~~Confidential~~

Helsinki, 16 August 2023

Addressee(s)
Registrant(s) of MSC_247-979-2 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
02/12/2022

Registered substance subject to this decision ("the Substance")
Substance name: 2,3-epoxypropyl neodecanoate
EC number/List number: 247-979-2

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***21 November 2028***.

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

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

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

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

- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: EU C.1./OECD TG 203).

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

- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211);

- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210).

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

- Carcinogenicity study (Annex X, Section 8.9.1.; test method: OECD TG 451) by oral route, in rats.

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

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Reasons related to the information under Annex VII of REACH

1. Short-term toxicity testing on aquatic invertebrates

1 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

1.1. Information provided

2 You have provided a short-term toxicity study on daphnia magna (1983) with the Substance (study i).

1.2. Assessment of the information provided

3 To fulfil the information requirement, a study must comply with the OECD TG 202 and the specifications of the OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Characterisation of exposure

a) 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.

Additional requirements applicable to difficult to test substances

Preliminary solubility study

b) if the test material is forming dispersion or emulsions (*e.g.* certain surfactants, aliphatic amines), the dispersibility limit or the critical micelle concentration of the test material in the specific test solution under the test conditions is determined;

Test solutions preparation methods

c) surface-active test chemicals are tested at concentrations below their critical micelle concentration (CMC) in the test medium;

d) a solvent must not be used for multi-constituent substances and UVCBs;

e) if water-accommodated fractions (WAFs) are used, they must be prepared separately for each test concentration;

f) if water-accommodated fractions (WAFs) are used, a preliminary study must be conducted to determine that saturation has been achieved.

4 In the study provided:

Characterisation of exposure

1. no analytical monitoring of exposure was conducted.

Additional requirements applicable to difficult to test substances

Preliminary solubility study

g) the test material has a reported surface tension of 50 mN/m (i.e. is surface active) and no dispersibility limit or critical micelle concentration of the test material in the specific test solution under the test conditions is reported.

Test solutions preparation methods

h) the Substance is a surface-active test chemical and you have not demonstrated that it was tested below its critical micelle concentration (CMC) in the test medium;

i) the test material is a UVCB substance and you have used a solvent (i.e. Analar acetone);

j) the study report indicates the use of dilutions of stock solution to prepare the water-accommodated fractions (WAFs) for each test concentration;

k) you have used water-accommodated fractions (WAFs) and have not reported the results of the preliminary saturation study.

5 Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have not reported the results of the preliminary stability study (f) and you have not performed analytical monitoring of the test concentrations (a). Hence, you have not demonstrated that the reported effect values are representative of the exposure concentration.

6 Furthermore, the Substance is difficult to test due to its UVCB and surface active nature and there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have used solvent to prepare the WAFs (d) and WAF dilutions (e) and you have not demonstrated that both procedures did not affect the relative composition of the constituents of the Substance in solution. Additionally, the Substance is surface active and, as you did not report the critical micelle concentration (CMC) under test conditions (b), you have not demonstrated that the test concentrations were below the CMC (c) hence, that the reported effect concentration was representative of the bioavailable fraction of Substance in the test system. Taken together, based on the above deficiencies the hazard can be underestimated.

7 On this basis, the specifications of OECD TG 202 are not met and the information requirement is not fulfilled.

1.3. Study design and test specifications

8 The Substance is difficult to test due to the UVCB nature, adsorptive properties (Log K_{ow} 4.4), surface activity (50 mN/m) and hydrolysis potential (DT50 ca. 9 days). The OECD TG 202 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 202. 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.

9 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).

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

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (Guidance on IRs and CSA, Appendix R.7.8.1-1, Table R.7.8-3);
- 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.

11 In the comments to the draft decision, an addressee of the decision disagrees with the requested study. They propose to perform the long-term toxicity to aquatic invertebrates study (OECD TG 211) requested in this decision (Request 3) instead of short-term toxicity study (OECD TG 202) and to adapt with this study current information requirement, in accordance with Annex VII, Section 9.1.1., Column 2 of the REACH Regulation. They consider that this "approach would also be consistent with ECHA's updates regarding adaptation of long-term aquatic toxicity testing under Annex IX to REACH as well as the Board of Appeal decision on case A-011-2018".

12 ECHA notes that Annex VII section 9.1.1 column 2 of REACH Regulation specifies that the short-term toxicity study does not need to be conducted if a long-term aquatic toxicity study on invertebrates is available. At present no long-term toxicity study on aquatic invertebrates is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

Reasons related to the information under Annex VIII of REACH

2. Short-term toxicity testing on fish

13 Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

2.1. Information provided

14 You have provided:

(i) a short-term toxicity study on fish (1983) with the Substance;

(ii) a short-term toxicity study on fish (2003) with the Substance.

2.2. Assessment of the information provided

15 To fulfil the information requirement, a study must comply with the OECD TG 203 and the specifications of the OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Validity criteria

1. the analytical measurement of test concentrations is conducted.

Characterisation of exposure

l) 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.

Additional requirements applicable to difficult to test substances

Preliminary solubility study

m) if the test material is forming dispersion or emulsions (*e.g.* certain surfactants, aliphatic amines), the dispersibility limit or the critical micelle concentration of the test material in the specific test solution under the test conditions is determined.

Test solutions preparation methods

n) surface-active test chemicals are tested at concentrations below their critical micelle concentration (CMC) in the test medium;

o) a solvent must not be used for multi-constituent substances and UVCBs;

p) if water-accommodated fractions (WAFs) are used, they must be prepared separately for each test concentration;

q) if water-accommodated fractions (WAFs) are used, a preliminary study must be conducted to determine that saturation has been achieved.

16 In studies (i) and (ii):

Validity criteria

1. no analytical measurement of test concentrations was conducted in study (i).

Characterisation of exposure

r) no analytical monitoring of exposure was conducted in study (i). For study (ii), you have used total organic carbon (TOC) for analytical monitoring of exposure concentrations. You do not report the specificities of the method used, including detection and quantification limits.

Additional requirements applicable to difficult to test substances

Preliminary solubility study

s) the test material has a reported surface tension of 50 mN/m (i.e. is surface active) and no dispersibility limit or critical micelle concentration of the test material in the specific test solution under the test conditions is reported for both studies (i) and (ii).

Test solutions preparation methods

t) the Substance is a surface-active test chemical and you have not demonstrated that it was tested below it's critical micelle concentration (CMC) in the test medium;

u) the test material is a UVCB substance and you have used a solvent (i.e. Analar acetone) for study (i);

v) the study report indicates the use of dilutions of stock solution to prepare the water-accommodated fractions (WAFs) used for each test concentration in study (i);

w) you have used water-accommodated fractions (WAFs) and have not reported the results of the preliminary saturation study for both studies (i) and (ii).

17 Based on the above, the validity criteria of the OECD TG 203 are not met for study (i) since you have not performed analytical verification of the test concentrations (a, b).

18 Furthermore, the Substance is difficult to test due to it's UVCB and surface active nature and there are critical methodological deficiencies resulting in the rejection of the study (i) results. More specifically, you have used a solvent to prepare the WAFs (e) and WAF dilutions (f) and you have not demonstrated that both procedures did not affect the relative composition of the constituents of the Substance in solution.

19 Regarding study (ii), TOC is not considered a substance specific or sensitive method for monitoring exposure concentrations (b) hence, it is not a reliable quantification method. Unless properly justified, a more reliable method (e.g. HPLC) should be used, as explain in OECD GD 23. 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.

20 Moreover, there are critical methodological deficiencies resulting in the rejection of both studies (i) and (ii) results. More, specifically you have not reported the results of the preliminary stability study (g), nor you have reported the results of analytical monitoring at the end of the test for study (ii), hence, you have not demonstrated that the Substance was stable in solution during the test period. Additionally, the Substance is surface active and, as you did not report the critical micelle concentration (CMC) under test conditions (c) you have not demonstrated that the test concentrations were below the CMC (d) hence, that the reported effect concentration was representative of the bioavailable fraction of Substance in the test system. Taken together, based on the above deficiencies the hazard can be underestimated.

21 On this basis, the specifications of OECD TG 203 are not met and the information requirement is not fulfilled.

2.3. Study design and test specifications

22 The OECD TG 203 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 and test specifications" under request 1.

23 In the comments to the draft decision, an addressee of the decision disagrees with the requested study. They propose to perform the long-term toxicity study on fish (OECD TG 210) requested in this decision (Request 4) instead of short-term toxicity study (OECD TG 203) and to adapt with this study current information requirement, in accordance with Annex VIII, Section 9.1.3., Column 2 of the REACH Regulation. They consider that this "approach would also be consistent with ECHA's updates regarding adaptation of long-term aquatic toxicity testing under Annex IX to REACH as well as the Board of Appeal decision on case A-011-2018".

24 ECHA notes that Annex VIII section 9.1.3 column 2 of REACH Regulation specifies that the short-term toxicity study does not need to be conducted if a long-term toxicity study on fish is available. At present no long-term toxicity study on fish is provided in the IUCLID dossier, therefore no conclusion on the compliance can currently be made. You remain responsible for complying with this decision by the set deadline.

Reasons related to the information under Annex IX of REACH

3. Long-term toxicity testing on aquatic invertebrates

25 Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

3.1. Information provided

26 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1.

3.2. Assessment of the information provided

27 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to aquatic invertebrates referred to under Column 1, Section 9.1.5.

28 Your adaptation is rejected and therefore the information requirement is not fulfilled.

29 Comments to the draft decision were submitted by one of the addressees of the decision. ECHA understands that they agree with the requested study.

3.3. Study design and test specifications

30 The OECD TG 211 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 and test specifications" under request 1.

4. Long-term toxicity testing on fish

31 Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

4.1. Information provided

32 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1.

4.2. Assessment of the information provided

33 Under Annex IX, Section 9.1., Column 2 is not a basis for omitting information on long-term toxicity to fish referred to under Column 1, Section 9.1.6.

34 Your adaptation is rejected and therefore the information requirement is not fulfilled.

35 Comments to the draft decision were submitted by one of the addressees of the decision. ECHA understands that they agree with the requested study.

4.3. Study design and test specifications

36 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.).

37 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 and test specifications" under request 1.

Reasons related to the information under Annex X of REACH

5. Carcinogenicity study

38 A carcinogenicity study is an information requirement (Annex X, Section 8.9.1.) if

1. the substance has a widespread dispersive use or there is evidence of frequent or long-term human exposure, and
2. the substance is classified as germ cell mutagen category 2 or there is evidence from the repeated dose study(ies) that the substance is able to induce hyperplasia and/or pre-neoplastic lesions.

5.1. Triggering the information requirement

5.1.1. Condition(s) related to exposure are met

5.1.1.1. The substance has widespread dispersive uses

39 The term widespread dispersive uses means that the substance is used at many sites and/or by many users leading to potential for exposure (ECHA Guidance R.12 (pages 34-35)). In relation to this condition you have indicated that "the substance does not have widespread dispersive use".

40 However, the registration dossier include uses which are considered widespread dispersive.

41 Firstly, you have reported widespread uses by professional workers (in section 3.5.4 of IUCLID).

42 One member reported "Epoxy Flooring – professional application with [redacted]% substance." The following Process Descriptors (PROCs) demonstrate dispersion of the Substance:

43 PROC 5: Mixing or blending in batch processes

44 PROC 8a: Transfer of substance or mixture at non-dedicated facilities

45 PROC 10: Roller application or brushing

46 Further assessment in the related CSR does not demonstrate absence of release/exposure (rigorous containment), and in fact your exposure estimations for professional workers (for example, in exposure scenario 4, contributing scenario 1) confirm actual exposure.

47 Another member of the joint submission reported a "Professional use application." The following PROCs especially demonstrate dispersion of the Substance:

48 PROC 5: Mixing or blending in batch processes

49 PROC 8a: Transfer of substance or mixture at non-dedicated facilities

50 PROC 10: Roller application or brushing

51 PROC 11: Non industrial spraying

52 Further assessment in the related CSR does not demonstrate absence of release/exposure (rigorous containment), and in fact your exposure estimations for professional workers (for example, in exposure scenario 3, contributing scenario 9) confirm actual exposure.

53 Secondly, in addition to the professional uses described above, you have reported uses at industrial sites (in section 3.5.3 of IUCLID).

54 For some of these uses it is indicated that they take place on many sites: for example, "Automotive and Industrial Coatings – Resin manufacturing" takes place on 10-100 sites, and further assessment in the related CSR does not demonstrate absence of release/exposure (rigorous containment), in fact your exposure estimations (for example, in exposure scenario 5, contributing scenario 1) confirm actual exposure.

55 Furthermore, the industrial exposure scenarios and contributing scenarios that you include in your CSRs demonstrate significant exposure to the workers (many users). For example, in one CSR of the joint submission exposure scenario 3, contributing scenario 1, (Batch processing with [redacted]% substance) and in another CSR of the joint submission, in exposure scenario 1, contributing scenario 2, (Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) (PROC 5)).

56 Therefore, based on the information in your registration dossier there are widespread dispersive uses of your Substance.

5.1.1.2. The uses of the Substance lead to frequent human exposure

57 Frequent exposure is considered to be more than a few exposures per year, as according to the ECHA Guidance R.14, infrequent exposure relates to tasks performed only a few times per year. In addition, ECETOC Technical Report No 131 (2018) defines frequent as 52-365 events in year, meaning at least once a week.

58 In relation to this condition you have indicated that there is no evidence of frequent exposure.

59 However, the information in the CSRs shows evidence of frequent human exposure for both professional and industrial uses.

60 For professional and industrial uses, and exposure scenarios described in section above, the conditions of use in the CSRs state < 8 hours or <4 hours. This demonstrates that exposures to professionals and industrial workers take place daily, for several hours, and lead to frequent exposure.

61 Therefore, based on the information in your registration dossier the uses of the Substance lead to frequent human exposure.

5.1.1.3. The uses of the Substance lead to long-term human exposure

62 Long-term (chronic) human exposure is considered to be exposure over a period of several months or years.

63 In relation to this condition you have indicated that there is no long-term human exposure.

64 However, you have professional and industrial uses and workers have the potential to be exposed to the registered substance long-term, even throughout their career/working-life.

65 Therefore, based on the information in your registration dossier the uses of the Substance lead to long-term exposure.

66 Comments to the draft decision were submitted by one of the addressees of the decision.

67 This registrant indicated that considering the use conditions of the Substance, they do not believe that the risk of human exposure is sufficient to justify the request for a carcinogenicity study. They state that uses under industrial setting are performed in closed processes and that for both industrial and professional uses proper chemical hygiene practices are in place, and personal protective equipment is used. They conclude that "Consistent with Chapter R.12 of ECHA's Guidance on Information Requirements and Chemical Safety Assessment, this information on the absence of release/exposure should be considered."

68 ECHA considers that the claim of absence of exposure is unsupported. In particular, the registrant has not demonstrated the absence of release/exposure, such as by describing rigorous containment throughout the life-cycle of the substance. Furthermore, the information available in registration dossiers for this Substance contradicts the registrant's claim. According to the exposure scenarios in their CSRs, as well as in the CSR of another addressee of this decision, as noted above in section 5.1.1.1, both industrial and professional uses of the substance confirm that professional and industrial workers are exposed to the Substance. Moreover, there is evidence that the uses of the Substance lead to frequent and long-term exposure (as noted above in sections 5.1.1.2. and 5.1.1.3.)

69 Furthermore, while the registrant mentions that there is proper chemical hygiene practices and use of personal protective equipment in place for both industrial and professional uses, ECHA notes that this cannot be used to demonstrate absence of exposure. According to the principles of the hierarchy of control, technical measures (such as rigorous containment) should be given priority to ensure absence of exposure rather than relying upon personal protective equipment (REACH Guidance E.2.5.1., 2016).

70 Therefore, ECHA concludes that the information in the comments does not demonstrate absence of exposure. ECHA considers that the conditions related to exposure are met, as explained above separately.

5.1.2. Condition related to the hazard/classification

71 The condition sets that the substance is classified as germ cell mutagen category 2 or there is evidence from the repeated dose study(ies) that the substance is able to induce hyperplasia and/or pre-neoplastic lesions.

72 In relation to this condition you have indicated that "there was no histopathological evidence of induced cell hyperplasia and/or pre-neoplastic lesion observed in a five-week rat oral repeated-dose study." You have not provided any considerations regarding the alternative condition relating to the classification.

73 However, as evident from your dossier you have self-classified the Substance as a germ cell mutagen category 2. Furthermore, ECHA's Risk assessment committee (RAC) has concluded that the available information on the Substance meets the criteria for the germ cell mutagen 2 and proposed harmonised classification for the Substance on 18 March 2022[2].

74 Although no histopathological evidence of induced cell hyperplasia and/or pre-neoplastic lesions are reported in available repeat dose toxicity studies, the other hazard criterion is met.

75 In your comments you confirm that the Substance is already classified as germ cell mutagen 2. You consider that precautions and controls are in place to minimize human exposure as a result of this classification. However, this is not sufficient as noted above and the hazard classification of the Substance is in fact one of the triggers for the current request.

76 Therefore, the condition related to the hazard/classification is met.

5.1.3. Conclusion on triggering

77 Based on above, the information on uses reported in the dossiers and CSRs demonstrates that not only one necessary condition relating to the exposure is met, but all three alternative exposure criteria as set out in Annex X, Section 8.9.1., Column 2 are fulfilled:

[2] https://echa.europa.eu/documents/10162/af871a8f-f316-6705-6cc0-3ce76d1423b2

1. widespread dispersive use, and
2. evidence of frequent exposure, and
3. evidence of long-term human exposure.

78 In addition, the Substance is classified as a germ cell mutagen category 2.

79 Therefore, the information requirement is triggered.

5.2. Information provided

80 You have not provided in your dossier any information to address the carcinogenic properties of the Substance.

81 In the comments to the draft decision, one of the addressees indicated that it would welcome the opportunity to work with ECHA to determine if data from structurally related substance is appropriate to address the information requirement.

82 However, your comments do not indicate which analogue substance you intended to use nor provide any new scientific information to address or adapt current information requirement. Therefore, the data gap remains.

5.3. Test selection

83 ECHA considers that a 2-year carcinogenicity study according to the OECD TG 451 is the appropriate test method because (a) this is an internationally agreed test method recognised by the Agency as being appropriate, as required by Article 13(3), and (b) this study protocol is designed specifically to assess carcinogenicity properties of a chemical. In particular, the OECD TG 451 study aims at: "The identification of the carcinogenic properties of a chemical, resulting in an increased incidence of neoplasms, increased proportion of malignant neoplasms or a reduction in the time to appearance of neoplasms, compared with concurrent control groups; the identification of target organ(s) of carcinogenicity; the identification of the time to appearance of neoplasms; characterisation of the tumour dose-response relationship; identification of a no-observed-adverse-effect level (NOAEL) or point of departure for establishment of a Benchmark Dose (BMD); extrapolation of carcinogenic effects to low dose human exposure levels; and provision of data to test hypotheses regarding mode of action."

5.4. Study design and test specifications

84 The OECD TG 451 sets that the three main routes of administration to be used are oral, dermal and inhalation. Considering the physical and chemical characteristics of the Substance, liquid with low vapour pressure, oral is the most appropriate route of administration.

85 According to the OECD TG 451, the rat is the preferred species.

86 Therefore, the study must be performed according to the OECD TG 451, in rats and with oral administration of the Substance.

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.12 Use description; ECHA (2015).
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

The Substance is listed in the Community rolling action plan (CoRAP) for substance evaluation, which was concluded in 2021.

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 1 February 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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

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

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[3].

(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 the careful identification and description of the characteristics of the Tests Materials in accordance with

[3] https://echa.europa.eu/practical-guides

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.

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).