~~Confidential~~

Helsinki, 14 May 2024

Addressees
Registrants of JS_141-98-0 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
21 December 2022

Registered substance subject to this decision ("the Substance")
Substance name: O-isopropyl ethylthiocarbamate
EC/List number: 205-517-7

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 ***19 February 2027***.

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).

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

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

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

5. 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.

6. If negative results are obtained in tests performed for the information requirement of Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. then: In vitro gene

mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: EU B.17./OECD TG 476 or EU B.67./OECD TG 490)

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

8. Adsorption/desorption screening (Annex VIII, Section 9.3.1.; test method: EU C.18/OECD TG 106).

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

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

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

11. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: EU C.25/OECD TG 309) at a temperature of 12°C.

12. Identification of degradation products (Annex IX, Section 9.2.3.; test method: EU C.25/OECD TG 309).

The reasons for the requests are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The 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. In addition, the studies relating to biodegradation and bioaccumulation are necessary for the PBT assessment. However, to determine the testing needed to reach the conclusion on the persistency and bioaccumulation of the Substance you should consider the sequence in which these tests are performed and other conditions described in this Appendix.

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 requests
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 requests

Reasons common to several requests

0.1. Substance-tailored exposure-driven testing adaptation rejected

1 ECHA understands that you have adapted the following standard information requirements under Annex XI, Section 3.2 (a) substance-tailored exposure-driven testing, for the following information requirements:

- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)
- Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.)

To support the adaptation, you have provided statements as summarized below:

- you consider that the CSA adequately addresses the relevant exposure scenarios showing the absence or no significant exposure to the test item throughout its life cycle;
- you consider the adaptation justified on the basis of a low risk demonstrated by RCRs of << 1 based on CHESAR/EUSES modelling.

0.1.1. Assessment of the information provided

2 A substance-tailored exposure-driven testing adaptation under Annex XI, Section 3.2(a) must fulfil the cumulative conditions set out under Annex XI, Sections 3(1) as well as 3(2)(a). ECHA has identified the following issues with the proposed adaptations.

0.1.1.1. Absence of or no significant exposure not demonstrated

3 Under Annex XI, Section 3(2)(a)(i), the results of the exposure assessment covering all relevant exposure throughout the life cycle of the substance must demonstrate absence of or no significant exposure in all scenarios of the manufacture and all identified uses.

4 You claim that there will be no discharge to the environment from the use of the Substance at industrial site as flotation agent. You state that [redacted]".

5 However, ECHA considers that spills, leaks, and runoff are not avoidable for this kind of operation. In addition, there is no indication that special measures are implemented to limit *e.g.* spills during transfer, loading, and cleaning/maintenance. The Substance is well soluble (WS of 2.96 g/L), and hence it can potentially migrate to and contaminate surface water and groundwater. Furthermore, considering its volatility (VP of 950 Pa at 20°C), release from air through evaporation or volatilisation, and distribution further via precipitations cannot be excluded.

6 Therefore, you have not demonstrated absence of or no significant exposure in all scenarios of the manufacture and all identified uses.

0.1.1.2. Lack of appropriate PNEC

7 Under Annex XI, Section 3.2(a)(ii), a relevant and appropriate predicted no effect concentration (PNEC) must be derived.

8 For the reasons explained under requests 3, 4, 7, 9 and 10, your dossier does not include reliable information on the hazardous properties of the substance on at least three trophic levels (Guidance on IRs and CSA, Section 7.8.5.3).

9 Therefore, you have not demonstrated that an appropriate PNEC can be derived.

0.1.1.3. Exposure always well below PNEC not demonstrated

10 The results of the exposure assessment must show that exposures are always well below the PNEC, i.e. RCRs must always be well below 1. This means that a high level of confidence is needed to demonstrate that every RCR is low enough to ensure that the risks are always controlled, under every plausible condition of the manufacture and all identified uses of the Substance. For this purpose, the possible sources of variability and uncertainty must be considered in the assessment of exposure (Guidance on IRs and CSA Chapter R.16, page 68).

11 Uncertainty must be taken into account, either by carrying out the environmental exposure assessment using conservative assumptions and default values, which are provided in Guidance on IRs and CSA Chapters R.16. (Guidance on IRs and CSA Chapter R.19).

12 Alternatively, when the environmental exposure assessment is not based on these generic assumptions, a stepwise, tiered approach including an uncertainty analysis must be conducted. This analysis can be qualitative, deterministic, or probabilistic, to demonstrate that the risk is adequately controlled (Guidance on IRs and CSA Chapter R.19 provides a framework for carrying out a stepwise, tiered approach to uncertainty analysis). The results must be provided in the dossier to demonstrate that the application of such tiered uncertainty analysis gives a clear indication that the risk is adequately controlled (e.g. an increased belief that the (distribution of the) RCR is less than 1).

13 You do not demonstrate that the worst cases conditions are covered in the CSA, as default parameters recommended by ECHA are not applied. In addition, you do not provide results of the uncertainty analysis for the environmental exposure assessment ensuring a high level of confidence that the risk is always adequately controlled.

14 Therefore, you have not demonstrated that your exposure assessment is always conservative enough and the RCRs always low enough to cover the possible sources of variability and uncertainty. Thus, exposures cannot be regarded as being always well below the PNEC.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

15 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

16 You have provided a modified Local Lymph Node Assay (LLNA) in mouse (2012) with the Substance.

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

1.2.1.1. Study not conducted using a recognised test method

17 Toxicological and eco-toxicological tests on substances must be conducted in compliance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or ECHA as being appropriate (Article 13(3) of REACH). According to Article 141(2), Article 13 applies from 1 June 2008.

18 You have provided a study according to Modified LLNA (IMDS = Integrated Model for the Differentiation of Skin Reactions) that you claim is equivalent to the Local Lymph Node Assay (OECD TG 429). Based on the results you consider that the Substance is not a skin sensitiser.

19 The provided study was not conducted using a recognised method. The IMDS test method has not been validated or considered to be scientifically valid by international bodies in respect to how and what measurements are performed and what is the appropriate cut off value for the determination of skin sensitisation potential. This deficiency significantly affects the reliability of these sources of information and therefore its ability to predict the properties of the Substance.

20 Therefore, the study is rejected.

21 On this basis, it cannot be concluded whether the Substance causes skin sensitisation.

1.2.2. No assessment of potency

22 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).

23 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.

24 Therefore, the information requirement is not fulfilled.

1.3. Study design

25 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.

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

27 In your comments to the initial draft decision you agree with the request.

2. *In vitro* gene mutation study in bacteria

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

2.1. Information provided

29 You have provided an *in vitro* gene mutation study in bacteria (2012) with the Substance.

2.2. Assessment of the information provided

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

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

a) triplicate plating is used at each dose level;

b) concurrent strain-specific positive controls, both with and without metabolic activation, are included in each assay and the number of revertant colonies per plate induced by the positive controls demonstrates the effective performance of the assay;

c) a concurrent negative control is included in each assay and the number of revertant colonies per plate for the concurrent negative control is inside the historical control range of the laboratory;

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.

31 In the provided study:

a) triplicate plating was not used at each dose level;

b) the number of revertant colonies per plate induced by the concurrent positive controls are not provided to demonstrate the effective performance of the assay;

c) the number of revertant colonies per plate for the concurrent negative control was not reported;

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

e) no repeat experiment was performed to confirm the negative results and no justification was provided.

32 The information provided in your registration dossier does not cover the specifications required by the OECD TG 471.

33 Therefore, the information requirement is not fulfilled.

34 In your comments to the draft decision, you address the study deficiencies identified above. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set in the decision.

3. Short-term toxicity testing on aquatic invertebrates

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

3.1. Information provided

36 You have provided a short-term toxicity study on daphnia magna (2013) performed according to the OECD TG 202 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

37 To fulfil the information requirement, a study must comply with OECD TG 202 and the specifications of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). The Substance is difficult to test due to its volatility (950 Pa at 20°C) and surface active property (54 mN/m). Therefore, the following specifications must be met:

Reporting of the methodology and results

a) the test design is reported (e.g. number of replicates);

b) the test procedure is reported (e.g. composition of the test medium, loading in number of Daphnia per test vessel);

c) the number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation;

d) the dissolved oxygen and pH measured at least at the beginning and end of the test is reported;

e) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.

38 In the provided study:

Reporting of the methodology and results

a) on the test design, you have not specified number of replicates, age and number of test organisms used, test temperature, nominal concentrations used;

b) on the test procedure, you have not specified composition of the test medium (particulate matter, total organic carbon, and hardness), loading in number of Daphnia per test vessel;

c) tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control are not reported;

d) the dissolved oxygen, pH and temperature measured at least at the beginning and end of the test is not reported;

e) on the analytical method adequate information, i.e. performance parameters of the method are not reported and the results of the analytically determined exposure concentrations are not provided.

39 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability and its validity.

40 On this basis, the specifications of OECD TG 202 are not met.

41 Therefore, the information requirement is not fulfilled.

3.3. Study design

42 The Substance is difficult to test due to its volatility (950 Pa at 20°C) and surface active property (54 mN/m). OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

4. Growth inhibition study aquatic plants

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

4.1. Information provided

44 You have provided a Growth inhibition study on aquatic algae (2013), performed according to the OECD TG 201 with the Substance.

4.2. Assessment of the information provided

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

45 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). The Substance is difficult to test due to its volatility (950 Pa at 20°C) and surface active property (54 mN/m). Therefore, the following specifications must be met:

Reporting of the methodology and results

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

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

c) the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported;

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

e) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided.

46 In the provided study:

Reporting of the methodology and results

a) on the test design, you have not specified number of replicates, nominal concentrations used, geometric progression used. In your comments to the draft decision, your provided the missing information;

b) on the test conditions, you have not specified composition of the test medium, test temperature, biomass density at the beginning of the test, pH measurements of the control medium. In your comments to the draft decision, your provided the missing information;

c) the method used to determine algal biomass is not reported. In your comments to the drafted decision, you provided the information;

d) tabulated data on the algal biomass determined daily for each treatment group and control are not reported. In your comments to the draft decision, you have provided tabulated data;

e) on the analytical method adequate information, i.e. performance parameters of the method are not reported and the results of the analytically determined exposure concentrations are not provided. In your comment to the draft decision, you provide following information:

- The chemical analyses were performed by Cheminova (not by the CRO). This was not done under GLP conditions;
- the concentrations were measured in abiotic flasks run concurrently with the biotic flasks;
- There was no chemical concentration determination in the biotic flask.

47 Based on your comment to the draft decision, you address the study deficiencies identified point a)-d). However, you also provided information that the test media prepared specifically for analysis of exposure concentrations during the test was not treated identically to those used for testing (*i.e.,* inoculated with algae and incubated under identical conditions). Under such conditions, the reported measured values may not be representative of true exposure levels. In addition, your measured concentrations at nominal concentrations of 1.0 and 2.0 mg/L indicate that the concentrations of the test material have not been maintained within ±20 % of the nominal or measured initial concentration throughout the test. Therefore, EC10 and NOEC could be lower than currently reported values (i.e., 1.4 and 1.0 mg/L based on nominal concentrations respectively).

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

49 Therefore, the information requirement is not fulfilled.

4.1. Study design

50 OECD TG 202 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design" under request 3.

Reasons related to the information under Annex VIII of REACH

5. In vitro micronucleus study

51 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.

52 You have provided an *in vitro* cytogenicity study in mammalian cells OECD 473 (2012) with the Substance.

5.1. Assessment of the information provided

5.1.1. The provided study does not meet the specifications of the test guidelines

53 To fulfil the information requirement, the study has to be an *in vitro* chromosomal aberration test or an *in vitro* micronucleus test conducted in mammalian cells. The study must comply with the OECD TG 473 or the OECD TG 487, respectively (Article 13(3) of REACH). 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.

54 In the provided study:

a) the maximum tested concentration did not induce 55+5% of cytotoxicity compared to the negative control, and it did not induce the precipitation of the tested substance, and it was less than 10 mM, 2 mg/mL or 2 µL/mL. Cytotoxicity starting at 1029 µg IPETC /mL is reported but the actual data are not provided.

b) the number of metaphases scored per concentration was not reported;

c) you have not reported if the positive control data is compatible with those generated in the historical positive control database;

d) you have not reported if the positive control did produce a statistically significant increase in the induced response when compared with the concurrent negative control;

e) you have not reported if the negative control did show 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) 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) are missing to conclude on a negative outcome.

55 The information provided in your registration dossier does not cover the specifications required by the OECD TG 473.

56 Therefore, the information requirement is not fulfilled.

57 ECHA therefore considers that an appropriate *in vitro* micronucleus study is necessary to further investigate the mutagenicity of the Substance and to help identify the most adequate follow-up in vivo study.

58 In your comments to the draft decision, you address the study deficiencies identified above. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set in the decision.

5.2. Study design

59 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).

60 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.

61 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).

5.2.1. Assessment of aneugenicity potential

62 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.

63 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 fragments) and/or aneugenic events (i.e. micronuclei contain whole chromosomes).

[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).

6. In vitro gene mutation study in mammalian cells

64 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.

6.1. Triggering of the information requirement

65 For the reasons explained under Request 2 and 5 *in vitro* gene mutation study in bacteria and *in vitro* cytogenicity study in mammalian cells are not valid.

66 The result of the study required under request 2. (*in vitro* gene mutation study in bacteria) and under request 5. (*in vitro* cytogenicity study in mammalian cells) 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.

67 Consequently, you are required to provide information for this information requirement, if the *in vitro* gene mutation study in bacteria / the *in vitro* micronucleus study in mammalian cells provide a negative result.

6.2. Information provided

68 You have provided an *in vitro* gene mutation study (2013) according to OECD TG 476 with the substance.

6.3. Assessment of the information provided

6.3.1. The provided study does not meet the specifications of the test guidelines

69 To fulfil the information requirement, a study must comply with the OECD TG 476 or the OECD TG 490 (Guidance on IRs and CSA, Table.7.7-2) (Article 13(3) of REACH). 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) at least 4 concentrations are evaluated, in absence and in presence of metabolic activation;

c) a positive control is included in the study;

d) 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;

e) the concurrent positive controls produce a statistically significant increase compared with the concurrent negative control / For the Mouse Lymphoma Assay (MLA), the concurrent positive control meets the acceptability criteria recommended by the MLA Expert Workgroup of the International Workshop for Genotoxicity Testing (IWGT) in terms of mutant frequency and/or small colony induction and described in paragraph 58 of OECD TG 490;

f) the negative control data is ideally within the 95% control limits of the distribution of the laboratory's historical negative control database / For the Mouse Lymphoma Assay (MLA), the concurrent negative control meets the acceptability criteria recommended by the MLA Expert Workgroup of the International Workshop for Genotoxicity Testing (IWGT) in terms of mutant frequency, cloning efficiency and suspension growth and described in paragraph 57 of OECD TG 490;

g) data on the cytotoxicity and the mutation frequency for the treated and control

cultures are reported.

70 In the provided study:

a) you have not reported if the maximum tested concentration did induce 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance, and if it was less than 10 mM, 2 mg/mL or 2 µL/mL;

b) the number of concentrations (i.e., less than 4 concentrations) evaluated in absence and in presence of metabolic activation was not reported;

c) no positive control was included in the study without metabolic activation;

d) the positive control did not induce responses that are compatible with those generated in the historical positive control database and/or induces more than 90% of cytotoxicity compared to the negative control;

e) you have not reported if the positive control did produce a statistically significant increase in the induced response when compared with the concurrent negative control;

f) you have not reported if the response of the negative control was inside the historical control range of the laboratory;

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

71 The information provided in your dossier does not cover the specifications required by the OECD TG 476.

72 Therefore, the information requirement is not fulfilled.

73 In your comments to the draft decision, you address the study deficiencies identified above. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set in the decision.

6.1. Study design

74 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.

7. Short-term toxicity testing on fish

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

7.1. Information provided

76 You have provided a short-term toxicity study on fish (2012), performed according to the OECD TG 203 with the Substance.

7.2. Assessment of the information provided

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

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

The Substance is difficult to test due to its volatility (950 Pa at 20°C) and surface active property (54 mN/m). Therefore, the following specifications must be met:

Reporting of the methodology and results

a) the test design is reported (number of test animals, nominal concentrations tested);

b) the test procedure is reported (composition of the test medium such as particulate matter, and fish loading);

c) for semi-static tests, dissolved oxygen, pH, salinity (if relevant) and temperature measured prior to and after each water renewal are reported. The results of hardness and TOC determinations in the dilution water are reported;

d) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided;

e) mortalities and sub-lethal effects (*e.g.* with regard to equilibrium, appearance, ventilator and swimming behaviour) are reported. The frequency of observations includes at least 2 observations within the first 24 hours and at least two observations per day from day 2 to 4.

78 In the provided study:

Reporting of the methodology and results

a) on the test design, you have not specified number of test animals and nominal concentrations tested;

b) on the test procedure, you have not specified composition of the test medium such as particulate matter, and fish loading;

c) the dissolved oxygen and pH, temperature, hardness, and TOC measured are not reported;

d) on the analytical method, adequate information, performance parameters of the method are not reported and the results of the analytically determined exposure concentrations are not provided;

e) tabulated data on mortalities and sub-lethal effects (e.g. with regard to equilibrium, appearance, ventilator and swimming behaviour) obtained on at least 2 observations within the first 24 hours and at least two observations per day from day 2 to 4 for each treatment group and control are not reported.

79 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability and validity.

80 On this basis, the specifications of OECD TG 203 are not met.

81 Therefore, the information requirement is not fulfilled.

7.3. Study design

82 OECD TG 203 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design" under request 3.

8. Adsorption/desorption screening

83 Adsorption/desorption screening is an information requirement under Annex VIII to REACH (Section 9.3.1).

8.1. Information provided

84 You have adapted this information requirement by using Column 2 of Annex VIII, Section 9.2.2.1. To support the adaptation, you have provided the following statement: "*the study does not need to be conducted because the substance has a low octanol water partition coefficient and the adsorptive properties of the substance are solely driven by lipophilicity.* The test item has a low potential for adsorption as log Pow at 30 °C is 2.3".

In your comments to the draft decision, you mention the availability of OECD TG 121 study in the technical dossier. However, we did not find such study record in your dossier.

8.2. Assessment of the information provided

8.2.1. Low potential for adsorption based on physicochemical properties not demonstrated

85 Under Annex VIII, Section 9.3.1, Column 2, first indent, the study may be omitted if the substance can be expected to have a low potential for adsorption (e.g. the substance has a low octanol-water partition coefficient). In order to adapt this information requirement based on low octanol-water partition coefficient (log K_{ow}), lipophilicity must be the sole characteristic driving the adsorption potential of a substance. However, for some groups of substances (e.g. ionisable substances, surfactants) other mechanisms than lipophilicity may drive adsorption.

86 You claim that the Substance has a low octanol-water partition coefficient and has therefore low potential for adsorption/desorption.

87 However, you have not provided any relevant evidence or argument demonstrating that the Substance can be expected to have a low potential for adsorption.

88 In addition, in section 4.10 of your dossier, you report that the surface tension of the Substance is 54.9 ± 1.3 mN/m at 20ºC (OECD TG 115, 2012).

89 Therefore, the information in your dossier indicates that the Substance is surface active based on surface tension <60 mN/m.

90 Based on this property of the Substance, other mechanisms than lipophilicity may drive absorption.

91 You have not demonstrated that lipophilicity is the sole characteristic driving adsorption potential and that log K_{ow} is not a valid descriptor for assessing the adsorption potential of the Substance.Based on the above, your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

In your comments to the draft decision, you agree that the adsorption/desorption screening study may be necessary because the Substance is ionisable at pH 4-9. You propose to use the available OECD TG 121 study to address this information requirement. However, as we do not find the study record in your technical dossier, no conclusion on the compliance can currently be made. You remain responsible for complying with this information requirement by the set deadline.

8.3. Study design

92 To fulfil the information requirement, the test method(s) according to OECD TG 106 or 121 are in general appropriate. You must ensure that the Substance is within the applicability domain of the chosen test method. Because the OECD TG 121 is not applicable for surface

active substances, OECD TG 106 is the appropriate method for the Substance considering its surface active properties.

93 In your comments to the draft decision, you do not agree to perform OECD TG 106 study and propose to use available OECD TG 121 study instead, because you believe the Substance is not surface active. You state that the Substance is ionisable and in the technical dossier, you report pKa=8.67 at 20.6 ºC. ECHA points out that OECD TG 121 may not be suitable for ionisable substances, especially for those which dissociate at pH>7.5. Therefore, ECHA still considers that OECD TG 106 is more appropriate method for the Substance than OECD TG 121, taking account the reported properties in your dossier. If you nevertheless consider that the information available justify using the OECD TG 121 study, you remain liable for complying with this information requirement. In any case you are responsible for ensuring that the Substance falls within the applicability domain of the test method you will choose.

Reasons related to the information under Annex IX of REACH

9. Long-term toxicity testing on aquatic invertebrates

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

9.1. Information provided

95 You have adapted this information requirement by using Annex XI, Section 3.2(a) (substance-tailored exposure-driven testing). To support the adaptation, you have provided the statements which is summarised in the section 0.1 above.

9.2. Assessment of the information provided

9.2.1. Substance-tailored exposure-driven testing adaptation rejected

96 As explained in Section 0.1., your adaptation based on exposure-based waiving under Annex XI, Section 3.2(a) is rejected.

97 Therefore, the information requirement is not fulfilled.

9.3. Study design

98 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" under request 3.

10. Long-term toxicity testing on fish

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

10.1. Information provided

100 You have adapted this information requirement by using Annex XI, Section 3.2(a) (substance-tailored exposure-driven testing). To support the adaptation, you have provided the , you have provided the statements which is summarised in the section 0.1 above.

10.1. Assessment of the information provided

10.1.1. Substance-tailored exposure-driven testing adaptation rejected

101 As explained in Section 0.1., your adaptation based on exposure-based waiving under Annex XI, Section 3.2(a) is rejected.

102 Therefore, the information requirement is not fulfilled.

10.2. Study design

103 OECD TG 210 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design" under request 3.

11. Simulation testing on ultimate degradation in surface water

104 Simulation testing on ultimate degradation in surface water is an information requirement under Annex IX to REACH (Section 9.2.1.2.).

11.1. Information provided

105 You have adapted this information requirement by using Annex XI, Section 3.2(a) substance-tailored exposure-driven testing. To support the adaptation, you have provided the statements which are summarised in the section 0.1 above.

11.2. Assessment of the information provided

11.2.1. Substance-tailored exposure-driven testing adaptation rejected

106 As explained in Section 0.1., your adaptation based on exposure-based waiving under Annex XI, Section 3.2(a) is rejected.

107 Therefore, the information requirement is not fulfilled.

11.3. Study design

108 In your comments to draft decision, you point out that according to a recent decision from the Board of Appeal (A-001-2022), NER cannot be requested by ECHA under the compliance check procedure. ECHA took your comments into account and revised the study design specifications and deleted the reference to NER from the request. However, please note that in some cases you may need to assess NER as explained below in the study design.

109 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

110 You must perform the test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (Guidance on IRs and CSA, Section R.11.4.1.1.3.).

111 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

112 As specified in Guidance on IRs and CSA, Section R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test material concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Paragraph 52 of the OECD TG 309 provides that the "*total recovery (mass balance) at the end of the experiment should be between 90% and 110% for radiolabelled substances, whereas the initial recovery at the beginning of the experiment should be between 70% and 110% for non-labelled substances*". NERs contribute towards the total recovery. Therefore, the quantity of the (total) NERs must be accounted for the total recovery (mass balance), when relevant, to achieve the objectives of the OECD TG 309 to derive degradation rate and half-life. The reporting of results must include a scientific justification of the used extraction procedures and solvents.

113 For the persistence assessment by default, total NERs is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NERs may be differentiated and quantified as irreversibly bound or as degraded to biogenic NERs, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website (NER - summary 2019 (europa.eu)).

114 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 309; Guidance on IRs and CSA, Section R.11.4.1.).

12. Identification of degradation products

115 Identification of abiotic and biotic degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).

116 You have not submitted any information for this requirement.

117 Therefore, the information requirement is not fulfilled.

12.1. Study design

118 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

119 Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported. In addition, identified transformation/degradation products must be considered in the CSA including PBT assessment.

120 You must obtain this information from the degradation study requested in request 11.

121 To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (request 11) must be conducted at 12°C and at a test concentration < 100 µg/L. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline, e.g. 20°C) and at higher application rate (i.e. > 100 µg/L).

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 05 June 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 amended the request(s).

Following the Board of Appeal's decision in case A-001-2022 ECHA revised the study design specifications for meeting the information requirement for simulation testing on ultimate degradation in surface water (Annex IX, first column, section 9.2.1.2).

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: Addressees 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]

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).

2. General recommendations for conducting and reporting new tests

2.1 Strategy for the PBT/vPvB assessment

Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. You must assess the PBT properties of each relevant constituent of the Substance present in concentrations at or above 0.1% (w/w) and of all relevant transformation/degradation products. Alternatively, you would have to justify why you consider these not relevant for the PBT/vPvB assessment.

You are advised to consult Guidance on IRs & CSA, Sections R.7.9, R.7.10 and R.11 on PBT assessment to determine the sequence of the tests needed to reach the conclusion on PBT/vPvB. The guidance provides advice on 1) integrated testing strategies (ITS) for the P, B and T assessments and 2) the interpretation of results in concluding whether the Substance fulfils the PBT/vPvB criteria of Annex XIII.

In particular, you are advised to first conclude whether the Substance fulfils the Annex XIII criteria for P and vP, and then continue with the assessment for bioaccumulation. When determining the sequence of simulation degradation testing you are advised to consider the intrinsic properties of the Substance, its identified uses and release patterns as these could significantly influence the environmental fate of the Substance. You must revise your PBT assessment when the new information is available.

References to Guidance on REACH and other supporting documents can be found under Appendix 1.