~~Confidential~~

Helsinki, 27 June 2022

Addressees
Registrant(s) of JS_214-426-1 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
06/06/2017

Registered substance subject to this decision ("the Substance")
Substance name: N-butyl phenyl ether
EC number: 214-426-1

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 ***2 April 2024***.

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

Information required from 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)

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

2. Simulation testing on ultimate degradation in surface water (triggered by Annex VIII, Section 9.2.; test method: EU C.25./OECD TG 309) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

3. Identification of degradation products (triggered by Annex VIII, Section 9.2; test method: using an appropriate test method or EU C.25./OECD TG 309)

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the 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. Short-term toxicity testing on aquatic invertebrates

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

1.1. Information provided

2 You have provided the following information:

i. a key study (1991) performed according to OECD TG 202 on the Substance;
ii. a supporting study (1993) performed according to non-specified test method on the Substance;
iii. an adaptation according to Annex XI, Section 1.3 ((Q)SAR) of REACH supported by the following information: a prediction of toxicity to aquatic invertebrates derived from ECOSAR v1.11 (2016) using the Substance as an input structure.

1.2. Assessment of the information provided

3 We have assessed this information and identified the following issues:

1.2.1. The provided studies do not meet the information requirement

4 To fulfil the information requirement, a study must comply with OECD TG 202 (Article 13(3) of REACH). Therefore, the following specifications must be met:

- the test duration is 48 hours or longer;
- at least 20 animals are used at each test concentration and for the controls;
- the number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation;
- adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided;

5 Your registration dossier provides a key OECD TG 202 study and a supporting study performed according to non-specified test method both showing the following:

- the test duration was 24 hours;
- 10 animals were used at each test concentration and for the control;
- tabulated data on the number of immobilised daphnids after 24 and 48 hours for each treatment group and control are not reported;
- on the analytical method adequate information, performance parameters of the method and the results of the analytically determined exposure concentrations are not provided;

6 Based of the above, the reporting of the studies is not sufficient to conduct an independent assessment of its reliability including fulfilment of the validity criteria of OECD TG 202. Furthermore, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically the test duration was shorter and smaller number of animals per concentration/control was used than required by OECD TG 202 which may affect the sensitivity and reliability of the studies. Therefore, the requirements of OECD TG 202 are not met for both provided experimental studies.

1.2.2. Assessment of adaptation according to Annex XI, Section 1.3

7 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.

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

9 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).

10 Your registration dossier provides the following information:

- You explain that "*The short-term daphnia toxicity of butyl phenyl ether was estimated using quantitative structure-activity relationship (QSAR). ECOSAR (Ecological Structure-Activity Relationships, ECOSAR v1.11) was chosen because it uses a training set based on mostly public data in a transparent empirical model. Butyl phenyl ether was assessed by the model for Neutral Organics defined in ECOSAR which is deemed adequate.*"
  "*The daphnia 48 h LC50 of butyl phenyl ether is estimated to be 3.3 mg/L. This estimation is deemed reliable because butyl phenyl ether is in the applicability domain of the model and the estimated aquatic toxicities of structural analogues agree well with existing experimental data.*"
- A predicted (by ECOSAR) K_{OW} octanol-water partition coefficient of the compound equal to 3.55 and was used to predict toxicity of the Substance to aquatic invertebrates.
- The octanol/water partition coefficient (log K_{ow}) for butyl phenyl ether is 4.26 which was estimated following the OECD Guideline 117: HPLC method.
- The list of structural analogues which were evaluated for the model performance. The list contains only one substance (trans-Anethole) which has aromatic ring and ether group in its structure.

11 You have not justified the use of predicted log Kow instead of measured log Kow, although the later, being a measured data, would have less uncertainties and thus would be more reliable. Therefore, you have not demonstrated having used a reliable parameter.

12 Furthermore, the Substance has an aromatic ring and ether group in its structure. However, the analogues identified from within the training set have limited coverage of relevant substructures present in the target (ether, aryl). There is only one substance (CAS 4180-23-8) having both such structural features present in the list of structural analogues which were used by you to evaluate the model performance.

13 You have not justified how such structural analogues present in the training/test sets of the model would be sufficient to confirm the model performance and ensure the sufficient level of reliability for the Substance. Thus, it can not be confirmed that the model predicts well for the Substance.

14 Therefore, you have not demonstrated that the prediction for the Substance is adequate for the purpose of classification and labelling and/or risk assessment.

15 Therefore, the information requirement is not fulfilled.

1.3. Study design and test specifications

16 The Substance is difficult to test due to the low water solubility (36.6 mg/L, OECD TG 105), adsorptive properties (Log kow of 4.26, OECD TG 117) and potential volatility (due to vapour pressure of 84 Pa at 25 °C, OECD TG 104 and water solubility of 36.6 mg/l at 20 °C). OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

Reasons related to the information under Annex VIII of REACH

2. Simulation testing on ultimate degradation in surface water

17 Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

18 This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (Guidance on IRs and CSA, Section R.11.4.). This is the case if the Substance itself or any of its constituent or impurity present in concentration ≥ 0.1% (w/w) or relevant transformation/degradation product meets the following criteria:

- it is potentially persistent or very persistent (P/vP) as:
  - it is not readily biodegradable (*i.e.* <60/70% degradation in an OECD 301D), and
- it is potentially bioaccumulative or very bioaccumulative (B/vB) as:
  - it has a high potential for bioaccumulation in air-breathing organisms (log K_{ow} >2 and log K_{oa} >5).

2.1. Information provided

19 The following information is provided:

- The Substance is not readily biodegradable (5.4% degradation after 28 days in OECD TG 301D);
- The Substance has a high potential for bioaccumulation in air-breathing organisms (Log K_{ow} of 4.26 based on OECD TG 117 and Log K_{oa} of 5.776 predicted by KOAWIN v 1.10, when experimental log Kow value is used);

20 Under section 7.1 of the registration dossier you note that "Experimental data on absorption, distribution, metabolism and excretion (ADME) are not available" for the Substance and provide "QSAR predictions of ADME properties in humans" and you summarise that the Substance "is not expected to bioaccumulate in human".

2.2. Assessment of the information provided

21 As explained in ECHA Guidance R.11, p. 81 "There is no universal elimination process–related threshold in B-assessment available which would cover all (aquatic/terrestrial - water breathing/air breathing) organisms because the elimination rate depends on several factors (e.g. species). Nor can any more specific cut off criteria be recommended to compare elimination ie, ADME] data with the B/vB criteria."

22 Furthermore, once there is indication of potential PBT/vPvB properties, assessment information is required to conclude on PBT/vPvB.

23 However, the provided considerations are based on standalone QSAR predictions and as it is explained in Section 3.2.2. of Annex XIII and Guidance R.11 (section R.11.4.1.2.10 for "BCF-QSARs") QSAR results could be used in the weight of evidence approach for the PBT/vPvB assessment but not as stand alone for assessment information.

24 Finally, provided predictions address ADME properties in humans while there is no information on bioaccumulation potential in other air-breathing organisms (e.g. birds and other mammals) although these are also relevant for PBT assessment.

25 Therefore, the additional information from the section 7.1 of the registration dossier is not adequate to conclude that the Substance is not a potential B/vB in air-breathing organisms.

26 Based on the above, the available information on the Substance indicates that it is a potential PBT/vPvB substance. Further, the additional information from the section 7.1 of the registration dossier is not adequate to conclude on the PBT/vPvB properties of the Substance

2.3. Study design and test specifications

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

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

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

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

30 As specified in Guidance on IRs and CSA, Section R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test material concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Therefore, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents. By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

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

3. Identification of degradation products

32 Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

33 This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (Guidance on IRs and CSA, Section R.11.4.).

34 As already explained in Request on Simulation testing on ultimate degradation in surface water above, the Substance is a potential PBT/vPvB substance.

35 Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

3.1. Study design and test specifications

36 Regarding the selection of appropriate and suitable test method(s), the method(s) will have to be substance-specific. Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported, when analytically possible. In addition, degradation half-life, log K_{ow} and potential toxicity of the transformation/degradation may need to be investigated. You may obtain this information from the degradation study requested in the section 3 above or by some other measure. If any other method is used for the identification of the transformation/degradation products, you must provide a scientifically valid justification for the chosen method.

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

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; (ECHA 2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).

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 8 July 2021.

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

ECHA did not receive any comments within the commenting period.

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

2. General recommendations for conducting and reporting new tests

2.1. Strategy for the PBT/vPvB assessment

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

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

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