Helsinki, 01 September 2020

Addressees
Registrants of [redacted] 2-ethyl-hexyl nitrate listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
23/05/2018

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: 2-ethylhexyl nitrate
EC number: 248-363-6
CAS number: 27247-96-7

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

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***7 December 2021***.

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

A. Requirements applicable to all the Registrants subject to Annex VII of REACH

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

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

B. Requirements applicable to all the Registrants subject to Annex VIII of REACH

1. The same bioaccumulation in aquatic species as requested in C.1. (Annex I, sections 0.6.1. and 4.; Annex XIII, Section 2.1.; test method OECD TG 305).

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

1. Bioaccumulation study in aquatic species (Annex IX, Section 9.3.2; test method: OECD TG 305).

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

- Appendices entitled "Reasons to request information required under Annexes VII 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 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;

You are only required to share the costs of information that you must submit to fulfil your information requirements.

For certain endpoints, ECHA requests the same study from registrants 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; the registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants under Article 53 of REACH.

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". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations 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.

Approved[1] under the authority of Christel Schilliger-Musset, 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 VII of REACH

1. **Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)**

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex VII to REACH.

You have provided a study conducted on *Daphnia magna* and according to test guideline OECD 202.

We have assessed this information and identified the following issue(s):

Tests on substances must be conducted in accordance with the OECD test guidelines or other internationally recognised test method (Article 13(3) of REACH).

OECD TG 202, in combination with the revised OECD Guidance 23, ENV/JM/MONO(2000)6/REV1 for difficult to test substances, including volatile substances, require that the following conditions are met (among others):

- Effect concentrations must be based on measured values rather than nominal values unless the test concentrations remain within 80-120% of the nominal concentrations throughout testing.
- The analytical monitoring of the test concentrations must be performed using a sufficiently sensitive analytical method;
- The possibility of losses during sampling, sample treatment and analysis must be considered and documented;

Data contained in the dossier:
The Substance is volatile and has the potential to evaporate (Henry's law constant 375.49 $Pa.m^3/mol$).

In the study provided:

- The concentration levels of the test Substance were not analytically monitored;
- You have not demonstrated that the test concentrations were maintained during the test within the required 80-120% of the nominal concentrations;
- No precautions were taken to avoid the volatilisation of the Substance from the test vessels: the test was a static test and it was conducted with aeration.

In comparison, in the key studies for short-term toxicity to fish or for toxicity to algae, important losses were observed (measured concentrations were less than 80% of the nominal concentrations or even below the limit of quantification).

Based on the study design and properties of the Substance, it is expected that considerable losses occured during the exposure period of the *Daphnia* study as well.

Based on these elements, the aforementioned conditions of the test guideline are not met and the study is rejected.

Therefore, the information provided does not fulfil the information requirement.

2. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)**

Growth inhibition study on aquatic plants is a standard information requirement in Annex VII to REACH.

You have provided two studies, both on species *Pseudokirchneriella subcapitata* and performed according to test guideline OECD 201.

We have assessed this information and identified the following issue(s):

Tests on substances must be conducted in accordance with the OECD test guidelines or other internationally recognised test method (Article 13(3) of REACH).

OECD TG 201 in combination with the revised OECD Guidance 23, ENV/JM/MONO(2000)6/REV1 for difficult to test substances, including volatile substances, require that the following conditions are met (among others):

- Effect concentrations must be based on measured values rather than nominal values unless the test concentrations remain within 80-120% of the nominal concentrations throughout testing.
- For that purpose, the analytical monitoring of the test concentrations must be performed using a sufficiently sensitive analytical method;
- The possibility of losses during sampling, sample treatment and analysis must be considered and documented;

The Substance is volatile and has potential to evaporate (Henry's law constant 375.49 $Pa.m^3/mol$).

For the key study, the following results are reported:

- 72h-ErC50: <0.8 mg/L (based on measured concentrations), 3.22 mg/L (based on nominal concentrations)
- 72h-ErC10: <0.8 mg/L (based on measured concentrations), 1.54 mg/L (based on nominal concentrations)

All measured concentrations were below the limit of quantification (0.8 mg/L) for the corresponding nominal test concentrations of 3.75 mg/L or less. In the study summary you mention that "*there is sufficient uncertainty in what was the actual concentration that caused the algal growth inhibition that we should not use the value of <0.8 mg/l as the EC50 value for 2-ethylhexyl nitrate. We therefore propose that you use the nominal concentration to calculate the EC50*".

In the supporting study, the test concentrations were not analytically monitored.

For the key study, effects were observed at concentrations below the limit of quantification (LoQ) of the analytical method.

This indicates that:

- the test concentrations were not maintained within 80-120% of the nominal concentrations,
- the analytical method was not sufficiently sensitive to derive effect concentrations based on measured concentrations
- important substance losses occurred during the test or during the analysis procedures

You chose to base effect concentrations on nominal concentrations. However, effect concentrations based on nominal concentrations are not reliable considering that the test concentrations were not maintained within 80-120% of the nominal concentrations.

Similarly, the results obtained from the supporting study are regarded as invalid as no analytical monitoring was performed.

Therefore, the information provided does not fulfil the information requirement.

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

Under Articles 10(b) and 14(1) of REACH, a technical dossier registered at 10 to 100 tonnes or more per year must contain a chemical safety report (CSR) which must document the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I to REACH.

Annex I, Section 4 of REACH requires that the chemical safety assessment includes the PBT (persistent, bioaccumulative and toxic) and vPvB (very persistent and very bioaccumulative) assessments.

1. The same bioaccumulation study in aquatic species as requested in C.1 (Annex I, sections 0.6.1. and 4.; Annex XIII, Section 2.1)

Bioaccumulation in aquatic species is required for the purpose of the PBT/vPvB assessment (Annex I, Sections 0.6.1 and 4 to REACH).

Annex I, Section 4 requires that the CSA includes the PBT (persistent, bioaccumulative and toxic) and vPvB (very persistent and very bioaccumulative) assessments.

In accordance with Annex XIII, Section 2.1., if the result of the screening tests or other information indicate that the substance may have PBT or vPvB properties, further testing on bioaccumulation as set out in Section 3.2 is required.

You have provided an assessment of PBT/vPvB properties of the Substance in section 8 of your CSR. You concluded that the Substance was not bioaccumulative (not B or vB) and therefore not PBT/vPvB.

ECHA has assessed this information and concluded that this information requirement is triggered based on the following reasons:

For the identification of PBT and vPvB substances, Annex XIII of REACH makes the distinction between so-called 'screening information' (Section 3.1) and 'assessessment information' (Section 3.2).

Section 2.1. of Annex XIII requires that you must generate assessment information if the results from screening tests indicate that the Substance may have PBT or vPvB properties. This Section further specifies that assessment information does not have to be generated for the purpose of the PBT/vPvB assessment only if screening information does not indicate potential P or B properties.

Therefore, as long as a piece of screening information indicates that the Substance could potentially be persistent (P) and bioaccumulative (B), then assessment information needs to be generated.

This is the case if the Substance, a constituent, an impurity or a transformation/degradation product meets the following screening criteria (see ECHA Guidance R.11, Section R.11.4):

- The Substance is potentially bioaccumulative or very bioaccumulative:
  - E.g. log Kow > 4.5 or potential for bioaccumulation in air-breathing organisms (log Kow >2 and log Koa >5)

- The Substance is potentially persistent or very persistent:
  - E.g. the Substance not readily biodegradable according to OECD 301 or OECD 310 test(s)

For the B/vB assessment, results from a bioconcentration or bioaccumulation study in aquatic species constitutes assessment information for B or vB properties (Section 3.2.2. of Annex XIII of REACH). However, QSAR predictions are not mentioned as possible assessment information for the PBT/vPvB assessment. (Q)SAR models may however be used together with other information in a Weight-of-Evidence approach (see ECHA Guidance R.11, Section R.11.4.1.2.10).

Screening information provided in your dossier indicates that:

- the Substance has a log Kow 5.24, and
- the Substance showed no mineralisation after 28 days in OECD 310 test.

You have also reported a BCF value of 1330 for the Subtance. This value was calculated using the regression method of the BCFBAF v3.01 model (in software EPI Suite v4.11) and using the experimental log Kow value of 5.24 as input parameter to this model.

The experimental log Kow value of 5.24 is a valid piece of screening information which indicates that the Substance could be bioaccumulative or very bioaccumulative.

Similarly, the Substance is not readily biodegradable, indicating that the Substance could be in addition persistent or very persistent.

The BCF value of 1330 is regarded as a 'screening information' (Section 3.1, Annex XIII of REACH), not as 'assessment information' (Section 3.2, Annex XIII of REACH) as it is based on a QSAR prediction. Furthermore, from the training set provided in the help file of the BCFBAF v3.01 model, it is possible to calculate the prediction interval for this prediction. For a log Kow of 5.24, the prediction for log BCF is 3.12 and the 95% prediction interval (in the log scale) is 1.922 – 4.327. In the linear scale, this corresponds to a predicted BCF of 1330 with a 95% prediction interval ranging from 84 to 21212. Therefore, the model prediction does not rule out that the Substance may be bioaccumulative (B) or very bioaccumulative (vB).

The information you have provided cannot reverse the conclusion that the Substance may have PBT/vPvB properties, since there is already valid screening information (log Kow of 5.24 and the absence of degradation observed in the ready biodegradability test) to establish this.

Therefore, the provided information indicates that the Substance is potentially PBT/vPvB.

Therefore, this information requirement is triggered.

The assessment of the information provided for this information requirement and specifications of the requested study are explained under Appendix C, Section 1.

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

1. Bioaccumulation study in aquatic species (Annex IX, Section 9.3.2)

Bioaccumulation in aquatic species, preferably fish is a standard information requirement at Annex IX of REACH.

You have provided a QSAR prediction using model BCFBAF v3.01 (in software EPI Suite v4.11).

ECHA has assessed this information and identified the following issue(s):

Annex XI, Section 1.3. states that results obtained from valid QSAR models may be used instead of testing when an adequate justification is provided and the following cumulative conditions are met:

1. results are derived from a QSAR model whose scientific validity has been established;
2. the substance falls within the applicability domain of the QSAR model;
3. adequate and reliable documentation of the applied method is provided; and
4. the results are adequate for classification and labelling and/or risk assessment.

Further, Section 2.1. of Annex XIII requires that you must generate 'assessment information', such as a bioaccumulation study, if the results from screening information indicate that the Substance may have PBT or vPvB properties.

Your dossier only contains a QSAR prediction.

As provided under Appendix B, Section 1, the Substance is potentially PBT/vPvB. The proposed QSAR cannot reverse this conclusion from the existing screening information (log Kow of 5.24 and the absence of degradation observed in the ready biodegradability test); and it cannot qualify as assessment information under Annex XIII of REACH.

Therefore, further information on bioaccumulation is required for the PBT/vPvB assessment and your adaptation is rejected for that purpose.

Bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to investigate bioaccumulation (ECHA *Guidance, Chapter R.7c, R.7.10.3.1)*. Whenever technically feasible, the aqueous route of exposure (OECD TG 305-I) must be used as the results obtained can be used directly for comparison with the B and vB criteria of Annex XIII of REACH. If testing through aquatic exposure is technically not possible, you must provide scientifically valid justification for the infeasibility. In case you conduct the study using the dietary exposure route (OECD 305-III), you must also attempt to estimate the corresponding BCF value from the dietary test data according to Annex 8 of the OECD 305 TG and OECD Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation, ENV/JM/MONO (2017)16. In any case you must report all data derived from the dietary test as listed in the OECD TG 305-III.

Appendix D: 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

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

Appendix E: General recommendations when conducting and reporting new tests for REACH purposes

A. Strategy for the PBT/vPvB assessment

You are advised to consult ECHA Guidance R.7b (Section R.7.9.), R.7c (Section 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.

Appendix F: 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 18 June 2019.

The decision making followed the procedure of Articles 50 and 51 of REACH, as described below:

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

ECHA did not receive any comments within the notification period.

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

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix G: 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)[5]

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[6]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[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] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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 H: List of the registrants to which the decision is addressed and the corresponding information requirements applicable to them

Registrant Name	Registration number	(Highest) Data requirements to be fufilled
[redacted]	[redacted]	[redacted]
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Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.