Decision number: TPE-D-2114350342-60-01/F Helsinki 20 December 2016

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

For Cashew (Anacardium occidentale) Nutshell Extract, Decarboxylated, List No 941-216-3, 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 Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, List No. 941-216-3, submitted by [redacted] (Registrant) using the registered substance Cashew (Anacardium occidentale) Nutshell Extract, Decarboxylated, List No. 941-216-3

- Sub-chronic Oral Toxicity – Rodent: 90-day study according to OECD TG 408 in rat;
- Pre-natal developmental Toxicity Study according to OECD TG 414 in rat.

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 Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, List No. 941-216-3, submitted by [redacted] (Registrant) using the analogue substance Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No. 700-991-6):

- Bioaccumulation aquatic/sediment (OECD 305);
- Long-term toxicity to aquatic invertebrates (OECD 211);
- Sediment toxicity (OECD 218);

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. This decision does not take into account any updates after 21 July 2016, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

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 May 2014.

ECHA held a third party consultation for the testing proposals from 15 July 2014 until 29 August 2014. ECHA did not receive information from third parties.

On 14 November 2014, 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 19 December 2014, ECHA received comments from the Registrant on the draft decision. On 20 February 2015, the Registrant updated his registration (submission number [redacted]) as agreed with ECHA. In the update the Registrant submitted a new grouping and read-across rationale in which he proposes to fulfil the standard information requirements across the group, by a one-to-one read-across (analogue approach) using the source substance "Distilled Grade" (List No. 700-991-6) and the registered substance "Technical grade" (List No. 941-216-3), while he originally proposed testing only one substance, the "Distilled Grade".

In addition, in this update the Registrant also modified the testing proposals 90-day oral toxicity study (OECD TG 408) in rats and the Developmental toxicity /teratogenicity study (OECD TG 415). In the initial testing proposal, he requested the test to be performed with the analogue substance Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No. 700-991-6) while in the update the 90-day oral toxicity study (OECD TG 408) in rats and the Developmental toxicity /teratogenicity study (OECD TG 414) was proposed to be performed with the registered substance Cashew (Anacardium occidentale) Nutshell Extract, Decarboxylated, List No. 941-216-3.

The ECHA Secretariat considered the Registrant's comments and update. On basis of this information, Section II was amended in relation to Sub-chronic Oral Toxicity (OECD TG 408) and a Pre-natal developmental Toxicity Study (OECD TG 414). The Statement of Reasons (Section III) was changed accordingly. For the Bioaccumulation aquatic/sediment (OECD TG 305), Long-term toxicity to aquatic invertebrates (OECD TG 211) and Sediment toxicity (OECD TG 218), the information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

On 21 July 2016, 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, proposal(s) for amendment to the draft decision were submitted.

On 26 August 2016, ECHA notified the Registrant of the proposal(s) for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposal(s) for amendment within 30 days of the receipt of the notification.

The ECHA Secretariat reviewed the proposal(s) for amendment received and amended the draft decision.

On 5 September 2016, ECHA referred the draft decision to the Member State Committee.

By 26 September 2016, in accordance to Article 51(5), the Registrant provided comments on the proposals for amendment. In addition, the Registrant provided comments on the draft decision. The Member State Committee took the comments on the proposals for amendment of the Registrant into account. The Member State Committee did not take into account the Registrant's comments on the draft decision as they were not related to the proposals for amendment made and are therefore considered outside the scope of Article 51(5).

After discussion in the Member State Committee meeting on 25–27 October 2016, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 27 October 2016.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Testing required

A. Tests required pursuant to Article 40(3)

The Registrant shall carry out the following tests pursuant to Article 40(3)(a) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated (List No. 941-216-3):

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

The Registrant shall carry out the following additional tests pursuant to Article 40(3)(c) and 13(4) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated (List No. 941-216-3):

3. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method Bioaccumulation in Fish: Aqueous or Dietary Exposure Bioaccumulation Fish Test, OECD 305);
4. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: *Daphnia magna* reproduction test, EU C.20/OECD 211);
5. Long-term toxicity to sediment organisms (Annex X, Section 9.5.1.; test method: Sediment-water Chironomid toxicity using spiked sediment, OECD 218);

while the tests listed in Section I above originally proposed, to be carried out using the analogue substance (Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled, List No 700-991-6) are 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

A. Tests required pursuant to Article 40(3)

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant on the registered substance and on two analogue substances to the registered substance.

0. Grouping approach and read-across hypothesis proposed by the Registrant

ECHA notes that based on the manufacturing process, the Cashew Nutshell Extract, Decarboxylated ("Technical Grade", the registered substance), with List No. 941-216-3, is distilled, resulting in the two other substances of the group, namely Cashew Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade"), with List No. 941-212-1 and Cashew Nutshell, Decarboxylated, Distilled (Distilled Grade) with List No. 700-991-6.

a) Legal background on ECHA's assessment and preliminary considerations

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. In accordance with these objectives, ECHA shall assess 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.

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 from information from structurally related substances (grouping or read-across), "*provided that the conditions set out in Annex XI are met*". According to Annex XI, Section 1.5 there needs to be structural similarity among the substances within a group or a category and furthermore, it is required that the relevant properties of a substance within the group can be predicted from the data for reference substance(s) within the group by interpolation.

The Registrant has submitted testing proposals, intended to fulfil the information requirements for three endpoints, namely, (i) Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.), (ii) Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5., and (iii) Long-term toxicity to sediment organisms (Annex X, Section 9.5.1), It is noteworthy that under the evaluation of the testing proposals, ECHA has not performed a compliance check on other endpoints and may do so at any time at its own discretion. ECHA is developing below in the relevant sections, its further considerations on the read-across approach proposed by the Registrant.

b) Introduction of the grouping approach and read-across hypothesis 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 group consists of the following three substances:
- Registered substance: Cashew Nutshell Extract, Decarboxylated ("Technical Grade"), with List No. 941-216-3;
- Cashew Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade"), with List No. 941-212-1; and
- Cashew Nutshell, Decarboxylated, Distilled ("Distilled Grade"), the analogue (or source) substance to be tested with EC number List No. 700-991-6.

In their comment to the draft decision and subsequent dossier update, the Registrant proposes to fulfil the standard information requirements across the group, by a one-to-one read-across (analogue approach) using the source substance "Distilled Grade" (List No. 700-991-6) and the registered substance "Technical grade" (List No. 941-216-3), while they originally proposed testing only one substance, the "Distilled Grade".

According to the Registrant, the read-across hypothesis is based on the assumption that common functional groups and common constituents can be identified between the registered substance and the proposed source substance. In ECHA's understanding the grouping is based on the fact that all substances that are members of the category share a structural similarity; i.e. they have the same constituents as, the Registrant indicated that *"the studies for distilled grade (proposed in this dossier) are considered relevant for read across to "distillation residue" grade since the two substances:*

- *Contain the same constituents ([redacted]), generally in similar proportions.*
- *Have similar physico-chemical properties in terms of their water solubility, vapour pressure and octanol-water partition coefficient".*

In their updated dossier, the Registrant also submitted a new grouping and read-across rationale ("[redacted]") which is based on the three substances of the group having *"common constituents or chemical classes"*, *"common functional groups"* and *"common mode of action for specific endpoints"*. The Registrants claims that *"[T]the commonality of the constituents or chemical classes in the three grades and the common modes of action for specific endpoints are manifest in physico-chemical, toxicological and ecotoxicological properties that are similar or follow a regular pattern as a result of the structural similarity"*.

In addition, the Registrant has provided further information (as indicated in the comments to the draft decision), for lower tier tests: *in vitro* eye irritation, *in vitro* skin irritation, skin sensitisation and *in vitro* mutagenicity studies.

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

Specifically, the *in vitro* skin/eye irritation results were inconclusive due to technical issues linked with the removing of the test substance from the *in vitro* system. The skin sensitisation potential was assessed only in the distilled grade and conclusion was extented to the other two grades of the group, based on tht fact that *"studies in humans also indicate that the sensitisation is largely due to the presence of cardols and, to a lesser extens, cardanol in all the three grades"*.

In vitro mutagenicity results indicated no evidence of mutagenic activity in this test system. In addition, the Registrant has submitted a comparative matrix, addressing the commonalities between the three grades.

Furthermore, although the Registant claims in their comments and updated dossier, that the similar properties were resulting from the common constituents (attachment name: [redacted]), they did not provide an appropriate justification to support their read-across approach. The Registrant has sufficiently addressed the similarities of properties among the three grades due to common constituents, however they have not discussed and not concluded upon how the different proportions of constituents would not affect the overall common properties.

ECHA notes that based on the manufacturing process, the Cashew Nutshell Extract, Decarboxylated ("Technical Grade"), with List No. 941-216-3, is distilled, resulting in the two other substances of the group, namely Cashew Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade"), with List No. 941-212-1, and Cashew Nutshell, Decarboxylated, Distilled (Distilled Grade) with List No. 700-991-6.

ECHA considers that it is not possible to predict the properties of the third member of the grouping ("Distillation residue Grade") on basis of the properties of the "Distilled Grade" and the "Technical Grade" substances. This is because the "Distillation residue Grade" substance contains higher concentrations of specific compounds than are present in the other two substances. Likewise, ECHA considers it would not be possible to predict the properties of the "Distilled Grade" substance, from knowing the properties of the "Technical Grade" and "Distillation residue Grade" substances, and this is because the "Distilled Grade" substance contains higher concentrations of specific compounds than are present in the other two substances.

ECHA is therefore requesting testing on the registered substance.

d) Conclusion

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 has analysed the dossier together with the requirements of Annex XI, Section 1.5. The read-across hypothesis is currently not considered acceptable for the reasons outlined because the hypothesis is not supported by sufficient toxicological or ecotoxicological data.

More explicitly, for environmental endpoints, ECHA notes that e.g. (a) carefully selected available (long-term) ecotoxicity bridging study/ies together with (b) bioavailability data for List No. 700-991-6 and on one or both target substances (List No. 941-216-3 and List No. 941-212-1) – could improve the read-across by providing substantiation for the hypothesis suggested by the Registrant. However, all terrestrial studies have been waived in the source and both target substance dossiers.

On this basis, the read-across cannot be accepted because the Registrant has not demonstrated that human health or environmental effects may be predicted from data on the source substance within the group by interpolation to other substances in the group. Consequently, the proposed adaptation according to Annex XI, Section 1.5, cannot be accepted, and the tests must be performed on the registered substance. In addition based on the current and the two related decisions, the Registrant is recommended to reconsider their proposed testing strategy. Further clarifications are provided in the relevant section of this decision.

1. Sub-chronic toxicity study (90-day), oral route (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.

In their updated dossier, 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 TG 408) to be performed with the registered substance, with the following justification: *"It is proposed that a subchronic oral toxicity study be conducted for Cashew Nutshell Extract, Decarboxylated, (Technical Grade) according to OECD Guideline for testing of chemicals 408 "Subchronic Oral Toxicity – Rodent: 90-day study" and to GLP. On the grounds of animal welfare, it would have to be conducted using an oral route of exposure even though this is not the likely route of human exposure. For this study, the preferred species is the rat and at least three dose levels and a control group should be used with 20 animals (10 females and 10 males) at each dose level. The animals will be treated for 90 days with observation. Appropriate clinical examinations (ophthalmological, haematology, clinical biochemistry and urinalysis when appropriate) and pathology (gross necropsy and histopathology) will be carried out and reported with interpretation.*

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 physico-chemical properties of the substance (liquid with very low vapour pressure classified as irritating to the skin and damaging to the eyes) and the information provided on the uses and human exposure (i.e., 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 TG 408, the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

b) Outcome

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

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

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 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.

In their updated dossier, the Registrant has submitted the following proposal and justification: *"It is proposed that a subchronic oral toxicity study be conducted for Cashew Nutshell Extract, Decarboxylated, (Technical Grade) according to OECD Guideline for testing of chemicals 408 "Subchronic Oral Toxicity – Rodent: 90-day study" and to GLP. Combined with this study would be a reproductive and development toxicity study conducted according to OECD Guideline for testing of chemicals 414 "Pre-natal developmental Toxicity Study". This combined study would be the best for animal welfare while yielding the information required for an appropriate assessment of the potential reproductive and developmental toxicity of Cashew Nutshell Extract, Decarboxylated, (Technical Grade). In addition to the requirements of the 90-day test outlined above, which would give the appropriate level and duration of dosing of male and female animals, mating would occur and observations made on dams, live pups and litter sizes. The clinical examination and pathology would be carried out as outlined above for the 90-day test but would include gross necropsy of dead or moribund pups and detailed pathological examination of the reproductive organs of adult animals."*

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation in a first species, as the proposed test guideline meets the standard information requirement pursuant to Annex IX, Section 8.7.2. The Registrant specified that the species to be used is the rat, and the route for testing is the oral intubation. According to the test method EU B.31/OECD TG 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) Outcome

Therefore, pursuant to Article 40(3)(a) 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, by oral route (test method: EU B.31/OECD TG 414).

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, Section 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, they should include in the update of their 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, they should update their technical dossier by clearly stating the reasons for proposing to adapt the standard information requirement of Annex X, Section 8.7.2. of the REACH Regulation.

3. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(c) and (d) 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.

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2. 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.

Originally the Registrant has submitted a testing proposal for testing the analogue substance Cashew (Anacardium occidentale) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade"), with List No. 700-991-6, for bioaccumulation in aquatic species (Bioaccumulation in Fish: Aqueous and Dietary Exposure, OECD 305) with the following justification: *"To clarify the potential for bioaccumulation of Cashew Nutshell Extract, Decarboxylated, Distilled (Distilled Grade) it is proposed that, if technically feasible, a fish bioaccumulation study is conducted according to OECD Test Guideline 305 "Bioconcentration: Flow through Fish Test" and to GLP."*. ECHA considers that the proposed test guideline is appropriate to fulfil the information requirement of Annex IX, Section 9.3.2. of the REACH Regulation.

The Registrant proposed testing with the analogue substance Nutshell Extract, Decarboxylated, Distilled (Distilled Grade) with List No. 700-991-6. The proposed adaptation according to Annex XI, Section 1.5, is not accepted, and the test must be performed on the registered substance subject to the present decision.

Given the nature of the registered substance as an extract of unknown or variable composition, complex reaction products or biological materials (UVCB), analytical challenges can be expected. More specifically, from the testing proposal description referring to the *"technically feasible"* as a condition to perform the study, it is not clear if the Registrant will include all of the constituents in the study. Bearing this in mind, the bioconcentration factor should be related to single constituents rather than to the overall UVCB substance to allow for the interpretation of the results.

In the comment to the draft decision and subsequent dossier update, the Registrant has provided information on the composition and properties of the registered substance subject to the present decision.

The Registrant has justified the testing proposal as follows:
"Bioaccumulation refers to the uptake from water, food and sediment. The substance has a log Kow = >6.2 and because it exceeds the ECHA Guidance threshold of log Kow of 3 it is considered to have the potential to bioaccumulate. However, its water solubility is low (0.3 mg/l) and close to the cut-off point of 0.1 mg/l for tests with substances for which reliable results cannot be obtained due to the difficulty of maintaining exposure concentrations .

To clarify the potential for bioaccumulation of Cashew Nutshell Extract, Decarboxylated, Distillation Residue (Distilled Residue Grade) it is proposed that, if technically feasible, a fish bioaccumulation study is conducted according to OECD Test Guideline 305 "Bioconcentration: Flow through Fish Test" and to GLP. The test will be carried out using Cashew Nutshell Extract, Decarboxylated, Distilled (Distilled Grade) source (EC: 700-991-6) (see read across justification)."

ECHA notes that there is uncertainty concerning the logKow of the individual constituents. The Registrant did not attempt to estimate logKow values and BCF values (e.g. with valid QSARs) for (the constituents of) the source and target substances. In this respect ECHA notes that the logKow should not be expressed as one single value but as a range or as individual logKow values for the different constituents. Similarly, BCF values derived from experimental results should normally be given for individual constituents, especially those considered as worst-case constituents.
Since there is only a limited data set on toxicological and ecotoxicological effects on the substances that the Registrant proposes would create a category, the proposed read-across hypothesis is not substantiated and there is no basis for predicting the properties of the registered substance as required by Annex XI, Section 1.5. ECHA therefore considers the proposed read-across not acceptable to fulfil the information requirements of this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7c* (version 2.0, November 2014), bioaccumulation in fish: aqueous and dietary exposure (test method EU C.13. / OECD TG 305) is the preferred test to cover the standard information requirement of Annex IX, Section 9.3.2".

ECHA's Guidance defines further that results obtained from a test with aqueous exposure can be used directly for comparison with the B and vB criteria of Annex XIII of REACH Regulation and can be used for hazard classification and risk assessment. Comparing the results of a dietary study with the REACH Annex XIII B and vB criteria is more complex and has higher uncertainty. Therefore, the aqueous route of exposure is the preferred route and shall be used whenever technically feasible. If you decide to conduct the study using the dietary exposure route, you shall provide scientifically valid justification for your decision. Data obtained from a dietary study will also need to be used to estimate BCF values.

b) Outcome

Therefore, pursuant to Article 40(3)(c) of the REACH Regulation, the Registrant is required to carry out the proposed study using the registered substance subject to the present decision: Bioaccumulation in aquatic species, preferably fish (Annex IX, 9.3.2 Bioaccumulation in Fish: Aqueous or Dietary Exposure Bioaccumulation Fish Test, OECD TG 305), while the study proposed on an analogue substance has to be rejected pursuant to Article 40(3)(d) of the REACH Regulation as not appropriate.

Notes for consideration by the Registrant

Before conducting testing, the Registrant is advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapters R.11., PBT/vPvB assessment, which provides further guidance on what should be considered as relevant constituents for UVCBs (substances of Unknown or Variable composition, Complex reaction products or Biological materials).

In addition, the Registrant is advised to consult the ECHA Guidance on the standard information requirements and chemical safety assessment, Chapters R.4, 5, 6, R.7b and R.7c., where the Registrant decides to adapt the testing requested 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. Also, ECHA refers the Registrant to the advice provided in the practical guide on "How to use alternatives to animal testing to fulfil your information requirements for REACH registration and on How to use and report (Q)SARs".

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

a) Examination of the testing proposal

Pursuant to Article 40(3)(c) and (d) 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.

"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 testing the analogue substance Cashew (Anacardium occidentale) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade"), with List No. 700-991-6, for long-term toxicity testing on aquatic invertebrates *Daphnia magna* reproduction test, OECD 211 with the following justification: *"In order to refine the PNECwater values and confirm the Toxicity (T) element of the PBT assessment it is initially proposed to conduct a long-term Daphnia magna reproduction study. This test is proposed rather a long-term fish toxicity test to avoid unnecessary animal testing."* ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 9.1.5 of the REACH Regulation.

The Registrant proposed testing with the analogue substance Nutshell Extract, Decarboxylated, Distilled (Distilled Grade) with List No. 700-991-6. The proposed adaptation according to Annex XI, Section 1.5, is not accepted, and the test must be performed on the registered substance.

According to ECHA *Guidance on information requirements and chemical safety assessment* (version 1.2., November 2012), 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. There was no indication in the dossier from the short-term toxicity studies on aquatic species that the 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. However, if a risk is indicated, long-term fish testing may need to be conducted.

In their comment to the draft decision, the Registrant submitted information on the composition and properties of the registered substance subject to the present decision in relation to the proposed read-across substance ("distilled grade"). The Registrant states in their grouping and read-across rationale [redacted] that *'No reliable comparative acute and chronic data for the three grades of unprocessed cashew nutshell extract are available for any ecotoxicity endpoints.* '

The Registrant has demonstrated the presence of similar constituents and functional groups among the different grades of substance being considered. Additionally, the Registrant has provided evidence of similar modes of action, which he claims are mediated by the similar functional groups encountered across the different grades of cashew nutshell extract.

The Registrant has also compared the acute toxicity of cardanol and cardol to the results obtained in 48 h studies on brine shrimp. However, the results presented by the Registrant are defined as Klimisch 4, thus not reliable.

ECHA considers that in this case, although the proposed read-across substance may be similar, i.e. have similar intrinsic properties, to the registered substance, there is a limited data set on toxicological and ecotoxicological effects on the substances that the registrant proposes would create a category and therefore the proposed read across hypothesis is not substantiated.

As there is no basis for predicting the properties of the substance as required by Annex XI, Section 1.5. ECHA therefore considers the proposed read-across not acceptable to fulfil the information requirements of this endpoint.

b) Outcome

Therefore, pursuant to Article 40(3)(c) 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), while the study proposed on an analogue substance has to be rejected pursuant to Article 40(3)(d) of the REACH Regulation as not appropriate.

Notes for consideration by the Registrant

As further explained in section IV of this decision it is important to ensure that the particular sample of substance selected to be tested in the studiy is appropriate to assess the properties of the registered substance. Hence, it is critical that those constituents which are most relevant should be present at appropriate concentrations in any sample tested.

Once results of the proposed test on long-term toxicity to aquatic invertebrates are available, the Registrant shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation. If the revised chemical safety assessment indicates the need to investigate further the effects on aquatic organisms, the Registrant shall submit a testing proposal for a long-term toxicity test on fish in order to fulfil the standard information requirement of Annex IX, 9.1.6. If the Registrant comes to the conclusion that no further investigation of effects on aquatic organisms is required, he shall update his technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex IX, section 9.1.6..

Due to the low solubility of the substance in water OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA Guidance, Chapter R7b, table R. 7.8-3 summarising aquatic toxicity testing of difficult substances should be consulted by the Registrant for choosing the design of the requested long-term ecotoxicity tests and for calculation and expression of the result of this test.

In addition, regarding the use of the Water Accommodated Fraction (WAF) approach, which the Registrant confirmed they would use for the long term toxicity testing on *Daphnia* study in their comments on the proposals for amendment, please note that the WAF approach is problematic when used with a test substance containing several constituents, as in the case of the registered substance.

In such cases the toxicity cannot be allocated to specific constituents directly and interpretation of the results in the risk assessment requires careful consideration taking into account differences in fate of the constituents in the environment. When constituents of varying solubility are present there can be partitioning effects which limit dissolution in the water. These effects should be minimised and appropriate loadings selected accordingly to allow an appropriate determination of the toxicity of the different constituents.
In that respect, it is critical that a robust chemical analysis is carried out to identify those constituents present in the water to which the test organisms are exposed. Additionally, chemical analysis to demonstrate attainment of equilibrium in WAF preparation and stability during the conduct of the test is required. Methods capable of identifying gross changes in the composition of WAFs with time are required such as ultra-violet spectroscopy or total peak area have been used successfully for this purpose. Due to the low sensitivity of the Total organic carbon analysis observed in the acute aquatic toxicity testing, this method is not recommended.

5. Long-term toxicity to sediment organisms (Annex X, Section 9.5.1.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(c) and (d) 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.

"Long-term toxicity to sediment organisms" is a standard information requirement as laid down in Annex X, Section 9.5.1. 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 testing the analogue substance Cashew (Anacardium occidentale) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade"), with List No. 700-991-6, for long-term toxicity testing on sediment organisms Sediment-water Chironomid toxicity test using spiked sediment (OECD 218) with the following justification: *"It is proposed that the study is carried out according to OECD Test Guideline 218 "Sediment-Water Chironomid Toxicity using Spiked Sediment" and to GLP. This study will assess the effects of prolonged exposure of Cashew Nutshell Extract, Decarboxylated, Distilled (Distilled Grade) to the sediment-dwelling larvae of the freshwater dipteran Chironomus sp."*

The Registrant proposed testing with the analogue substance Nutshell Extract, Decarboxylated, Distilled (Distilled Grade) with List No. 700-991-6. The proposed adaptation according to Annex XI, Section 1.5, is not accepted, and the test must be performed on the registered substance.

ECHA considers that the proposed study is appropriate to further investigate long-term toxicity to sediment organisms (Annex X, Section 9.5.1. of the REACH Regulation).

In their comment to the draft decision, the Registrant submitted information on the composition and properties of the registered substance in relation to the proposed read-across substance. The Registrant states in their grouping and read-across rationale ("[redacted]") that *'No reliable comparative acute and chronic data for the three grades of unprocessed cashew nutshell extract are available for any ecotoxicity endpoints. '*

The Registrant has demonstrated the presence of similar constituents and functional groups among the different grades of substance being considered. Additionally, the Registrant has provided evidence of similar modes of action, which they claim are mediated by the similar functional groups encountered across the different grades of cashew nutshell extract.

ECHA considers that in this case, although the proposed read-across substance may be similar, i.e. have similar intrinsic properties, to the registered substance, there is a limited data set on toxicological and ecotoxicological effects on the substances that the registrant proposes would create a category and therefore the proposed read across hypothesis is not substantiated. As there is no basis for predicting the properties of the substance as required by Annex XI, section 1.5., ECHA therefore considers the proposed read-across not acceptable to fulfil the information requirements of this endpoint.

c) Outcome

Therefore, pursuant to Article 40(3)(c) 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 to sediment organisms (Annex X, 9.5.1.; test method: Sediment-water Chironomid toxicity using spiked sediment, OECD 218), while the study proposed on an analogue substance has to be rejected pursuant to Article 40(3)(d) of the REACH Regulation as not appropriate.

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 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. 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 Ofelia Bercaru, Head of Unit, Evaluation E3

[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.