EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-2114350797-37-01/F Helsinki, 19 December 2016

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

For Fatty acids, tall oil and rosin, reaction products with maleic anhydride, List No 940-281-5, registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 40(1) of the REACH Regulation, ECHA has examined the following testing proposals submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(d) thereof for Fatty acids, tall oil and Rosin, reaction products with maleic anhydride, List No 940-281-5, submitted by [redacted] (Registrant).

- Long term aquatic toxicity study according to OECD Guideline 211 (Daphnia magna Reproduction Test);
- Repeated dose toxicity study according to OECD Guideline 408 in rats, using the analogue substance Rosin, maleated (CAS RN 8050-28-0); and
- Pre-natal developmental toxicity study according to OECD Guideline 414 in rats, oral route, using the analogue substance Rosin, maleated (CAS RN 8050-28-0).

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 100 to 1000 tonnes per year. This decision does not take into account any updates after 29 April 2015, i.e. 30 calendar days after the end of the commenting period.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

The examination of the testing proposals was initiated upon the date when receipt of the complete registration dossier was confirmed on 22 September 2013.

ECHA held a third party consultation for the testing proposals from 18 February 2014 until 4 April 2014. ECHA did not receive information from third parties.

On 19 February 2015 ECHA sent the draft decision to the Registrant and invited them to provide comments within 30 days of the receipt of the draft decision.

On 18 March 2015 ECHA received comments from the Registrant on the draft decision.

The ECHA Secretariat considered the Registrant's comments.

On basis of this information, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

On 3 November 2016 ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

II. Testing required

A. Tests required pursuant to Article 40(3)

The Registrant shall carry out the following test pursuant to Article 40(3) and 13(4) of the REACH Regulation using the indicated test methods and using the analogue substance *Rosin, maleated* (CAS RN 8050-28-0, EC No 232-480-4):

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

The Registrant shall carry out the following tests pursuant to Article 40(3) and 13(4) of the REACH Regulation using the indicated test method and the registered substance subject to the present decision:

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31/OECD 414) in rats or rabbits, oral route; and
3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211);

while the originally proposed test for a prenatal developmental toxicity study according to OECD Guideline 414 (Prenatal Developmental Toxicity Study) in rats, oral route, proposed to be carried out using the the analogue substance *Rosin, maleated* (CAS RN 8050-28-0, EC No 232-480-4) is rejected pursuant to Article 40(3)(d) of the REACH Regulation.

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.

B. Deadline for submitting the required information

Pursuant to Articles 40(4) and 22(2) of the REACH Regulation, the Registrant shall submit to ECHA by **3 January 2019** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report. The timeline has been set to allow for sequential testing as appropriate.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant for the registered substance.

Tests required pursuant to Article 40(3)

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)

a) Examination of the testing proposal

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

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats via the oral route (EU B.26/OECD 408) to be performed with the analogue substance Rosin maleated (CAS RN 8050-28-0, EC No 232-480-4).

Read-across assessment (related to both repeated dose toxicity and prenatal developmental toxicity testing proposals)

i. Read-across hypothesis

The Registrant provided a read-across justification document entitled "[redacted]".

In his read-across justification document the Registrant provides information on the manufacture of the registered substance and its composition. According to the Registrant, the registered substance comprises [redacted]

The proposed source substance, rosin maleated, contains [redacted].

Furthermore, the Registrant provides data matrices and additional explanatory text on physicochemical properties, environmental fate/ ecotoxicology and toxicological endpoints for three substances, i.e. the two source substances (1) TOFA maleated (CAS RN 68139-89-9, List No 800-760-0) and (2) Rosin maleated (CAS RN 8050-28-0, EC No 232-480-4), and (3) the target substance (registered substance).

The Registrant argues that the two source substances (1) TOFA maleated and (2) Rosin maleated are suitable because together they cover all identified components of the target substance as both source substances are reaction products of TOFA and Rosin with maleic anhydride, respectively, which leads to partially maleated end products of TOFA and Rosin (typically [redacted] % remains unreacted; for the composition of the source substances see table 2 on page 4 of the read-across justification document).

ECHA notes, however, that although the Registrant identified two source substances, testing with only one of them is proposed, namely Rosin maleated, to fulfil the standard information requirement of Annex IX, 8.6.2. (sub-chronic toxicity) and Annex IX, 8.7.2 (pre-natal developmental toxicity). Therefore, ECHA concludes that the Registrant proposed an analogue-approach for read-across using the source substance Rosin maleated as explained in section 2 of the read-across justification document entitled "[redacted]".

With respect to the selection of Rosin maleated as the only source substance, the Registrant referred to his comparison of the results of the provided OECD 422 studies: "*The results of the three studies are indicative for the fact that maleated compounds show similar systemic toxicity. Because no effects on reproduction were seen for the source and the target substances at dose levels below doses showing maternal toxicity, a read-across to the target substances is considered appropriate. In view of the lower NOAELs found for Rosin maleated and the fact that this substance contains the components of fatty acids, tall oil and rosin, reaction products with maleic anhydride that are most likely to be absorbed (see section on toxicokinetics), this substance is considered as a worst case representative for the toxicity of fatty acids, tall oil and rosin, reaction products with maleic anhydride. Consequently, the testing proposal for the higher tier testing will be based on rosin maleated.*" With respect to toxicokinetics, the Registrant stated that only some absorption of the registered substance is expected and that mainly Rosin maleated and to a minor extend Rosin are absorbed because in the available OECD 422 study with the registered substance effects on parental animals are reported.

ii. Read-across assessment

ECHA understands that the Registrant's read-across is based on the assumption that
(i) Rosin maleated represents the worst case for sub-chronic toxicity and pre-natal developmental toxicity because in the OECD 422 study on this source substance lower NOAELs were observed; and
(ii) Mainly Rosin maleated and to a minor extend Rosin are absorbed.

OECD 422 studies

Developmental effects

ECHA notes that in the OECD 422 study on the registered substance, difficulties at parturition and inadequate nursing of the pups were observed at 250 mg/kg bw/day which results in a NOEL (P, female) ≥ 75 mg/kg bw/day. In this respect, the Registrant states in the corresponding endpoint-study record that "*at 250 mg/kg and 750 mg/kg a dose related increase in the number of females that died during delivery or failed to nurse their offspring. This is reflected in a lower gestation index, but considered to be related to generic non-specific toxicity in maternal animals.*" However, ECHA considers that these effects are adverse (in particular due to their dose dependency) and warrant by themselves further investigation with regards to reproductive toxicity. ECHA considers that for developmental effects the registered substance presents the worst case and the read across cannot be accepted for this endpoint.

Systemic toxicity

In comparison to the registered substance, ECHA notes that effect levels of the OECD 422 study for Rosin maleated are as follows: NOAEL (P, male) ≥ 188 mg/kg bw/day based on lower food consumption and body weight; and NOAEL (P, female) ≥ 225 mg/kg bw/day based on mortality, food consumption, and body weight. For the source substance mortality

was present in female during the pre-pairing stage already at approximately 300 mg/kg. Therefore, ECHA agrees that the source substance (Rosin maleated) constitutes the "worst case" in terms of systemic toxicity because in the corresponding OECD 422 study adverse effects (deaths) are observed at a level which is close to the NOAEL of the target substance.

Absorption

With respect to the Registrant's assumption that mainly Rosin maleated and to a minor extend Rosin are absorbed, ECHA notes that this conclusion are derived from theoretical considerations on average molecular weight, water solubility and partition coefficient as disclosed in section 7.1. of the IUCLID dossier. Furthermore, ECHA notes that differing adverse effects were observed in the provided OECD 422 studies on the registered substance and the source substance Rosin maleated (see above) which might stem from a different absorption patterns. Therefore, ECHA concludes that this might result from absorption of TOFA maleated at significant levels. Furthermore, it is generally known that the components of TOFA (in particular fatty acids such as palmitic, stearic, oleic acid, and linoleic acid) are readily absorbed after ingestion and ECHA has no evidence to the contrary that this would not apply to the components of TOFA maleated when considering the mechanism of fat uptake in the small intestine. Therefore, ECHA cannot agree with the Registrant's assumption that mainly Rosin maleated and, to a minor extent, Rosin are absorbed from the registered substance.

Supporting evidence (data matrices)

With respect to physicochemical properties, environmental fate and ecotoxicology, the Registrant concludes that source and target substances show similar properties and that slight differences in physicochemical properties can be explained on the basis of differences in the degree of adduction and/or the presence of TOFA.

Similarities between some physicochemical, environmental and ecotoxicological properties are observed, and ECHA considers that these similarities exclude substantial differences in the measured parameters, which may provide limited support to a read-across at a general level. ECHA considers that the similarities of these physicochemical, environmental and ecotoxicological properties, per se, do not provide a basis for predicting specific toxicological properties such as sub-chronic toxicity or pre-natal developmental toxicity.

With respect to toxicological properties, the Registrant states that "*based on chemical similarity, toxicokinetics and tests with the components or structural analogues of the components it is concluded that the toxicodynamic properties of fatty acids, tall oil and Rosin, reaction products with maleic anhydride are expected to be similar to those of its components.*"

iii. Summary and conclusion

Considering the above-mentioned aspects, ECHA concludes the following:

- The OECD 422 study on the source substance Rosin maleated can be considered worst case in terms of systemic toxicity when compared to the OECD 422 study on the registered substance;
- The information on toxicokinetics is insufficient to be able to verify the Registrant's conclusions about the relative amount of absorption (or other toxicokinetic parameters); in particular, the Registrant has not convincingly demonstrated that "*mainly Rosin maleated and to a minor extend Rosin*" are absorbed.
- ECHA considers that for developmental effects the registered substance presents the worst case and the read across cannot be accepted for this endpoint.

The hypothesis can be considered plausible for predicting the properties of the registered substance using the proposed source substance Rosin maleated and, therefore, the read-across approach can be accepted for the endpoint sub-chronic repeated dose toxicity. The read across cannot be accepted for this endpoint.

Testing requested

ECHA considers that the proposed study via the oral route is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation because the proposed route is the most appropriate route of administration having regard to the likely route of human exposure due to the following reasons. The Registrant proposed testing by the oral route. In light of the properties of the substance (i.e. viscous liquid with high boiling point and very low vapour pressure; not classified as corrosive/irritating to the skin and/or damaging/irritating to the eyes) and the information provided on the uses and human exposure (i.e., no uses with spray application), ECHA considers that testing by the oral route is most appropriate.

The Registrant proposed testing in rats. According to the test method EU B.26/OECD 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

The Registrant proposed testing with the analogue substance Rosin maleated (CAS RN 8050-28-0, EC No 232-480-4). As explained above ECHA can accept the proposed read-across approach.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study using the the analogue substance Rosin, maleated (CAS RN 8050-28-0, EC No 232-480-4): Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26/OECD 408).

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) and (c) of the REACH Regulation, ECHA may reject a proposed test and require the Registrant to carry out other tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for a pre-natal developmental toxicity study in rats according to EU B.31/OECD 414 to be performed with the analogue substance Rosin maleated (CAS RN 8050-28-0, EC No 232-480-4). ECHA considers that the proposed test guideline (OECD TG 414) is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

The Registrant proposed testing with the analogue substance Rosin maleated (CAS RN 8050-28-0, EC No 232-480-4). However, for prenatal developmental toxicity, ECHA cannot

accept the proposed read-across as explained in the read across assessment in section III.1.a) i-iii above. Hence testing is to be performed on the registered substance.

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.

From the comments provided to the draft decision, ECHA understands that the Registrant agrees to will revise the analogue justification and testing-proposals accordingly..

b) Outcome

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is requested to carry out the following study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in rats or rabbits, oral route (test method: EU B.31/OECD 414), while the originally proposed test for a prenatal developmental toxicity study according to OECD Guideline 414 (Prenatal Developmental Toxicity Study) in rats, oral route, proposed to be carried out using the the analogue substance *Rosin, maleated* (CAS RN 8050-28-0, EC No 232-480-4) is rejected pursuant to Article 40(3)(d) of the REACH Regulation.

3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

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.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

The Registrant has submitted a testing proposal for long-term toxicity testing on aquatic invertebrates *Daphnia magna* reproduction test, EU C.20/OECD 211/ with the following justification: "*Due to the poor water solubility of test substance, the exposure to the aquatic compartment is very low. No testing for prolonged toxicity to fish is proposed. The outcome of the risk assessment shows that the RCR is <0.1 and thus no additional testing is considered. The available information is sufficient to draw conclusions on classification and labelling. A daphnia reproduction study is proposed to refine the risk assessment*". ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 9.1.5 of the REACH regulation.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 2.0, November 2014), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. ECHA did not assess the read-across regarding acute toxicity to aquatic organisms. Based on the available information in the dossier, there were no indications from the short-term toxicity studies on aquatic species that fish would be substantially more sensitive than aquatic invertebrates. In such case, according to the integrated testing strategy, the *Daphnia* study is to be

conducted first. If based on the results of the long-term *Daphnia* study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted.

b) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study using the registered substance subject to the present decision: Long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211).

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 has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In addition is important to ensure that the particular sample of substance tested in the new studies is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured. If the registration of the substance covers different grades, the sample used for the new studies must be suitable to assess these.

Finally, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the studies to be assessed.

V. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the ECHA's internet page at http://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

Authorised[1] by Leena Ylä-Mononen, Director of Evaluation

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.