~~Confidential~~

Helsinki, 06 November 2023

Addressee
Registrant of JS_Phenyl 4-hydroxybenzoate as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
07 February 2019

Registered substance subject to this decision ("the Substance")
Substance name: phenyl 4-hydroxybenzoate
EC/List number: 241-698-9

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 ***13 November 2025***.

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

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

1. Skin sensitisation (Annex VII, Section 8.3.)
    a) *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.); and
    b) only if the *in vitro/in chemico* test methods specified under point a) above are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429).

2. *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, OECD TG 471 (2020)).

3. Long-term toxicity testing on aquatic invertebrates (triggered by Annex VII, Section 9.1.1., Column 2; test method: EU C.20./OECD TG 211).

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

5. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. C/D/E/F/OECD TG 301B/C/D/F or EU C.29./OECD TG 310).

The reasons for the requests are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressee of the decision and its corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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 requirements for testing and reporting new tests under REACH, see Appendix 4.

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

Appendix 1: Reasons for the request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 1: Reasons for the request(s)

Contents

Reasons common to several requests

0.1. Read-across adaptation rejected

1 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5.:

- Long-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1., column 2)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Ready biodegradability (Annex VII, Section 9.2.1.1.)

2 ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following sections.

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

4 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

0.1.1. Scope of the grouping of substances

5 You provide a read-across justification in sections 5.2.1, 6.1.4 and 6.1.5 of IUCLID.

6 You predict the properties of the Substance from information obtained from the following source substance:

- Benzyl 4-hydroxybenzoate, EC 202-311-9 (source substance 1).

7 You provide the following reasoning for the prediction of ecotoxicological and environmental fate properties: "Both substances are structural homologues regarding the functional groups at the ester (phenyl vs benzyl group). Both esthers have similar physico-chemical properties. Both are moderately/poorly water soluble (108 g/L vs 0.05 mg/L), exhibit similar log Kow values (3.97 vs 3.21), have similar boiling points (355 °C vs 241 °C) and vapour pressure (3.37x10-6 mm Hg vs 8.17x10-6 mm Hg)."

8 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

0.1.2. Predictions for ecotoxicological and fate properties

0.1.2.1. Read-across hypothesis contradicted by existing data

9 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information must strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and

establishing that the properties of the Substance can be predicted from the data on the source substance(s) (Guidance on IRs and CSA R.6., Section R.6.2.2.1.f.).

10 The observation of differences in the physico-chemical properties between the source substance(s) and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the source substances. An explanation why such differences do not affect the read-across hypothesis must to be provided and supported by scientific evidence.

11 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar and physicochemically similar Substance and source substance cause the same type of effect(s).

12 However, contrary to your claim, the source substance and the Substance do not share similar physicochemical properties. For the source you have provided a solubility (108 g/L) and for the Substance a solubility (<0.05 mg/L). This difference may be expected to lead to differences in the bioavailability of the source substance and the Substance, which may affect their ecotoxicological effects and fate.

13 Therefore, the available set of data on the Substance and on the source substance indicates differences in the physicochemical properties of the substances. This contradicts your read-across hypothesis whereby the Substance and source substances cause the same type of effect(s) based on similar physico-chemical properties. However, you have not supported and scientifically justified why such differences in the physico-chemical properties do not affect your read-across hypothesis.

0.1.2.2. Missing supporting information to compare the properties of the substances

14 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).

15 As indicated above, your read-across hypothesis is based on the assumption that the structurally and physico-chemically similar source substance cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the source substance 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 with the Substance and the source substance.

16 In your dossier, you provide studies on the source substance to fulfill the information requirements on long-term toxicity to aquatic invertebrates, growh inhibition to aquatic plants and ready biodegradation. Apart from these studies, your read-across justification or the registration dossier does not include any robust study summaries or descriptions of data for the Substance that would confirm that both substances cause the same type of effects and have a similar fate. In particular, you provided no study on the target substance relevant to the adapted information requirements (bridging study).

17 In the absence of such information, you have not established that the Substance and the source substance are likely to have similar properties. Therefore you have not provided sufficient supporting information to scientifically justify the read-across.

0.1.2.3. Inadequate or unreliable studies on the source substance(s)

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

(1) be adequate for the purpose of classification and labelling and/or risk assessment;

(2) have adequate and reliable coverage of the key parameters addressed in the corresponding study that shall normally be performed for a particular information requirement;

(3) cover an exposure duration comparable to or longer than the corresponding study that shall normally be performed for a particular information requirement if exposure duration is a relevant parameter.

19 Specific reasons why the studies on the source substance do not meet these criteria are explained further below under the applicable information requirement sections 3, 4 and 5. Therefore, no reliable predictions can be made for these information requirements.

0.1.3. Conclusion

20 Based on the above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

21 Skin sensitisation is an information requirement under Annex VII, Section 8.3. Under Section 8.3., Column 1, the registrants must submit information allowing (1) a conclusion whether the substance is a skin sensitiser and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

1.1. Information provided

22 You have provided:

(i) a non-guideline loose-fit coculture-based sensitisation assay (LCSA) (2015) with the Substance;

(ii) Positive Vega QSAR skin sensitisation model (CAESAR) 2.1.6 prediction implemented in the QSAR tool VEGA (version 1.2.4.);

(iii) QSAR Toolbox (Version 4.0), which revealed a positive structural alert for protein binding: Acylation (Protein Binding by OASIS v1.4 and Protein Binding by OECD).

23 Based on the presented sources of information, you conclude that "[...] based on an assessment of the available data in a weight-of-evidence approach, the target substance must be considered as a skin-sensitiser".

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

24 To fulfil the information requirement, the information available must allow a conclusion whether the Substance is a skin sensitiser.

25 You consider that based on the information available (studies i to iii) the Substance is a skin sensitiser and have classified the Substance as Skin sensitiser Cat 1.

26 ECHA agrees with your assessment that the Substance is a skin sensitiser, therefore this requirement has been fulfilled.

1.2.2. No assessment of potency

27 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), as required under Annex VIII, 8.1, column 1. Information on potency is crucial for the correct classification and risk management of the Substance.

28 Although the information provided allows to conclude that the Substance is considered to cause skin sensitisation, we have assessed the information you provided in relation to skin sensitisation potency (Cat 1A vs. 1B) and we identified the following issues.

1.2.2.1. the study (i) provided does not comply with the prescriptions of Article 13

29 According to Annex XI, section 1.4 of REACH Regulation, results obtained from suitable in vitro methods, that have not been formally validated or adopted by international organisations, can be used, if they indicate a presence of certain dangerous property. Under Article 13 of the REACH Regulation, "where tests on substances are required to generate information on intrinsic properties of substances, they shall be conducted in accordance

with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the Agency as being appropriate".

30 You have provided result of an in vitro study conducted according to loose-fit coculture-based sensitisation assay (LSCA). The results of the study indicated that the Substance has skin sensitisation potential.

31 However, the method used to perform study (i) is not a test method laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the Agency as being appropriate for predicting skin sensitisation potency.

1.2.2.2. The QSAR result is not equivalent to results obtained from the required experimental test (studies ii and iii)

32 Results from (Q)SAR models are adequate for risk assessment or classification and labelling when they are equivalent to results obtained from the required experimental test. The corresponding information needs to allow (1) a conclusion whether the substance is a skin sensitiser and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A). This information can either be obtained by performing in vitro test battery covering three key events (molecular interactions with skin proteins, inflammatory response in keratinocytes and activation of dendritic cells) or via the in vivo LLNA (OECD TG 429).

33 You have provided a prediction from a VEGA (Q)SAR skin sensitisation model (CAESAR) v. 2.1.6 (ii), which predicts whether the substance is skin sensitiser. You have also provided an alert from QSAR Toolbox (iii), but this alert only flags protein binding potential.

34 The models predict skin sensitisation (study ii) and protein binding potential (study iii), but do not measure potency. Therefore, the prediction is not adequate to meet the information requirement for skin sensitisation for the purpose of classification and labelling and/or risk assessment.

35 Based on the above, your QSAR adaptation under Annex XI, Section 1.3. is rejected.

36 On this basis, it cannot be concluded whether the Substance is presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

37 Therefore, the information requirement is not fulfilled

38 In your comments on the draft decision you claim that the information currently in your dossier already informs on several key events. More specifically:

- Molecular interaction with skin proteins: you state "*ECHA guidance R7a (version 6) proposes the use of the profiler OASIS for protein binding, which* "revealed a positive structural alert for protein binding: Acylation". *This in-formation has been submitted within the endpoint summary and answers REACH requirements for this first AOP key event assessment*". ECHA notes, that indeed the OASIS profiler does provide a structural alert for protein binding, as explained above under 1.2.2.2. However, it does not provide any information on reactivity rates that could be used to estimate the skin sensitisation potency, as required under REACH.
- Activation of dendritic cells: referring to study (i), you claim that "*this method has been the subject of 9 publications on Pubmed, the last co-published by the* [redacted]". You state that "*This methods allows to assess the sensitizing potency, as mentioned in (Sonnenburg A. et al., 2015)*". However, for the reasons already explained under

1.2.2.1., ECHA cannot consider study (i) a relevant assay to inform on potency. ECHA further notes, that based on the information provided in the publication, it is not described to which potency classification system the comparison is made. Based on the four different potency categories, it appears that ECETOC potency classes are used (Contact sensitisation: classification according to potency Technical report no [redacted], 2003). The ECETOC potency classes differ from the CLP potency classification and cannot be transferred to the CLP potency categories. Even if the method would be formally validated and internationally accepted for potency assessment, this information cannot be used for classification and labelling.

- Inflammatory responses in keratinocytes: you agree in your comments to generate information according to the OECD TG 442D.

39 None of your comments provide new information that fully address the concerns raised under Section 1.2.2. as they do not provide information on skin sensitisation potency.

40 Therefore, your comments on the draft decision do not change ECHA's assessment. You remain responsible for complying with this decision by the set deadline.

1.3. Study design

41 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

42 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or newly generated data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

43 Please also note that if, based on the available information, a substance is considered as a skin sensitiser, a Defined Approach (DA) to skin sensitisation, especially the Integrated Testing Strategy DA as described in the OECD guideline 497 can be applied to conclude on the skin sensitisation potency (Cat 1A vs 1B of CLP). Alternatively, you may consider applying the kinetic Direct Peptide Reactivity Assay (kDPRA), as described in OECD TG 442C to conclude on the skin sensitisation potency (Cat 1A vs 1B of CLP).

2. In vitro gene mutation study in bacteria

44 An in vitro gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

2.1. Information provided

45 You have provided:

(i) an *in vitro* gene mutation study in bacteria (2018) with the Substance;

2.2. Assessment of the information provided

2.2.1. The provided study does not meet the specifications of the test guideline

46 To fulfil the information requirement, a study must comply with OECD TG 471 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the maximum dose tested induces 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 corresponds to 5 mg/plate or 5 µl/plate;

b) the mean number of revertant colonies per plate is reported for the treated doses and the controls.

47 In study(i):

a) You claim that the test item concentrations (top concentration 1000 µg/plate) in the main experiments were based on a preliminary cytotoxicity test in TA100. However, it was not reported that the maximum dose tested induced a reduction in the number of revertant colonies per plate, as compared to the negative control, or that the top dose (which was was less than 5 mg/plate or 5 µl/plate) resulted in precipitation of the tested substance;

b) the mean number of revertant colonies per plate for the treated doses and the controls was not reported.

48 The information provided does not cover the specification(s) required by the OECD TG 471.

49 In your comments on the draft decision you provide the full study report of study (i) and address the concerns listed above. However, this data is currently not in your dossier. On this basis, the information requirement is not fulfilled and you remain responsible for complying with this decision by the set deadline.Study design

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

3. Long-term toxicity testing on aquatic invertebrates

51 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII, Column 1, Section 9.1.1. However, under Column 2, long-term toxicity testing on aquatic invertebrates may be required by the Agency if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

3.1. Triggering of the information requirement

52 In section 4.8 of IUCLID, you have provided information which indicates that the Substance is poorly water soluble (solubility <0.05 mg/L).

53 As the Substance is poorly water soluble, information on long-term toxicity on aquatic invertebrates must be provided.

3.2. Information provided

54 You have adapted the long term toxicity to invertebrates information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

(i) long-term toxicity testing on aquatic invertebrates (2009) with the analogue substance benzyl 4-hydroxybenzoate EC 202-311-9;

(ii) long-term toxicity testing on aquatic invertebrates (2011) with the analogue substance benzyl 4-hydroxybenzoate EC 202-311-9.

3.3. Assessment of the information provided

3.3.1. Read across adaptation rejected

55 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified the specific issue addressed below.

3.3.1.1. Inadequate or unreliable studies on the source substance

56 To fulfil with the information requirement for long-term toxicity on aquatic invertebrates, a study must comply with the OECD TG 211. Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

a) parental animals are not first brood progeny;
b) the test duration is 21 days or sufficient to produce at least three broods;
c) the test temperature is within 18°C and 22°C and not varying by over ±1°C;

Characterisation of exposure

d) analytical monitoring must be conducted. A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;

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e) the test design is reported (*e.g.* semi-static or flow-through, number of replicates, number of parents per replicate);
f) detailed information on feeding, including amount (in mgC/daphnia/day) and schedule is reported;
g) the nominal test concentrations and the results of all analyses to determine the concentration of the test substance in the test vessels are reported;
h) the full record of the daily production of living offspring during the test [by each parent animal/in each replicate] is provided;
i) the number of deaths among the parent animals (if any) and the day on which they occurred is reported;
j) the coefficient of variation for control reproductive output is reported;
k) the test medium fulfils the following condition(s): total organic carbon (TOC) ≤ 2 mg/L.

57 In the studies provided:

Technical specifications impacting the sensitivity/reliability of the test

a) in studies i) and ii) it is not specified if parental animals were first brood progeny;
b) in study i) the test duration is 10 days and you have not demonstrated that this duration was sufficient to produce at least three broods;
c) in study i) the test temperature was 24 °C;

Characterisation of exposure

d) for study ii) no analytical monitoring of exposure is specified;

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e) on the test design of study i), you have not specified the frequency of water renewal;
f) in study ii) the food provided to Daphnids is not reported, whereas in studies i) and ii) the feeding rate is not reported;
g) in studies i) and ii) the results of all analyses to determine the concentration of the

test substance in the test vessels are not reported;

h) in studies i) and ii) the full record of the daily production of living offspring during the test by each parent animal is not provided;
i) for studies i) and ii) the number of deaths among the parent animals (if any) and the day on which they occurred is not reported;
j) in studies i) and ii) the coefficient of variation for control reproductive output is not reported;
k) for study i) the test was conducted with a test medium for which total organic carbon is unknown.

58 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, in study i) test duration is shorter than required and test temperature is higher than the guideline range. For study ii) no analytical monitoring is specified. Further, for studies i) and ii) it is not indicated if parent animals were first brood progeny.
- the reporting of the studies i) and ii) is not sufficient to conduct an independent assessment of their reliability and validity. Specifically, for studies i) and ii) the full record of daily production of living offspring during the test by each parent animal is not provided.
- there are further reporting issues associated with study i) since the frequency of water renewal and the TOC concentration in water are not reported. For study ii) the food provided to daphnids is not reported. In both studies, the feeding rate, the justification of the use of nominal concentrations through the provision of measured concentrations, the number of deaths among parent animals and the coefficient of variation for control reproductive output are not reported.

59 On this basis, the specifications of OECD TG 211 are not met.

60 On this basis, you have not provided adequate information for long-term aquatic toxicity study on invertebrates. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

61 In the comments to the draft decision, you acknowledge the registration dossier evaluation in the CCH draft decision, including on environnemental fate and ecotoxicology for which you have no comment and agree with the deadline set in this decision. You remain responsible for complying with this decision by the set deadline.

3.4. Study design

62 The Substance is difficult to test due to the low water solubility (<0.05 mg/L). OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 211. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

4. Growth inhibition study aquatic plants

63 Growth inhibition study on aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

4.1. Information provided

64 You have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

(i) Growth inhibition study on aquatic plants/algae (2011) with the source substance benzyl 4-hydroxybenzoate, EC 202-311-9.

4.2. Assessment of the information provided

4.2.1. Read-across adaptation rejected

65 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified the specific issue addressed below.

4.2.1.1. Study (i) does not meet the specification of the test guideline

66 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 201. Therefore, the following specifications must be met:

Characterisation of exposure

a) analytical monitoring must be conducted. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

b) the results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within ±20 % of the nominal or measured initial concentration throughout the test;

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c) the test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);

d) the test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);

e) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

67 In study (i):

Characterisation of exposure

a) no analytical monitoring of exposure was conducted or at least it is not specified in the report;

b) You have expressed the effect values based on nominal concentrations. The concentrations of the test material are unknown and measured concentrations were not provided/measured as to justify the use of nominal;

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c) on the test design, you have not specified the test concentrations and geometric progression used;

d) on the test conditions, you have not specified hardness, pH, dissolved oxygen biomass density at the start of the test;

e) tabulated data on the algal biomass determined daily for each treatment group and control are not reported.

68 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, analytical monitoring is not specified and the use of nominal concentrations is not justified through the provision of measured concentrations that show that the substance concentration is maintained within 80% nominal.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, tabulated data on the algal biomass determined daily for each treatment group and control are not reported. In addition, tested concentrations and test conditions (i.e.: PH, hardness, dissolved oxygen and initial cell density) are not reported.

69 On this basis, the specifications of OECD TG 201 are not met.

70 Based on the above, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameters specified in the corresponding OECD TG.

71 Therefore, the information requirement is not fulfilled.

72 In the comments to the draft decision, you acknowledge the registration dossier evaluation in the CCH draft decision, including on environnemental fate and ecotoxicology for which you have no comment and agree with the deadline set in this decision. You remain responsible for complying with this decision by the set deadline.

4.3. Study design

73 OECD TG 201 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 request 3.4.

5. Ready biodegradability

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

5.1. Information provided

75 You have adapted this information requirement by using Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs). To support the adaptation, you have provided the following information:

(i) a prediction from QSAR VEGA 2018 on the Substance;

(ii) a prediction from QSAR Biowin 4.1 on the Substance.

76 In addition, ECHA understands that you have adapted this information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

(iii) a ready biodegradability study (2007) with the source substance benzyl 4-hydroxybenzoate, EC 202-311-9.

5.2. Assessment of the information provided

5.2.1. Read-across adaptation rejected

77 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified the specific issue addressed below.

5.2.1.1. Study (iii) does not meet the specification of the test guideline

78 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 301 or 310. Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

a) a reference compound, which meets the criteria for ready biodegradability, is tested in parallel in all tests. Appropriate reference compounds include aniline (freshly distilled), sodium acetate and sodium benzoate;

b) the test duration is normally 28 days. The duration of the test may only be shortened if the biodegradation curve has reached a plateau for at least three consecutive determinations;

c) determination is carried out at least in duplicate;

d) the dilution water does not contain more than 10% of the organic carbon content introduced by the test material;

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

f) when losses due to adsorption cannot be ruled out, an adsorption control is included, which is inoculated and poisoned;

g) the concentration of the test material is in the range of 10-40 mg DOC/L;

Reporting of the methodology and results

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

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

79 In study (iii):

Technical specifications impacting the sensitivity/reliability of the test

a) it is assumed that a reference compound was not tested in parallel in all testsas no reference compound was speficied;

b) the test duration was 15 hours and you have not demonstrated that a plateau was reached for at least three consecutive determinations;

c) it is unknown if determinations were or were not carried out in at least duplicate;

d) the dilution water contains 2.4 mg/L TOC whereas the substance concentration is 100 µg/L;

e) it is unknown if the inoculum was pre-adapted to the test material;

f) the test material is adsorptive (log Kow of 3.97) and therefore expected to be adsorptive. However, no adsorption control was included;

g) the concentration of the test material was 100 µg/L;

Reporting of the methodology and results

h) the inoculum concentration and cell density in the test and any pre-conditioning treatment are not reported;

i) the results of measurements at each sampling point in each replicate is not reported in a tabular form.

80 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically the reference compound is not specified, the test duration was 15 hours and it was not demonstrated that a plateau was reached, it is unknown if determinations were done in duplicate, no information on inoculum pre adaptation is provided. Also the substance concentration is 100 µg/L whereas the Guideline 301A recommends 10-40 mg/L DOC. This value is much lower than the TOC of the river water used in the test. Finally, an adsorption control should have been performed comnsidering the adsorptive properties of the Substance.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, the results of measurements at each sampling point in each replicate is not reported and the degradation of the reference compound, if used, is also unknown. Further, the inoculum concentration and cell density in the test and any pre-conditioning treatment are not reported.

81 On this basis, the specifications of OECD TG 301A are not met.

82 Based on the above, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameters of/ cover an exposure duration comparable to or longer than the one specified in the corresponding OECD TG.

5.2.1. (Q)SAR results only are not sufficient to fulfil the information requirement under Annex VII, Section 9.2.1.1.

83 Guidance on IRs and CSA, Section R.7.9.5.1. specifies that (Q)SARs for predicting ready biodegradation are not yet sufficiently accurate to predict rapid degradation. However, when no useful information on degradability is available (either experimentally derived or estimated), (Q)SAR predictions can be used as supporting evidence of that the substance is not rapidly degradable.

84 For the reasons explained above, the provided experimental study on the analogue substance (study iii) cannot be seen as a reliable source of information./ In the absence of any other additional useful information on degradability, the (Q)SARs predictions you have submitted do not enable alone to conclude on the persistence of the Substance. Consequently, your adaptation is rejected.

85 Therefore, the information requirement is not fulfilled.

86 In the comments to the draft decision, you acknowledge the registration dossier evaluation in the CCH draft decision, including on environnemental fate and ecotoxicology for which you have no comment and agree with the deadline set in this decision. You remain responsible for complying with this decision by the set deadline.

5.3. Study design

87 To fulfil the information requirement, the test method(s) according to OECD TG 301B/C/D/F or OECD TG 310 are in general appropriate. You can choose any of these methods, but you must ensure that the Substance is within the applicability domain of the test method chosen.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2012).
***Guidance on intermediates*;** ECHA (2010).
All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017).
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs; ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: 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 07 October 2022.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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

ECHA took into account your comments and did not amend the requests.

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 3: Addressee(s) of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- 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.

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

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

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1 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 (https://echa.europa.eu/practical-guides).

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2 Test material

(1) Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

- the 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.

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (https://echa.europa.eu/manuals).