EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000004372-79-06/F Helsinki, 14 August 2014

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

For Rosin, maleated, CAS No 8050-28-0 (EC No 232-480-4), 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)(e) thereof for Rosin, maleated, CAS No 8050-28-0 (EC No 232-480-4), submitted by [redacted] (Registrant). The dossier contains a document "Testing strategy for a UVCB category comprising Rosin Adducts and Rosin Adduct salts", which can be summarised as follows:

- Sub-chronic toxicity studies (OECD Guideline 408, rat, oral route) to be performed on the substance subject to this decision.
- Pre-natal developmental toxicity study (OECD Guideline 414, rat, oral route) to be performed on the substance subject to this decision.
- Two-generation reproduction toxicity study (OECD Guideline 416, rat, oral) to be performed on Rosin, fumarated (CAS No. 65997-04-8).
  - An additional two-generation reproduction toxicity study will be proposed by the Registrant for the substance subject to this decision if the results from the proposed sub-chronic toxicity (90-day; OECD Guideline 408) studies or available/ on-going combined repeated dose toxicity study with the reproduction/ developmental toxicity screening (OECD Guideline 422) studies on this substance indicate differences in toxicity relative to Rosin, fumarated (CAS No. 65997-04-8).

The present decision relates solely to the examination of the testing proposals for sub-chronic toxicity (90-day) and pre-natal developmental studies. The testing proposal for the two-generation reproductive toxicity study is addressed in a separate decision although the testing proposals were initially addressed together in the same draft decision.

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more per year. In order to follow the procedure outlined in Articles 50(1) and 51 of the REACH Regulation and to allow ECHA to complete the necessary administrative practices for the Member States Competent Authorities' referral, ECHA took into consideration dossier updates pertinent to the decision received by the deadline of 7 January 2014 as agreed between ECHA and the Registrant.

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.

On 12 November 2010, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposal set out by the Registrant in the registration dossier for the substance mentioned above, in relation to pre-natal developmental toxicity based on a read-across argumentation.

ECHA held a third party consultation for the testing proposal from 6 March 2012 until 20 April 2012. ECHA did receive information from third parties (see section III.2.b. below).

The dossier was later updated by the registrant with additional testing proposals for sub-chronic toxicity (90-day) and two-generation reproductive toxicity and additional substances covered by the category.

On 18 June 2013, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposals set out by the Registrant in the updated registration dossier.

ECHA held a third party consultation for the testing proposal from 2 July 2013 until 16 August 2013. ECHA did not receive information from third parties.

On 23 October 2013 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

On 22 November 2013 ECHA received comments from the Registrant agreeing to ECHA's draft decision.

ECHA considered the Registrant's comments received. On the basis of the comments, the deadline in Section II was amended. The Statement of Reasons (Section III) was changed accordingly and to reflect that one substance was removed from the category.

On 6 March 2014 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 2014 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 did not amend the draft decision.

On 22 April 2014 ECHA referred the draft decision to the Member State Committee.

By 12 May 2014, in accordance to Article 51(5), the Registrant provided comments on the proposals for amendment. The Member State Committee took the comments of the Registrant on the proposals for amendment into account.

A unanimous agreement of the Member State Committee on the draft decision relating to the Sub-chronic toxicity (90-days) and Pre-natal development toxicity studies was reached on 26 May 2014 in a written procedure launched on 15 May 2014. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Testing required

The Registrant has requested to carry out the required tests using the registered substance as part of a read-across and grouping approach, in accordance with Annex XI, 1.5. with respect to fulfilling the endpoints of Annex IX, 8.6.2 and Annex IX, 8.7.2.

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

1. Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2.; test method: EU B.26/OECD 408); and

2. Pre-natal developmental toxicity study in rats or rabbits, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414).

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 request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

Data from a second pre-natal developmental toxicity study on another species is a standard information requirement according to Annex X, 8.7.2. of the REACH Regulation. The Registrant should firstly take into account the outcome of the pre-natal developmental toxicity on a first species and all other relevant available data to determine if the conditions are met for adaptations according to Annex X, 8.7. column 2, or according to Annex XI. If the Registrant considers that testing is necessary to fulfil this information requirement, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species.

At any time, the Registrant shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other Registrants.

3. Deadline for submitting the required information

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **21 August 2017** an update of the registration dossier containing the information required by this decision. 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 substance subject to the present decision and scientific information submitted by third parties.

The Registrant has requested to carry out the required tests using the registered substance as part of a read-across and grouping approach, in accordance with Annex XI, 1.5.

According to the Registrant, the substance subject to this decision can be grouped with other substances in a category for the purpose of read-across. The grouping is based on the premise that all substances that are members of the category are structurally related, i.e. all the substances are UVCBs (substances of Unknown or Variable composition, Complex reaction products or Biological materials) derived from the UVCB starting material Rosin (CAS No. 8050-09-7, EC No. 232-475-7), and are chemically modified in a similar manner.

The Registrant considers substances that fulfil the following criteria as members of the category:

- The substances are formed by the reaction of maleic anhydride, maleic acid or fumaric acid with rosin. The reaction (a Diels-Alder addition reaction) is specific to resin acids which contain a conjugated double bond;
- The reaction products are isomeric mixtures comprising maleopimaric acid anhydride and either (cis-)maleopimaric tricarboxylic acid or fumaropimaric tricarboxylic acid (the latter being the trans-isomer of (cis-)maleopimaric tricarboxylic acid);
- Non-reacted resin acids derived from the parent substance Rosin predominate in all the substances of the category;
- Rosin-derived neutral and fatty acid fractions are present in all the substances of the category at low levels;
- The fumarated adduct contains relatively high levels of fumaropimaric acid and maleopimaric anhydride, while the maleated adduct is relatively high in maleopimaric acid or maleopimaric anhydride and low in fumaropimric acid;
- The adduct salts will ionise in solution to give the parent adduct and associated cation, as is the case for any type of weak acid/ base.

In ECHA's understanding, the Registrant's read-across hypothesis is that if the substance selected for higher tier testing fully covers the structural diversity within the category, this will enable accurate predictions of the toxicological properties within the category. Furthermore, the hypothesis assumes that all substances within the category will exhibit similar toxicity; because the Registrant assumes that the same fraction of the substances will be absorbed.

1. Sub-chronic toxicity study (90-day)

a) Examination of the testing proposal

Pursuant to Article 40(3) 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.

ECHA notes that the Registrant has submitted an oral combined repeated dose toxicity and reproduction/ developmental toxicity screening study (OECD Guideline 422) on the analogue substance Rosin, fumarated (CAS No. 65997-04-8); this study provides information about sub-acute toxicity, but does not meet the information requirement for sub-chronic toxicity (90-day) according to section 8.6.2 of Annexes IX. In addition, the Registrant has submitted a testing proposal, for sub-chronic toxicity study (90-day; EU B.26/OECD 408), proposed to be carried out, in rats, via the oral route on the substance subject to this decision.

The Registrant proposed testing by the oral route. In the light of the physico-chemical properties of the substance and the information provided on the uses and human exposure, ECHA considers that testing by the oral route is appropriate.

b) Consideration of the information received during third party consultation

ECHA did not receive third party information concerning the testing proposal on this endpoint during the third party consultation.

c) Outcome

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

2. Pre-natal developmental toxicity study

a) Examination of the testing proposal

Pursuant to Article 40(3) 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 an oral combined repeated dose toxicity and reproduction/ developmental toxicity screening study (OECD Guideline 422) on the analogue substance Rosin, fumarated (CAS No. 65997-04-8); and reproduction/ developmental toxicity screening studies (OECD Guideline 421) on two substances (Rosin [CAS No. 8050-09-7] and Rosin, pentaerythritol ester [CAS No. 8050-26-8]) not part of the category '*Rosin adducts and rosin adduct salts*'. In addition, the Registrant has submitted a testing proposal for a pre-natal developmental toxicity study (EU B.31/OECD 414), proposed to be carried out, in rats, via the oral route with the substance subject to this decision.

While ECHA considers that OECD Guideline 421/422 studies useful to screen substances for potential to cause reproduction/ developmental toxicity, the tests are not sufficient to meet the information requirement for pre-natal developmental toxicity according to Section 8.7.2 of Annexes IX and X.

In addition, ECHA notes that as neither Rosin nor Rosin, pentaerythritol ester is a member of the category '*Rosin adducts and rosin adduct salts*' as defined by the Registrant; therefore, these studies can only be considered as supporting evidence.

The Registrant proposed testing in rats 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.

A third party has referred to "*the applicants' summaries and conclusions for each substance*" stating that "*recent reproductive/ developmental screening tests have not suggested any evidence of toxicity to reproduction or development*" and that "*the weight of existing evidence clearly indicates that further testing is unnecessary.*"

ECHA points out that the absence of reproductive and developmental effects in one screening study cannot be used as basis for adapting the information requirement. Furthermore, ECHA has taken the information provided by the third party into account and concludes that it is insufficient for demonstrating that the conditions of Annex XI, Section 1.2 (weight of evidence) of the REACH Regulation are met. More specifically, the weight of evidence referred to by the third party is not sufficient to assume that the substance has or has not a particular dangerous property and that the standard information requirement for a pre-natal developmental toxicity study could be adapted.

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

c) Outcome

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

d) Notes for consideration by the Registrant

In addition, a pre-natal developmental toxicity study on a second species is part of the standard information requirements as laid down in Annex X, section 8.7.2. for substances registered for 1000 tonnes or more per year (see sentence 2 of introductory paragraph 2 of Annex X).

When considering the need for a testing proposal for a pre-natal developmental toxicity study in a second species, the Registrant should take into account the outcome of the pre-natal developmental toxicity study on the first species and all available data to determine if the conditions are met for adaptations according to Annex X, 8.7. column 2, or according to Annex XI; for example if the substance meets the criteria for classification as toxic for reproduction Category 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment, or alternatively, if Weight of Evidence assessment of all relevant available data provides scientific justification that the study in a second species is not needed. If the Registrant considers that the conditions for adaptations are not fulfilled, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species. If the Registrant comes to the conclusion that the conditions for these adaptations can be fulfilled, he should update his

technical dossier by clearly stating the reasons for proposing to adapt the standard information requirement of Annex X, 8.7.2. of the REACH Regulation.

3. Deadline for submitting the required information

In the draft decision communicated to the Registrant, the deadline to provide the requested information was 36 months from the date of adoption of the decision. In his comments on the draft decision of 22 November 2013 the Registrant requested an extension of the timeline to 48 months.

The Registrant put forward several arguments. Firstly, he highlights the complexity of the testing strategy, which requires sequential testing for several endpoints and substances, and thereafter reassessment of the read-across and category approach in view of the results. Secondly, in order to minimise variability and facilitate interpretation of data for the category the Registrant intends to perform the tests in the same testing facility.

Considering the complexity of the overall testing strategy, number of tests to be performed and need for sequential testing, ECHA concluded that there are justified reasons to extend the deadline. Therefore, the deadline was extended to 48 months in the draft decision communicated to the Member State Competent Authorities. This deadline took into account the fact that the draft decision also requested a reproductive toxicity study (Annex X, 8.7.3). As the testing proposal for this study is not addressed in the present decision, ECHA considers that a reasonable time period for performing the remaining test(s) is 36 months from the date of the adoption of the decision. Therefore, ECHA changed the deadline from 48 months to 36 months.

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 relation to the proposed tests, the sample of substance used for the new studies must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given by the joint registrants. It is the responsibility of all joint registrants of the same substance to agree to the tests proposed (as applicable to their tonnage level) and to document the necessary information on their substance composition.

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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies must be suitable to assess these grades.

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. General requirements for the generation of information and Good Laboratory Practice

ECHA reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP).

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

VI. 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://echa.europa.eu/appeals/app_procedure_en.asp. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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