EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 05 May 2021

Addressees
Registrant(s) of CO Butandiol 810 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
10/07/2013

Registered substance subject to this decision ("the Substance")
Substance name: A mixture of: but-1,3-diyl didecanoate; but-1,3-diyl dioctanoate; but-1,3-diyl 1-decanoate-3-octanoate; but-1,3-diyl 1-octanoate-3-decanoate
EC number: 424-180-9
CAS number: NS

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 ***10 August 2022***.

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

A. 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: EU B.13/14. /OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

2. Long-term toxicity testing on aquatic invertebrates also requested below (triggered by Annex VII, Section 9.1.1., Column 2; test method: EU C.20./OECD TG 211)

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

1. If negative results are obtained in tests performed for the information requirement of Annex VII, Section 8.4.1. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

2. Long-term toxicity testing on fish also requested below (triggered by Annex VIII, Section 9.1.3., Column 2; test method: OECD TG 210)

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

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

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

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 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.

Authorised[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. In vitro gene mutation study in bacteria

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

You have provided:

i. [redacted] (1997) with the following strains, TA 98, TA 100, TA 1535, and TA 1537 which all gave negative results.

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

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[2] (1997). One of the key parameters of this test guideline includes: 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).

The reported data for the study you have provided did not include the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

The information provided does not cover one of the key parameters required by OECD TG 471.

Therefore, the information requirement is not fulfilled.

Study design

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

In your comments on the draft decision you agree to conduct the requested test as specified in the decision.

2. Long-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.). Long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

You have provided the following information:

- A short-term toxicity study on aquatic invertebrates according to OECD TG 202, and
- A long-term toxicity study on aquatic invertebrates according to OECD TG 211.

We have assessed this information and identified the following issue:

Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for these 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).

[2] ECHA Guidance R.7a, Table R.7.7-2, p.557

As already explained under Appendix A.2., the Substance is poorly water soluble (< 1mg/L). Therefore, relevant and reliable information on long-term toxicity on aquatic invertebrates 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 C.1.

Your comments to the draft decision are also addressed under section C.1.

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

1. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

i. Triggering of the study

Your dossier contains: (i) insufficient date for an *In vitro* gene mutation study in bacteria, and (ii) negative results in an *In vitro* cytogenicity study in mammalian cells.

The *in vitro* gene mutation study in bacteria provided in the dossier is insufficient for the reasons provided in section A.1.

The result of the request for information in Appendix A, section 1 will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

ii. Assessment of information provided

Your dossier does not contain any study or adaptation in accordance with column 2 of Annex VIII, Section 8.4.3. or with the general rules of Annex XI for this standard information requirement.

Therefore, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

In your comments on the draft decision, you agree to conduct the requested test as specified in the decision if it is triggered by the outcome of the requested OECD TG 471 (Appendix A., Request 1.).

2. 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 a short-term toxicity study on fish according to an OECD TG 203 and a justification to omit a long-term toxicity study on fish based on Annex IX, Section 9.1, Column 2 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 do not give a true measure of toxicity for these 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).

As already explained under Section A.2., the Substance is poorly water soluble (< 1mg/L). Therefore, relevant and reliable information on long-term toxicity on fish must be provided.

The examination of the adaptation provided, as well as the selection of the requested test and the test design are addressed under section C.2.

Your comments to the draft decision are also addressed under section C.2.

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

1. Long-term toxicity testing on aquatic invertebrates

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

You have provided the following information: a key study according to OECD TG 211 ([redacted] 2001).

We have assessed this information and identified the following issues:

To fulfil the information requirement, a study must comply with the OECD TG 211 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) (Article 13(3) of REACH). Therefore, the following specifications must be met:

Measurements and analytical determinations:

- A reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available;

Furthermore if the test material is poorly water soluble:

- Evidence must be provided that the test solution preparation allowed achieving the maximum dissolved concentration under test conditions;
- A justification for, or validation of, the separation technique is provided, especially if filtration is used, as it can cause losses due to adsorption onto the filter matrix.

Your registration dossier provides a key study according to OECD TG 211 showing the following:

- In your registration dossier the analytical method is unidentified and no details on analytical method are reported.

- The maximum dissolved concentration that can be achieved in the specific test solution is not reported in the study listed above;
- The test substance in your study has been filtered using a cellulose nitrate filter (pore size 0.45 µm), but a justification for, or validation, of the separation technique is not provided.

Based on the above,

- There are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the study does not provide adequate information on the characterisation of exposure during the test as no information on the analytical method used are given and adequacy of the analytical method cannot be confirmed;
- As explained under section A.2 , the Substance is difficult to test (poor water solubility) and the specific requirements of OECD GD 23 are not met in the study above. You have not demonstrated that the method applied in the study allowed achieving maximum dissolved concentrations, nor have you justified the use of filter as a separation method.

Therefore, the requirements of OECD TG 211 are not met and on this basis, the information requirement is not fulfilled.

In your comments on the draft decision you claim that the available OECD TG 211 study would

cover the requirements listed above. In your comments you identify the analytical method used in the test (gas chromatography) and provide some details on the analytical method such as detection and quantification limits, mean recoveries of the fortified samples, and mean test item concentrations in freshly prepared filtrate samples and in aged filtrate samples. You also indicate in your comments that you intend to provide more details in an updated Robust Study Summary.

ECHA has assessed the information provided in the comments against the requirements in OECD TG 211. ECHA acknowledges the new information in your comments related to the analytical method and the analysis of the test substance and considers that the new information in your comments provides adequate information on the characterisation of exposure.

However, ECHA notes that no information on the other requirements listed above is provided in your comments (e.g. achievement of maximum dissolved concentrations with method applied in the study or the justification for, or validation of, the used separation technique).

Since the new information does not cover all the issues identified in the decision and you intend to provide more details in the updated dossier, no conclusions can currently be made. Hence data gap remains.

Study design

The Substance is difficult to test due to the low water solubility (< 0.1 mg/L). OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

2. 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:

- 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 provided the following justification:

"According to column 2 of EC 1907/2006 Annex IX 9.1.6 long-term toxicity testing shall only be proposed if the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms. No results from the existing long-term test with Daphnia magna give concern to investigate the long-term toxicity to fish due to the following reasons: The screening test on biodegradation in water showed that the substance is readily biodegradable and thus, will not persist in the aquatic environment. Furthermore the short-term tests for all three trophic levels showed no toxicity of the test substance up to the limit of its water solubility. There was no sign, that fish are more sensitive than Daphnia. Thus, it can not be expected that a long-term test with fish will generate different results than the existing long-

term test with Daphnia magna (no effect up to the limit of the water solubility of the tested substance). Therefore no further long-term test with fish is proposed due to animal welfare."

In your comments on the draft decision you claim that the available data adequately cover this endpoint and fulfil the information requirement because the short-term data show that the fish is not the most sensitive species as the test substance do not exhibit toxicity within its limit of solubility in any aquatic test across the three trophic levels.

We have assessed this information and identified the following issue:

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).

In addition, as explained in Appendix B.2, due to the Substance properties acute toxicity studies cannot be used to conclude on long-term hazards of poorly soluble substances.

Your adaptation is therefore rejected.

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.).

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 Appendix C.1.

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[3].

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[4].

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

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

A. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in ECHA Guidance R.11 (Section R.11.4.2.2), you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

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 16 April 2020.

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

ECHA took into account your comments and amended the draft decision by removing one of the requests.

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 G: List of references - ECHA Guidance[5] 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)[6]

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

[5] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[6] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[7] 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: 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]
[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.