EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000004948-58-05/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 Fatty acids, tall oil, oligomeric reaction products with maleic anhydride and rosin, calcium magnesium[..], CAS No 160901-14-4 (EC No 500-451-8), 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 Fatty acids, tall oil, oligomeric reaction products with maleic anhydride and rosin, calcium magnesium[..], CAS No 160901-14-4 (EC No 500-451-8, submitted by [redacted] (Registrant). The dossier contains a document "*Analogue approach for CAS No 160901-14-4*", which can be summarised as follows:

- Sub-chronic toxicity studies (OECD Guideline 408, rat, oral route) to be performed on Rosin, fumarated (CAS No. 65997-04-8), Rosin, maleated (CAS No. 8050-28-0), and Rosin (CAS No. 8050-09-7);
- Pre-natal developmental toxicity studies (OECD Guideline 414, rat, oral route) to be performed on Rosin, maleated (CAS No. 8050-28-0) and Rosin (CAS No. 8050-09-7);
- Two-generation reproductive toxicity studies (OECD Guideline 416, rat, oral) to be performed on Rosin, fumarated (CAS No. 65997-04-8) and Rosin (CAS No. 8050-09-7).

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 6 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 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 proposed at that time by the Registrant.

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

On 22 November 2013 ECHA received comments from the Registrant.

On 7 January 2014 the Registrant updated his registration dossier (submission number [redacted]. In the updated registration dossier the Registrant substantially changed the read-across approach. In particular, the read-across based on grouping was replaced by an analogue approach and the substances proposed to be tested as well as the number of proposed tests for each of the endpoints were changed.

ECHA considered the Registrant's comments and update. On basis of this information, 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 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 analogue substances as part of a read-across approach (analogue approach), in accordance with Annex XI, 1.5.

ECHA emphasises that any final determination on the validity of the read-across proposed by the Registrant would be premature at this point in time. The eventual validity of the read-across hypothesis and analogue 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. 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)(a) 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 analogue substances Rosin, fumarated (CAS No. 65997-04-8), Rosin, maleated (CAS No. 8050-28-0) and Rosin (CAS No. 8050-09-7); 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 the analogue substances Rosin, maleated (CAS No. 8050-28-0) and Rosin (CAS No. 8050-09-7).

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.

ECHA notes that after having received the draft decision, the originally proposed read-across approach based on grouping was abandoned by the Registrant and replaced by an analogue read-across approach in the updated dossier. This newly proposed analogue approach demanded a completely new evaluation, the results of which are presented hereafter.

In relation to the testing proposals subject to the present decision, the Registrant has proposed to use a read-across (analogue approach), in accordance with Annex XI, 1.5, and to perform the proposed tests on analogue substances. 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 analogue approach (preliminary considerations; Section 0, below), before assessing the testing proposed (Sections 1 and 2, below).

ECHA emphasises that the analogue substances are also proposed to be tested in their respective technical dossiers (see ECHA decisions with the following communication numbers: TPE-D-0000004346-74-03/F, TPE-D-0000004372-79-06/F and TPE-D-0000004345-76-06/F.

0. Read-across approach/ analogue approach (preliminary considerations)

0.1. Legal Background on ECHA's assessment of the analogue approach 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 such that the relevant properties of a substance can be predicted from the data for reference substance(s).

The Registrant has submitted testing proposals, based on read-across approach (analogue approach), intended to fulfil information requirements for sub-chronic toxicity (90-day; Annex IX, Section 8.6.2.) and pre-natal developmental toxicity (Annexes IX and X, Section 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. Analogue approach and read-across hypothesis as proposed by the Registrant

According to the Registrant, an analogue approach can be applied from the reference substances Rosin, fumarated (CAS No. 65997-04-8), Rosin, maleated (CAS No. 8050-28-0), and Rosin (CAS No. 8050-09-7) to the substance subject to this decision for the purpose of read-across.

The analogue approach is based on the presumption that all substances are chemically related UVCB substances (substances of Unknown or Variable composition, Complex reaction products or Biological materials), *i.e.* the substance subject to the present decision and the analogue substances Rosin, fumarated (CAS No. 65997-04-8) and Rosin, maleated (CAS No. 8050-28-0) are UVCBs derived from the UVCB starting material Rosin (CAS No. 8050-09-7; EC No. 232-475-7).

The Registrant states that "*the target substance and Rosin, maleated are UVCB homologues formed by the reaction of levoprimaric acid present in both with maleic anhydride or maleic acid, with additional neutralisation of fatty acids present in the target substance to give divalent calcium, magnesium and zinc salts. The Diels-Alder reaction of levopimaric acid with maleic anhydride or maleic acid results in the formation of maleopimaric anhydride or acid and the (cis-) maleopimaric tricarboxylic acid (Soltes and Zinkel, 1989). Rosin, fumarated is formed through the Diels-Alder reaction of levopimaric acid with fumaric acid and results in the formation of fumaropimaric tricarboxylic acid (the trans-maleopimaric tricarboxylic acid) and maleopimaric acid anhydride (Soltes and Zinkel, 1989). Overall, these reactions involve Diels-Alder addition of a nucleophile such as maleic anhydride, maleic acid or fumaric acid. The reaction products are isomeric mixtures comprising (i) maleopimaric acid anhydride and (ii) either (cis-) maleopimaric tricarboxylic acid or fumaropimaric tricarboxylic acid where the latter is the trans-isomer of cis-maleopimaric tricarboxylic acid.*"

According to the Registrant, the "*the target and source substances are UVCBs, with similarities in underlying composition i.e. their principle components are non-adducted resin acids, maleoprimaric acids/anhydride, fumaropimaric acids, fatty acids and neutral fraction*".

In ECHA's understanding, the Registrant's read-across hypothesis is that the substances selected for higher tier testing fully cover the structural variability of the target substance (*i.e.* the substance subject to the present decision) which will enable predictions of the toxicological properties from the reference substances to the target substance. Furthermore, the Registrant hypothesises that the overall observed toxicity of the target substance as well the reference substances is low and that all substances will exhibit similar toxicity based on the assumption that similar fractions of the substances are absorbed. ECHA also understands that the starting material Rosin is proposed as reference substance to address

the constituents of the target substance which remain unchanged during chemical modification of Rosin.

0.3. Information submitted by the Registrant to support the analogue approach and read-across hypothesis

The Registrant has provided justification documents for the analogue approach entitled "*Analogue approach for CAS No 160901-14-4*" and "*Arguments to prove that the testing strategy for TOFA, oligomeric products with maleic anhydride and rosin, calcium magnesium zinc salts is fully appropriate and justified despite the ECHA draft decision letter of October 23*". The justification document "*Analogue approach for CAS No 160901-14-4*" contains an explanation on the underlying hypothesis for the analogue approach; a list of the analogue substances; information on the underlying chemistry of adducted rosin; an analogue approach justification including a summary of toxicological properties of the substances; data matrices on compositional information, physico-chemical properties and toxicological properties; and additional information on the testing proposals for sub-chronic toxicity (90-day) and pre-natal developmental toxicity. The justification document also addresses *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 confidence in the analogue approach.

The Registrant has provided an oral combined repeated dose toxicity and reproduction/ developmental toxicity screening (OECD 422) study on the analogue substance Rosin, fumarated (CAS No. 65997-04-8). Therein, 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 for reproductive effects (651-889 mg/kg/day for males; 449-995 mg/kg/day for females). Based on these results, the Registrant concluded that no reproductive toxicity was observed at the highest dose tested.

Furthermore, the Registrant has provided an oral reproduction/ developmental toxicity screening test (OECD 421) on the analogue substance Rosin (CAS No. 8050-09-7). Therein, the Registrant reports that following administration of Rosin in feed, the NOAEL for reproductive toxicity was considered to be 3000 ppm (P; male/female) and 10000 ppm for developmental toxicity (F1; male/female). Based on these results, the Registrant concluded that "*there was no clear evidence of test substance-related effects on reproduction of F0 males and females or on survival and development of F1 pups.*"

In addition, the Registrant commits in the testing programme to conduct *ex vivo* absorption tests on all the source substances and the target substance (*i.e.* the substance subject to the present decision). In this respect, the Registrant states that "*no toxicokinetic data are available for the source or target substances; however studies are in progress to assess the likely bioavailability using an ex vivo gut sac model. Results from these investigations are expected January 2014.*" Furthermore, the Registrant commits to conduct combined repeated dose toxicity study with the reproduction/ developmental toxicity screening tests (OECD Guideline 422) on the substance subject to the present decision (CAS No 160901-14-4) and the reference substances Rosin, maleated (CAS No. 8050-28-0) and Rosin (CAS No. 8050-09-7).

The Registrant intends to use the information obtained from the *ex vivo* absorption studies as a quantitative indication of uptake and as a qualitative assessment of which chemical species are absorbed. The *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.

0.4. ECHA analysis of the selection of substances to be tested for sub-chronic toxicity (90-day) and pre-natal developmental toxicity

In ECHA's understanding, the Registrant hypothesises that the substances selected for higher tier testing fully cover the chemical composition of the substance subject to the present decision which will enable accurate predictions of the toxicological properties from the reference substances to the target substance. Furthermore, ECHA understands that the Registrant assumes that the overall observed toxicity of the target substance and reference substances is low and that all substances will exhibit similar toxicity based on the assumption that similar fractions of the substances are absorbed.

ECHA has considered each substance proposed to be tested in the light of the Registrant's hypothesis, available toxicological information for reference substances and target substance.

The Registrant has proposed to test three substances for sub-chronic toxicity (90-day):

i. Rosin (CAS No. 8050-09-7) is the starting material for the manufacture of the substance subject to the present decision and the other two source substances, and this substance contains up to [redacted]% non-adducted resin acids, up to [redacted]% fatty acids and up to [redacted]% neutral fraction;
ii. Rosin, maleated (CAS No. 8050-28-0) contains up to [redacted]% non-adducted resin acids, up to [redacted]% maleopimaric acids, up to [redacted]% maleopimaric anhydride, up to [redacted]% fumaropimaric acids, up to [redacted]% fatty acids, and up to [redacted]% neutral fraction; and
iii. Rosin, fumarated (CAS No. 65997-04-8) contains up to [redacted]% non-adducted resin acids, up to [redacted]% maleopimaric acids, up to [redacted]% maleopimaric anhydride, up to [redacted]% fumaropimaric acids, up to [redacted]% fatty acids, and up to [redacted]% neutral fraction.

ECHA notes that the differences in composition with respect to non-adducted resin acids (up to [redacted]% in the substance subject to this decision compared to up to [redacted]% in Rosin), maleopimaric anhydride (up to [redacted]% in the substance subject to this decision compared to up to [redacted]% in Rosin, fumarated and Rosin, maleated), and fatty acids (up to [redacted]% in the substance subject to this decision compared to up to [redacted]% in Rosin) do not raise toxicological concern with respect to sub-chronic toxicity (90-day). Furthermore, also the presence of calcium, magnesium and zinc does not raise toxicological concern, in particular when considering that "*Mg and Zn salts of TOFA, rosin and maleated rosin*" amount to [redacted] to [redacted]% each.

For pre-natal developmental toxicity, the Registrant has already submitted a reproductive/ developmental toxicity screening study (OECD Guideline 422) for Rosin, fumarated (CAS No. 65997-04-8) and a reproduction/ developmental toxicity screening test (OECD 421) on the substance Rosin (CAS No. 8050-09-7). The Registrant has proposed to test two substances for pre-natal developmental toxicity:

i. Rosin (CAS No. 8050-09-7) is the starting material for the manufacture of the substance subject to the present decision and the other two source substances, and this substance contains up to [redacted]% non-adducted resin acids, up to [redacted]% fatty acids and up to [redacted]% neutral fraction; and
ii. Rosin, maleated (CAS No. 8050-28-0) contains up to [redacted]% non-adducted resin acids, up to [redacted]% maleopimaric acids, up to [redacted]% maleopimaric anhydride, up to [redacted]% fumaropimaric acids, up to [redacted]% fatty acids, and up to [redacted]% neutral fraction.

ECHA notes that the differences in composition with respect to non-adducted resin acids (up to [redacted]% in the substance subject to this decision compared to up to [redacted]% in Rosin), maleopimaric anhydride (up to [redacted]% in the substance subject to this decision compared to

up to [redacted]% in Rosin, maleated), and fatty acids (up to [redacted]% in the substance subject to this decision compared to up to [redacted]% in Rosin) do not raise toxicological concern with respect to pre-natal developmental toxicity. Furthermore, also the presence of calcium, magnesium and zinc does not raise toxicological concern, in particular when considering that "*Mg and Zn salts of TOFA, rosin and maleated rosin*" amount to [redacted] to [redacted]% each.

ECHA notes that the substances proposed to be tested cover most of the compositional diversity of the target substance.

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 analogue and read-across approach is based on structural similarity. This structural similarity results from the common UVCB starting material Rosin and that the reference substances Rosin, maleated and Rosin, fumarated are formed by subjecting Rosin to a Diels-Alder reaction. Because the composition of the reference substances is very similar to the composition of the target substance, and because the differences in composition between the reference substances and the target substance do not raise toxicological concerns, the analogue approach is considered suitable for the purpose of read-across. ECHA has analysed the analogue approach proposed by the Registrant and considers that the reference substances are sufficiently characterised.

ECHA understands that the read-across hypothesis is that the substances selected for higher tier testing cover the composition of the target substance; this enables prediction of toxicological properties from the reference substances to the target substance. Furthermore, the Registrant hypothesises that the overall observed toxicity of the target substance as well the reference substances is low and that all substances will exhibit similar toxicity based on the assumption that similar fractions of the substances are absorbed. ECHA also understands that the starting material Rosin is proposed as reference substance to address the constituents of the target-substance composition which remain unchanged during chemical modification.

Based on the available compositional information and limited toxicological information, ECHA considers the read-across approach/ analogue approach plausible with respect to sub-chronic toxicity (90-day) and pre-natal developmental toxicity. However, the limited toxicological information currently available does not allow reaching a conclusion on the assumption of general low and/ or similar toxicological profiles of the substances. This circumstance creates uncertainties that will have to be addressed by the Registrant in order to meet the condition 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 and committed to undertake additional studies intended to strengthen the toxicological information for the read-across approach. This includes combined repeated dose toxicity studies with the reproduction/ developmental toxicity screening tests (OECD 422) on fatty acids, tall oil, oligomeric reaction products with maleic anhydride and rosin, calcium magnesium[..] (CAS No 160901-14-4; *i.e.* the substance subject to the present decision), Rosin, maleated (CAS No. 8050-28-0) and Rosin (CAS No. 8050-09-7).

Furthermore, the Registrant has committed to provide *ex vivo* absorption data on the substance subject to this decision and all reference substances, *i.e.* Rosin, fumarated (CAS No. 65997-04-8), Rosin, maleated (CAS No. 8050-28-0) and Rosin (CAS No. 8050-09-7). 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, and that 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 will have to be addressed by the Registrant. Nevertheless, ECHA considers that information on bioavailability is useful to strengthen the read-across argumentation and considers it to be an essential condition for the ultimate acceptance and use of read-across for the category.

The Registrant has proposed to test three reference substances for sub-chronic toxicity taking into account the structural variability of target substance. Furthermore, two reference substances are proposed to be tested for pre-natal developmental toxicity which also cover the structural variability of the target substance. ECHA considers that the substances proposed for testing may allow the Registrant to predict toxicolological properties and that the read-across/analogue approach may ultimately be acceptable for ECHA.

In case that the proposed source substances exert identical adverse effects for the endpoints concerned, the read-across is considered plausible. However, if the toxicological effects differ from one substance to another, the read-across can only be considered acceptable if the most conservative effects are used for risk assessment.

In the case where the result of the proposed studies performed in accordance with the present decision would not confirm the 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 requirement 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)(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 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 of the analogue substance, but does not meet the information requirement for sub-chronic toxicity (90-day) according to section 8.6.2 of Annex IX.

In addition, the Registrant has submitted a testing proposal, based on read-across (analogue approach), for sub-chronic toxicity studies (90-day; EU B.26/OECD 408), proposed to be carried out, in rats, via the oral route with the analogue substances Rosin, fumarated (CAS No. 65997-04-8), Rosin, maleated (CAS No. 8050-28-0) and Rosin (CAS No. 8050-09-7).

Based on ECHAs preliminary considerations on the read-across approach (see Section 0, above) ECHA considers that the approach proposed is plausible.

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)(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 analogue substances Rosin, fumarated (CAS No. 65997-04-8), Rosin, maleated (CAS No. 8050-28-0), and Rosin (CAS No. 8050-09-7).

2. Pre-natal developmental toxicity study

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 an oral combined repeated dose toxicity and reproduction/ developmental toxicity screening study (OECD Guideline 422) on Rosin, fumarated (CAS No 65997-04-8) and a reproduction/developmental toxicity screening study (OECD Guideline 421) on Rosin (CAS No. 8050-09-7).

In addition, the Registrant has submitted a testing proposal, based on read-across (analogue approach), 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 substances Rosin, maleated (CAS No. 8050-28-0) and Rosin (CAS No. 8050-09-7).

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.

Based on ECHAs preliminary considerations on the grouping of substances and read-across approach (see Section 0, above) ECHA considers that the approach proposed is plausible.

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.

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 a screening study cannot be used as basis for adapting the information requirement. The general statement relating to "*the weight of existing evidence*" does not provide sufficient information and adequate evidence for the respective standard information requirement.

Therefore, the information provided by third parties is not sufficient to fulfil 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 analogue substances Rosin, maleated (CAS No. 8050-28-0) and Rosin (CAS No. 8050-09-7).

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 prenatal 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 concludes 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 tests 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.

[redacted]

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