~~Confidential~~

Helsinki, 29 May 2024

Addressee(s)
Registrant(s) of JS_C1618AEP as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
09 October 2013

Registered substance subject to this decision ("the Substance")
Substance name: Alcohols, C16-18, ethoxylated, phosphates
EC/List number: 500-295-0

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 ***3 September 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. 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).

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

3. *In vitro* micronucleus study (Annex VIII, Section 8.4.2., test method: OECD TG 487). The aneugenic potential of the Substance must be assessed with an additional positive control group for aneugenicity on top of the positive control group for clastogenicity, if the Substance induces an increase in the frequency of micronuclei.

4. If negative results are obtained in test performed for the information requirement of Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490).

5. Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.) by oral route, in rats, to be combined with the screening for reproductive/developmental toxicity requested below.

6. Screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats.

7. Long-term toxicity testing on fish (triggered by Annex VIII, Section 9.1.3., Column 2; test method: EU C.47./OECD TG 210).

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)

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.:

- Skin sensitisation (Annex VII, Section 8.3.)
- *In vitro* micronucleus study (Annex VIII, Section 8.4.2.)
- *In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

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. Predictions for toxicological properties

5 You provide a read-across justification document in IUCLID Section 13.

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

- Alcohols C16-18 (even numbered), ethoxylated (< 2.5 EO), EC 500-212-8 (which you define as 'source substance 1');
- Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-hydroxy-, mono-C11-14-isoalkyl esters, C13-rich, phosphates, EC 616-610-0 (which you define as 'source substance 5');
- Poly(oxy-1,2-ethanediyl), alpha-hydro-omega-hydroxy-, mono-C8-10 (even numbered)-alkyl esters, phosphates, EC 614-291-2 (which you define as 'source substance 7').

7 You provide the following reasoning for the prediction of toxicological properties: the substances share the common functional groups, similar physico-chemical properties, similar properties for environmental fate & eco-toxicological profile of the analogue members, similar metabolic pathways, common levels and mode of human health related effects.

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 substances.

0.1.1.1. Missing supporting information to compare properties of the substancess

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 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(s) (Guidance on IRs and CSA R.6., Section R.6.2.2.1.f.).

10 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar source substances cause the same type of effects. In this context, relevant, reliable and adequate information allowing to compare the properties of the source substances 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 Substance and of the source substances.

11 As indicated in your read-across justification document, the Substance and the source substances differ in the presence or absence of phosphates, the alkyl chain length and degree of ethoxylation. You have provided studies with the source substances 1, 5 and 7 to inform on the toxicological properties of the Substance. While these studies provide relevant information on the properties of the respective source substances, ECHA notes that you did not provide any experimental data, in particular bridging studies of comparable design and duration on the Substance and relevant for the properties under consideration.

12 In the absence of such information, you have not established that the Substance and the source substances are likely to have similar properties despite their compositional differences. Therefore you have not provided sufficient supporting information to scientifically justify the read-across.

0.1.2. Conclusion

13 Based on the above, you have not established that relevant properties of the Substance can be predicted from data on the source substances. 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

14 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

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

(i) an OECD Guideline 406 test (1995) with the source substance 1.

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

1.2.1.1. Read-across adaptation rejected

16 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 endpoint-specific issue addressed below.

17 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 the OECD TG 406. Therefore, the following specifications must be met:

a) a dose level selection rationale is provided;

b) the induction concentration is the highest causing mild irritation to the skin;

c) the challenge dose is the highest non-irritation concentration;

d) positive and negative controls are included to establish the sensitivity and reliability of the experimental technique.

18 In study (i):

a) no dose level selection rationale was provided;

b) you did not provide information whether the concentration used for induction caused mild irritation;

c) you did not provide information whether the challenge concentration caused irritation;

d) no information on positive group(s) was provided.

19 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 parameter(s) of the OECD TG 406.

20 On this basis, the information provided does not contribute to the assessment whether the Substance causes skin sensitisation.

1.2.2. No assessment of potency

21 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).

22 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.

23 Therefore, the information requirement is not fulfilled.

1.3. Study design

24 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.

25 In your comments to the draft decision, you indicate that "*the feasibility of conducting the in vitro skin sensitisation tests relies on the fulfilment of the applicability domain criteria. This has to be determined with the help of pre-tests*". You further elaborate on the nature of the pre-tests applicable to the different in vitro assays listed in the OECD TGs 442C, D and E. You point out that "*If it is not feasible to run all three in vitro tests due to any of the tests not being suitable for the substance, or if it is not possible to conclude on hazard and/or potency on the basis of in vitro studies; additional in silico modelling will be used in a weight of evidence assessment according to OECD 497*".

26 In case the methods included in the defined approaches are suitable for the substance and conclusive prediction is obtained, a defined approach as presented in the OECD TG 497 can also be used to address the skin sensitisation information requirement of Annex VII, 8.3 provided that the results of the defined approach allows classification and risk assessment, including determination of the potency of the skin sensitisation properties of the Substance. It is the Registrant's responsibility to determine whether a defined approach is applicable and conclusive for a particular substance. More information on the use of defined approaches for skin sensitisation under REACH can be obtained in the document available at the following link on ECHA's website: https://echa.europa.eu/documents/10162/1128894/oecd_test_guidelines_skin_sensitisation_en.pdf

27 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or newly generated *in vitro* 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.

2. Long-term toxicity testing on aquatic invertebrates

28 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.

2.1. Triggering of the information requirement

29 In the provided EU Method A.6 (2012) study, the saturation concentration of the Substance in water was determined to be below 0.00053, i.e. below the limit of detection of the UV/VIS spectrophotometric method applied.

30 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

2.2. Information requirement not fulfilled

31 You have provided a short-term toxicity study on aquatic invertebrates but no information on long-term toxicity on aquatic invertebrates for the Substance.

32 Therefore, the information requirement is not fulfilled.

2.3. Study design

33 The Substance is difficult to test due to the low water solubility (<0.00053 g/L), adsorptive properties (Log K_{ow} = 5.83 - 16.04 and Log K_{oc} > 4) and surface active properties (ca. 45 dyne/cm). The OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in the 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 the 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.

34 For multi-constituents/UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key constituents or groups of constituents).

35 If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

36 In your comments to the draft decision, you agree to perform the requested study.

Reasons related to the information under Annex VIII of REACH

3. *In vitro* micronucleus study

37 An *in vitro* mammalian chromosomal aberration study or an *in vitro* mammalian micronucleus study is an information requirement under Annex VIII, Section 8.4.2.

3.1. Information provided

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

(i) an *in vitro* chromosome aberration study in mammalian cells (1995) with the source substance 1.

3.2. Assessment of the information provided

3.2.1. Read-across adaptation rejected

39 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 endpoint-specific issues addressed below.

40 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 the OECD TG 473. Therefore, the following specifications must be met:

a) the maximum concentration tested induces 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration corresponds to 10 mM, 2 mg/mL or 2 µL/mL, whichever is the lowest;

b) at least 300 well-spread metaphases are scored per concentration;

c) the positive controls induce responses compatible with those generated in the historical positive control database;

d) the positive controls produce statistically significant increase compared with the negative control;

e) the negative control data is ideally within the 95% control limits of the distribution of the laboratory's historical negative control database;

f) data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures is reported;

g) to conclude on a negative outcome, a negative response is obtained in all three experimental conditions described in paragraph 28 of OECD TG 473, using a short-term treatment with and without metabolic activation and long-term treatment without metabolic activation.

41 In study (i):

a) there was no information provided whether the maximum tested concentration induced 55+5% of cytotoxicity compared to the negative control, it was only mentioned that cytotoxicity was induced;

b) there was no information provided of how many metaphases were scored per concentration;
c) there was no information provided whether the positive control data was compatible with those generated in the historical positive control database. The positive controls were described as 'valid', however no validity criteria were provided;
d) there was no information provided whether the positive control produced a statistically significant increase in the induced response when compared with the concurrent negative control. The positive controls were described as 'valid', however no validity criteria were provided;
e) there was no information provided whether the negative control showed a response within the historical control range of the laboratory;
f) data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures were not reported;
g) there was no information provided whether all three experimental conditions described in paragraph 28 of OECD TG 473 (i.e., a short-term treatment with metabolic activation, a short-term treatment without metabolic activation, a long-term treatment without metabolic activation) were met to conclude on a negative outcome.

42 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 parameter(s) of the corresponding OECD TG.

43 Therefore, the information requirement is not fulfilled.

3.3. Study design

44 According to the Guidance on IR & CSA, Section R.7.7.6.3., either the *in vitro* mammalian chromosomal aberration ("CA") test (test method OECD TG 473) or the *in vitro* mammalian cell micronucleus ("MN") test (test method OECD TG 487) can be used to investigate chromosomal aberrations *in vitro*. However, while the MN test detects both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the CA test detects only clastogenicity, as OECD TG 473 is not designed to measure aneuploidy (see OECD TG 473, paragraph 2).Therefore, you must perform the MN test (test method OECD TG 487), as it enables a more comprehensive investigation of the chromosome damaging potential *in vitro*. Moreover, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen [1] (OECD TG 487, paragraphs 33 to 35).

45 In your comments to the draft decision, you agree to perform the requested study.

3.3.1. Assessment of aneugenicity potential

46 If the result of the MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance.

47 In line with the OECD TG 487 (paragraph 4), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

[1] According to the TG 487 (2016) "At the present time, no aneugens are known that require metabolic activation for their genotoxic activity" (paragraph 34).

4. *In vitro* gene mutation study in mammalian cells

48 An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII, Section 8.4.3., in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

4.1. Triggering of the information requirement

49 Your dossier contains (I) a negative result for *in vitro* gene mutation study in bacteria and (II) inadequate data for the other study (*in vitro* chromosomal aberration study in mammalian cells).

50 The *in vitro* chromosomal aberration in mammalian cells study provided in the dossier is rejected for the reasons provided in request 3.

51 The result of the request 3 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3. is triggered.

52 Consequently, you are required to provide information for this information requirement, if the *in vitro* micronucleus study in mammalian cells provides a negative result.

4.2. Information provided

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

(i) an *in vitro* gene mutation study in mammalian cells (1995) with the source substance 1.

4.3. Assessment of the information provided

4.3.1. Read-across adaptation rejected

54 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 endpoint-specific issues addressed below.

55 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 476 or the OECD TG 490 (Guidance on IRs and CSA, Table.7.7-2). Therefore, the following specifications must be met:

a) the maximum concentration tested induces 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration corresponds to 10 mM, 2 mg/mL or 2 µL/mL, whichever is the lowest;

b) the concurrent positive controls induce responses that are compatible with those generated in the historical positive control database and does not induce more than 90% of cytotoxicity compared to the negative control

c) the concurrent positive controls produce a statistically significant increase compared with the concurrent negative control

d) the negative control data is ideally within the 95% control limits of the distribution of the laboratory's historical negative control database

e) data on the cytotoxicity and the mutation frequency for the treated and control cultures are reported.

56 In study (i):

a) there was no information provided whether the maximum tested concentration induced 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. It was only mentioned that in the dose finding test the solubility limit was 100 µg/ml and in the results section 'cytotoxicity' was mentioned, but no further details were provided;

b) there was no information provided whether the positive control induced responses that are compatible with those generated in the historical positive control database and whether it induced more than 90% of cytotoxicity compared to the negative control. The positive controls were described as 'valid', however no validity criteria were provided;

c) there was no information provided whether the positive control produced a statistically significant increase in the induced response when compared with the concurrent negative control. The positive controls were described as 'valid', however no validity criteria were provided;

d) there was no information provided whether the response of the negative control was inside the historical control range of the laboratory. The negative controls were described as 'valid', however no validity criteria were provided;

e) data on the cytotoxicity and the mutation frequency for the treated and control cultures were not reported.

57 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 parameter(s) of the corresponding OECD TG.

58 Therefore, the information requirement is not fulfilled.

4.4. Study design

59 To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

60 In your comments to the draft decision, you agree to perform the requested study.

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

61 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1.

5.1. Information provided

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

(i) a combined repeated dose and reproduction / developmental screening study (2009) with the source substance 5;

(ii) a combined repeated dose and reproduction / developmental screening study (2009) with the source substance 7.

5.2. Assessment of the information provided

5.2.1. Read-across adaptation rejected

63 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.

64 Therefore the information requirement is not fulfilled.

5.2.2. Information provided in your comments on the draft decision

65 Your comments on the draft decision for this request are addressed together with your comments on the request for information requirement related to the screening study for reproductive/developmental toxicity study in section 6.2.2 below.

5.3. Study design

66 When there is no information available neither for the 28-day repeated dose toxicity (EU B.7, OECD TG 407), nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

67 The study design is addressed in request 6.

6. Screening study for reproductive/developmental toxicity

68 A screening study for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1.

6.1. Information provided

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

(i) a combined repeated dose and reproduction / developmental screening study (2009) with the source substance 5;

(ii) a combined repeated dose and reproduction / developmental screening study (2009) with the source substance 7.

6.2. Assessment of the information provided

6.2.1. Read-across adaptation rejected

70 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.

6.2.2. Information provided in your comments on the draft decision

71 In your comments on the draft decision, you acknowledge the lack of bridging studies to support the read-across adaptation.

72 You indicate to proceed in a "*step-wise approach*" whereby the first step is to "*to submit a new read-across adaptation to cover the short-term repeated dose toxicity and the screening for reproductive/developmental toxicity studies; and only move on to request the OECD 422 which involves vertebrate animal testing at later stage, if required*".

73 As part of your comments, you have described your read-across hypothesis, outlined elements of structural similarities between the Substance and the source substance EC 500-155-9 and presented a data matrix mapping out the physico-chemical and (eco)toxicological properties of these substances. You have also indicated that as part of this new read-across adaptation, you intend to generate the following supporting information:

- In vitro Caco2 assay for both the target and source substances to determine if they have a comparable absorption in the gastrointestinal tract.

- 3T3 NR (Neutral Red) uptake test acute toxicity for target and source substances to determine similar acute toxicity potential.

- in vitro testing (ReproTracker/DevTox) for both target and source substances to generate bridging data for the developmental toxicity endpoint.

74 When the conditions for an adaptation are not met and there is a data gap, ECHA has the duty to request the missing information, which is a standard information requirement. ECHA does not breach the principle of testing as last resort in Article 25(1) of the REACH Regulation by requesting the study, but this does not prejudice your obligation to consider alternatives as set out in the REACH Regulation.

75 In any case, as your testing strategy relies on a read-across approach that has not yet been fully described and justified, with elements of the adaptation missing such as the robust study summary for the source study as well as on supporting information which is yet to be generated, no conclusion on the compliance of the proposed adaptation can be made.

76 Therefore, the information requirement is not fulfilled.

6.3. Study design

77 A study according to the test method EU B.64/OECD TG 422 must be performed in rats.

78 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex VIII, Section 8.7.1., Column 1).

79 Therefore, the study must be conducted in rats with oral administration of the Substance.

7. Long-term toxicity testing on fish

80 Short-term toxicity testing on fish is an information requirement under Annex VIII, Column 1, Section 9.1.3. However, long-term toxicity testing on fish may be required by the Agency (Section 9.1.3., Column 2) if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

7.1. Triggering of the information requirement

81 As already explained in request 2, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

7.2. Information requirement not fulfilled

82 You have provided a short-term toxicity study on fish but no information on long-term toxicity on fish for the Substance.

83 Therefore, the information requirement is not fulfilled.

7.3. Study design

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

85 The OECD TG 210 specifies that, for difficult to test substances, the 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 2.

86 In your comments to the draft decision, you agree to perform the requested study.

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 (2023).
***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 14 March 2023.

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 request(s).

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]
[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/group of constituents on the test results for the endpoint to be assessed. For example, if a constituent/group of constituents of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/group of constituents.

(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 the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

- The reported composition must also include other parameters relevant for the property to be tested.

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).