~~Confidential~~

Helsinki, 5 January 2023

Addressees
Registrants of JS_104-75-6_2-EH as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
31/10/2018

Registered substance subject to this decision ("the Substance")
Substance name: 2-ethylhexylamine
EC/List number: 203-233-8

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 the deadline of ***14 April 2025***.

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

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

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: OECD TG 471, 2020) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

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

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

3. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

4. 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

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

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

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.

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 decision
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 decision

Contents

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

1 An in vitro gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

1.1. Information provided

2 You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence). In support of your adaptation, you have provided the following studies on the Substance:

(i) *In vitro* bacterial reverse mutation assay according to OECD TG 471 (1999);
(ii) *In vitro* bacterial reverse mutation assay similar to OECD TG 471 (1988).

1.2. Assessment of the information provided

3 Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

4 According to ECHA Guidance R.4.4, a weight of evidence adaptation involves an assessment of the relative values/weights of different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance of the information for the given regulatory information requirement. Subsequently, relevance, reliability, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

5 Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

6 However, for each relevant information requirement, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property.

7 In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation and identified the following issues.

8 For this endpoint your study needs to have adequate and reliable coverage of the key parameters foreseen to be investigated in an OECD TG 471 test. The key parameter investigated by this test is detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria including data on the number of revertant colonies.

9 The studies (i) and (ii) investigate the above mentioned key parameter. Therefore, they provide information that could contribute to the conclusion on this key parameter.

10 However, the reliability of these sources of information is affected by the following issue:

11 The conditions of OECD TG 471 specify that the test must be performed with 5 strains: four strains of S. typhimurium (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101)

12 Nevertheless, the reported data for the sources of information (i) and (ii) do not include the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101), which can detect certain oxidising mutagens, cross-linking agents and hydrazines.

13 Accordingly, the sources of information (i) and (ii) only provide a partial coverage of the key investigations required to conclude on the intrinsic property under investigation.

14 Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous property foreseen to be investigated by the required study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

1.3. Specification of the study design

15 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) should be performed using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

2. Ready biodegradability

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

2.1. Information provided in the dossier

17 You have provided a study according to ISO 14593 (2002), i.e. similar to OECD TG 310, on the Substance.

2.2. Additional information provided in the comments to the draft decision

18 In your comments on the draft decision, you also provide ready biodegradability estimates based on QSAR results from seven different models and state that *"The Registrant adapts the information requirement under Annex VII of REACH with regards to ready biodegradability testing in accordance with Annex XI, Section 1.3 by providing the requested information using an appropriate QSAR method. The QSAR results (Table 1) support the conclusion on the ready biodegradability of the substance."*

19 The QSAR estimates are based on the following methods:

i. MultiCASE CASE Ultra model for Not Ready Biodegradability (v1; Danish QSAR Group at DTU Food);
ii. Leadscope Enterprise model for Not Ready Biodegradability (v1; Danish QSAR Group at DTU Food);
iii. SciMatics SciQSAR model for Not Ready Biodegradability (v1; Danish QSAR Group at DTU Food)
iv. Battery model for Not Ready Biodegradability (Danish QSAR Group at DTU Food);
v. BIOWIN v4.10 (EPI Suite v4.11):
    a. BIOWIN3 (ultimate survey model), and
    b. BIOWIN5 (MITI linear biodeg probability;
vi. CATALOGIC Kinetic 301F v14.17 (OASIS Catalogic v5.14.1.5)

2.3. Assessment of information provided in the dossier

2.3.1. The provided study does not follow the specifications of the applicable test guideline

20 To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 310, the following requirements must be met:

21 Technical specifications impacting the sensitivity/reliability of the test

a) For test vessels containing the substance, blank controls and test vessels containing the reference substance, at least three replicate test vessels are analysed at regular intervals. At least five replicate test vessels are analysed at the end of the test;

22 Reporting of the methodology and results

b) The mean amount of inorganic carbon content (IC) present in the blank controls at the end of the test is ≤ 3mg C/L;
c) The volume of inoculum used is generally 1-10 mL and must be adequate so that:
- a bacterial cell density of 10^2 to 10^5 colony-forming units is reached in the test vessel, and
- it contributes to ≤ 10% of the initial concentration of organic carbon introduced by the test material, and
- the suspended solid concentration is 4 mg/L (suspended solid concentrations up to 30 mg/L may be used provided the above criteria are met and the mean amount of TIC present in the blank controls at the end of the test is ≤ 3mg C/L);

23 Your registration dossier provides a study similar to OECD TG 310 showing the following:

24 Technical specifications impacting the sensitivity/reliability of the test

a) Only 1 replicate test vessel was analysed at the end of the test. In your comments to the draft decision, you state that the study was performed with three replicate vessels each for all treatments. Further, you specify that no additional vessels were sampled on day 28. As specified above, the OECD TG 310 requires that five replicate samples are analysed at the end of the test at least for the test vessels (i.e. test material), blank controls and reference substance.

25 Reporting of the methodology and results

b) The inorganic carbon content (IC) of the test material suspension in the mineral medium at the beginning of the test (%) of the total carbon (TC) was not reported; In your comments you provided this information, 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 out in the decision.
c) The concentration of the inoculum is described as 4 mg/L dry substance, however, the bacterial cell density in the test vessel is not reported.

26 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, an insufficient number of relicates were analysed at the end of the test and therefore the test does not meet the requirements of the test guideline.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, the applied method cannot be fully assessed, since the bacterial cell density at the beginning of the test is not known and deviation from the standard cell density range could lead to unreliable results.

  In your comments on the draft decision, you state that *"According to OECD TG 310, the inoculum may be derived from a variety of sources"* and further refer to paragraph 26 of OECD TG 310, which gives e.g. a range for colony-forming units

and concentration of suspended solids. After that you state that *"However, in paragraph 32 of the guideline, it is clearly stated that "4 mg/L activated sludge solids" should be used as the concentration of the inoculum. This value was followed in the study* […]*. OECD TG 310 does not give a specific number of colony-forming units with regards to activated sludge. This information can be relevant if other sources than activated sludge are used for the inoculum."*

ECHA points out that table 2 of OECD TG 301 is entitled "test conditions" and therefore should be seen as the conditions under which the various test methods described in the test guideline must be conducted. The limit values for the inoculum density in mg/L (e.g., for sludge or soil) or mL/L (e.g., for surface water or effluent) are set to ensure that the introduction of exogeneous organic matter in the test system is within an acceptable range. Such parameter does not provide a direct estimate of bacterial biomass (as the density of bacteria in, for e.g., a sludge sample or a secondary effluent may vary by orders of magnitude). Accordingly, Appendix R.7.9-1 of ECHA Guidance on IRs and CSA specifies inoculum conditions as cell density (cells/mL) present in a relevant media (e.g. surface waters, unchlorinated sewage treatment works, activated sludge). In the absence of supporting information to demonstrate that the sludge concentration used in this study allowed reaching an adequate bacterial density, you have not demonstrated that the inoculum density was consistent with the specifications of OECD TG 310.

27 Therefore, the requirements of OECD 310 are not met.

2.4. Assessment of additional information provided in your comments to the draft decision

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

28 Under Section 1.3., first paragraph, third indent of Annex XI to REACH, a study may be omitted if QSAR results are adequate for the purpose of classification and labelling and/or risk assessment, including PBT assessment. ECHA Guidance R.7.9.5.1. specifies that (Q)SARs for predicting ready biodegradation (e..g using the Danish QSAR group at DTU Food models (MultiCASE, Leadscope, SciQSAR, Battery model), BioWIN models or CATALOGIC) are not yet sufficiently accurate to predict rapid degradation. However, when no useful information on degradability is available (either experimentally derived or estimated), (Q)SAR predictions can be used as supporting evidence of that the substance is not rapidly degradable.

29 Your comment to the draft decision provides (Q)SARs predictions from the Danish QSAR group at DTU Food models (MultiCASE, Leadscope, SciQSAR, Battery model), BioWIN models and CATALOGIC, These models are are considered insufficient to predict rapid degradation in the environment. However, you have used this information to conclude that the Substance is readily biodegradable. As explained above, (Q)SARs predictions alone is not adequate to conclude on the persistence of the Substance. Therefore, this information does not fulfil the information requirement and your adaptation is rejected.

Therefore, your adaptation under Annex XI, Section 1.3. is rejected.

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

Reasons related to the information under Annex VIII of REACH

3. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

31 An in vitro cytogenicity study in mammalian cells or an in vitro micro-nucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

3.1. Information provided

32 You have adapted this information requirement by using Column 2 of Annex VIII, Section 8.4.1. To support the adaptation, you have provided following information:

(i) A study according to OECD TG 474 (2007) with the source substance octylammonium chloride with EC 205-574-8

3.2. Assessment of the information provided

3.2.1. Column 2 adaptation criteria not met

33 Under Section 8.4.2., column 2 of Annex VIII to REACH, the study usually does not need to be conducted "if adequate data from an in vivo cytogenicity test are available". The Guidance on IRs and CSA, Section R.7.7.6.3 and Table R.7.7–3 clarifies that the in vivo somatic cell cytogenicity test must be either a micronucleus test or a chromosomal aberration test, performed according to OECD TG 474 or 475, respectively.

34 For the data from an in vivo somatic cell cytogenicity test to be considered adequate, the in vivo study you submitted has to meet the requirements of OECD TG 474, and the specifications/conditions of this test guideline include:

a) The highest dose studied must be the maximum tolerated dose (MTD), i.e. the highest dose that is tolerated without evidence of toxicity (e.g. body weight depression or hematopoietic system cytotoxicity, but not death or evidence of pain, suffering or distress necessitating humane euthanasia). The highest dose can also be a dose that produces toxicity in the bone marrow (e.g. a reduction in the proportion of immature erythrocytes among total erythrocytes in the bone marrow or peripheral blood);
b) In order to provide a clear negative outcome, the data available must show that "*bone marrow exposure to the test Substance occurred*".

35 The study (i) is described as OECD TG 474. However, the following specifications are not performed according to the requirements of OECD TG 474:

a) a maximum studied dose that is a MTD or induces toxicity;
b) a demonstration that the systemic or target tissue (bone marrow) exposure to the Substance or its metabolites.

36 The information provided does not cover specifications/conditions required by OECD TG 474. The column 2 criteria are not met.

37 Therefore, your adaptation is rejected and the information requirement is not fulfilled.

3.3. Specification of the study design

38 To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

4. Short-term toxicity testing on fish

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

4.1. Information provided

(i) a study according to DIN 38412, part 15 (1982);
(ii) A non-guideline study (1972).

4.2. Assessment of the information provided

4.2.1. The provided studies do not follow the sepcicifations of the applicable test guideline

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

41 Validity criteria

a) the analytical measurement of test concentrations is conducted;

42 Technical specifications impacting the sensitivity/reliability of the test

b) the test duration is 96 hours or longer;
c) the fish-to-water loading rate is ≤ 0.8 g of fish (wet weight) per litre of water for static and semi-static tests;

43 Reporting of the methodology and results

d) the test procedure is reported (*e.g.* fish size and age, composition of the test medium, fish loading, number of tested concentrations).

44 Your registration dossier provides two studies showing the following:

45 You dossier indicates adsorptive properties (log Koc = 3.91 and is ionisable under environmentally relevant pH). Under the OECD GD 23 the Substance is difficult to test. Therefore, the provide studies must follow the specific requirements set out in OECD GD 23 also identified above.

46 Validity criteria

a) no analytical measurement of test concentrations was conducted in studies i and ii. In your comments to the draft decision, you state that "*the test concentrations are expected to have been stable in the study based on the experiences of the algal growth inhibition test and the substance's physicochemical properties*". To support this, you specify that the Substance evaporatates slowly due to high water solubility (2.5 g/L), low Henry's Law Constant (HLC = 8.27 Pa m³/mol at 25 °C) and ionisation at environmentally relevant pHs (pKa=10.4) and conclude that "*evaporation of the Substance into the atmosphere is assessed to be not relevant*". In addition, based on the stability of the Substance in the algal growth inhibition test you conclude that "*the test concentrations are expected to have been stable under the test conditions*"

47 Technical specifications impacting the sensitivity/reliability of the test

b) the test duration was only 48 hours in study ii. In your comments you acknowledge this deficiency;
c) the test was conducted using a static setup and the fish-to-water loading rate was

1.9 g of fish (wet weight) per litre of water in study i;

48 Reporting of the methodology and results

d) on the test procedure, you have not specified fish size and age in study i, composition of the test medium, the loading rate was not reported in study ii and no information on tested concentrations was provided for study ii.

49 Based on the above,

- the validity criteria of OECD TG 203 are not met, since no analytical monitoring is performed in studies i and ii; In your comments you argued that the test concentrations are expected to have been stable. ECHA does not agree with this statement since the analytical monitoring of the test material during a fish test is a basic requirement to demonstrate that nominal test concentrations are representative of the actual (i.e. measured) exposure concentrations over the exposure phase. Also in this case, the Substance has adsorptive properties and its behaviour under different test conditions may vary. Therefore stability of measured exposure concentrations in an algal test is not a proof that no reduction in exposure would occur in a short-term fish test. Finally, the analytical monitoring of exposure concentration at the beginning of the test is needed to demonstrate that no experimental error occurred when preparing the test solutions. For these reasons, you have not demonstrated that the applied nominal test concentrations provide reliable estimates of the actual test material concentrations in these tests.
- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically,
  - the test duration in study ii was only 48 hours instead of standard 96 hours. In your comments on the draft decision, you explain that this study "*will not further be used to assess the toxicity to fish*"
  - the fish-to-water loading rate exceeded recommended 0.8 g of fish per litre of water in study i. The higher than standard loading rate could influence water quality and test material concentrations and result in unreliable results.
    In your comments, you consider that the higher loading rate was considered acceptable as it had no "*negative impact on the vitality of the fish*" and allowed to reach oxygen concentrations above the "*minimum level of 80 % air saturation*". You consider that this deficiency did not impact exposure concentrations as fish mortality was only observed in the absence of pH adjustment.
    ECHA notes that water quality is not limited to oxygen levels in the test solutions and maintains that high loading rate may have impacted exposure concentrations. ECHA further notes that your comments on the impact of pH adjustment on mortality does not address this issue.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. The study summary contains very few details on the test procedure in study i, for example, fish age and size are not reported.

50 Therefore, the requirements of OECD TG 203 are not met.

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

4.3. Study design and test specifications

52 The Substance is difficult to test. OECD TG 203 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 203. 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 solutions.

Reasons related to the information under Annex IX of REACH

5. Long-term toxicity testing on aquatic invertebrates

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

5.1. Information provided in the dossier

54 You have provided a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you did not provide a justification/provided the following justification: "*The risk charaterisation of 2-ethylhexylamine shows that the RCRs are < 1, indicating no uncacceptable risks for the aquatic environment. Moreover, the substance is neither a PBT nor a vPvB substance. Therefore, long-term toxicity testing in aquatic invertebrates is not provided*".

5.2. Additional information provided in the comments to the draft decision

55 In your comments to the draft decision, you explain that you intend to adapt this information requirement under Annex XI, Section 1.3. ((Q)SARs). Youu have provided information derived from experimental data from a group of substances (analogues) using the OECD QSAR Toolbox and flagged the information as QSAR.

56 As the group of substances (analogues) are used as source substances to predict the property of the Substance, we understand that you have adapted the standard information requirements under Annex XI, Section 1.5 of REACH (grouping and read-across).

5.3. Assessment of the information provided in the dossier

5.3.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study

57 Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. It must be understood as a trigger for providing further information on aquatic invertebrates if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

58 Your adaptation is therefore rejected.

5.4. Assessment of additional information provided in your comments to the draft decision

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

60 Supporting information must include information on the long-term toxicity to aquatic invertebrates of parent source compounds including the robust study summaries and bridging studies to compare ecotoxicological and physicochemical properties of the category members.

61 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar category members cause the same type of effect(s). In this context,

relevant, reliable and adequate information allowing to compare the properties of the category members is necessary to confirm that the substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the category members.

62 For the source substances, you do not provide any studies used in the prediction. In addition, your supportive documentation provided in the comments does not include any robust study summaries or descriptions of data for the source substances that would confirm the ecotoxicological effects and physicochemical properties of the substances in the category. Also, you have not provided documentation as to why the information from the source substances is relevant for the Substance and thus why the properties of the Substance may be predicted from information on the source substance(s).

63 In the absence of such information, you have not established that the category members are likely to have similar properties. Therefore, you have not provided sufficient supporting information to scientifically justify the read-across.

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

5.5. Study design and test specifications

65 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 4.

6. Long-term toxicity testing on fish

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

6.1. Information provided in the dossier

67 You have provided a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you did not provide a justification/provided the following justification: "*The risk charaterisation of 2-ethylhexylamine shows that the RCRs are < 1, indicating no uncacceptable risks for the aquatic environment. Moreover, the substance is neither a PBT nor a vPvB substance. The results from short-term toxicity tests on fish, Daphnia and algae demonstrate that fish is not the most sensitive trophic level tested. Therefore, it may be concluded that results from a long-term test in fish would not reveal a greater hazard than already determined by the available data.Therefore, and for reasons of animal welfare, long-term toxicity testing in fish is not provided*".

6.2. Additional information provided in the comments to the draft decision

68 In your comments to the draft decision, you provide also an adaptation under Annex XI, Section 3.2(a) stating that "[…] *it can be demonstrated in the risk assessment that the manufacture and the use of the substance do not pose an unacceptable risk for all environmental compartments as the risk characterization ratios (RCRs) of the chemical safety assessment are below 1 for all compartments* […]". In your comments you also claim that fish is not the most sensitive organism.

6.3. Assessment of the information provided in the dossier

6.3.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study

69 Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

70 Your adaptation is therefore rejected.

6.4. Assessment of additional information provided in your comments to the draft decision

6.4.1. Lack of appropriate PNEC

71 Under Annex XI, Section 3, this information may be omitted based on the exposure scenario(s) developed in the Chemical Safety Report. The justification must be based on a rigorous exposure assessment in accordance with Annex I, Section 5 and, for an adaptation according to Annex XI, Section 3.2(a), must demonstrated that all the following conditions are met:

i. the absence or no significant exposure in all scenarios of the manufacture and all identified uses referred to in Annex VI, Section 3.5., and
ii. a PNEC can be derived from available data, which:
    - must be relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes and therefore must be based on reliable information on the hazardous properties of the substance on at least three trophic levels;
    - must take into account the increased uncertainty resulting from the omission of the information requirement, in this case by selecting an appropriate assessment factor (AF) as described in Guidance on IRs and CSA, Section R.10.3.
iii. the ratio between the results of the exposure assessment (PECs) and the PNEC are always well below 1 .

72 Your dossier does not include reliable information on the hazardous properties of the Substance on at least three trophic levels as the hazard information on short-term toxicity to fish is also missing (request 4).

73 Therefore, you have not demonstrated that an appropriate PNEC can be derived and your adaptation is rejected.

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

6.5. Study design and test specifications

75 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.).

76 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 4.

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).

All Guidance on REACH is 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 06 July 2021.

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

ECHA took into account your comments and amended the requests. The following requests were removed:

- In vitro gene mutation in mammalian cells (Annex VIII, Section 8.4.3.) which had erroneously been specified in the decision
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

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 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]

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[2].

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 and other parameters relevant for the property to be tested.

This information is needed to assess 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[3].

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