EUROPEAN CHEMICALS AGENCY

Helsinki, 15 November 2018

Addressee: [redacted]

Decision number: CCH-D-2114449868-28-01/F
Substance name: (Z)-3-hexenyl salicylate
EC number: 265-745-8
CAS number: 65405-77-8
Registration number: [redacted]
Submission number: [redacted]
Submission date: 31/10/2017
Registered tonnage band: 100-1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408) in rats with the registered substance**

2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2. test method: OECD TG 414) in a first species with the registered substance**

3. **Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: Daphnia sp. Acute immobilisation test, EU C.2./OECD TG 202) with the registered substance;**

4. **Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: Fish, acute toxicity test, OECD TG 203) with the registered substance;**

5. **Effect concentrations based on the geometric mean measured test concentrations for the growth inhibition study in aquatic plants and use these effect concentrations for the Chemical Safety Assessment of the substance (Article 13(3));**

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 adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by ***23 November 2020***, except for the information requested under point 1 for a Sub-chronic toxicity study (90-day) which shall be submitted in an updated registration dossier by ***22 November 2019***. You shall also update the chemical safety report, where relevant.

The reasons of 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 Kevin Pollard, Head of Unit, Evaluation E1

[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

(ECO)TOXICOLOGICAL INFORMATION

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX 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 the endpoints sub-chronic toxicity (90-day) study (Annex IX, 8.6.2.), pre-natal developmental toxicity study (Annex IX, 8.7.2.), and short-term toxicity tesing on fish (Annex VIII, 9.1.3.) adaptation arguments in form of a read-across approach under Annex XI, Section 1.5. of the REACH Regulation. ECHA has considered first the scientific and regulatory validity of your read-across approach in general (section 0) before assessing the individual endpoints (sections 1, 2, and 4).

0. Grouping of substances and read-across approach

You have sought to adapt the information requirements listed above by applying a read-across approach in accordance with Annex XI, Section 1.5. 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. 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, 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- (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 proposed by you

You consider to achieve compliance with the REACH information requirements for the registered substance (Z)-3-hexenyl salicylate using data of structurally similar substance Benzoic acid, 2-hydroxy-, cyclohexyl ester (CAS no 25485-88-5) (hereafter the 'source substance').

You have provided a read-across documentation as a separate attachment in the registration.

You use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group:

From the QSAR Toolbox data, that you report in the attachement, you state that "*it can be seen that the two substances share structural similarities and also 'mechanistic action' similarities which are both general and endpoint specific. A difference in the protein binding mechanism was reported, however it is important to remember that most of these identified similarities represent the substance itself and not always its biologically relevant metabolites. The main difference observed is structural. The target substance ((z)-3-hexenyl salicylate) contains an acyclic hexenyl chain and the source substance (cyclohexyl salicylate) contains a cyclic hexyl group.*"

ECHA understand that your read-across hypothesis is based on the assumption that the source and the registered substance have similar properties of repeated dose toxicity, pre-natal developmental toxicity and short-term fish toxicity. ECHA considers that this information is your read-across hypothesis.

In support of your read-across hypothesis you have provided QSAR documentation, a data matrix, and a generic group justification. You also provided a comparison of some core physico-chemical parameteres (partition coeffient, water solubility and boiling point), and a comparison of acute oral toxicity and dermal toxicity data as well a comparison of ready biodegradability and 48h fish toxicity information.

In addition, ECHA observes that in the technical dossier of the target substance you have provided studies for the source substance Benzoic acid, 2-hydroxy-, cyclohexyl ester (CAS no 25485-88-5). These studies are further discussed under the respective endpoints below.

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:

a) Substance characterisation of source and target substances

The substance characterisation of the source substance need to be sufficiently detailed in order to assess whether the attempted prediction is not compromised by the composition and/or impurities. In the ECHA's Practical Guide on "How to use alternatives to animal testing to fulfil your information requirements" (chapter 4.4), it is recommended to follow the ECHA *Guidance for identification and naming of substances under REACH and CLP* (version 2.1, May 2017) also for the source substances. This ensures that the identity of the source substance and its impurity profile allows an assessment of the suitability of the substances for read-across purposes.

Currently the identity of the source substance and its impurity profile cannot be assessed using the information provided in the registration dossier and the suitability of the substances for read-across purposes cannot be verified. Therefore, ECHA cannot reach a conclusion whether the source substances can be used to predict properties for the registered substance.

b) Explanation on why and how the structural similarities allow predictions

In order to meet the provisions in Annex XI, Section 1.5. to predict human health effects from data for a reference substance within the group by interpolation to other substances in the group, ECHA considers that structural similarity alone is not sufficient. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. In particular, the structural similarities must be linked to a scientific explanation of how and why a prediction is possible.

ECHA notes the following observations: In your read-across justification document you have stated: "*The main difference observed is structural. The target substance ((z)-3-hexenyl salicylate) contains an acyclic hexenyl chain and the source substance (cyclohexyl salicylate) contains a cyclic hexyl group.*"

ECHA concludes that you have not addressed the obvious structural differences between the source substances and the target substance and did not explain, why those differences would not lead to differences in the (eco)toxicity profile of target and source substances.

c) Support of a similar or regular pattern as a result of structural similarity

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances.* One prerequisite for a prediction based on read-across therefore is that the substances involved are structural similar and are likely to have similar properties. One important aspect in this regard is the analysis of the data matrix to compare the properties of source and target substances and to establish whether indeed they are similar or follow a regular pattern.

ECHA notes the following:

1. Acute oral and acute dermal toxicity tests are made both with the registered and with the source substance and the results are rather similar. In addition, the Screening study for reproductive/developmental toxicity, OECD TG 422 and the *In vitro* gene mutation study in bacteria, OECD TG 471 (Ames test) are made with the registered substance, but for those endpoints studies with the source substance are not provided, and thus a similar or regular pattern of toxicity has not been documented. Other genotoxicity studies, repeated dose toxicity study, and pre-natal developmental toxicity study are only provided for the source substance of the read-across and therefore, a similar or regular pattern of toxicity has not been documented.
2. Similarity has been observed in the QSAR Toolbox results for some physico-chemical, fate properties and for a limited set of human health endpoints. However, the modelling results, which you have reported in your read-across justification document do not cover the three endpoints, compliance of which depends on the read-across, i.e. repeated systemic toxicity, developmental toxicity and short-term fish toxicity. Furthermore, you have not documented that the two substances fall within the applicability domain of the QSAR model which you have used, as required in Annex XI, 1.3. "Qualitative or Quantitative structure-activity relationship ((Q)SAR)".
3. There is some, although preliminary evidence that the target substance is more toxic than the source substance. More notably, the NOAEL of the OECD TG 422 screening study with the registered substance is 50 mg/kg, whereas the NOAELs of the one-generation study with the read-across source substance are 180 mg/kg (for parent females and for development of F1 generation) and 540 mg/kg (for parent males). In ECHAs opinion, this difference prevents the conclusion that the two substances would have similar toxic effects. Moreover, you have not shown, how a prediction of the toxic properties of the registered substance can be obtained, which would ensure the safety of the exposed humans.
4. Furthermore, ECHA observes that results of profiling by the OECD QSAR Toolbox reported in the read-across justification document indicate more functional groups and bioaccumulation (metabolism) alerts for the target substance than for the source substance. It is not explained how these differences would affect predictions of the repeated systemic toxicity, developmental toxicity and short-term fish toxicity.

ECHA concludes that the presented evidence in the data matrix does not support a similar or regular pattern of toxicity as a result of structural similarity. Therefore it cannot be verified that the proposed analogue substance can be used to predict properties of the registered substance.

d) Toxicokinetics

One important aspect in establishing that substances have similar effects or follow a regular pattern is the comparison of absorption, distribution, metabolism and elimination of source and target substances. This allows assessing the qualitative and quantitative internal systemic exposure of the test organism when exposed to source and target.

ECHA notes the following observations:

1. Information that you have provided on absorption is based on physico-chemical properties and on assumptions based on the existing animal studies. No experiemental data addressing specifically the absorption of the target or sources

substance has been provided.
2. Furthermore, the metabolic pathway for(Z)-3-hexenyl salicylate shown in the registration dosser is "postulated" and is not based on experimental data.

ECHA concludes that you did not address important aspects such as the toxicokinetics of the parent substance and their metabolic fate / (bio)transformation and the resulting possible difference in the metabolite profile. Therefore, it is not possible to verify the substances which are likely to govern the toxicity profiles of source and target substances. In the absence of such information there is not an adequate basis for predicting the properties of the registered substance from the data obtained with the source substance.

iv. Conclusion on the read-across approach

The adaptation of the standard information requirements for repeated dose toxicity, pre-natal developmental toxicityand short-term fish toxicity in the technical dossier is based on the proposed read-across approach examined above. ECHA does not consider the read-across justification to be a reliable basis to predict the properties of the registered substance for the reasons set out above. Thus, the adaptation does not comply with the general rules of adaptation as set out in Annex XI, 1.5. Therefore, ECHA rejects all adaptations in the technical dossier that are based on Annex XI, 1.5.

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

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. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided:

A screening study for reproductive/developmental toxicity OECD TG 422 with registered substance was provided, rats, gavage, reliability 2.

However, this study does not provide the information required by Annex IX, Section 8.6.2., because the exposure duration is less than 90 days and the number of animals examined per dose group for histopathology and clinical chemistry is significantly lower than in the 90 day sub-chronic toxicity study (OECD TG 408).

In addition, a 28-day oral study EU B.7 (1984) with read-across substance Benzoic acid, 2-hydroxy-, cyclohexyl ester; rats, gavage, reliability 2. The doses were 40, 100, 250 mg/kg of body weight. However, this study does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days and the number of animals per dose group is significantly lower than in the 90 day sub-chronic toxicity study (OECD TG 408) . Therefore, the sensitivity of a 28-day study is much lower than that of a 90-day study.

Furthermore, you have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a 90-day oral study OECD 408 (1995) with the analogue substance Benzoic acid, 2-hydroxy-, cyclohexyl ester (CAS no 25485-88-5) in rats, via gavage, reliability 2.
However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

Therefore, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA has evaluated the most appropriate route of administration for the study. ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 5.0, December 2016) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, the available oral studies indicate a concern for systemic toxicity (*kidney toxicity and reproductive toxicity*) that requires further information on repeated dose toxicity by the oral route. Hence, the test shall be performed by the oral route using the test method OECD TG 408.

According to the test method OECD TG 408 rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

ECHA received your comments to the draft decision submitted during the 30-day commenting period. ECHA acknowledges your agreement to perform the requested test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 90-day oral toxicity study (test method: OECD TG 408) in rats.

Notes for your considerations

The Extended one-generation reproductive toxicity study (EOGRTS) according to Annex IX, Section 8.7.3. is not part of this decision because the results of the Sub-chronic toxicity study (90-day) are considered crucial to inform on the study design of the EOGRTS. Therefore, the results of the Sub-chronic toxicity study (90-day) should be used, among other relevant information, to decide on the study design of the EOGRTS.

ECHA may therefore launch a separate compliance check at a later stage addressing the EOGRTS information requirement.

Alternatively, you may also consider submitting a testing proposal for an Extended one-generation reproductive toxicity study together with the results of the requested Sub-chronic toxicity study (90-day). The testing proposal should include a justification for its study design following ECHA Guidance on information requirements and chemical safety assessment Chapter R.7a, Section R.7.6 (version 6.0, July 2017), taking into account the results of the Sub-chronic toxicity study (90-day).

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

A "pre-natal developmental toxicity study" (test method OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH

Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a pre-natal developmental toxicity study OECD TG 414 with analogue substance Benzoic acid, 2-hydroxy-, cyclohexyl ester (CAS no 25485-88-5) in rats, via gavage, reliability 2, according to GLP.

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

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

ECHA considers 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, ECHA concludes that testing should be performed by the oral route.

ECHA received your comments to the draft decision submitted during the 30-day commenting period. ECHA acknowledges your agreement to perform the requested test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: OECD TG 414) in a first species (rat or rabbit) by the oral route.

3. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)

"Short-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex VII, Section 9.1.1. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for the key study (title of reference: [redacted]; static design of the test; dissolved organic carbon was measured only at the start of the test while there is no information available on analytical monitoring of the test material at the end of the test). However, this study does not provide the information required by Annex VII, Section 9.1.1., because it is not adequate, as explained in the following.

ECHA observes that the effect levels for the key study reported in the dossier are estimated on the basis of measured initial concentrations of the test material. At the same time, based on available information on the properties of the substance reported in the registration dossier, you concluded that the substance has potential to volatilise from aqueous medium

(estimated Henry law constant, when based on expiremental values of water solubility and vapour pressure provided in the registration dossier, is app. 6.578 Pa-m3/mole), is readily biodegradable and has potential for adsorption (log Koc equal to 3.25). As noted in the ECHA *Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7b* (version 4.0, June 2017) substances with such properties can be lost from the aquatic test system. Consequently, ECHA considers that the substance has potential for being lost from the test system during aquatic toxicity testing. Thus, in order to gather adequate results for the purpose of classification/labelling and risk assessment, analytical verification of exposure concentrations of the substance is necessary for the aquatic toxicity testing, especially for the static test design. However, as noted above there is no information on analytical monitoring of the test material at the end of the study available. Therefore, ECHA considers that the results of the study reported in the registration dossier are not adequate for the purpose of classification/labelling and risk assessment, as required by section 1.1.2. of Annex IX and Annex I, section 3 to the REACH Regulation.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Daphnia sp. acute immobilisation test (test method EU C.2. / OECD TG 202) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.1.

ECHA received your comments to the draft decision submitted during the 30-day commenting period. ECHA acknowledges your agreement to perform the requested test and that a further review of PNECs will also take into account new test data from this test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: *Daphnia* sp. Acute immobilisation test, EU C.2./OECD TG 202).

4. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)

"Short-term toxicity testing on fish" is a standard information requirement as laid down in Annex VIII, Section 9.1.3. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a short-term fish toxicity study (according to the "*German Federal Environment Agency [UBA] - Proposed procedure 'Lethal effect on zebra danio (Brachydanio rerio)*") with analogue substance Benzoic acid, 2-hydroxy-, cyclohexyl ester (CAS no 25485-88-5), reliability 2 (reliable with restrictions), according to GLP.

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

Furthermore, ECHA notes that in the technical dossier you have provided a study record for the supporting study with the registered substance (title of reference [redacted]; static design of the test; no information on analytical

monitoring of the test material, i.e. effect concentrations are based on nominal concentration of the test substance,and on GLP status of the study; 48h exposure duration; reliability 3 (not reliable)). However, this study does not provide the information required by Annex VIII, Section 9.1.3., because it is not adequate for the purpose of classification/labelling and risk assessment, as explained in the following. ECHA notes that information on fish toxicity after 96h exposure duration is needed for the purpose of classification/labelling and risk assessment, while reported supporting study was of only 48h exposure duration. Furthermore, as noted in the section 3 above in order to gather adequate results for the purpose of classification/labelling and risk assessment, analytical verification of exposure concentrations of the substance is necessary for the aquatic toxicity tests. Finally, ECHA notes that fulfilment of validity criteria of the used test guideline is not confirmed by you for the supporting study in the study summary reported in the registration dossier.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint and that a further review of PNECs will also take into account new test data from this test.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) fish acute toxicity test (test method EU C.1. / OECD TG 203) is the preferred test to cover the standard information requirement of Annex VIII, Section 9.1.3.

ECHA received your comments to the draft decision submitted during the 30-day commenting period. ECHA acknowledges your agreement to perform the requested test.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Fish, acute toxicity test (test method: EU C.1./OECD TG 203).

Notes for your consideration

Due to the volatility, degradability and adsorption potential of the substance 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, Chapter R7b* (version 4.0, June 2017), Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity tests requested under section 4-5 above and for calculation and expression of the result of the tests.

Furthermore, ECHA reminds you that substances are classified into chronic categories as hazardous to the aquatic environment on the basis of short-term and long-term aquatic toxicity information as described in the Figure 4.1.1. and Table 4.1.0 of the Annex I of Regulation No 1272/2008.

5. Effect concentrations based on the geometric mean measured test concentrations for the growth inhibition study in aquatic plants (Article 13(3))

Pursuant to Article 13(3) of the REACH Regulation the tests on substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in

accordance with other international test methods recognised by the Commission or the Agency as being appropriate.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

According to the OECD TG 201 "*the actual exposure concentrations may be difficult to define, especially for adsorbing substances tested at low concentrations. In such cases, disappearance of the test substance from solution by adsorption to the increasing algal biomass does not mean that it is lost from the test system. When the result of the test is analysed, it should be checked whether a decrease in concentration of the test substance in the course of the test is accompanied by a decrease in growth inhibition. If this is the case, application of a suitable model describing the decline of the concentration of the test substance (7) may be considered. If not, it may be appropriate to base the analysis of the results on the initial (nominal or measured) concentrations.*"

ECHA notes that in the technical dossier you have provided a study record for the growth inhibition study in aquatic plants (title of reference: [redacted]; reliability 2 (reliable with restrictions); analytical monitoring of exposure concentrations of the test material was performed). ECHA observes that you explained that "*Analysis of the test preparations at 72 hours showed a significant decline in measured test concentrations in the range of less than the limit of quantitation (LOQ). As the preliminary stability analyses indicated that the test substance was stable in culture medium, this decline was attributed to the absorption of the test substance to the algal cells. Whilst the preliminary recovery analyses conducted in the presence of algal cells indicated that no immediate absorption occurred, this does not preclude long-term adsorption over the test period.* [...] *As the test substance was known to be stable in aqueous test medium and the decline observed attributed to adsorption to algal cells it was considered that the algal cells present were exposed to equivalent 0-hour measured concentrations of the test substance throughout the test.*" As noted under section 3 above, the registered substance could be lost from the test medium by evaporation and degradation in addition to the adsorption. ECHA notes that there is no documentary evidence provided in the registration dossier supporting your conclusion that the test substance from the solution was lost exclusively by adsorption. Therefore, ECHA considers that the effect concentrations for the growth inhibition study in aquatic plants should be based on the calculated geometric mean measured test concentrations.

ECHA received your comments to the draft decision submitted during the 30-day commenting period. ECHA acknowledges your agreement that the substance effect concentration to be based on geometric mean measured test concentrations.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit in the regsitration dossier and use in the Chemical Safety Assessment of the substance effect concentrations based on the geometric mean measured test concentrations for the growth inhibition study in aquatic plants.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 1 March 2018.

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.

ECHA took into account your comments 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 compliance check decision does not prevent ECHA from initiating further compliance checks on the present 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 your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample 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 material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests 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 or imported by each registrant.

   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.