, the reliability of these studies is significantly affected and thus cannot contribute to the conclusion on this key element.

Blood chemistry, and organ and tissue toxicity

Information on blood chemistry must include haematological (full-scale) and clinical chemistry analysis (full-scale), and other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary). Organ and tissue toxicity must include information on terminal observations on organ weights, gross pathology and histopathology (full-scale) and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory, endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory).

The sources of information provide information on haematological (full-scale) (iv and v) and clinical chemistry analysis (full-scale) (iv and v), other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary) (iv), terminal observations on organ weights (i, ii, iv and v), gross pathology (i, ii, iii, and iv) and histopathology (full-scale) (i, ii, iv, and v), and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory, endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory) as foreseen to be investigated in OECD TG 408.

However, the reliability of all sources of information is significantly affected by the reliability issues *1)* and *2)* already described above. Therefore, they cannot contribute to the conclusion on this key element.

Therefore, the reliability of these studies is significantly affected and thus cannot contribute to the conclusion on this key element.

Conclusion on your weight of evidence adaptation

Taken together, the sources of information provide information on systemic toxicity in intact, non-pregnant and young adult males and females from: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity. However, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, 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 408. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In your comments on the draft decision, you state that:

- ECHA rejects the weight of evidence on the basis of individual studies not meeting the requirements of the OECD 408.
- "*ECHA rejects the WoE primarily on the basis of the weakness of the description of the category and grouping justification*."

However, in your comments you do not address the reliability issues of the studies (i, iii and v) listed above. Overall, you provide no new specific information to contradict the conclusion explained above. ECHA acknowledges your intentions to improve the read-across approach. As indicated in your comments, this strategy relies essentially on information which is yet to be provided, therefore no conclusion on the compliance can currently be made. Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

Study design

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the Substance is a liquid of very low vapour pressure And, although uses with industrial, professional and consumer spray application are reported in the chemical safety report, the reported concentrations are low (<3%).

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

2. Pre-natal developmental toxicity study in one species

Pre-natal developmental toxicity study (in one species (rat or rabbit)) is an information requirement in Annex IX to the REACH Regulation (Section 8.7.2.)

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 sources of information:

i. a study according to OECD TG 421 on the Substance (2011)
ii. a non-guideline developmental toxicity study on the analogue substance cinnamaldehyde, EC No. 203-213-9 (1987)
iii. a developmental toxicity study according to a protocol from the Japanese Ministry of Health and Welfare on the analogue substance cinnamaldehyde, EC No. 203-213-9 (1989)
iv. a non-guideline developmental toxicity on the analogue substances cinnamic acid and cinnamic alcohol, respectively EC No. 210-708-3 and EC No. 203-212-3 (1975)
v. a non-guideline developmental toxicity on the analogue substance cinnamic alcohol, EC No. 203-212-3 (1973)

As explained in the Appendix on Reasons common to several requests, it would be sufficient to reject your weight-of-evidence adaptation based on the fact that you have not submitted any justification of your adaptation. In addition, endpoint specific issues are described below.

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

Prenatal developmental toxicity

Prenatal developmental toxicity includes information after prenatal 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 provide information on embryonic/foetal survival (number of live foetuses; number of resorptions and dead foetuses, postimplantation loss) (i, ii, iii, iv, v), growth (body weights and size) (i, ii, iii, iv, v) and structural malformations and variations (external, visceral and skeletal) (iii, iv, v) as foreseen to be investigated in OECD TG 414.

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

1) Your read-across adaptation is rejected

Information from source substance(s) can contribute to weight of evidence adaptation only if the read-across is acceptable. Studies (ii-v) are performed with analogue substances. However, for the reasons explained under section 1 of the Appendix on Reasons common to several requests, the provided studies performed on source substances cannot be considered reliable sources of information that could contribute to the conclusion on the key parameters investigated by the required OECD TG 414.

In addition, the reliability of the sources of information is also affected by the following issues:

2) The sources of information i.-v. are not reliable

The specifications of OECD TG 414, include the following:
a) testing of at least three dose levels and a concurrent control,
b) highest dose level should aim to induce some developmental and/or maternal toxicity,

c) 20 female animals with implantation sites for each test and control group,
d) dosing of the Substance from implantation until the day prior to scheduled caesarean section

The reported data for the studies you have provided include the following:
a) The studies (iv and v) you have provided were conducted with one or two dose levels.
b) The highest dose level in the study (iv and v) did not induce any developmental and/or maternal toxicity and you have not shown that the aim was to induce toxicity.
c) The studies (i, iii, and iv) you have provided were conducted with respectively 8, 15-17 or 6-9 pregnant females for each test group.
d) In the studies (studies ii, iii, and v) you have provided, the animals were exposed during respectively GD 6-13, GD 7-17, and GD 4/GD 10-12.

Therefore, the reliability of these studies is significantly affected and thus cannot contribute to the conclusion on these key elements.

Maternal toxicity and Maintenance of pregnancy

Maternal toxicity includes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in dams. 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 provide information on maternal survival (i and ii), body weight (i, ii and iii) and clinical signs (i and iii) and inform on abortions and/or early delivery and other potential aspects of maintenance of pregnancy (i and iv).

However, the reliability of all sources of information is significantly affected by the reliability issues *1)* and *2)* already described above. Therefore, they cannot contribute to the conclusion on this key element.

Therefore, the reliability of these studies is significantly affected and thus cannot contribute to the conclusion on this key element.

Conclusion on your weight of evidence adaptation

Taken together, the sources of information provide information on pre-natal developmental toxicity. However, their reliability is affected so significantly that they cannot be taken into consideration in a weight of evidence approach.

Therefore, 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 an OECD TG 414 study with a design described in this decision. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

In your comments on the draft decision, you state that:
- ECHA rejects the weight of evidence on the basis of individual studies not meeting the requirements of the OECD 408.
- "*ECHA rejects the WoE primarily on the basis of the weakness of the description of the category and grouping justification*."

However, in your comments you do not address the reliability issues of the studies (i, iii and v) listed above. Overall, you provide no new specific information to contradict the conclusion explained above. ECHA acknowledges your intentions to improve the read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be provided, therefore no conclusion on the compliance can currently be made. Please note that this decision does not consider updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation). You remain responsible for complying with this decision by the set deadline.

Study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[5] administration of the Substance. The oral route is requested for the reasons that are already explained under Appendix C.1.

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:

i. 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: *"A chronic study on Daphnia magna was proposed and performed. A toxic effect (adult immobility and reproduction) was found after 21 days of exposure. However, this study must be used with care because solvent was used during the test. Under normal circumstances a chronic fish study could also be requested, however for several reasons this study is considered unjustified. Firstly, due to the low solubility in water of the substance and its capacity to form emulsions when used in conjunction with a solvent (as has been observed in acute studies), the long-term fish study would be technically difficult to perform. Secondly, this substance is expected to adsorb to organic matter and sediment and would therefore not be expected to be present at concentrations that could cause toxicity in the pelagic compartment. For this reason, sediment studies have been proposed in order to characterise any potential risk for the compartment at greatest risk of exposure*."

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.

On this basis, the information requirement is not fulfilled.

In your comments you have agreed to provide the information.

Study design

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

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.).

OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.2.

4. Long-term toxicity on terrestrial invertebrates

Short-term toxicity to invertebrates is an information requirement under Annex IX to REACH (Section 9.4.1). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

Based on the information from your registration dossier:

- the Substance is considered to have high adsorption potential to soil as you report predicted log Kow and log Koc values above 5 and 4 respectively for the Substance;

On this basis information on long-term toxicity on terrestrial invertebrates must be provided.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix D.2.

In your comments you state that the Substance is "*a soft electrophile (MechoA 3.2),* [it] *is therefore highly reactive and* [it] *is not expected to persist in soils for more than a few hours/days*". Nevertheless, you have agreed to provide the information.

5. Effects on soil micro-organisms

Effects on soil microorganisms is a standard information requirement under Annex IX to REACH (Section 9.4.2).

You have adapted this information requirement under Annex IX, Section 9.4., Column 2, second paragraph with the following justification: "*The substance HCA is readily biodegradable […] and therefore is not expected to reside for long periods in the soil compartment. Moreover the Chemical Safety Assessment does not suggest that there may be a risk to soil dwelling invertebrates based on the RCR. It has been shown that micro-organisms in STPs are not sensitive to HCA (see IUCLID section 6.1.7). Therefore, no tests on the effects on soil micro-organisms are proposed."*

We have assessed this information and identified the following issue:

> Under Annex IX, Section 9.4., column 2, in the absence of toxicity data to soil organisms, the equilibrium partitioning method (EPM) may be applied to assess the hazard to soil organisms. The choice of the appropriate tests depends on the outcome of the chemical safety assessment.
>
> In this context, ECHA Guidance R.7.11.6. describes an integrated testing strategy (ITS) for soil toxicity, which rely on the assignment of the Substance to a "soil hazard category" and on an initial screening assessment using the EPM, in order to decide the information needed for the chemical safety assessment. Substances that have a high potential to adsorb to soil or are very persistent and that are very toxic to aquatic organisms (i.e. lowest short-term EC/LC50 < 1 mg/L and/or long-term NOEC < 0.1 mg/L) fall under Hazard Category 4. For such substances, long-term toxicity tests according to the standard information requirement of Annex X, Section 9.4 must be provided.

As already explained under Appendix C.4., the Substance is concluded to have a high potential to adsorb to soil.

Under Section 6.1.5. of your technical dossier, you report a chronic toxicity to aquatic invertebrates test as per OECD TG 211 (2011). The NOEC reported was 63 µg/L and EC50 > 157 µg/L for reproduction and immobilisation. On this basis the Substance is concluded to be very toxic to aquatic organisms (Aquatic Chronic 2).

The information from your dossier indicates that the Substance belongs to Hazard Category 4 as described in the ITS for soil toxicity. For such substances the screening assessment based on the EPM is not recommended and information on long-term toxicity to terrestrial invertebrates and terrestrial plants (as described in Annex X, Section 9.4) must be provided. Therefore, you adaptation is rejected.

On this basis, the information requirement is not fulfilled.

In your comments you have agreed to provide the information.

Study design

ECHA Guidance R.7.11.3.1. specifies that Soil Microorganisms: Nitrogen Transformation Test (EU C.21/OECD TG 216) is considered suitable for assessing long-term adverse effects on soil microorganisms for most non-agrochemicals.

6. Long-term toxicity on terrestrial plants

Short-term toxicity to terrestrial plants is an information requirement under Annex IX to REACH (Section 9.4.3). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

Based on the information from your registration dossier:

- the Substance is considered to have high adsorption potential to soil as you report predicted log Kow and log Koc values above 5 and 4 respectively for the Substance;

Therefore, the Substance has a high potential to adsorb to soil. On this basis information on long-term toxicity on terrestrial plants must be provided.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix D.3.

In your comments you have agreed to provide the information with the same argumentation as for C.4.

Appendix D: Reasons to request information required under Annex X of REACH

1. Pre-natal developmental toxicity study in a second species

Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is a standard information requirement under Annex X to REACH.

You have not provided information on a second species. In order to be compliant and enable concluding if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in two species.

On this basis, the information requirement is not fulfilled.

In your comments you have agreed to provide the information.

Study design

A PNDT study according to the OECD TG 414 study should be performed in the rabbit or rat as the preferred second species, depending on the species tested in the first PNDT study (See Appendix C.2. in this decision).

The study shall be performed with oral[6] administration of the Substance. he oral route is requested for the reasons that are already explained under Appendix C.1.

2. Long-term toxicity on terrestrial invertebrates

Long term toxicity testing on soil invertebrates (Section 9.4.4.) is a standard information requirement under Annex X.

You have adapted this information requirement under Annex IX, Section 9.4., Column 2 with the following justification: "*The substance HCA is readily biodegradable […] and therefore is not expected to reside for long periods in the soil compartment. Moreover the Chemical Safety Assessment does not suggest that there may be a risk to soil dwelling invertebrates based on the RCR.* "

However, for the reasons already explained in Appendix C.5., your adaptation under Annex IX, Section 9.4., Column 2 is rejected.

On this basis, the information requirement is not fulfilled.

In your comments you have agreed to provide the information with the same argumentation as for C.4.

Study design

ECHA Guidance R.7.11.3.1. specifies that the earthworm reproduction test (OECD TG 222), the Enchytraeid reproduction test (OECD TG 220), and the Collembolan reproduction test (OECD TG 232) are appropriate to cover the information requirement for long-term toxicity testing on terrestrial invertebrates. ECHA is not in a position to determine the most appropriate test protocol since this decision is dependent upon species sensitivity and substance properties. However, when log Kow >5 and log Koc >4, as in this case, the test OECD 232 is not appropriate as the dominant route of exposure for Collembolans is via pore water.

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

3. Long-term toxicity on terrestrial plants

Long term toxicity testing on soil invertebrates (Section 9.4.6.) is a standard information requirement under Annex X if the substance has a high potential to adsorb to soil or is very persistent.

You have adapted this information requirement under Annex IX, Section 9.4., Column 2 with the following justification: "*The substance HCA is readily biodegradable […] and therefore is not expected to reside for long periods in the soil compartment. Moreover the Chemical Safety Assessment does not suggest that there may be a risk to soil dwelling invertebrates based on the RCR.*".

However, for the reasons already explained in Appendix C.5., your adaptation under Annex IX, Section 9.4., Column 2 is rejected.

On this basis, the information requirement is not fulfilled.

In your comments you have agreed to provide the information with the same argumentation as for C.4.

Study design

ECHA Guidance R.7.11.3.1. specifies that the Plant Test: Seedling Emergence and Seedling Growth Test (test method: OECD TG 208) is appropriate to cover the information requirement for long-term toxicity on terrestrial plants.

The OECD TG 208 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 must 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.

Appendix E: 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 F: Procedure

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS. Similarly the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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

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

The compliance check was initiated on 03 February 2021.

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

In your comments on the draft decision, you requested an extension of the deadline to provide information from 24 to 30 months from the date of adoption of the decision.

ECHA took into account your comments and amended the deadline to 30 months.

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[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)[11]

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[12]

[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
[11] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[12] 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 their corresponding information requirements

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

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

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