EUROPEAN CHEMICALS AGENCY

Helsinki, 28 March 2018

Addressee: [redacted]

Decision number: TPE-D-2114398036-43-01/F
Substance name: Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated ("Technical Grade")
List number: 941-216-3
CAS number: NS
Registration number: [redacted]
Submission number: [redacted]
Submission date: 15/08/2017
Registered tonnage band: Over 1000

## DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation ((EC) No 1907/2006) (the REACH Regulation), ECHA examined your testing proposal(s) and decided as follows.

Your testing proposals are accepted and you are requested to carry out:

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats using the analogue substances Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No. 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No. 941-212-1).**
2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route using the analogue substances Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No. 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No. 941-212-1)**
3. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) using the analogue substances Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No. 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No. 941-212-1).**
4. **Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305, aqueous exposure) using the analogue substances Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No. 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No. 941-212-1).**

5. **Long-term toxicity to sediment organisms (Annex X, Section 9.5.1.; test method: Sediment-water Chironomid toxicity using spiked sediment, OECD TG 218) using the analogue substances Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No. 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No. 941-212-1).**

You 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 to the REACH Regulation.
To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and an adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by **6 April 2020**. You also have to update the chemical safety report, where relevant.

The reasons for this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

## Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2

[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.

**Appendix 1: Reasons**

The decision of ECHA is based on the examination of the testing proposals submitted by you.

TOXICOLOGICAL AND ECOTOXICOLOGICAL INFORMATION

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Your registration dossier contains for multiple endpoints adaptation arguments in the form of a grouping and read-across approach according to Annex XI, 1.5. of the REACH Regulation. ECHA has assessed first the scientific and regulatory validity of your Grouping and read-across approach in general before the individual endpoints (sections 1 to 5).

**Grouping of substances and read-across approach**

You have sought to adapt information requirements by applying a read-across approach in accordance with Annex XI, Section 1.5, for the endpoints:

- sub-chronic toxicity (90-day) study (Annex IX, Section 8.6.2.)
- pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- bioaccumulation in aquatic species (Annex IX, Section 9.3.2.)
- long-term toxicity to sediment organisms (Annex X, Section 9.5.1.

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (read-across approach). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances[2]. This hypothesis explains why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern. The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration. Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests. Similarly, biotic and abiotic degradation may alter the fate and bioavailability of compounds as well as be themselves hazardous, bioaccumulative and/or persistent. Thus,

[2] For further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.

physicochemical and degradation properties influence the human health and environmental properties of a substance and should be considered in read-across assessments. However, the information on physicochemical and degradation properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis[3]- (1) (Bio)transformation to common compound(s)- the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s)- the read-across hypothesis is that the organism is exposed to different compounds which have similar (eco)toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common compounds).

Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

### i. Description of the grouping and read-across approach you proposed

You consider to achieve compliance with the REACH information requirements for the registered substance Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated ("Technical Grade" or TG) (List No 941-216-3) using data of structurally similar substances Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade" or DG) (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade" or DRG) (List No 941-212-1) (hereafter the 'source' substances).

You have provided a read-across documentation as a separate attachment in the category object of the updated registration dossier. Furthermore you have provided a data matrix document and a description of the testing proposals that you submitted.

You use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group:
*"The available data for the three grades [...] support the assertion that thay can be considered as a category (or group) with regard to the use of read-across because Distilled, Technical and Distillation Residue grades are all derived from a Natural Complex Substance, namely cashew nutshell extract (or cashew nutshell oil) [...].* [redacted]."

[3] ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

As a result of structural similarity, you state that the data of the TG can be predicted "*by interpolation*" from the results generated in tests on the DG and DRG, namely physico-chemical parameters, environmental fate and local effect mammalian toxicity, such as *in vitro* mutagenicity, and *in vitro* skin and eye irritation tests. You consider that "*interpolation is the estimation of a value for a member of the group using measured values from other members on both sides of that member within the defined group spectrum.*"

You add that a "*comparision of the test data for Distilled grade for the skin sensitisation, in vitro mutagenicity [...], acute oral and acute dermal toxicity endpoints, with the predicted values for the different forms of cardanol and cardol, using the OECD QSAR Toolbox, indicate that these constituents are responsible for any observed effects. Predicted data could not be generated for the polymeric fraction since no information on the chemical structure and/or physico-chemical properties of this constituent was available. Therefore it has not been possible to predict the toxicity of the Technical and Distillation Residue grades for these endpoints.*"

As an integral part of this prediction, you conclude that "*given the compositional spectrum of the three grades, TG lies between DG and DRG. As a result it would be feasible to reliably determine the toxicity of TG for appropriate endpoints from the data generated in tests on DG and DRG by interpolation. The use of data from the two source substances (DG and DRG) to read-across to TG is considered to provide greater confidence in the predicted data for the target (registered) substance.*"

ECHA considers that this information is your read-across hypothesis, for the above-mentioned information requirements.

**ii. ECHA analysis of the grouping and read-across approach in light of the requirements of Annex XI, 1.5.**

With regard to the proposed predictions ECHA has the following observations:

Your proposed adaptation argument is that the registered (TG) substance is fractionated by distillation into the two source substances (DG and DRG) and so testing the two source substances is a sufficient basis for predicting the properties of the registered substance for other (eco)toxicological endpoints.

You have provided supporting evidence regarding :

- The common functional groups by providing characterisation of the source and registered substances by IR and UV-Vis spectroscopic analysis;
- The common mode of action for local and systemic effect by indicating that the local effects are probably due to the presence of the irritant cardol and to a lesser extent cardanol, of relevance for endpoint such as skin and eye irritation and skin sensitisation;
- Consistent physico-chemical parameters, such water solubility, Log $K_{ow}$, vapour pressure;
- Comparable environmental fate properties;
- Comparable lower-tier endpoints for mammalian toxicity endpoints, accepting that data is mainly available for the DG substance, and that QSAR information on cardol and cardanol are also to be taken into consideration.

Finally you have concluded that "*for Annex IX and X endpoints, where the testing of DG and DRG is proposed, comparable results for these source substances will mean that the salem results (whether a demonstrable effect or an absence of effects) is predicted for the target substance, TG. This will mean that the differences in proportion of low molecular weight cardanols and high molecular weight polymeric fractrion beetween the grades do not evidently affect the responses observed in the 3 substances in the specified test. This result*

*would indicate that all possible toxicokinetic and toxicodynamic interactions among the source substances' constituents are also inherently reflected in the test result for the target substance. The absence of effect for a particular Annex IX and X endpoint in tests with DG and DRG will indicate that none of the constituents present in the three grades in siginificant proportions cause adverse effect for that endpoint. [...] Therefore, the interpolated response for a particular endpoint for the target substance [TG] will lay between those measured for the two source substances [DG and DRG]."*

ECHA considers that your proposed adaptation argumentation is plausible and that the supporting evidence reported in your read-across justification document provides a sufficient basis for predicting the properties of the registered substance. ECHA concludes that you have sufficiently established why a prediction by interpolation can be considered as reliable for the human health/ environmental endpoints for which the read across is claimed, from data for reference substance(s) within the group.

**iii. Conclusion on the read-across approach**

The adaptation of the standard information requirements, sub-chronic toxicity (90-day) study (Annex IX, Section 8.6.2.), pre-natal developmental toxicity study (Annex IX, Section 8.7.2.), long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.), bioaccumulation in aquatic species (Annex IX, Section 9.3.2.), long-term toxicity to sediment organisms (Annex X, Section 9.5.1.), in the technical dossier is based on the proposed read-across approach examined above.

For the reasons as set out above, ECHA considers that the read-across justification and the supporting evidence to be a sufficiently adequate and reliable basis to predict the properties of the registered substance by interpolation from the two source substances.

Thus, the adaptation does comply with the general rules of adaptation as set out in Annex XI, 1.5. Therefore, ECHA accepts all adaptations in the technical dossier that are based on Annex XI, 1.5.

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

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.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to EU B.26./OECD TG 408 to be carried out with two analogue substances: Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade") (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No 941-212-1).

ECHA requested your considerations for alternative methods to fulfil the information requirement for Sub-chronic toxicity (90-day): oral. ECHA notes that you provided your considerations and you applied read-across to fulfil the respective information requirement, and no other alternative methods were available. ECHA has taken these considerations into account.

ECHA has evaluated your proposal to perform the test with the two source substances, DG and DRG, "*with the required data for TG being interpolated by read-across*". As explained above at the beginning of Appendix 1 of this decision, ECHA agrees that the read-across approach is plausible and that you can rely on the results of studies performed with Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade") (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade").

You argued that, "*on the grounds of animal welfare, these tests would have to be conducted using an oral route of exposure even though this is not the likely route of human exposure. For these studies, 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. Furthermore, 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.

You 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.

ECHA notes your agreement to perform the test as requested.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study: Sub-chronic toxicity study (90-day) in rats, by oral route (test method: EU B.26/OECD TG 408), with two analogue substances, Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue) (List No 941-212-1).

**2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species**

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.

You have submitted a testing proposal for a pre-natal developmental toxicity study in rats according to EU B.31./OECD TG 414 by the oral route with two analogue substances: Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade") (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No 941-212-1).

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (pre-natal developmental toxicity). ECHA notes that you provided your considerations and you applied read-across to fulfil the respective information requirement, and no other alternative methods were available. ECHA has taken these considerations into account.

ECHA has evaluated your proposal to perform the test with the two source substances, DG and DRG, "*with the required data for TG being interpolated by read-across*". As explained above at the beginning of Appendix 1 of this decision, ECHA agrees that the read-across approach is plausible and that you can rely on the results of studies performed with Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade") (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade").

ECHA considers that the proposed study performed with the analogue substances, detailed above, is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

You proposed testing with the rat as a first species. According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with the rat or rabbit as a first species.

You proposed testing by the oral route. ECHA agrees that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid (with very low vapour pressure classified as irritating to the skin and damaging to the eyes), ECHA concludes that testing should be performed by the oral route.

Furthermore you indicated that "*the study will include three concentrations of the test substance and a control group, each group will contain 20 female animals. Measurements (weighing) and clinical daily observations will be conducted. After terminating the females (one day prior to the expected day of delivery), the uterine contents will be examined, and the foetuses will be evaluated for soft tissue and skeletal changes. Further reproductive and developmental studies may potentially be proposed based on the result of developmental studies (OECD TG414) conducted on the Distilled and the Distillation Residue grades.*" ECHA notes, that it is at your discretion to perform the intended examinations during the testing program as long as the examination are in line with the examinations according to test method OECD TG 414.

ECHA notes your agreement to perform the test as requested.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study: Pre-natal developmental toxicity study in a first species (rats or rabbits), oral route (test method: EU B.31./OECD TG 414), with two analogue substances, Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue) (List No 941-212-1).

*Notes for your consideration*

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017), Chapter R.7a, Section R.7.6.2.3.2.

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, you 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 you consider that the conditions for adaptations are not fulfilled, you should include in the update of their dossier a testing proposal for a pre-natal developmental toxicity study on a second species. If you conclude that the conditions for these adaptations can be fulfilled, you should update your 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. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

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.

You have submitted a testing proposal for two analogue substances: Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade") (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No 941-212-1) for long-term toxicity testing on aquatic invertebrates *Daphnia magna* reproduction test, EU C.20/ OECD TG 211 with the following justification: *"This test is proposed rather than a long-term fish toxicity test (to address Annex IX – 9.1.6) to avoid unnecessary vertebrate testing. This approach is consistent with ECHA Guidance on information requirements and assessment: Chapter R.10: Dose (concentration)-response for environment which states that: "A long-term test has to be carried out for substances showing no toxicity in short-term tests if the log Kow >3 (or BCF >100) and if the $PEC_{local/regional}$ is >1/100th of the water solubility. The long-term toxicity test should normally be a test on invertebrate (preferred species Daphnia) to avoid unnecessary vertebrate testing."*
*The data from the long-term Daphnia study will be used to assess the risks posed by the test substance to the aquatic environment in different use scenarios based on the Risk Characterisation Ratios (RCRs) generated in a revised chemical safety assessment. If all of these RCRs are shown to be below 1, then the Consortium would not conduct a long-term fish study to avoid unnecessary vertebrate testing. However, if RCR values above one for the aquatic environment are indicated than the conduct of a long-term fish test such as the Fish Sexual Development Test (OECD TG 234) will be considered."*

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 4.0, June 2017), 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 were no indications 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.

ECHA notes your agreement to perform the test as requested.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed test: Long-term toxicity testing on aquatic invertebrates (test method: *Daphnia magna* reproduction test, EU C.20/ OECD TG 211), with two analogue substances, Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue) (List No 941-212-1).

*Notes for your consideration*

Once results of the proposed test on long-term toxicity to aquatic invertebrates are available, you 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, you 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 you come to the conclusion that no further investigation of effects on aquatic organisms is required, you shall update your technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex IX, 9.1.6.

Due to the low solubility of the substance in water, you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, table R. 7.8-3 summarising aquatic toxicity testing of difficult substances 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 you confirmed you would use for the long term toxicity testing on *Daphnia* study, 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.

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

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

"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.

You have submitted a testing proposal for testing two analogue substances: Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade") (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No 941-212-1) for a bioaccumulation in aquatic species (Bioaccumulation in Fish, by aqueous exposure, OECD TG 305) with the following justification: *"The test substance Cashew Nutshell Extract, Decarboxylated (Technical Grade) has a log $K_{ow}$ = >6.2 with the log $K_{ow}$ values for the different forms of cardanol and cardol predicted from the OECD QSAR Toolbox being from 8.37 to 8.96 and 7.89 to 8.46 respectively. Since the log $K_{ow}$ values for the substance as a whole and for individual constituents exceed the ECHA Guidance threshold of log $K_{ow}$ = 3 Technical grade is considered to have the potential to bioaccumulate and the specific adaptation possibilities of Annexes VI to X (and Column 2 thereof) of the REACH Regulation are not adequate to generate the necessary information. In addition the exposure scenarios for Technical grade used in the Chemical Safety Report indicate a potential for direct exposure of the aquatic environment."*

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 9.3.2. of the REACH Regulation.

ECHA requested your considerations for alternative methods to fulfil the information requirement for bioaccumulation in aquatic species. ECHA notes that you provided your considerations and you applied read-across to fulfil the respective information requirement, and no other alternative methods were available. ECHA has taken these considerations into account.

ECHA notes your agreement to perform the test as requested.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study: Bioaccumulation in aquatic species, preferably fish (Annex IX, 9.3.2 Bioaccumulation in Fish: Aqueous Exposure Bioconcentration Fish Test, OECD TG 305), with two analogue substances, Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue) (List No 941-212-1).

*Notes for your consideration*

Before conducting testing, you are advised to consult the ECHA *Guidance on the information requirements and chemical safety assessment* (version 3.0, June 2017), Chapter R.11. PBT/vPvB assessment, in particular to first conclude on whether the registered substance is

not persistent (P) and not very persistent (vP) or whether it may fulfil Annex XIII of the REACH Regulation criteria of being P or vP and to consult the PBT assessment for Weight-of-Evidence determination and the integrated testing strategy for bioaccumulation assessment, in particular concerning relevant constituents, impurities, additives and degradation/transformation products. Also, you need to carefully consider the potential formation of stable degradation products with PBT/vPvB properties.

In addition, you are advised to consult the ECHA *Guidance on information the information requirements and chemical safety assessment*, Chapters R.4, 5, 6, R.7b and R.7c. If you decide to adapt the testing requested according to the specific rules outlined in Annexes VI to X and/or according to general rules contained in Annex XI of the REACH Regulation, you are referred to the advice provided in ECHA's Practical Guides 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".

Due to the low solubility of the substance in water and high octanol-water partition coefficient, you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), , Chapter R7b (table R.7.8-3 summarising aquatic toxicity testing of difficult substances) for choosing the design of the requested test and calculation and expression of the results of the test.

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

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

"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.

You have submitted a testing proposal for testing two analogue substances: Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled ("Distilled Grade") (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No 941-212-1) for long-term toxicity testing on sediment organisms Sediment-water Chironomid toxicity test using spiked sediment (OECD TG 218) with the following justification: "*The current Risk Characterisation exercise for Technical grade within the Chemical Safety Report indicates that there is a potential risk to freshwater and marine sediments from certain exposure scenarios. However, the perceived risk may be a consequence of the rather precautionary PNECs for freshwater and marine water sediments which have been derived using the Equilibrium Partitioning approach in the absence of experimental data.*
*The data for Technical grade will be used to refine the PNECsediment, for freshwater and marine sediments which is consistent with the specific adaptation possibilities in Column 2 of Section 9.5.1 of REACH Annex X.*"

You argued that "*This study will assess the effects of prolonged exposure of Distilled and Distillation Residue grades to the sediment-dwelling larvae of the freshwater dipteran Chironomus sp. First instar chironomid larvae will be exposed to at least five concentrations of the test chemical in sediment-water systems. The test substances will be spiked into the sediment and first instar larvae will be subsequently introduced into test beakers in which the sediment and water concentrations have been stabilised. Chironomid emergence and*

*development rate will be measured at the end of the test. The maximum exposure duration is 28 days for C. riparius, C. yoshimatsui, and 65 days for C. tentans. Larval survival and weight may also be measured after 10 days if required (using additional replicates as appropriate).*

*The study report will include the development time and the total number of fully emerged midges (sex and number are recorded daily), the observation of any abnormal behaviour the number of visible pupae that have failed to emerge and any egg masses deposition. The testing will be supported by appropriate analytical confirmation of the exposure concentrations of key constituents such as cardanol and cardol."*

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).

ECHA notes your agreement to perform the test as requested.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study: Sediment-water Chironomid toxicity using spiked sediment (test method: OECD TG 218), with two analogue substances, Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No 700-991-6) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue) (List No 941-212-1).

*Notes for your consideration*

Due to substance properties, you are advised to consider the feeding recommendations given in the OECD test guidelines 218 and 233. The guidelines recommend that when testing strongly adsorbing substances (typically with log $K_{ow}$ > 5), in order to cover the dietary exposure food should be added to the formulated sediment before the stabilisation period (paragraph 31 of OECD TG 218 or 233).

## Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 15 August 2017.

This decision does not take into account any updates after **13 December 2017,** 30 calendar days after the end of the commenting period.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments.

In your comments you agreed to the draft decision. ECHA took your comments into account and did not amend the request(s).

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.

**Appendix 3: Further information, observations and technical guidance**

1. This decision does not imply that the information provided in your 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.

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.

3. In relation to the information required by the present decision, the sample of the substances used for the new tests must be suitable for use by all the joint registrants. Hence, the samples should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test materials and to document the necessary information on their substances' composition. In addition, it is important to ensure that the particular samples of the substance tested in the new tests are appropriate to assess the properties of the registered substance.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.

4. ECHA would like to draw your attention to the obligation imposed by Article 53 of the REACH Regulation on registrants who are required by ECHA to perform the same test on the same substance. According to this provision, those registrants '*shall make every effort to reach an agreement as to who is to carry it out on behalf of the other registrants* [...] *and to inform the Agency accordingly within 90 days*'. This provision also sets out the conditions of the cost-sharing obligation between the registrants concerned.

   We remind you that you have been required to perform the same studies on the two source substances, which have already been subject to a decision: Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distilled (List No. 700-991-6 - decision reference TPE-D-2114350280-62-01/F ) and Cashew (*Anacardium occidentale*) Nutshell Extract, Decarboxylated, Distillation Residue ("Distillation residue Grade") (List No. 941-212-1 – decision reference TPE-D-2114350287-48-01/F).

5. If the required tests are conducted with one or more analogue substances in the context of a read-across approach, the identity of the test materials used to perform the test should be specified in line with the ECHA's Practical Guide on "How to use alternatives to animal testing to fulfil your information requirements" (chapter 4.4). This is required to show that the test materials are representative of the analogue substances identified in the read-across approach and used to predict the properties of the registered substance.