ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114309016-62-01/F Helsinki, 30 September 2015

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

For Copolymer of neodecanoic acid oxiranylmethyl ester and 4-methylbenzenesulfonic acid, EC No 500-281-4 (CAS No 98362-33-5), 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 Copolymer of neodecanoic acid oxiranylmethyl ester and 4-methylbenzenesulfonic acid, EC No 500-281-4 (CAS No 98362-33-5), submitted by [redacted] (Registrant).

- Bioaccumulation aquatic/sediment (OECD 305);
- 90-day oral toxicity study (OECD 408) in rats;
- Developmental toxicity / teratogenicity study in rats, oral route (OECD 414).

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 16 May 2015, i.e. 30 calendar days after the end of the commenting period.

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.

The examination of the testing proposals was initiated upon the date when receipt of the complete registration dossier was confirmed on 24 May 2013.

ECHA held a third party consultation for the testing proposals from 15 July 2014 until 29 August 2014. ECHA received information from third parties (see section III below).

On 10 March 2015 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 16 April 2015 the Registrant did not provide any comments on the draft decision to ECHA.

On 11 June 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 17 July 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 27 July 2015 ECHA referred the draft decision to the Member State Committee.

By 17 August 2015, in accordance to Article 51(5), the Registrant provided comments on the proposals for amendment. The Member State Committee took the comments on the proposals for amendment of the Registrant into account.

A unanimous agreement of the Member State Committee on the draft decision was reached on 31 August 2015 in a written procedure launched on 20 August 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 test pursuant to Article 40(3)(a) and (b) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

1. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method Bioaccumulation in Fish: Aqueous or Dietary Exposure Bioaccumulation Fish Test, OECD 305).

Moreover, 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:

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.

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 **9 October 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. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.)

a) Examination of the testing proposal

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

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2. 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 testing the registered substance for bioaccumulation in aquatic species (Bio-concentration: Flow-through Fish Test, OECD 305) and has also included the following information in the endpoint summary: *"Based on the log Kow of 4.2 the substance has to be considered as bioaccumulative. Due to the fact that the substance is an UVCB substance and the results of the hydrolysis study, the study design has to be developed in close agreement with the competent authority. The test substance was found to be not hydrolytically stable. However, its components differ significantly in their liabilities to hydrolysis: For some of them the MS peak areas decreased in the course of the preliminary study while for others they increased. The total peak area decreased by* [redacted] *%, which, however, does not allow quantitative conclusions because of the variation of the sensitivity of the detection system towards differing molecular species."*

One Member State proposal for amendment raised some uncertainty regarding the reasoning for requesting the bioaccumulation in aquatic species test, whether "*the reason for conducting this test is for PBT/vPvB assessment (rather than secondary poisoning risk assessment)*". In the Registrant's comments on the proposal for amendment, the Registrant acknowledges that the reasoning, "*ensuring that the new studies meet real information needs*", needs to be clarified.

ECHA has considered the available information submitted in the technical dossier and agrees with the Registrant that the available information does not meet the conditions set out in Annex IX, 9.3.2. of the REACH Regulation. i.e. the results obtained from the bioaccumulation screening do not allow an assumption/conclusion that the registered substance subject to the present decision has or has not bioaccumulation potential in aquatic species. Hence, the available data are not adequate for the purpose of classification and labelling and/or risk assessment.

ECHA notes that the test method OECD 305 was revised and a new version was adopted on 2nd October 2012. One of the main goals of the updated Test Guideline is "*to incorporate a dietary bioaccumulation test suitable for determining the bioaccumulation potential of substances with very low water solubility*".

As described in the current version of test guideline OECD 305, ECHA underlines that the Registrant shall select the appropriate exposure route based on consideration of the substance properties, therefore selecting either the aqueous (the registered substance has an octanol-water partition coefficient, Log Kow, between 4.1 and 4.3, seems moderately sorptive and is soluble in water) or dietary exposure route (the registered substance is unstable in water solutions and in water solubility testing the formation of colloids was observed). ECHA notes that further guidance on the importance of considering the stability in aqueous solution when selecting the relevant exposure route can be retrieved in the test guideline 305 paragraphs 5 and 8.

In addition to considerations contained in the above-mentioned OECD 305 test guideline paragraphs, ECHA notes that, as concluded by the Registrant, the substance is not hydrolytically stable, therefore the Registrant should consider whether or not it may be more relevant to test the hydrolysis product(s) instead of the registered substance. ECHA *Guidance on information requirements and chemical safety assessment,* R.7.10.3.4 states: "*The effect of hydrolysis may be a significant factor for substances discharged mainly to the aquatic environment: the concentration of a substance in water is reduced by hydrolysis so the extent of bioconcentration in aquatic organisms would also be reduced. Where the half-life, at environmentally relevant pH values (4-9) and temperature, is less than 12 hours, it can be assumed that the rate of hydrolysis is greater than that for uptake by the exposed organisms. Hence, the likelihood of bioaccumulation is greatly reduced. In these cases, it may sometimes be appropriate to perform a BCF test on the hydrolysis products, if identified, instead of the parent substance. However, it should be noted that, in most cases hydrolysis products are more hydrophilic and as a consequence will have a lower potential for bioaccumulation.*"

Therefore, for the selection of the appropriate exposure route and overall design of the test, the Registrant is advised to consult both the OECD 305 test guideline as well as ECHA *Guidance on information requirements and chemical safety assessment* (version 1.1., November 2012), Chapter R7c.

Moreover, given the nature of the registered substance as an extract of unknown or variable composition, complex reaction products or biological materials (UVCB), analytical challenges can be expected. More specifically, ECHA observes that the bioconcentration factor should be related to single constituents rather than to the overall UVCB substance to allow for the interpretation of the results.

One Member State proposal for amendment has indicated that "*Instead of the whole UVCB substance only these components and hydrolysis products with the strongest*

bioaccumulation concern should be tested according to OECD 305. Ideally, the tested substances should be radiolabelled".

In the Registrant's comments on the proposal for amendment, in summary the Registrant indicates that following identification of those constituents with a potential to bioaccumulate using non-testing data like QSAR predictions, read across data etc. at first and due to the high complexity of the composition of the registered substance, it is not feasible to isolate part of the constituents for a bioaccumulation study, all constituents will be determined unless analytical problems arise.

ECHA draws the attention of the Registrant to the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapters R.11., PBT/vPvB assessment Section R.11.4.1. which provides further guidance on what should be considered as relevant constituents and for UVCBs (substances of Unknown or Variable composition, Complex reaction products or Biological materials), Section R.11.4.2.2 which provides further guidance on how to carry out a PBT/vPvB assessment.

In the Registrant's comments on the proposal for amendment, the Registrant indicates that "*Since bioaccumulation mainly is a problem if associated with persistence, there is more value in testing a sample where the non-persistent constituents have had sufficient time for conversion to more stable hydrolysis products (e.g. by means of WAF). Accordingly the testing in aqueous solution seems more reasonable than a feeding study. Furthermore it is likely that a number of constituents or hydrolysis products may be sufficiently mobile to cross biological membranes and therefore have the possibility to bioaccumulate. At the time being we assume that the analytical methods in the study will be sufficiently sensitive for the quantification of all relevant constituents without radiolabelling. We will consider radiolabelling if this assumption turns out to be false*".

ECHA draws the attention of the Registrant to the OECD 305 test guideline which provides further guidance that a radiolabelled test substance can facilitate the analysis of fish samples, and may be used to determine whether identification and quantification of metabolites will be necessary.

Given the physicochemical properties of the registered substance (log Kow between 4.1 and 4.3 and its water solubility of 614 mg/L at pH 2.6), the Registrant is reminded that the most appropriate route of exposure according to the provisions outlined in the OECD 305 test guideline has to be chosen.

Furthermore, due to the nature of the registered substance (UVCB), the Registrant is advised to consult the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 1.1., November 2012), Chapter R7b, table R. 7.8-3, which summarises aquatic toxicity testing methods of difficult substances in order to select the design of the test.

With regards to the PBT screening information in the technical dossier, the Registration dossier states the substance is not readily biodegradable in the 10-d-window (OECD 301B ready biodegradability test). ECHA notes based on the available screening biodegradation information indicates that the registered substance may have persistent or very persistent (P or vP) properties. The most sensitive acute species is short-term invertebrates on Daphnia with an EL50 value of 26.3 mg/L. No simulation biodegradation or long term aquatic toxicity testing was provided but adaptations were stated. The registered substance

not classified as carcinogenic (cat. 1A or 1B), germ cell mutagenic (cat. 1 or 1B) or toxic to reproduction (class 1A, 1B or 2) or STOT RE 1, or STOT RE 2.

b) Outcome

Therefore, pursuant to Article 40(3)(a) and (b) of the REACH Regulation, the Registrant is required to carry out the proposed study using the registered substance subject to the present decision: Bioaccumulation in aquatic species, preferably fish (Annex IX, 9.3.2.; test method: Bioaccumulation in Fish: Aqueous or Dietary Exposure Bioaccumulation Fish Test, OECD 305).

Notes for consideration by the Registrant

Before conducting testing, the Registrant is advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapters R.11., PBT/vPvB assessment, in particular it may be relevant to conclude on whether the registered substance is not persistent and not very persistent or whether it may fulfil Annex XIII of the REACH Regulation criteria of being persistent or very persistent and to consult on PBT assessment for the integrated testing strategy for bioaccumulation assessment in particular concerning, relevant constituents, impurities, additives and degradation/transformation products. Careful consideration needs to be given to the formation of stable degradation products with PBT/vPvB properties.

In addition, the Registrant is advised to consult the ECHA Guidance on the standard information requirements and chemical safety assessment (version 2.0, November 2014), Chapters R.4, 5, 6, R.7b and R.7c.Where the Registrant decides to adapt the testing requested 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, ECHA refers him to the advice provided in practical Guides 4, 5 and 6.

2. Sub-chronic toxicity study (90-day), oral route (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 (EU B.26/OECD 408) to be performed with the registered substance subject to the present decision.

ECHA considers that the proposed study via the oral route is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation.

The Registrant proposed testing by the oral route. In light of the physico-chemical properties of the substance (liquid with very low vapour pressure and not classified as corrosive/irritating to the skin and/or damaging/irritating to the eyes) and the information

provided on the uses and human exposure (although uses by brushing and spraying application are reported, the exposure estimates do not indicate high inhalation exposure), 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, by 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 Guideline 414, to be performed with the registered substances with the following justification: *"It is proposed to conduct the study with rats by using oral exposure, because other exposure routes like nose-only inhalation exposure is technically very difficult especially because very young and hence very small animals have to be used in this study"*

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

The Registrant proposed testing in rats and proposed testing by the oral route. 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) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

Third party information:

The third party has indicated: *"Results of a transgenic rodent somatic mutation assay with the constituent 2,3-epoxypropyl neodecanoate showed mutagenic effects in the liver, kidney and bone marrow of mice. Accordingly, the registrant proposed classification of the reaction products for germ cell mutagenicity as Muta. 2 (H341: Suspected of causing genetic defects). The hazard profile indicates that the chemical should only be handled with strict risk management measures. On this background testing for reproductive toxicity may not be required (cf. REACH Guidance R.7.6.6.3)."*

ECHA notes that it is the Registrant's responsibility to consider and justify in the registration dossier any adaptation of the information requirements in accordance with Annex IX, Section 8.7., column 2, second indent.

This adaptation specifies that in case the substance is known to be a germ cell mutagen (which corresponds to a classification as germ cell mutagen category 1A or 1B) and appropriate risk management measures are implemented, the pre-natal developmental toxicity study does not need to be conducted.

However, ECHA notes that the registered substance is classified as germ cell mutagen category 2 but not as category 1A or 1B.

Therefore, the information provided by third parties is not sufficient to adapt this information requirement.

c) Outcome

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

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.

In addition, 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.

Finally, 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.

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2.

[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.