~~Confidential~~

Helsinki, 04 May 2022

Addressees
Registrant(s) of JS - dihexyl ether as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
22/12/2020

Registered substance subject to this decision ("the Substance")
Substance name: Dihexyl ether
EC number: 203-987-8

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 ***11 May 2023***.

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

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

1. Long-term toxicity testing on fish also requested below (triggered by Annex VIII, Section 9.1.3., column 2)

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

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

2. Long-term toxicity testing on terrestrial invertebrates (triggered by Annex IX, Section 9.4.1., column 2; test method: OECD TG 222 or 220)

3. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: EU C.21./OECD TG 216, AND test method: EU C.22./ OECD TG 217)

4. Long-term toxicity to terrestrial plants (triggered by Annex IX, Section 9.4.3., column 2; test method: OECD TG 208 with at least six species or ISO 22030)

Reasons for the request(s) are explained in the following appendices:

- Appendices entitled "Reasons to request information required under Annexes VIII to IX of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa.

For certain endpoints, ECHA requests the same study at different tonnages. In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given. Only one study is to be conducted.

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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

[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 A: Reasons to request information required under Annex VIII of REACH

1. Long-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.). Long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

You have provided three studies, including an OECD TG 203 study for short-term toxicity to fish, and a (Q)SAR prediction for long-term toxicity to fish for the Substance.

We have assessed this information and identified the following issues:

Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (ECHA Guidance R.7.8.5).

In the provided OECD TG 105 study, the saturation concentration of the Substance in water was determined to be 2.71 mg/L at 20°C.

Furthermore, you indicate that in the provided OECD TG 201 study, the geometric mean measured concentration corresponding to the 100% saturated solution was 0.0670 mg/L.

You indicate that in the provided OECD TG 202 study, the measured concentration corresponding to the 50% saturated solution was 0.371 mg/L.

In the comments to the initial draft decision, you argue that the solubility of the Substance in the test medium used for a fish study will not be equivalent as that observed in the daphnia and algae culture media in the abovementioned studies.

This would be:

- Because the water solubility of any substance would be significantly influenced by the other dissolved components (i.e. those in the culture media); and
- Based on the measured values from the water solubility (OECD 105) study in deionized water and the analytical monitoring of exposure concentrations in the semi-static short-term fish toxicity (OECD 203) study conducted in dechlorinated tap water.

Based on the information reported in the registration dossier, ECHA notes that the results of the analytical monitoring of exposure concentrations of the Substance provided in two of the registration dossier aquatic toxicity studies (OECD TG 201, OECD TG 202) indicate that the Substance during duration of these tests was mostly present in the test solutions at concentrations below 1 mg/L. This indicates that the Substance may be considered poorly water soluble and that steady-state conditions may not be reached in the provided short-term toxicity studies with fish and aquatic invertebrates.

The considerations provided in your comments are unsubstantiated generic comments that do not exclude the above indication.

Therefore, for the purposes of short-term and long-term aquatic toxicity testing, the Substance is considered to be poorly water soluble and information on long-term toxicity on aquatic organisms, including fish, must be provided.

The examination of the information provided, as well as the selection of the requested test and the test design are addressed under section B.1.

Appendix B: Reasons to request information required under Annex IX of REACH

1. Long-term toxicity testing on fish

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

You have provided the following information:

i. key study with results derived from (Q)SAR model EPISuite v4.11 / ECOSAR v1.11.

We have assessed this information and identified the following issues:

Assessment of your (Q)SAR adaptation

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

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

With regard to these conditions, we have identified the following issue(s):

The prediction is not adequate due to low reliability

Under ECHA Guidance R.6.1.3.4 a prediction is adequate for the purpose of classification and labelling and/or risk assessment when the model is applicable to the chemical of interest with the necessary level of reliability. ECHA Guidance R.6.1.5.3. specifies that, among others, the following cumulative conditions must be met:

- the model predicts well substances that are similar to the substance of interest, and
- reliable input parameters are used, and
- the prediction is consistent with information available for other related endpoint(s).

Your registration dossier provides the following information:

- an experimental partition coefficient derived from a supporting OECD TG 117 (HPLC method) study indicating that the Log Kow of the Substance is 6.08 at 25°C.

The following information is also available for the Substance used as input for the prediction:

- a calculated partition coefficient derived from a key study using EPISuite (v4.11) / KOWWIN (v1.68) indicating that the Log Kow value of the Substance is 4.98 at 25°C.

You fail to explain in the dossier why the lower calculated Log Kow value of 4.98 at 25°C is used as input for the ECOSAR predictions rather than the higher experimental Log Kow value of 6.08 at 25°C.

The Log Kow prediction for the Substance used as input, 4.98 at 25°C is not the value giving rise to the highest concern as it differs more than 1 log unit from an available experimental Log Kow value (6.08 at 25°C). Log Kow is a key parameter in predicting of aquatic toxicity. Using a lower Log Kow prediction value of 4.98 at 25°C for the substance will underestimate the long-term toxicity of Fish aquatic toxicity for the substance. There is no justification provided in the registration dossier why the Log Kow value of 6.08 at 25°C has not been used as an input value to predict the long-term toxicity of Fish for the substance. There is no justification provided in the registration dossier why the Log Kow value of 4.98 at 25°C for the Substance used as an input value is so much lower than the available experimental Log Kow value of 6.08 at 25°C. The Log Kow value of 4.98 at 25°C differs by over 1 log unit from the available experimental log Kow, raising concerns on the reliability of the predicted Log

Kow used as input for the ECOSAR predictions reported by the you. Therefore, you have not demonstrated that the Log Kow input value used for the prediction for the Substance is reliable. Consequently, you have not demonstrated that the prediction for the Substance is adequate for the purpose of classification and labelling and/or risk assessment.

Lack of or inadequate documentation of the prediction (QPRF)

ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You provided the following information about the prediction: identifiers of the predicted substance; information about the prediction (including the predicted endpoint, name and version of the model used, equation used by the model, predicted values); some information about the applicability domain of the model (descriptor domain).

The information you provided about the prediction lacks the following elements:
List of substances that are considered to be structural analogues of the predicted substance and are present in the training or test sets and considerations on how predicted and experimental data for analogues support the prediction.

In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

On this basis, the information requirement is not fulfilled.

In the comments to the initial draft decision, you disagree with the request. You provide the following information:

1) The water solubility of the Substance based on measurements from water solubility study (i.e., OECD 105) and the water solubility of the Substance based on analytical monitoring data from bioassays (i.e., OECD TG 201, TG 202, TG 203).
2) Differences in species sensitivity to the Substance, as measured by short-term test results from tests done with algae, daphnia, and fish.
3) Animal welfare considerations.

A registrant may only adapt this information requirement based on the general rules set out in Annex XI. It is noted that Column 2 of Annex IX, Section 9.1, does not allow omitting the need to submit information on long-term toxicity to fish under Column 1 (Decision of the Board of Appeal in case A-011-2018).

Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH.

Therefore, this request is not changed.

Study design

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

As explained in Appendix A.1., under conditions of aquatic toxicity tests the Substance is considered to be poorly water soluble.

The Substance is difficult to test due to the low water solubility (see Appendix A.1.). OECD TG 210 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 210. 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.

2. Long-term toxicity on terrestrial invertebrates

Short-term toxicity to invertebrates is an information requirement under Annex IX to REACH (Section 9.4.1.). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

In Section 5.4 of the registration dossier, you report a predicted Log Koc value above 4.3 for the Substance. Therefore, the Substance is considered to have a high potential for adsorption to soil and information on long-term toxicity on terrestrial invertebrates must be provided.

You have adapted this information requirement under Annex IX, Section 9.4., Column 2 with the following justification:

"The test substance is not supposed to be directly applied to soil and an indirect exposure to soil via sewage sludge transfer is unlikely since the substance is readily biodegradable. For a substance being considered as „readily biodegradable", it can be assumed that it will be biodegraded within the STP process and as a consequence a transfer to the soil compartment is not expected. Therefore, soil macroorganisms are not exposed and, consequently, the respective test is not required."

We have assessed this information and identified the following issue:

Adaptation based on exposure

Column 2 of Annex IX, Section 9.4. states that studies on terrestrial organisms do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.

Based on data you have provided in Section 3.5. of the registration dossier, the Substance has a number of industrial, professional and consumer uses. These include multiple uses described by the Environmental Release Categories (ERC) ERC 8a, ERC 8c, ERC 8d, ERC 9b.

Significant direct and indirect exposure to soil cannot be excluded from those uses; in particular, based on data you have provided in Section 3.5 of the registration dossier, the Substance is used as a co-formulant in liquid plant protection products that have foliar application, outdoors – a use indicating direct soil exposure.

Therefore, you have not demonstrated that direct or indirect exposure of the soil compartment is unlikely.

On this basis, the information requirement is not fulfilled.

Study design

ECHA Guidance R.7.11.3.1. specifies that the earthworm reproduction test (OECD TG 222), the Enchytraeid reproduction test (OECD TG 220), and the Collembolan reproduction test (OECD TG 232) are appropriate to cover the information requirement for long-term toxicity testing on terrestrial invertebrates.

ECHA is not in a position to determine the most appropriate test protocol, since this decision is dependent upon species sensitivity and substance properties. However, when Log Koc > 4, as in this case, the test OECD 232 is not appropriate as the dominant route of exposure for Collembolans is via pore water.

3. Effects on soil micro-organisms

Effects on soil microorganisms is a standard information requirement under Annex IX to REACH (Section 9.4.2).

You have adapted this information requirement under Annex IX, Section 9.4., Column 2 with the following justification:

"The test substance is not supposed to be directly applied to soil and an indirect exposure to soil via sewage sludge transfer is unlikely since the substance is readily biodegradable. For a substance being considered as „readily biodegradable", it can be assumed that it will be biodegraded within the STP process and as a consequence a transfer to the soil compartment is not expected. Therefore, soil microorganisms are not exposed and, consequently, the respective testing is not required."

We have assessed this information and identified the following issue:

Adaptation based on exposure

Column 2 of Annex IX, Section 9.4. states that studies on terrestrial organisms do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.

As explained above in Appendix B.2., the substance has widespread uses and significant direct and indirect exposure to soil cannot be excluded.

Therefore, you have not demonstrated that direct or indirect exposure of the soil compartment is unlikely.

On this basis, the information requirement is not fulfilled.

In the comments to the initial draft decision, you agree to conduct the requested Soil Microorganisms: Nitrogen Transformation Test (EU C.21/OECD TG 216).

But you disagree with the request for the Soil Micro-organisms: Carbon Transformation Test (EU C.22/OECD TG 217). You provide the following information:

- The Substance has not been used or placed on the market for the agrochemical uses described in the registration dossier.
- You plan to remove uses in biocidal and plant protection products (PC 8 and 27) from the registration dossier of the Substance.

We have assessed this information and note the following:

The removal of the agricultural uses from the registration dossier would remove the need for the Soil Micro-organisms: Carbon Transformation Test (EU C.22/OECD TG 217). However, the additional use information provided in your comments to the draft decision is not included in the current version of the registration dossier. Therefore, currently there is a data gap for this information requirement.

You should therefore submit this additional use information in an updated registration dossier by the deadline set out in the decision.

Study design

According to ECHA Guidance, the Nitrogen Transformation Test is considered sufficient for most non-agrochemicals (R.7c, Section R.7.11.3.1.). However, as the Substance has identified agrochemical uses, i.e. used as a co-formulant in plant protection products with spraying application, both the Soil Microorganisms: Nitrogen Transformation Test (EU C.21/OECD TG 216) and Soil Micro-organisms: Carbon Transformation Test (EU C.22/OECD TG 217) must be performed simultaneously.

4. Long-term toxicity on terrestrial plants

Short-term toxicity to plants is an information requirement under Annex IX to REACH (Section 9.4.3). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

As explained above in Appendix B.2., the Substance has a high potential for adsorption to soil and information on long-term toxicity on terrestrial plants must be provided.

You have adapted this information requirement under Annex IX, Section 9.4., Column 2 with the following justification:

> *"The test substance is not supposed to be directly applied to soil and an indirect exposure to soil via sewage sludge transfer is unlikely since the substance is readily biodegradable. For a substance being considered as „readily biodegradable", it can be assumed that it will be biodegraded within the STP process and as a consequence a transfer to the soil compartment is not expected. Therefore, terrestrial plants are not exposed and, consequently, the respective testing is not required."*

We have assessed this information and identified the following issue:

Adaptation based on exposure

Column 2 of Annex IX, Section 9.4. states that studies on terrestrial organisms do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.

As explained above in Appendix B.2., the substance has widespread uses and significant direct and indirect exposure to soil cannot be excluded.

Therefore, you have not demonstrated that direct or indirect exposure of the soil compartment is unlikely.

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the Seedling Emergence and Seedling Growth Test (test method EU C.31/OECD TG 208) with at least six species tested, or the Soil quality — Biological methods — Chronic toxicity in higher plants (test method ISO 22030:2005) is the most appropriate (ECHA Guidance R.7.11.3.1.).

Appendix C: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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].

B. Test material

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 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.

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

Appendix D: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 14 December 2020.

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

ECHA took into account your comments and did not amend the request(s).

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix E: List of references - ECHA Guidance[4] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[5]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[6]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[7]

[4] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[5] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[6] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[7] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix F: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[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.