EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000004406-76-06/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, CAS No 8050-09-7 (EC No 232-475-7), 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 jointly submitted registration dossier in accordance with Articles 10(a)(ix) and 12(1)(e) thereof for Rosin, CAS No 8050-09-7 (EC No 232-475-7), hereinafter referred to as "the substance subject to this decision", submitted by [redacted] (Registrant). The dossier contains a document "Testing strategy for a UVCB category comprising Rosins and their salts", which can be summarized as follows:

- Sub-chronic toxicity studies (OECD Guideline 408, rat, oral route) to be performed on Rosin (CAS No. 8050-09-7), i.e. the substance subject to this decision, Rosin hydrogenated (CAS No. 65997-06-0) and Rosin, reaction products with formaldehyde (CAS No. 91081-53-7).
- Pre-natal developmental toxicity study (OECD Guideline 414, rat, oral route) to be performed on Rosin (CAS No. 8050-09-7), i.e. the substance subject to this decision.
- Two-generation reproduction toxicity study (OECD Guideline 416, rat, oral), or Extended one-generation reproductive toxicity study on Rosin, (CAS No. 8050-09-7), i.e. the substance subject to this decision.

The present decision relates solely to the examination of the testing proposal for Sub-chronic toxicity study (90–days) and Pre-natal development toxicity studies. The testing proposals for Two-generation reproductive toxicity study are 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 21 September 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. below).

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

On 26 April 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 receive information from third parties (see section III. below).

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. That draft decision was based on submission number [redacted].

On 22 November 2013 ECHA received comments from the Registrant on the draft decision.

ECHA considered the Registrant's comments received. On basis of the comments, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

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 amended 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 Sub-chronic toxicity study (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.

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

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

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 fulfill 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 registered substance 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 presumption 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.

The Registrant's working read-across hypothesis is that the substance(s) selected for higher tier testing can address the limited structural diversity within the category, and this will enable prediction of the toxicological properties within the category. Additionally, the Registrant assumes, based on chemicals similarity and currently limited other data that substances will exhibit similar toxicity, and that bioavailability and toxicity of the substances belonging to this category are relatively low. To confirm the hypothesis the Registrant is proposing to test several substances which are members of the category; this includes the substance subject to this decision.

ECHA has considered, for the purpose of the read-across and grouping approach, each substance proposed to be tested and provided conclusions in respective draft decisions on the substances that are members of the category.

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

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.

ECHA notes that the Registrant has submitted an oral (feeding) Reproduction/Developmental Toxicity Screening Test (OECD Guideline 421) on Rosin CAS No. 8050-09-7. This study provides information about sub-acute toxicity, but does not meet the information requirement for sub-chronic toxicity (90-days) according to section 8.6.2 of Annexes IX.

The Registrant has also submitted a testing proposal for a sub-chronic toxicity, proposed to be carried out, in rats, via the oral route on Rosin (CAS No. 8050-09-7), i.e. the substance subject to this decision, and on two other substances, Rosin, reaction products with formaldehyde (CAS No. 91081-53-7) and on Rosin hydrogenated (CAS No. 65997-06-0). ECHA notes that one of the substances proposed to be tested is the substance subject to the present decision. Therefore, ECHA considers that for the purpose of this decision, testing

with the substance subject to the present decision is sufficient to fulfil the information requirements for sub-chronic toxicity.

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. However, the Registrant has stated in the technical dossier for Rosin (CAS 8050-09-7) that reduced food consumption and associated reduction in body weight gain was observed in oral feeding studies (e.g. the OECD 421 studies) which may stem from low palatability of the feed. If the Registrant has reasons to assume that food consumption is significantly reduced in the oral studies, ECHA advises the Registrant to consider that oral administration via intubation (gavage) for sub-chronic toxicity is the most 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)(a) 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 the present decision.

2. Pre-natal developmental toxicity study

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.

ECHA notes that the Registrant has submitted an oral (feeding) Reproduction/Developmental Toxicity Screening Test (OECD Guideline 421) on Rosin CAS No. 8050-09-7.

In addition, the Registrant has submitted a testing proposal for Pre-natal developmental toxicity study (OECD Guideline 414), proposed to be carried out, in rats, via the oral route with Rosin, CAS No. 8050-09-7, i.e. the substance subject to this decision.

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

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 that testing with the rat or the rabbit as a first species is appropriate. With regard to the route of

administration, the Registrant has stated in the technical dossier for Rosin (CAS 8050-09-7) that reduced food consumption and associated reduction in body weight gain was observed in oral feeding studies (e.g. the OECD 421 studies) which may stem from low palatability of the feed. Furthermore, according to EU B.31/OECD 414 "*the test substance is usually administered orally by intubation*" (gavage). Therefore, ECHA considers that testing by the oral route via intubation (gavage) is most appropriate.

b) Consideration of the information received during third party consultation

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

Third party information 1:
A third party refers to column 2 of Annex IX and X of Regulation (EC) No 1907/2006 according to which the study does not need to be conducted if "the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure".

ECHA points out that while the existing data suggest that rosin is of low toxicity, mild signs of toxicity have been observed in repeated dose toxicity studies (effects on liver weight and histology of the kidneys). Therefore, the first criteria of Annex IX, 8.7, column 2 does not apply. Secondly the available data on absorption suggests that the bioavailability is below 5%, and thus it cannot be proved that no systemic absorption occurs. Furthermore, these toxicokinetic data have been obtained by using a substance, which does not belong to the category specified by the Registrant. Thirdly, from the data provided it can be preliminary concluded that the human exposure is low. However, since there is multitude of uses of rosin and rosin based products it cannot be claimed that "there is no or no significant human exposure". It is also noteworthy that the Registrant has not claimed that these criteria of column 2 would apply to the registered substance.

Therefore, due to the reasons explained above, the information provided by third parties is not sufficient to fulfill this information requirement.

c) Outcome

Therefore, pursuant to Article 40(3)(a) 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 the present 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. The Registrant must note, however, that this information, or the information submitted by other registrants of the same substance, has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

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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