~~Confidential~~

Helsinki, 02 November 2023

Addressee(s)
Registrant(s) of JS_propionitrile_203-464-4 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
10 February 2021

Registered substance subject to this decision ("the Substance")
Substance name: propiononitrile
EC/List number: 203-464-4

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***9 February 2026***.

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

The reasons for the request(s) 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 addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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

information requirements.

How to comply with your information requirements

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

You must follow the general 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. Weight of evidence adaptation rejected

1 ECHA understands that you have adapted the following standard information requirements by using Annex XI, Section 1.2. (weight of evidence):

- Skin sensitisation (Annex VII, Section 8.3.)
- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

2 Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

3 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

4 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 on the corresponding information requirement.

0.1.1. Lack of documentation justifying the weight of evidence adaptation

5 Annex XI, Section 1.2. requires that adequate and reliable documentation is provided to describe a weight of evidence approach. This documentation must include robust study summaries of the studies used as sources of information and a justification explaining why the sources of information together provide a conclusion on the information requirement.

6 You have not included a justification for your weight of evidence adaptation for each of the relevant information requirements, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

7 Beside this critical deficiency common to all information requirements under consideration, your weight of evidence approach has additional deficiencies.

8 Additional deficiencies that are specific for each of the information requirements individually are addressed under request(s) 1 and 2.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

9 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

10 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following:

(i) a category read-across approach using the OECD QSAR Toolbox v.4.3.1;
(ii) a qualitative structure-activity relationship ((Q)SAR) prediction with Toxtree v2.6.13 profilers.

11 Based on the presented sources of information, you consider that "The combination of the QSAR prediction and the read-across from closely-related substances gives confidence to the conclusion that propiononitrile will not cause skin sensitisation".

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

12 In addition to the deficiencies identified in Section 0.1., ECHA identified endpoint specific issue(s) addressed below.

1.2.1.1. Missing robust study summaries for source of information (i)

13 Annex XI, Section 1.2. requires that whenever weight of evidence is used adequate and reliable documentation of the applied method must be provided. Such documentation must include a robust study summary for each source of information used in the adaptations.

14 A robust study summary must provide a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).

15 In addition, for weight of evidence adaptations, the robust study summary must clearly indicate which key parameters of the study normally required for the information requirement are investigated in the study.

16 With the source of information (i) you intend to predict the skin sensitisation properties of the Substance from data obtained with analogue (source) substances in a read-across category approach as part of your weight of evidence adaptation.

17 However, you do not provide any information on the studies from the analogue substances used in the read-across category approach, but provide only the effect values in the Prediction report and indicate they relate to in vivo skin sensitisation data.

18 You have not provided detailed information on the methods, results and conclusions, allowing for an independent assessment of the studies used in your read-across category approach, as source of information (i), contributing to the overall weight of evidence for the information requirement under consideration.

19 In the absence of robust study summaries, the coverage of the key parameters of skin sensitisation by source of information (i) and the reliability of its contribution on these parameters to your weight of evidence adaptation cannot be evaluated.

20 ECHA concludes that you have failed to provide robust study summaries for the studies used in your read-across category approach as source of information (i).

21 Consequently, source of information (i), as lacking robust study summaries, cannot be considered as contributing to the overall weight of evidence for the information requirement under consideration.

22 Beside this critical deficiency, ECHA has also assessed the other aspects of your adaptation.

1.2.1.2. Assessment of relevance of the information provided

23 Information that can be used to support a weight of evidence adaptation for the information requirements of Section 8.3 at Annex VII includes similar information to that investigated by the internationally recognised in vitro, in chemico and/or in vivo test methods on skin sensitisation. The key investigations of such test methods address each of the 3 key events of skin sensitisation, either individually or in an integrated approach as follows:

(1) investigation of cell proliferation in the draining lymph nodes (local lymph node assay), or
investigation of local responses in animals or humans (guinea pig assays or human studies), or
(2) investigation of molecular interaction with proteins, inflammatory response in keratinocytes and activation of dendritic cells (*in vitro* and *in chemico* assays).

24 For the reasons explained in Section 1.2.1.1, the source of information (i) that is lacking robust study summaries cannot be considered as contributing to the key parameters of skin sensitisation with any relevant and reliable information.

25 The source of information (ii) may provide some relevant information for skin sensitisation as it investigates predicted properties on skin sensitisation referring to "skin sensitisation reactivity domain alerts", that include alerts for protein binding.

26 Therefore, it provides some information on investigation of molecular interaction with proteins, but does not cover other parts of the key elements, i.e. inflammatory response in keratinocytes and activation of dendritic cells.

1.2.1.3. Reliability of the read-across approach (source of information (i))

27 You intend to predict the skin sensitisation properties of the Substance from data obtained with source substances in a read-across category approach as part of your weight of evidence adaptation.

28 For this information to reliably contribute to the weight of evidence approach, it would have to meet the requirements for Grouping of substances and read-across approaches.

29 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used.

30 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.

31 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.

32 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).

33 You provide the following documents in the endpoint study record, which we understand are the read-across justification documents:

- a Category report
- a Prediction report
- a Data matrix
- a document titled "[redacted]".

34 You list the following substances as members of the category: suberonitrile (D 7800-8) (CAS 629-40-3), butanenitrile (CAS 109-74-0), adiponitrile (CAS 111-69-3); as 4th member of the category you indicate either acetonitrile (CAS 75-05-8) in the Data matrix and "[redacted]" document, or octanenitrile (CAS 124-12-9) in the Category report.

35 In addition to the critical shortcomings identified in section 1.2.1.1. above, ECHA notes the following shortcomings with regards to the reliability of the contribution of the information of the analogue substances to your weight of evidence adaptations.

1.2.1.3.1. Grouping of substances

36 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 identifies "the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made" (Guidance on IRs and CSA, Section R.6.2.1.2.).

37 Therefore, to reliably predict properties within a category, the applicability domain should be described. Such description must cover the borders of the category, define unambiguous inclusion- and exclusion criteria, and include a justification for these.

38 You describe the applicability domain of the substances covered by the grouping as "short-chained (C<=8) nitriles without branching" in the Category report and as "short-chained (C<=6) nitriles without branching" in the "[redacted]"document, and you state that "All molecules consist of solely carbon, hydrogen and nitrogen. Molecules have either one or two nitrile groups" in both documents. You add that the substances have "a low log Kow (< 1)" in the "[redacted]"document, but indicate the variation of the octanol/water partition coefficient as "-0.32÷2.75" in the Category report.

39 Based on the different statements in different parts of your read-across justification, it is not clear how you define the boundaries of the category in terms of chain length and logKow, and which source substances you include in your category to make the prediction.

40 Therefore, the applicability domain and 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, are not defined unambiguously.

1.2.1.3.2. Prediction for toxicological properties

41 You provide the following reasoning for the prediction of toxicological properties: "Because these molecules differ only in their carbon chain length and/or the number of nitrile groups (1 or 2)" and "as no other elements or functional groups are present", "their toxic properties are expected to be very similar."

42 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.

43 You indicate that the properties of your Substance are predicted by taking "the highest mode value from the 4 nearest neighbours".

Read-across hypothesis

44 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 include an explanation why the properties of the Substance may be predicted from other substances in the group, i.e. a read-across hypothesis. This hypothesis should be based on recognition of the structural similarities and differences between the substances (Guidance on IRs and CSA, Section R.6.). It should explain why the differences in the chemical structures should not influence the toxicological properties or should do so in a regular pattern, taking into account that variations in chemical structure can affect both toxicokinetics (uptake and bioavailability) and toxicodynamics (e.g. interactions with receptors and enzymes) of substances (Guidance on IRs and CSA, Section R.6.2.1.3.).

45 Your read-across hypothesis is based on the structural similarity between the source substance(s), which you consider a sufficient basis for predicting the properties of the Substance. However, your hypothesis does not explain why the structural differences between the substances, such as the number of nitrile groups and the chain length, do not influence the toxicological properties.

46 While structural similarity is a prerequisite for applying the grouping and read-across approach, it does not necessarily lead to predictable or similar toxicological properties. You have not provided a well-founded hypothesis to establish a reliable prediction for the toxicological properties, explaining why the structural differences do not influence toxicokinetics and toxicodynamics of the substances, and thus why the properties of the Substance may be predicted from information on the source substances.

47 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s).

1.2.1.4. Reliability of the (Q)SAR prediction (source of information (ii))

48 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(1) the prediction needs to be derived from a scientifically valid model,
(2) the substance must fall within the applicability domain of the model,
results need to be adequate for the purpose of risk assessment or classification and labelling, and
(3) adequate and reliable documentation of the method must be provided.

1.2.1.4.1. Inappropriate measures of robustness of the model

49 The Guidance on IRs and CSA R.6.1.3. states that for (Q)SAR models, to be scientifically valid, i.e. condition (1), they must fulfil the principles listed in the OECD Principles for (Q)SAR validation (ENV/JM/MONO(2007)2). The fourth of these principles requires that a model has appropriate measures of the internal performance (i.e. goodness-of-fit and robustness) and predictivity.

50 You use structural alert profilers with the Toxtree software v2.6.13, described in the dossier as "reactivity domain alerts". You use the profilers to make a prediction for the endpoint without measures of internal performance and predictivity of the profiler for the prediction of this endpoint.

51 Profilers are models developed for the purpose of identifying potential reactivity for example for screening or finding analogues in the context of read-across, but not to make

predictions. In absence of measures of internal performance and predictivity, a profiler is not considered a scientifically valid approach to meet this information requirement.

52 Therefore, ECHA cannot establish that the prediction can reliably contribute to the weight of evidence approach.

1.2.1.5. Conclusion on the weight of evidence

53 In summary, while the source of information (ii) may provide information on some element of the key event for skin sensitisation, it does not investigate other necessary elements. Moreover, the source of information (ii) has deficiencies affecting its reliability that prevents reaching a conclusion on the element investigated.

54 As noted in relation to the source of information (i), the lack of robust study summaries for the studies at the basis of the read-across prediction prevents to fully assess the relevance, the coverage of key parameters of the information requirement, as well as the reliability of the contribution to your weight of evidence.

55 In addition, there are some obvious deficiencies for the source of information (i) affecting the reliability of your read-across approach.

56 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement of whether the Substance causes skin sensitisation.

57 Based on the above, your weight of evidence adaptation under Annex XI, Section 1.2. is rejected.

1.2.2. No assessment of potency

58 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).

59 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section 1.2.1 above), this condition cannot be assessed.

60 On this basis, the information requirement is not fulfilled.

1.3. Study design

61 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.

62 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the newly generated in vitro/in chemico data, an 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.

2. In vitro gene mutation study in bacteria

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

2.1. Information provided

64 ECHA understands that you have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following:

(i) an *in vitro* study of genetic toxicity (mitotic recombination and mitotic chromosome loss) to Saccharomyces cerevisiae (1991) with the Substance;

(ii) an *in vitro* gene mutation study in bacteria (1988) with the Substance;

(iii) an *in vitro* chromosome aberration and sister chromatid exchange tests (1990) with the Substance;

(iv) an *in vivo* Drosophila aneuplody test (1991) with the Substance.

2.2. Assessment of the information provided

65 In addition to the deficiencies identified in Section 0.1., ECHA identified endpoint specific issue(s) addressed below.

66 Information that can be used to support weight of evidence adaptation for the information requirement of Annex VII, Section 8.4.1. includes similar information that is produced by the OECD TG 471. OECD TG 471 requires the study to investigate the following key parameter(s):

- Detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies;
- Data provided on 5 bacterial 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).

67 The sources of information (i, iii and iv) do not provide relevant information on the detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria.

68 More specifically, study (i) provides information on mitotic recombination and mitotic chromosome loss in Saccharomyces cerevisiae, study (iii) provides information on in vitro chromosome aberration and sister chromatid exchange in cultured mammalian cells, and study (iv) provides information on induction of aneuplody in drosophila.

69 Consequently, these studies do not provide relevant information for this information requirement.

70 The source of information (ii) provides relevant information on some of the key elements. More specifically, only the following strains were investigated in this study: S. typhimurium TA98, TA100, TA1535, TA1537 and TA97). The strain S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101) is missing.

71 Therefore, information on a strain which is capable of detecting oxidising mutagens, cross-linking agents and hydrazines is missing.

72 In addition, the reliability of the source of information (ii) is affected by the following deficiencies:

2.2.1. Methodological deficiencies of study (ii)

73 The evaluation of the reliability of the contribution of each relevant line of information to the weight of evidence approach includes an assessment of each source of information against the specifications of the test guideline followed.

74 Study (ii) is reported as in vitro gene mutation study in bacteria and has been performed to a test protocol similar to the OECD TG 471. This test guideline requires that:

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) at least 5 doses are evaluated, in each test condition;
c) triplicate plating is used at each dose level;
d) the mean number of revertant colonies per plate is reported for the treated doses and the controls;
e) negative results are confirmed in a repeat experiment with modification of study parameters to extend the range of conditions assessed, or a justification why confirmation of negative results is not considered necessary is provided.

75 In study (ii):

a) details on the dose selection and the maximum dose tested are not reported
b) the number of doses used is not reported
c) it is not reported whether triplicate plating was used at each dose level;
d) the mean number of revertant colonies per plate for the treated doses and the controls is not reported;
e) no repeat experiment was performed to confirm the negative results and no justification is provided.

76 The unclarity regarding how the results were obtained introduces uncertainty in the results which must be considered.

77 Therefore, the provided study (ii) cannot be considered a reliable source of information that could contribute to the conclusion on the detection and quantification of gene mutations in cultured bacteria investigated by the required study.

2.2.2. Conclusion on the weight of evidence

78 In summary, there is no information provided on some elements of detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies, for the required 5 bacterial strains. More specifically, the required strain S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101) is missing.

79 And even for the elements covered, the corresponding source of information has deficiencies affecting its reliability.

80 In absence of reported details, the unclarity regarding how the results were obtained introduces uncertainty in the results, which prevents drawing the conclusion on the detection and quantification of gene mutations of the strains investigated.

81 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for in vitro gene mutation study in bacteria.

82 Based on the above, your weight of evidence adaptation under Annex XI, Section 1.2. is rejected.

83 Therefore, the information requirement is not fulfilled.

2.3. Study design

84 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) is considered suitable.

3. Growth inhibition study aquatic plants

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

3.1. Information provided

86 You have provided:

(i) Growth inhibition study on algae (2007) with the Substance;

3.2. Assessment of the information provided

3.2.1. The provided study does not meet the specifications of the test guideline(s)

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

Validity criteria

a) exponential growth in the control cultures is observed over the entire duration of the test;

b) at least 16-fold increase in biomass is observed in the control cultures by the end of the test;

c) 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%;

d) the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with *Pseudokirchneriella subcapitata*;

Technical specifications impacting the sensitivity/reliability of the test

e) the test duration is 72 hours. However, the test duration may be shortened to at least 48 hours as long as the biomass of control cultures increase by at least 16-fold;

Characterisation of exposure

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

g) the concentrations of the test material are measured at least at the beginning and end of the test:

- at the highest, and
- at the lowest test concentration, and
- at a concentration around the expected EC_{50}.
- for volatile, unstable or strongly adsorbing test substances, additional samplings for analysis at 24 hour intervals is required;

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. If the concentration of the test material has not been maintained within ±20 % of the nominal or measured initial concentration throughout the test, results must be based on the geometric mean of measured concentrations during exposure or on a model describing the decline of the concentration of the test material over the exposure period;

88 In study (i):

Validity criteria
No information is provided on:

a) exponential growth in the control cultures;

b) the biomass at the start and end of the test, respectively;

c) the mean coefficient of variation for section-by-section specific growth in the control;

d) the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures;

Technical specifications impacting the sensitivity/reliability of the test

e) the test duration was 48 h and no information is provided if the biomass in the control culture increased by at least 16-fold;

Characterisation of exposure

f) no analytical monitoring of exposure was conducted;

g) you have expressed the effect values based on nominal concentrations without further justification or proof that the test concentrations remained within ± 20 % of nominal or measured initial concentration throughout the test. The Substance is volatile (vapor pressure = 5950 – 6306 Pa at 25° C), and no additional sampling for analysis at 24 h interval was conducted;

89 Based on the above,

- it cannot be confirmed wether the validity criteria (a – d) of OECD TG 201 are met
- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the exposure duration was shorter than 72 hours without further justification or proof that biomass of control culture increased by at least 16 fold during this time (e). A shorter exposure period might lead to less pronounced effects and thus underestimate the hazard
- in addition, the Substance is difficult to test due to its volatility and there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, in the lack of analytical monitoring it cannot be confirmed that the test material stable during the course of the test (f -g). Therefore, the hazard might be underestimated if effect values are based on nominal concentrations and the results of this study are not reliable.

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

91 Therefore, the information requirement is not fulfilled.

3.3. Study design

92 The Substance is difficult to test due to its volatility (vapor pressure = 5950 – 6306 Pa at 25° C). OECD TG 201 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.

93 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.

94 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 201.

95 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.

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 23 August 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 did not receive any comments within the commenting period.

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]
[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

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.

With that detailed information, ECHA can confirm 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 (https://echa.europa.eu/manuals).