EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000004371-81-07/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, fumarated, CAS No 65997-04-8 (EC No 266-040-8), 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, fumarated, CAS No 65997-04-8 (EC No 266-040-8), 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 Rosin, maleated (CAS No. 8050-28-0).
  - An additional pre-natal developmental toxicity study will be proposed by the Registrant for the substance subject to this decision if the results from the proposed sub-chronic toxicity (90day; 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, maleated (CAS No. 8050-28-0).

- Two-generation reproduction toxicity study (OECD Guideline 416, rat, oral), to be performed on the substance subject to this decision.

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 too 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 October 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 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 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 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 endpoint of Annex IX, 8.6.2.

Furthermore, the Registrant has requested to carry out one of the required tests using an analogue substance as part of a read-across and grouping approach, in accordance with Annex XI, 1.5 with respect to fulfilling the endpoint of Annex IX, 8.7.2. ECHA emphasises that any final determination on the validity of the read-across, including the grouping approach proposed by the Registrant would be premature at this point in time. The eventual validity of the read-across hypothesis and grouping approach will be reassessed once the requested information from studies is submitted. Nevertheless, based on the information currently submitted, ECHA considers that the approach proposed by the Registrant is plausible with respect to fulfilling the endpoint of Annex IX, 8.7.2. In the light of this assessment ECHA has taken the following decision:

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 substances indicated below:

1. Sub-chronic toxicity study (90-day) in rats, oral route (Annex IX, 8.6.2.; test method: EU B.26/OECD 408) on the substance subject to this decision; 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)

   on either:

   a. the analogue substance Rosin, maleated (CAS No. 8050-28-0, EC No. 232-480-4), if the result of the proposed OECD 408 studies or available/ on-going OECD 422 studies indicate no difference in toxicity between Rosin, fumarated (CAS No. 65997-04-8, EC No. 266-040-8) and Rosin, maleated (CAS No. 8050-28-0, EC No. 232-480-4); or

   b. the substance subject to the present decision, if the result of the proposed OECD 408 studies or available/ on-going OECD 422 studies indicate difference in toxicity between Rosin, fumarated (CAS No. 65997-04-8, EC No. 266-040-8) and Rosin, maleated (CAS No. 8050-28-0, EC No. 232-480-4).

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.

In relation to the testing proposals subject to the present decision, the Registrant has proposed to use a read-across and grouping approach, in accordance with Annex XI, 1.5, and to perform the proposed tests on either the substance subject to this decision or an analogue substance that is a member of the same category. To the extent that all proposed testing relies upon an identical read-across justification, ECHA has considered first the scientific validity of the proposed read-across and grouping approach (preliminary considerations; Section 0, below), before assessing the testing proposed (Section 1 and 2, below).

0. Grouping of substances and read-across approach (preliminary considerations)

0.1. Legal Background on ECHA's assessment of the grouping of substances and read-across hypothesis brought forward by the Registrant

The evaluation by ECHA of testing proposals submitted by registrants aims at ensuring that generation of information is tailored to real information needs. To this end, it is necessary to consider whether programmes of testing proposed by Registrants are appropriate to fulfil the relevant information requirements and to guarantee the identification of health and environmental hazards of substances. In that respect, the REACH Regulation aims at promoting wherever possible the use of alternative means, where equivalent results to the prescribed test are provided on health and environmental hazards.

Article 13(1) of the REACH Regulation requires information on intrinsic properties of substances on human toxicity to be generated whenever possible by means other than vertebrate animal tests, including information from structurally related substances (grouping or read-across), "provided that the conditions set out in Annex XI are met".

According to Annex XI, 1.5 there needs to be structural similarity among the substances within a group such that the relevant properties of a substance within the group can be predicted from the data for reference substance(s) by interpolation.

The Registrant has submitted a testing proposal, based on a grouping and read-across approach, intended to fulfil the information requirement for pre-natal developmental toxicity (Annexes IX and X, 8.7.2.).

The first Recital and the first Article of the REACH Regulation establish the "promotion of alternative methods for assessment of hazards of substances" as an objective pursued by the Regulation. In accordance with that objective, ECHA considers whether a prediction of the relevant properties of the substance subject to this decision by using the results of the proposed tests is sufficiently plausible based on the information currently available.

0.2. Grouping of substances and read-across hypothesis as proposed by the Registrant

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.

0.3. Information submitted by the Registrant to support the grouping of substances and read-across hypothesis

The Registrant has provided a justification document for the category of '*Rosin adducts and rosin adduct salts*'. This document contains an overview of the grouping approach proposed; additional information on the testing proposals for sub-chronic toxicity (90-day), pre-natal developmental toxicity and toxicity to reproduction, including a rationale for selection of test material(s); a summary of the composition ranges and physico-chemical properties of the substance concerned by the category; information on the underlying chemistry; and an overview of planned/ on-going experimental work (*ex vivo* absorption tests and combined repeated dose toxicity study with the reproduction/ developmental toxicity screening tests, OECD Guideline 422) intended to increase the scientific reliability of the grouping and read-across approach.

The Registrant has provided an oral combined repeated dose toxicity and reproduction/ developmental toxicity screening (OECD Guideline 422) study on the substance Rosin, fumarated (CAS No. 65997-04-8; *i.e.* the substance subject to the present decision). The Registrant reports that following administration of Rosin, fumarated in feed the NOAEL for parental systemic toxicity was considered to be 3000 ppm (221-288 mg/kg/day for males; 196-292 mg/kg/day for females) and 10000 ppm (651-889 mg/kg/day for males; 449-995 mg/kg/day for females) for reproductive effects. Based on these results, the Registrant concluded that no reproductive toxicity was observed (at the highest dose tested). However, ECHA notes that the highest dose tested did not reach the "limit dose", therefore the conclusion of no reproductive effects is not fully supported. In addition, reproduction/ developmental toxicity screening tests (OECD Guideline 421) on Rosin (CAS No. 8050-09-7) and Rosin, pentaerythritol ester (CAS No. 8050-26-8) have been provided to support the proposed read-across. ECHA notes that these two substances are not members of the category as defined by the Registrant.

Furthermore, as there is very limited toxicological information available for the substances in this category, the Registrant commits in the testing programme to address this deficiency by conducting *ex vivo* absorption tests on all the substances in the category, in combination with a repeated dose toxicity study with the reproduction/ developmental toxicity screening tests (OECD Guideline 422) on Rosin, maleated (CAS No. 8050-28-0); and Rosin, fumarated, reaction products with formaldehyde (CAS No. 95009-65-7). The Registrant intends to use the information obtained from the absorption study as a quantitative indication of uptake and as a qualitative assessment of which chemical species that are absorbed. Both *ex vivo* absorption and OECD 422 studies are intended to support the read-across hypothesis and provide information to what extent the toxicological properties vary amongst the substances in the category.

0.4. ECHA analysis of the selection of substances to be tested for pre-natal developmental toxicity

According to the Registrant's testing strategy document, the structural variation within the category is caused by the fact that the starting material Rosin is reacted with either maleic anhydride, maleic acid or fumaric acid. Depending on the reagent used, the relative proportions of maleopimaric acid anhydride and either (cis-)maleopimaric tricarboxylic acid or fumaropimaric tricarboxylic acid (the latter being the trans-isomer of (cis-)maleopimaric tricarboxylic acid) will vary between the substance covered by the category. The Registrant has proposed to test Rosin, maleated with the intention to cover the structural variability of the substance subject to the present decision. ECHA has considered each substance proposed to be tested in the light of the relative proportions of these structural element(s).

a. The substances in the category can contain up to [redacted]% of maleopimaric acid anhydride. The Registrant proposes to test Rosin, fumarated for sub-chronic toxicity (90-day), and Rosin, maleated for pre-natal developmental toxicity. ECHA notes that both substances proposed have similar content (up to [redacted]%) of the maleopimaric acid anhydride and that this is the high end of the category.

b. The substances in the category can contain up to [redacted]% (cis-)maleopimaric tricarboxylic acid. The Registrant proposes to testRosin, fumarated (up to [redacted]% (cis-)maleopimaric tricarboxylic acid) for sub-chronic toxicity (90-day), and Rosin, maleated for pre-natal developmental toxicity. ECHA notes that Rosin, maleated has the highest content of (cis-)maleopimaric tricarboxylic acid within the category.

c. The substances in the category can contain up to [redacted]% fumaropimaric tricarboxylic acid. The Registrant proposes to test Rosin, fumarated (up to [redacted]% fumaropimaric tricarboxylic acid) for sub-chronic toxicity (90-day), and Rosin, maleated for pre-natal developmental toxicity. ECHA notes that Rosin, fumarated has the highest content of fumaropimaric tricarboxylic acid acid within the category.

In addition, all substances share the following structural elements: "*Fatty acids*", "*Neutral fraction*" and "*Non-reacted resin acids*". ECHA notes that the content of these structural elements is similar across the substances covered by the category.

ECHA notes that the substances proposed to be tested (Rosin, maleated and Rosin, fumarated) together cover the structural diversity within the category boundaries as defined by the Registrant.

0.5. ECHA analysis of the grouping approach and the read-across hypothesis of the Registrant in light of the requirements of Annex XI, 1.5

ECHA understands that the grouping approach is based on a structural similarity resulting from the common UVCB starting Rosin with variations in the relative proportions of (cis-)maleopimaric tricarboxylic acid and fumaropimaric tricarboxylic acid. Because the Registrant considers the compositional diversity within the category will be similar he further considers that the grouping is suitable for the purpose of read-across. ECHA has analysed the grouping approach proposed by the Registrant and considers that the criteria and the boundaries of the category have been sufficiently defined.

ECHA understands that the read-across hypothesis assumes that all substances within the category will exhibit similar toxicity after gastrointestinal absorption. Specifically, the Registrant assumes that Rosin, maleated and Rosin, fumarated will exhibit no difference in toxicity. Based on the available compositional information and supporting information about the underlying chemistry, ECHA considers the read-across hypothesis plausible.

However, ECHA notes that currently the read-across hypothesis is based only on the assumption of structural/ compositional similarity due to lack of toxicological information for all but one substance of the category (in which case ECHA already noted – section 0.3. above - that the result does not fully support the conclusion of no reproductive effects).

While ECHA recognises the relevance of structural/ compositional similarity, it concludes that the Registrant's assumption of similar toxicity for the category members is not supported by the currently available information. This circumstance creates uncertainties that will have to be addressed by the Registrant in order to meet the conditions set out in Annex XI, section 1.5. of the REACH Regulation.

The Registrant has recognised the necessity to provide sufficient toxicological information to substantiate the hypothesis for the substances in the category and committed to undertake additional studies intended to strengthen the toxicological information for the read-across approach. This includes two combined repeated dose toxicity studies with the reproduction/ developmental toxicity screening tests on Rosin, maleated and Rosin, fumarated (OECD 422). ECHA considers that generating this additional information on Rosin, maleated and Rosin, fumarated is therefore an essential condition for the ultimate compliance of the read-across approach in relation to pre-natal developmental toxicity.

The Registrant also committed to carry out combined repeated dose toxicity studies with the reproduction/ developmental toxicity screening tests (OECD 422) on one more substance: Rosin, fumarated, reaction products with formaldehyde (CAS No. 95009-65-7). Due to the compositional differences between the substance subject to the present decision and the substance Rosin, fumarated, reaction products with formaldehyde (CAS No. 95009-65-7), ECHA does not consider testing with this substance will provide relevant information for the substance subject to the present decision.

In addition, the Registrant has committed to provide *ex vivo* absorption data on all members of the category. Absorption information is to be generated using an "*everted gut-sac model*". ECHA considers that this model is currently not validated for this type of substances, that currently the Registrant has not demonstrated that the *ex vivo* absorption observed accurately predicts *in vivo* gastrointestinal absorption and ultimately correlates to the systemic toxicity observed in available toxicity studies. These uncertainties should be addressed by the Registrant. Nevertheless, ECHA considers that information on bioavailability is useful to strengthen read-across argumentation and considers it to be an essential condition for the ultimate acceptance and use of read-across for the category.

Furthermore, the Registrant assumes that the results of the above mentioned studies and the proposed sub-chronic toxicity (90-day) studies for Rosin, fumarated and Rosin, maleated, will demonstrate that these substances exhibit no difference in toxicity. However, ECHA notes that the Registrant has not specified any criteria on the basis of which the assumption can be confirmed.

In that respect, ECHA considers that the following criteria are decisive for the actual determination of absence of difference in toxicity:

- no adverse effects are observed in any organs or tissues for both source and target substances when tested up to the limit dose in a study of the same duration; or
- comparable effect(s) (*i.e.* in terms of type of effect, severity and incidence in the same species/ strain) are observed in the same organ(s), tissue(s) or parameters at equal dose level for both source and target substances when tested in a study of the same duration.

To assess whether the above criteria are met, the Registrant shall at least compare the parameters covered in the corresponding test guidelines and analyse the effects observed and thereafter conclude on the overall test results. The Registrant shall also consider the classification and labelling criteria given in Annex I of Regulation (EC) No 1272/2008, Chapters "*3.7 Reproductive toxicity*" and "*3.9 Specific target organ toxicity – repeated exposure*".

Additionally, the assessment has to consider differences in potential of the substances to cause reproduction/ developmental toxicity.

ECHA points out that such consideration can be obtained from the available/ on-going combined repeated dose toxicity study with the reproduction/developmental toxicity screening tests, and/ or from sub-chronic toxicity (90-day) tests if additional examinations of male and female reproductive parameters normally covered in the two-generation reproduction toxicity study are included in the proposed studies. ECHA considers that additional examinations of male and female reproductive parameters (oestrous cycle, sperm parameters, and certain reproductive and other organs/ tissues) as outlined for parental animals in EU test method B.35, sections 1.5.3., 1.5.4. and 1.5.6. to 1.5.8. can increase the reliability of the proposed read-across approach. ECHA wants to highlight that the sub-chronic toxicity (90-day) studies, modified to include additional examinations of reproductive parameters and organs/ tissues, are not considered to be an equivalent replacement for the information requirement of Annex IX, 8.7.2.

ECHA considers that the above criteria and information are therefore an essential condition for the valid justification of the similarity of toxicity of the substance covered by the category and, hence, for the ultimate compliance of the read-across approach to be submitted by the Registrant.

The Registrant proposes to test Rosin, fumarated for sub-chronic toxicity (90-day); and Rosin, maleated for pre-natal developmental toxicity.

Subject to the above considerations, ECHA concludes that it is plausible that the substances selected by the Registrant, cover the structural variability within the category boundaries as defined by the Registrant.

In the case where the result of the proposed OECD 408 studies or available/ on-going OECD 422 studies performed in accordance with the present decision would not confirm the grouping and read-across hypothesis relied upon by the Registrant, this outcome shall not alter the obligation of the Registrant to meet the standard information requirements. Should the read-across strategy be inadequate, it is the responsibility of the Registrant to ultimately submit reliable information or adaptations which is used in a way that does not underestimate hazards of the registered substance in relation to the relevant endpoints.

Finally, the read-across adaptation based on the results of the proposed tests shall ensure that any remaining uncertainties, including results of any existing studies which might give rise to concern, are analysed, minimized, and taken into account for the purpose of classification and labelling and/ or risk assessment.

In any case, following the update of the dossier submitting the information required in the present decision, ECHA will determine whether the documentation provided is sufficient to satisfactorily address the information requirements of Annex IX for the substance subject to the present decision.

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 substance subject to this decision; 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 the present 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 substance subject to this decision; 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, based on grouping of substances and read-across, 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 analogue substance Rosin, maleated (CAS No. 8050-28-0).

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). Depending on whether the result of the proposed OECD 408 studies or available/ on-going OECD 422 studies may or may not enable the Registrant to confirm its assumption of absence of difference of toxicity between the substances covered by the category, as explained in section III.0.5. above, the study shall be performed, respectively, on either:

a) the analogue substance Rosin, maleated (CAS No. 8050-28-0, EC No. 232-480-4), or
b) 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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