ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114303419-54-01/F Helsinki, 31 August 2015

**DECISION ON TESTING PROPOSAL(S) SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006**

**For 2-Butenedioic acid (Z)-, ester with 1,2-propanediol, compd. with 2-(dibutylamino)ethanol, CAS No 85204-10-0 (EC No 286-304-6), registration number:** [redacted]

**Addressee:** [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 40(1) of the REACH Regulation, ECHA has examined the following testing proposals submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for 2-Butenedioic acid (Z)-, ester with 1,2-propanediol, compd. with 2-(dibutylamino)ethanol, CAS No 85204-10-0 (EC No 286-304-6), submitted by [redacted] (Registrant).

- Viscosity of Liquids (OECD Test Guideline 114);
- *Daphnia magna* Reproduction Test (OECD Test Guideline 211);
- Fish, Juvenile Growth Test (OECD Test Guideline 215);
- Repeated Dose 90-Day Oral Toxicity in Rodents (OECD Test Guideline 408), in rats;
- Prenatal Developmental Toxicity Study (OECD Test Guideline 414), in rats;
- Two-Generation Reproduction Toxicity Study (OECD Test Guideline 416), in rats.

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of 100 to 1000 tonnes per year. This decision does not take into account any updates after 5 March 2015, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

ECHA received the registration dossier containing the above-mentioned testing proposals for further examination pursuant to Article 40(1) on 23 May 2013.

ECHA held a third party consultation for the testing proposals from 2 June 2014 until 17 July 2014. ECHA received information from third parties (see section III below).

On 11 November 2014 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

By 18 December 2014 the Registrant did not provide any comments on the draft decision to ECHA.

On 5 March 2015 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals for amendment of the draft decision within 30 days of the receipt of the notification.

Subsequently, proposals for amendment to the draft decision were submitted.

On 10 April 2015 ECHA notified the Registrant of the proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposals for amendment within 30 days of the receipt of the notification.

The ECHA Secretariat reviewed the proposals for amendment received and amended the draft decision.

On 20 April 2015 ECHA referred the draft decision to the Member State Committee.

By 11 May 2015 2015 the Registrant did not provide any comments on the proposals for amendment.

A unanimous agreement of the Member State Committee on the draft decision was reached on 26 May 2015 in a written procedure launched on 13 May 2015.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

## II. Testing required

### A. Tests required pursuant to Article 40(3)

The Registrant shall carry out the following proposed tests pursuant to Article 40(3)(a) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

1. Viscosity (Annex IX, Section 7.17.; test method OECD 114);
2. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26/OECD 408) in rats;
3. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414) in rats or rabbits, oral route.
4. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211);

The Registrant shall carry out the following additional test pursuant to Article 40(3)(c) and 13(4) of the REACH Regulation using the indicated test method and the registered substance subject to the present decision:

5. Fish, early-life stage (FELS) toxicity test (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage toxicity test, OECD 210);

while the originally proposed tests for a Fish, Juvenile Growth Test (OECD Test Guideline 215) and Two-Generation Reproduction Toxicity Study (OECD Test Guideline 416), in rats, are rejected pursuant to Article 40(3)(d) of the REACH Regulation.

Note for consideration by the Registrant:

The Registrant may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

Failure to comply with the requests in this decision, or to fulfil otherwise the information requirements with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

B. Deadline for submitting the required information

Pursuant to Articles 40(4) and 22(2) of the REACH Regulation, the Registrant shall submit to ECHA by **7 September 2017** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report. The timeline has been set to allow for sequential testing as appropriate.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant for the registered substance and scientific information submitted by third parties.

A. Tests required pursuant to Article 40(3)

1. Viscosity (Annex IX, Section 7.17.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

"Viscosity" is a standard information requirement as laid down in Annex IX, Section 7.17. of the REACH Regulation. The information on this endpoint is not available for the registered substance subject to the present decision but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for a Viscosity of liquids (OECD Test Guideline 114).

ECHA considers the proposed test appropriate and testing should be performed with the registered substance.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is requested to carry out the proposed test using the registered substance: Viscosity of liquids (test method: OECD 114).

2. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats via the oral route (OECD 408).

ECHA considers that the proposed study via the oral is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation because the proposed route is the most appropriate route of administration having regard to the likely route of human exposure due to the following reasons.

The Registrant proposed testing by the oral route. In light of the physic-chemical properties of the substance (liquid with low vapour pressure and as claimed by the Registrant "*highly viscous liquid limiting its availability as an inhalable aerosol*") and the information provided on the uses and human exposure, i.e. concentrations of the substance in mixtures applied via spraying are very low ([redacted]%), ECHA considers that testing by the oral route is most appropriate.

The Registrant proposed testing in rats. According to the test method EU B.26/OECD 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is requested to carry out the proposed study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408).

3. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for a pre-natal developmental toxicity study in rats according to OECD 414.

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

The Registrant proposed testing in rats. He did not specify the route for testing. According to the test method EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rat or the rabbit as a first species to be used.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in rats or rabbits, oral route (test method: EU B.31/OECD 414).

4. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for testing for long-term toxicity testing on aquatic invertebrates *Daphnia magna* reproduction test, OECD 211. ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 9.1.5 of the REACH regulation.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 1.2., November 2012), Chapter R7b (Section R.7.8.5), if based on acute aquatic toxicity data aquatic invertebrates are not shown to be substantially less sensitive than fish or algae, long-term study on aquatic invertebrates may be required. There were no compelling indications in the dossier from the short-term toxicity studies on aquatic species that the aquatic invertebrates would be substantially less sensitive than fish and algae. In such case, according to the integrated testing strategy, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study using the registered substance subject to the present decision: Long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211).

5. Fish, early-life stage (FELS) toxicity test (Annex IX, Section 9.1.6.1.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for testing for long-term toxicity testing on fish, Fish, Juvenile Growth Test, OECD 215. ECHA considers that the proposed study is, in principle, appropriate to fulfil the information requirement of Annex IX, Section 9.1.6 of the REACH regulation.

However, ECHA considers that for the endpoint of long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6., the FELS toxicity test according to OECD 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see ECHA *Guidance on information requirements and chemical safety assessment* (version 1.2., November 2012), Chapter R7b, Figure R.7.8-4 page 26). The test method OECD 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance R7b, version 1.2., November 2012, p. 26). For these reasons, ECHA considers the FELS toxicity test using the test method OECD 210 as appropriate and suitable. ECHA considers that in absence of a clear and valid scientific justification in the dossier why another guideline, such as the proposed OECD 215, is considered to be equally or more sensitive than OECD 210 for the registered substance, OECD 210 should be used for generating new long-term toxicity data on fish.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 1.2., November 2012), Chapter R7b, (Section R.7.8.5), if based on acute aquatic toxicity data fish is not shown to be substantially less sensitive than aquatic invertebrates or algae, long-term study on fish may be required. There were no compelling indications in the dossier from the short-term toxicity studies on aquatic species that the fish would be substantially less sensitive than aquatic invertebrates and algae. In such case, according to the integrated testing strategy, the *Daphnia* study is to be conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted.

b) Outcome

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is required to carry out the additional study using the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.; test method: Fish, early-life stage toxicity test, OECD 210), while the originally proposed tests for a Fish, Juvenile Growth Test (OECD Test Guideline 215) is rejected pursuant to Article 40(3)(d) of the REACH Regulation.

c) Notes for consideration by the Registrant

Before conducting any of the tests mentioned above in points 4 - 5 the Registrant shall consult the ECHA *Guidance on information requirements and chemical safety assessment*

*(version 1.2., November 2012)*, Chapter R7b, Section R.7.8.5 to determine the sequence in which the aquatic long-term toxicity tests are to be conducted and the necessity to conduct long-term toxicity testing on fish.

6. Two-generation reproductive toxicity study (Annex IX, Section 8.7.3.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) of the REACH Regulation, ECHA may reject a proposed test.

The Registrant has submitted a testing proposal for a two-generation reproductive toxicity study according to OECD 416 in rats. More specifically, in IUCLID section 7.8.1 of the technical diossier, the Registrant had selected "experimental study planned" indicating that the study is to be performed according to above-mentioned test guideline OECD 416, and with the following note provided: "*In the reproductive toxicity screening test no adverse effects were observed. Only if there were adverse effects on reproductive organs or tissues in the proposed 90 -day toxicity study a 2 -generation reproductive toxicity study will be proposed.*"

According to Annex IX, Section 8.7.3., a two-generation reproductive toxicity study is an information requirement if adverse effects on reproductive organs or tissues have been observed in a 28-day or 90-day repeated dose toxicity study.

ECHA notes that there are results of a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD 422) available in the registration dossier that did not indicate adverse effects on reproductive organs or tissues.

ECHA observes further that although proposing "experimental study planned", the Registrant has included a note that two-generation reproductive toxicity study would be proposed only if it is trigerred by adverse effects in the proposed 90-day repeated dose toxicity study. ECHA considers that the proposed study is at this stage not necessary to fulfil the information requirement of Annex IX, Section 8.7.3. of the REACH Regulation because no 90-day repeated dose toxicity study is currently available to evaluate if performance of a two-generation reproductive toxicity study is required at that tonnage level and no adverse effects on reproductive organs or tissues have been observed in a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD 422).

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation.

A third party has indicated that the the proposed study is not a standard information requirement and in terms of animal welfare a sequential testing strategy which gives priority to the proposed 90-day repeated dose toxicity study should be used. It means that the results of the proposed 90-day repeated dose toxicity study should be the basis to decide if a two-generation reproductive toxicity study is generally required. Furthermore, a third party noted that if further study on reproductive toxicity is triggered preferrably Extended One-Generation Reproductive Toxicity Study (EOGRTS) according to OECD 443 would be conducted for the registered substance.

As already stated under section III.6.a above, ECHA notes that according to Annex IX, Section 8.7.3., a two-generation reproductive toxicity study is an information requirement if adverse effects on reproductive organs or tissues have been observed in a 28-day or 90-day

repeated dose toxicity study. For the substance subject to the present decision no adverse effects on reproductive organs or tissues have been observed in a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD 422) and there is no 90-day repeated dose toxicity study available in the registration dossier that could trigger a two-generation reproductive toxicity study. Therefore, ECHA has rejected the testing proposal for a two-generation reproductive toxicity study.

c) Outcome

ECHA concludes that there is at this stage no information gap for the standard information requirement of Annex IX, Section 8.7.3. Therefore, pursuant to Article 40(3)(d) of the REACH Regulation, the proposed test for a two-generation reproduction toxicity study (OECD 416) is rejected.

d) Notes for consideration by the Registrant

Once the results from the sub-chronic toxicity study (Section II.2. above) are available, the Registrant should reconsider the information requirement of Annex IX, Section 8.7.3. If the sub-chronic toxicity study indicates adverse effects on reproductive organs or tissues a new testing proposal for the present endpoint would – in accordance with the REACH Regulation – have to be submitted, unless the information requirement could be adapted.

## IV. Adequate identification of the composition of the tested material

The process of examination of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the new studies meet real information needs. Within this context, the Registrant's dossier was sufficient to confirm the identity of the substance to the extent necessary for examination of the testing proposal. The Registrant must note, however, that this information has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

It is important to ensure that the particular sample of substance tested in the new studies is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured. If the registration of the substance covers different grades, the sample used for the new studies must be suitable to assess these.

Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the studies to be assessed.

## V. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the ECHA's internet page at http://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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[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.