~~Confidential~~

Helsinki, 30 September 2021

Addressees
Registrants of HX_256-905-8 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
23/01/2018

Registered substance subject to this decision ("the Substance")
Substance name: Vinyl neodecanoate
EC number: 256-905-8
CAS number: 51000-52-3

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***5 July 2024***.

Requested information must be generated using the Substance unless otherwise specified.

A. Information required from all the Registrants subject to Annex VII of REACH

1. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)

2. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202)

B. Information required from all the Registrants subject to Annex VIII of REACH

1. In vivo mammalian erythrocyte micronucleus test in mice or rats, oral route; or In vivo mammalian bone marrow chromosomal aberration test in mice or rats, oral route; or In vivo mammalian alkaline comet assay in rats, oral route, on the following tissues: liver, glandular stomach and duodenum (triggered by Annex VIII, Section 8.4., column 2)

2. Adsorption/ desorption screening (Annex VIII, Section 9.3.1.; test method: OECD TG 121)

3. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

C. Information required from all the Registrants subject to Annex IX of REACH

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

2. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

3. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

4. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: EU C.25./OECD TG 309) at a temperature of 12 °C

5. Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: EU C.24./OECD TG 308) at a temperature of 12 °C

6. Identification of degradation products (Annex IX, 9.2.3.; test method: using an appropriate test method)

D. Information required from all the Registrants subject to Annex X of REACH

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rabbit or rat), oral route;
2. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route, specified as follows:
   - Ten weeks premating exposure duration for the parental (P0) generation Dose level setting shall aim to induce systemic toxicity at the highest dose level;
   - Cohort 1A (Reproductive toxicity);
   - Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation which shall be followed to weaning;

   You must report the study performed according to the above specifications. Any expansion of the study must be scientifically justified.

Reasons for the request(s) are explained in the following appendix/appendices:

- Appendix entitled "Reasons common to several requests";
- Appendix/Appendices entitled "Reasons to request information required under Annexes VII to X of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

For certain endpoints, ECHA requests the same study from registrants at different tonnages. In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given. Only one study is to be conducted; the registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants under Article 53 of REACH.

How to comply with your information requirements

To comply with your information requirements you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

The studies relating to biodegradation and bioaccumulation are necessary for the PBT assessment. However, to determine the testing needed to reach the conclusion on the persistency and bioaccumulation of the Substance you should consider the sequence in which these tests are performed and other conditions described in Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes".

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[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 on Reasons common to several requests

1. **Assessment of your read-across approach under Annex XI, Section 1.5.**

You seek to adapt the following information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- In vivo mutagenicity test (triggered by Annex VIII, Section 8.4., column 2)
- Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following appendices.

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. 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 (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6 and related documents.

A. Predictions for toxicological properties

You have provided a read-across justification document in IUCLID Section 13.

You read-across between the structurally similar substances:
- vinyl neononanoate, EC no. 259-160-7, CAS No. 54423-67-5 and
- vinyl 2-ethyl hexanoate, EC No. 202-297-4, CAS No. 94-04-2

as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties:
- *"Analysis of actual test data (phys/chem, environmental, mammalian, genotoxicity) indicates that the vinyl esters produce comparable effects or no effects at all.";*
- *"QSAR analysis supports the test results";*
- *"given the close similarity in the many endpoints available for comparison, the vinyl esters would also produce similar effects in other endpoint tests, and that the results can be "read-across"."*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

In your comments to draft decision you explain that "*An updated read across justification will be provided addressing the current documents short comings. In addition the QSAR estimations will be performed with every constituent of both the target and source and updated in a future submission to further strengthen the read across justification*." You also informed that "*The vinyl 2-ethylhexanoate will be removed from the read across approach as further studies have shown it to be unsuitable for read across, therefore, only the vinyl neononanoate will be used as the source substance*."

ECHA notes the following shortcomings with regards to predictions of toxicological properties:

1) *Characterisation of the source substance(s)*

According to the ECHA Guidance, "*the purity and impurity profiles of the substance and the structural analogue need to be assessed"*, and "*the extent to which differences in the purity and impurities are likely to influence the overall toxicity needs to be addressed, and where technically possible, excluded*".[2] The purity profile and composition can influence the overall toxicity/properties of the Substance and of the source substance(s). Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substance(s) should be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities.

Furthermore, whenever the Substance and/or the source substances are UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances qualitative compositional information of the individual constituents of the substances needs to be provided; as well as quantitative characterisation in the form of information on the concentration of the individual constituents of these substances; to the extent that this is measurable.[3]

However, your read-across justification document does not contain compositional information for the source substances which are UVCB substances. In your comments to draft decision you argue that "*Both the target and source substances are UVCB's and therefore do not have any impurities. In depth compositions are included in both substance dossier, however they will be added to the justification to allow for easy reference and comparison. The target and source vary only by a single carbon on the aliphatic end of the molecule. Both vary in their branching from straight chain to highly branched, in fact a case can be made that there is more variation within the substance than between these two substances*." You also state that these substances are UVCB because they have a large number of constituents although they are known and well defined.

Nevertheless, without consideration of the all constituents present in the source substances, no qualitative or quantitative comparative assessment of the compositions of the Substance and of the source substances can be completed. Therefore, ECHA considers that it is not possible to assess whether the attempted predictions are compromised by the composition of the source substances.

2) *Read-across hypothesis contradicted by existing data*

The ECHA Guidance[4] indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s). The observation of differences in the toxicological properties between the source substance(s) and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on the source substances. An explanation why such differences do not affect the read-across hypothesis needs to be provided and supported by scientific evidence.

[2] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.3.1
[3] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.5.5
[4] Guidance on information requirements and chemical safety assessment (version 6.0, July 2017), Chapter R.6, Section R.6.2.2.1.f

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar target and source substances cause the same type of effect(s).

In the comments to the draft decision, you disagree that the data are contradictory and argued that they are "*a demonstration of the intrinsic property of toxicity studies and their uncertainty*."

However, the results of the information on mutagenicity and repeated dose toxicity obtained with the source substances and target vary. More specifically:

i. Mutagenicity data

A positive result is observed in the *in vitro* chromosomal aberration study (OECD TG 473) conducted with your Substance while negative results are reported for equivalent studies conducted for the source substances.

In the comments to draft decision, you argue that "*The positive in vitro chromosome aberration on vinyl neodecanoate may be just such an example of uncertainty*." You agreed on performing an *in vivo* micronucleus study identical to the micronucleus study with the vinyl neononanoate to clarify the genotoxicity endpoint.

ii. Repeated dose toxicity data

Different types of effects were noted in the repeated dose toxicity data:

- hyaline droplets and karyomegaly in the renal cortex in high dose males treated with the source substance, vinyl neononanoate for 28-d, and only significantly elevated group mean male kidney weights at 1000 mg/m^3 (not supported by clinical chemistry or histopathology) after 90-d treatment with the Substance; in the comments to the draft decision you argue that these "*results are not inconsistent. It is stated in the OECD 422 study report, 'The only abnormal findings at necropsy in males were in the Group II males (enlarged and/or pale enlarged kidneys in three animals) and they are consistent with the histopathology findings. Group II (high dose) kidney weights were also larger than control but the difference was not statistically significant despite histopathologic indications of nephrosis. There were no dose—related findings in females.' This result would also be consistant with a 2-microglobenemia in addition thr result could be less pronounce due to the shorter duration in exposure of the OECD 422 verses the 90-day of the neononanoate. The staining wasn't carried out in either the OECD 422 or the inhalation study to show there were no hyaline droplet formation. Additionally, The OECD 413 is an inhalation study where the systemic absorption can vary substantially from an oral study thus the hyaline droplet effect could be less pronounced due to less absorption."* However, these statements are not substantiated by any scientific evidence.
- significant evidence of haematotoxicity in males and females (i.e. anemia) at 1000 mg/kg bw/d after 14-d treatment with the source substance, vinyl 2-ethylhexanoate, while no significant reduction in red blood cells in the OECD TG 408 with the source substance, vinyl neononanoate or in the OECD 422 with the Substance. No haematotoxicity was observed in any of the inhalation studies. In the comments to draft decision you inform that Vinyl 2-ethylhexanoate will be removed as a source substance.
- No effects on the nervous system in any of the studies provided for the source substance, vinyl neononanoate and the Substance. However, effects on the nervous system at 1000 and 2000 mg/kg/bw/d in the 14-d study observed with the source

substance, vinyl 2-ethylhexanoate. In your comments you inform that Vinyl 2-ethylhexanoate will be removed as a source substance.

On this basis, the available set of data on the target and source substances indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the structurally similar target and source substances cause the same type of effect(s). Therefore you have not demonstrated and justified that the properties of the source substance(s) and of the Substance are likely to be similar despite the observation of these differences.

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substances. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

2. Assessment of the (Q)SAR adaptation under Annex XI, Section 1.3.

You seek to adapt the following standard information requirements by applying (a) (Q)SAR approach(es) in accordance with Annex XI, Section 1.3:

- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Adsorption/ desorption screening (Annex VIII, Section 9.3.1.)

ECHA has considered the scientific and regulatory validity of your (Q)SAR adaptation(s) in general before assessing the specific standard information requirements in the following appendices.

Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

1. the prediction needs to be derived from a scientifically valid model,
2. the substance must fall within the applicability domain of the model,
3. results need to be adequate for the purpose of risk assessment or classification and labelling, and
4. adequate and reliable documentation of the method must be provided.

With regard to these conditions, we have identified the following issues:

1) Input structure not consistent with the substance identity information given in the registration dossier

Under ECHA Guidance R.6.1.7.3. a prediction is adequate for the purpose of classification and labelling and/or risk assessment if the following condition is met:

- representative structure(s) for the assessment are selected.

Your registration dossier provides the following information:

- In Section 1.1 of your technical dossier, you define the Substance as a UVCB;
- In Section 1.2, you indicate the following constituents in the composition of your Substance (only constituents that have typical concentration ≥ 1% (w/w) are listed here):
  1) vinyl neononanoate (EC No: 259-160-7), typical concentration ca. [redacted] % (w/w)
  2) ethenyl 2,2,4,4-tetramethylhexanoate (EC and CAS No not available), ca.[redacted] %

(w/w)
3) ethenyl 2,4-dimethyl-2-propylpentanoate (EC and CAS No not available), ca. [redacted] % (w/w)
4) ethenyl 2,2,6-trimethylheptanoate + ethenyl 2-ethyl-2,5-dimethylhexanoate (EC and CAS No not available), ca. [redacted] % (w/w)
5) ethenyl 2,2,5-trimethylheptanoate + ethenyl 2,2-diethyl-4-methylpentanoate (EC and CAS No not available), ca. [redacted] % (w/w)
6) ethenyl 2-ethyl-2,4-dimethylhexanoate (EC and CAS No not available), ca. [redacted] % (w/w)
7) ethenyl 2,3-dimethyl-2-propylpentanoate (EC and CAS No not available), ca. [redacted] % (w/w)
8) ethenyl 2-methyl-2-(propan-2-yl) hexanoate + ethenyl 2-methyl-2-propylhexanoate (EC and CAS No not available), ca. [redacted] % (w/w) [redacted] % (w/w)
9) ethenyl 2-ethyl-2,3-dimethylhexanoate (EC and CAS No not available), ca. [redacted] % (w/w)
10) ethenyl 2,2,3-trimethylheptanoate (EC and CAS No not available), ca. [redacted] %
11) ethenyl 2,2-dimethyloctanoate + ethenyl 2-ethyl-2-methylheptanoate (EC and CAS No not available), ca. [redacted] % (w/w)
12) ethenyl 2,2-diethyl-3-methylpentanoate (EC and CAS No not available), ca. [redacted] % (w/w)
13) vinyl neoundecanoate (EC No: 298-612-8), ca. [redacted] % (w/w)

- For the assessment, you provided predictions for the following structures: ethenyl 7,7-dimethyloctanoate, i.e. vinyl neodecanoate (EC No: 256-905-8).

You have considered vinyl neodecanoate (EC No: 256-905-8) as the representative structure. However, you failed to justify your selection of the representative structure.

ECHA disagrees with the representative structure you selected because the input structure applied for the model is not consistent with the substance identity in the dossier. Since the substance is a UVCB and has 13 constituents that have typical concentration ≥ 1% (w/w) and also other constituents < 1% concentrations (not listed here), it is not demonstrated that the selected structure (vinyl neodecanoate, EC No: 256-905-8) represents all the constituents of the Substance. As a result the provided estimates do not reliably predict properties of the Substance.

2) Lack of or inadequate documentation of the prediction (QPRF)

ECHA Guidance R.6.1.6.3 states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the model prediction(s), including the endpoint,
- a precise identification of the substance modelled,
- the relationship between the modelled substance and the defined applicability domain,
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You have not provided sufficient information about the prediction:

- Inadequate documentation of the substance modelled,
- Inadequate documentation of the relationship between the modelled substance and the defined applicability domain,

- Inadequate documentation of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

On the basis of issues (1) and (2), the information requirement is not fulfilled.

Therefore, your adaptations are rejected.

Additional issues related to (Q)SAR are addressed under the corresponding Appendices.

Appendix A: Reasons to request information required under Annex VII of REACH

1. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

You have provided the following information:

i. Freshwater**:** OECD TG 202, key study ([redacted] 2000),
ii. [redacted]**:** ISO Guideline 14699, key study ([redacted] 2007),
iii. A non-guideline acute toxicity study on Daphnia magna, supporting study (Stephenson R.R., 1983),
iv. OECD TG 202, an acute toxicity study on Acartia tonsa, supporting study ([redacted] 1991),
v. U.S.E.P.A. ECOSAR, ver. 0.99 QSAR model. Estimated EC50. Supporting study ([redacted] 2007).

We have assessed this information and identified the following issues:

1) non-conformity with the applicable test guideline

To fulfil the information requirement, a study must comply with OECD TG 202 and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met:

Information on the test material

- The composition of the test substance must be provided.

  However, you have identified the test material as "(EC 256-905-8)" in studies (i) to (iv), without further information, including composition. In the absence of composition information on the test material, the identity of the test material and its impurities cannot be assessed and you have not demonstrated that the test material is representative for the Substance.

Characterisation of exposure

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available.

  However, you have not provided performance parameters of the analytical method in studies (i) to (iv).

Additional requirements applicable to difficult to test substances

- if water-accommodated fractions (WAFs) are used, they must be prepared separately for each dose level.

  However, the WAFs were not prepared individually for each test concentration and all concentrations were prepared from a single stock WAF of 100 mg/L in studies (i) and (ii).
- if water-accommodated fractions (WAFs) are used, a preliminary study must be conducted to determine that saturation has been achieved.

  However, from the information submitted in your dossier, a preliminary study was not conducted to demonstrate the saturation of the test substance in the exposure

medium in studies (i) and (ii).

Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results in studies i-iv. More specifically, the test substance identity is limited to the EC-number and since the Substance is a UVCB with known composition, the test substance composition should also be provided to allow independent assessment of its suitability as the test substance. In addition, the performance parameters of the analytical method and details on what was analysed are not provided and therefore, analytical results of the test substance and its components at different concentrations and reliability of the test setup cannot be assessed.

The Substance is difficult to test (UVCB) and there are critical methodological deficiencies supporting the rejection of the study results in studies i and ii. More specifically, the applied WAFs were not prepared individually for each test concentration as recommended in OECD GD 23 and all concentrations in the current test originated from a single stock WAF of 100 mg/L. As a result all the diluted test concentrations may vary in their composition and since there is no detailed analytical information on the composition of different test concentrations, the reliability of the applied method cannot be assessed.

In your comments to the draft decision, you stated that the listed missing information in the key studies (i) and (ii) is available and that you will provide this information in an update of your registration dossier. However, the information in your comments concerning the applied WAF method in study (i) is not sufficient for ECHA to assess the reliability of the test since the provided details on the analytical methods and results are not sufficiently detailed for all constituents of the Substance. As the test method did not follow the current recommendation in OECD GD 23 to prepare WAF separately for each dose level, the reasoning for deviations must be explained in detail with supporting analytical information on all constituents at each dose level that its reliability can be assessed. Similarly, in the study (ii) no further information of the WAF method was provided and it is currently considered as a non-reliable test. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation).

Therefore, the requirements of OECD TG 202 are not met in studies (i) – (iv).

2) *Invalidity of the QSAR adaptation*

You have also provided supporting information using data from qualitative or quantitative structure-activity relationship (QSAR) in accordance with Annex XI, Section 1.3. As explained in section 2 of the Appendix on Reasons common to several requests, you have not provided justification for your selection of the representative structure and documentation of the prediction. Therefore, the adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

The Substance is a UVCB comprising constituents with different properties. OECD GD 23 describes various techniques appropriate for aquatic toxicity testing of UVCBs. If you select the Water Accommodated Fraction (WAF) approach, you must in addition to the above:

- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any

remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner;
- develop an appropriate analytical method and monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key components);

No Observable Effect Loading Rate (NOELR) values can be used for the hazard and risk assessment only if the corresponding loading rate is sufficiently low to be in the solubility range of most constituents (or is consistent with the PEC value) (ECHA Guidance, Appendix R.7.8.1-1, Table R.7.8-3).

2. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

You have provided the following information:
i. OECD TG 201 key study ([redacted] 2007),
ii. OECD 201 supporting study ([redacted] 1983),
iii. U.S.E.P.A. QSAR model: ver. 0.99, supporting study ([redacted] 2007),

We have assessed this information and identified the following issues:

1) non-conformity with the applicable test guideline

To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH). Therefore, the following specifications must be met:

- The composition of the test substance must be provided.

  However, you have identified the test material as "(EC 256-905-8)" only without further information in studies (i) and (ii), including composition. In the absence of composition information on the test material, the identity of the test material and its impurities cannot be assessed and you have not demonstrated that the test material is representative for the Substance.

- exponential growth in the control cultures is observed over the entire duration of the test.

  However, you did not report section-by-section growth rates in the control cultures in studies (i) and (ii);

- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%.

  However, you have not reported this information in studies (i) and (ii);

- the coefficient of variation of average specific growth rates during the whole test period in replicate control cultures is ≤ 7% in tests with *Pseudokirchneriella subcapitata.*

  However, you have not reported this information in studies (i) and (ii);

- one of the two alternative growth medium (*i.e.* the OECD or the AAP medium) is used. Any deviations from recommended test media must be described and justified.

  However, in your dossier, the test medium is described as *agarified liquid medium* (study i) or *prepared according to* [redacted] *(1978)* (study ii) without more detailed composition of the medium. In addition, you have not provided a justification as why you did not use one of the two alternative growth medium of OECD TG;

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range must be available.

  However, in study (i) you have not provided performance parameters of the analytical method;

- the concentrations of the test material are measured at least at the beginning and end of the test:
  1) at the highest, and
  2) at the lowest test concentration, and
  3) at a concentration around the expected EC_{50}.

  However, in study (i) the concentration of the test material was determined but it is not clear if the determination was done throughout the experiment and at what time points (i.e. at the beginning of the test and after 24, 48 and 72 hours of exposure). In study (ii) the test material concentration was not measured in the exposure media;

- the method for determination of biomass and evidence of correlation between the measured parameter and dry weight are reported.
- the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

  However, you have not reported any of the above information in studies (i) and (ii);

- Algal biomass is determined based on dry weight per volume, or alternatively as cell counts or biovolume using microscopy or an electric particle counter. If an alternative method is used (*e.g.* flow cytometry, *in vitro* or *in vivo* fluorescence, or optical density), a satisfactory correlation with biomass must be demonstrated over the range of biomass occurring in the test.

  However, in study (i) you report that algal biomass was determined using Coulter Multisizer particle counter. However, you have not reported evidence of correlation between the measured parameter and dry weight. In study (ii) no method for algal biomass determination is provided;

- if water-accommodated fractions (WAFs) are used, they must be prepared separately for each dose level.

  However, in study (i) the WAFs were not prepared individually for each test concentration and all concentrations were prepared from a single stock WAF of 100 mg/L;

- if water-accommodated fractions (WAFs) are used, a preliminary study must be conducted to determine that saturation has been achieved.

However, in study (i) a preliminary study was not conducted to demostrate the saturation of the test substance in the exposure medium.

Based on the above, the validity criteria of OECD TG 201 are not met in studies i and ii. as the growth and growth rated related information is not available and independent assessment of growth and different growth variables are not possible. There are also critical methodological deficiencies resulting in the rejection of the study results. More specifically, the composition of the test substance is not provided and it is not clear if the composition of the test substance is the same as the composition of the Substance. There is no reason provided why other than recommended test medium is used and its full composition is not described. In addition, performance parameters of the analytical method are not reported and it is not clear what were the time points when the test substance samples were taken for analyses in study i. Furthermore, effective concentration in study ii are not reliable since test material concentration was not measured in the exposure media.

The reporting of the methodology and results is insufficient as the algal biomass data is not reported in detail. Furthermore, the correlation between the measured variable and biomass (dry weight) is not demonstrated in study I and therefore, it is not clear how well the measured variable predicts biomass of algae. Similar weakness is observed in study ii, since the method of biomass determination is not provided and therefore, the reliability of the reported biomass cannot be assessed.

The Substance is a UVCB and difficult to test (low water solubility of 5.9 mg/L and log Kow is 4.9) and the applied WAFs were not prepared individually for each test concentration in study i. In principle, the preparation of a WAF stock solution from a single concentration for all other test concentrations is not methodologically acceptable as specified in OECD GD 23. Also, it was not demonstrated with preliminary test that the test substance had reached saturation concentration in the exposure medium of the applied WAF method.

In your comments to the draft decision, you stated that the listed missing information in the studies (i) and (ii) is available and that you will provide this information in an update of your registration dossier. However, the information in your comments concerning the applied WAF method in study (i) is not sufficient for ECHA to assess the reliability of the test since the provided details on the analytical methods and results are not sufficiently detailed for all constituents of the Substance. As the test method did not follow the current recommendation in OECD GD 23 to prepare WAF separately for each dose level, the reasoning for deviations must be explained in detail with supporting analytical information on all constituents at each dose level that its reliability can be assessed. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation).

As a result of these deficiencies in methods and reporting, the reliability of the methods and results cannot be assessed independently.

Therefore, the requirements of OECD TG 201 are not met in studies (i) and (ii).

2) *Invalidity of the QSAR adaptation*

You have also provided supporting information using data from qualitative or quantitative structure-activity relationship (QSAR) study (iii) in accordance with Annex XI, Section 1.3. As explained in section 2 of the Appendix on Reasons common to several

requests, you have not provided justification for your selection of the representative structure and documentation of the prediction. Therefore, the adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

As already explained above, the Substance is a UVCB and difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.1.

Appendix B: Reasons to request information required under Annex VIII of REACH

1. In vivo mammalian erythrocyte micronucleus test; or In vivo mammalian bone marrow chromosomal aberration test or In vivo mammalian alkaline comet assay

Under Annex VIII, Section 8.4, column 2 of REACH, the performance of an appropriate *in vivo* somatic cell genotoxicity study must be considered if there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII.

Your dossier contains positive results for the *in vitro* cytogenicity test which raises the concern for chromosomal aberration.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. To support your adaptation you provided the following studies with the analogue substance vinyl neononanoate, EC no. 259-160-7:

i. *In vivo* mammalian somatic cell study: cytogenicity / erythrocyte micronucleus (1991), (OECD TG 474);
ii. *In vivo* mammalian cell study: DNA damage and/or repair (1982).

As explained in section 1 of the Appendix on Reasons common to several requests your adaptation is rejected.

Therefore, the information requirement is not fulfilled.

In your comments to draft decision you agree with the performing of the requested study.

ECHA considers that an appropriate *in vivo* follow up mutagenicity study is necessary to address the concern identified *in vitro*.

i. Test selection

According to the ECHA Guidance Chapter R.7a, Section R.7.7.6.3, the mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) or the mammalian bone marrow chromosomal aberration test ("CA test", OECD TG 475) are suitable to follow up a positive *in vitro* result on chromosomal aberration if the Substance or its metabolite(s) will reach the target tissue. Alternatively, the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) is a suitable test to be performed. Therefore, the MN test, the CA test and the comet assay are suitable tests to follow up the chromosomal aberration concern identified for the Substance.

ii. Test design

a. MN test / CA test

In case you decide to perform a MN or CA assay, according to the test methods OECD TG 474 / OECD TG 475, the test must be performed in mice or rats. Having considered the anticipated routes of human exposure and the need for adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

Regarding the exposure of the target tissue, the applicable test guideline (OECD TG 474 / OECD TG 475) states "If there is evidence that the test substance(s), or its metabolite(s), will not reach the target tissue, it may not be appropriate to use this test". Additionally, a negative test result can be considered reliable if "Bone marrow exposure to the test substance(s) occurred". Accordingly, if the Substance is negative in this test, but it is not possible to

demonstrate that bone marrow exposure to the Substance occurred, then ECHA will consider any remaining uncertainty concerning the mutagenic potential of the Substance and whether to request any further information.

b. Comet assay

In case you decide to perform the comet assay according to the test method OECD TG 489, the test must be performed in rats. Having considered the anticipated routes of human exposure and the need for adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

iii. Germ cells

A subsequent germ cell genotoxicity study (TGR/OECD TG 488, or CA on spermatogonia/OECD TG 483, depending on the concern raised by the substance) may still be required under Annex IX or X of REACH, in case 1) an *in vivo* genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity.

Therefore, in case you decide to perform the comet assay, you may consider to collect the male gonadal cells collected from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, in accordance to Annex IX or X, Section 8.4., column 2, you should consider analysing the slides prepared with gonadal cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

2. Adsorption/ desorption screening

Adsorption/desorption screening is a standard information requirement under Annex VIII to REACH (Section 9.3.1.).

You seek to adapt the standard information requirements by applying (a) (Q)SAR approach(es) in accordance with Annex XI, Section 1.3. You have provided the following information:

- Adsorption coefficient (Koc) based on model PCKOCWIN (ver 1.66), (2007), O.E.C.D.

We have assessed this information and as explained in section 2 of the Appendix on common to several requests, you have not provided a justification for your selection of the representative structure and documentation of the prediction.

Therefore, the adaptation is rejected and the information requirement is not fulfilled.

3. Short-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

You have provided the following information:

i. OECD TG 203, key study ([redacted] 2007),
ii. A non-guideline acute toxicity study on fish similar to O.E.C.D. TG 203 ([redacted]),
iii. U.S.E.P.A. ECOSAR, ver. 0.99, supporting study ([redacted] 2007),

We have assessed this information and identified the following issues:

1) non-conformity with the applicable test guideline

To fulfil the information requirement, a study must comply with OECD TG 203 [and the requirements of OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test] (Article 13(3) of REACH). Therefore, the following specifications must be met:

- the composition of the test substance should be provided.

  However, you have identified the test material as "(EC 256-905-8)" in studies (i) and (ii), without further information, including composition. In the absence of composition information on the test material, the identity of the test material cannot be assessed and you have not demonstrated that the test material is representative for the Substance.

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (i.e. detection and quantification) and working range must be available.

  However, in study (i) you have not provided performance parameters of the analytical method.

- in semi-static tests, test concentrations are measured at least twice over one exposure period (before and after renewal of test solutions).

  However, you have deviated from this requirement in study (ii) and no analytical monitoring of exposure is reported.

- if water-accommodated fractions (WAFs) are used, they must be prepared separately for each dose level.

  However, in study (i) the WAFs were not prepared individually for each test concentration and as a result all concentrations were prepared from a single stock WAF of 100 mg/L;

- if water-accommodated fractions (WAFs) are used, a preliminary study must be conducted to determine that saturation has been achieved.

  However, in study (i) a preliminary study was not conducted to demonstrate the saturation of the test substance in the exposure medium.

Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically in study (i) the composition of the test substance is not provided and it is not clear if the composition of the test substance is the same as the composition of the Substance. In addition, performance parameters of the analytical method were not provided and the reliability of the analytical method is not shown. In the supporting study (ii) analytical monitoring was not performed at all. Due to these shortcomings in the characterisation of exposure to test material, it is not possible to assess exposure of the test animals to the test material.

The Substance is difficult to test (water solubility 5.9 mg/L and log Kow 4.9) and there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically, the applied WAFs were not prepared individually for each test concentration and using a WAF stock solution from a single concentration for all other test concentrations is not methodologically acceptable. Also, it was not demonstrated that the test substance had reached saturation concentration in the exposure medium in the preparation of the WAF stock solution.

In your comments to the draft decision, you stated that the listed missing information in the key study (i) is available and that you will provide this information in an update of your registration dossier. However, the information in your comments concerning the applied WAF method in study (i) is not sufficient for ECHA to assess the reliability of the test since the provided details on the analytical methods and results are not sufficiently detailed for all constituents of the Substance. As the test method did not follow the current recommendation in OECD GD 23 to prepare WAF separately for each dose level, the reasoning for deviations must be explained in detail with supporting analytical information on all constituents at each dose level that its reliability can be assessed. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation).

Therefore, the requirements of OECD TG 203 are not met.

2) Invalidity of the QSAR adaptation

You have also provided supporting information using data from qualitative or quantitative structure-activity relationship (QSAR) study (iii) in accordance with Annex XI, Section 1.3. As explained in section 2 of the Appendix on Reasons common to several requests, you have not provided justification for your selection of the representative structure and documentation of the prediction. Therefore, the adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

As already explained above, the Substance is a UVCB and difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.1.

Appendix C: Reasons to request information required under Annex IX of REACH

1. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX to REACH.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. To support your adaptation you provided the following studies with the analogue substance vinyl neononanoate, EC no. 259-160-7:
i. Developmental toxicity study in rats, OECD TG 414, oral route, ([redacted], 2013)
ii. Developmental toxicity study in rabbits, OECD TG 414, oral route, ([redacted], 2017)

You also provided the following study with the Substance:
iii. Combined Repeated dose Toxicity with the Reproduction / Developmental Toxicity Screening Test, OECD TG 422, oral route, ([redacted], 2005)

We have assessed this information and identified the following issues:

A. Invalid Read-across adaptation

In your dossier you provided two studies (i. and ii. above) with the analogue substance vinyl neononanoate, EC no. 259-160-7. However, as explained in section 1 of the Appendix on Reasons common to several requests your adaptation is rejected.

In the comments to the draft decision you inform on your intention to update the read across justification addressing the current shortcomings.

B. Non-conformity of study iii. *with the applicable test guideline*

To fulfil the information requirement, a study must comply with OECD TG 414 (Article 13(3) of REACH). Therefore, the following specifications must be met:

- external, skeletal and visceral malformations and variations have to be investigated as described in OECD TG 414.

  However, you have provided a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (OECD TG 422). This study does not inform on skeletal and visceral malformations and variations as required by OECD TG 414. Hence, this study does not fulfil the requirements of the appropriate test guideline.

On this basis, the information requirement is not fulfilled.

Test design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[5] administration of the Substance.

[5] ECHA Guidance R.7a, Section R.7.6.2.3.2.

2. Long-term toxicity testing on aquatic invertebrates

AND

3. Long-term toxicity testing on fish

Long-term toxicity testing on aquatic invertebrates and fish are information requirements under Annex IX to REACH (Sections 9.1.5. and 9.1.6. respectively).

You have provided the following information:

- a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following statement:

  "In accordance with column 2 of REACH Annex IX, the long-term testing on invertebrates study (required in Section 9.1) is not required due to the Chemical Safety Assessment according to Annex I does not indicate the need to investigate further the effects on aquatic organisms."

In your comments to the draft decision you also state the following:

- *"Currently the substance is handled under strictly controlled conditions during manufacture except for the final stage of loading before the material is shipped to the customer.*

  Based on the use and disposal of the chemical, there is a "low potential for exposure" both to workers and to the general population following environmental release. Exposure to the substance may occur at workplaces where it is manufactured during loading and unloading operations, quality control sampling, or maintenance operations. Based on physical properties, the primary workplace exposure would be through dermal contact.

  The substance is handled in industrial manufacturing and processing facilities. Therefore, minimal consumer exposure is foreseen, since the consumer is only indirectly exposed through the use of the applications and uptake is expected to be low. There is no release to water air or soil. Waste from production is incinerated. Once the results of the acute aquatic studies have been clarified and updated in the dossier data will be present for all three trophic level. At the very least these long term aquatic endpoints can be waived due to exposure considerations. The environmental risks are certainly controlled."

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. It must be understood as a trigger for providing further information on aquatic invertebrates if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

Furthermore, with regard to your comments, ECHA understands that you intend to adapt this information requirement under Annex XI, Section 3. However, in the absence of an unambiguous reference to the provision(s) of Annex XI, Section 3 you intend (i.e. 3.2(a), (b) or (c)) to use and of the corresponding supporting information, ECHA cannot currently assess the validity of such adaptation. Please note that this decision does not take into account

updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation").

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.1.

4. Simulation testing on ultimate degradation in surface water

Simulation testing on ultimate degradation in surface water is an information requirement under Annex IX to REACH (Section 9.2.1.2.).

You have provided an adaptation under Annex IX, Section 9.2., Column 2 with the following justification:

> *"In accordance with column 2 of REACH Annex IX , The Biodegradation in water and sediments simultion test, (required in Section 9.2.1.2 and 9.2.1.4) does not need to be conducted as the chemical safety assessment according to Annex I does not indicate the need to investigate further the degradation of the substance and its degradation products."*

We have assessed this information and identified the following issue[s]:

Under Section 9.2., Column 2 of Annex IX to REACH, the study may be omitted if the chemical safety assessment (CSA) does not indicate the need for further biotic degradation testing. The CSA does indicate such need (Annex I, Section 4; Annex XIII, Section 2.1) if, for instance, the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4). This is the case if the Substance itself or any of its constituent or impurity present in concentration ≥ 0.1% (w/w) or relevant transformation/degradation product meets the following criteria:

- it is potentially persistent or very persistent (P/vP) as:
- it is not readily biodegradable (*i.e.* <60/70% degradation in an OECD 301D), and
- it shows <70% degradation within 7/14 days in an inherent biodegradation test OECD 302C and/or lag phase > 3 days;
- it is potentially bioaccumulative or very bioaccumulative (B/vB) as:
- it has a high potential to partition to lipid storage (*e.g.* log K_{ow} > 4.5);
- it has a calculated BCF > 2000;
- it meets the T criteria set in Annex XIII: NOEC or EC10 < 0.01 mg/L or classification as carc. 1A or 1B, muta. 1A or 1B, repro. 1A, 1B or 2, or STOT RE 1 or 2.

Your registration dossier provides the following:

- The Substance is not readily biodegradable (14-17% degradation after 28 days in OECD TG 301D
- The Substance is not inherently biodegradable (3-5% degradation after 28 days in OECD TG 302C with lag phase of > 28 days);
- The Substance has a high potential to partition to lipid storage (Log K_{ow} of 4.9 based on OECD TG 107);
- The Substance may meet the B criterion: the provided BCF estimate is based on the

ku/kd ratio, where the kd (depuration rate) is from the reported dietary test and the applied ku (uptake rate) is from one model only. However, there is no justification why the applied ku value is the most appropriate one for the BCF estimation and therefore there is high uncertainty in the reliability of the reported BCF value;

Furthermore, the information in your dossier is currently incomplete, since endpoints covering genotoxicity, developmental toxicity, long-term toxicity in fish and aquatic invertberates are not in compliance with standard information requirements and therefore: it is not possible to conclude on the toxicity of the Substance (see Appendices B.1, C.1-C.3 and D1. and D.2 of this decision). The information above indicates that the Substance is a potential PBT/vPvB substance.

Therefore, you have not demonstrated that the CSA does not indicate the need for further biotic degradation testing and your adaption is rejected.

In your comments to the draft decision, you have provided the same comment as in sections C.2 and C.3. As stated above, the CSA does indicate the need for further biotic degradation testing (Annex I, Section 4; Annex XIII, Section 2.1) since the substance is considered as a potential PBT/vPvB substance (ECHA Guidance R.11.4).

On this basis, the information requirement is not fulfilled.

Study design

Simulation degradation studies must include two types of investigations (ECHA Guidance R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

You must perform the test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (ECHA Guidance R.11.4.1.1.3.).

The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

As specified in ECHA Guidance R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test substance concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Therefore, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents. By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (ECHA Guidance R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

Relevant transformation/degradation products are at least those detected at ≥ 10% of the

applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 309; ECHA Guidance R.11.4.1.).

5. Sediment simulation testing

Sediment simulation testing is an information requirement under Annex IX to REACH (Section 9.2.1.4.) for substances with a high potential for adsorption to sediment.

You have provided an adaptation under Annex IX, Section 9.2., Column 2 as explained in section C.3 above.

The Substance has a low water solubility (5.9 mg/L), high partition coefficient (log K_{ow} 4.9) and high adsorption coefficient (log $K_{oc,soil}$ 2.7) and therefore has high potential for adsorption to sediment.

As explained in section C.3 above, the information in your dossier indicates that the Substance is a potential PBT/vPvB substance.

In your comments to the draft decision, you have provided the same comment as in sections C.2 and C.3. As stated above, the CSA does indicate the need for further biotic degradation testing (Annex I, Section 4; Annex XIII, Section 2.1) since the substance is considered as a potential PBT/vPvB substance (ECHA Guidance R.11.4).

Therefore, you have not demonstrated that the CSA does not indicate the need for further sediment simulation testing.

Study design

Simulation degradation studies must include two types of investigations (ECHA Guidance R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

In accordance with the specifications of OECD TG 308, you must perform the test using two sediments. One sediment should have a high organic carbon content (2.5-7.5%) and a fine texture, the other sediment should have a low organic carbon content (0.5-2.5%) and a coarse texture. If the Substance may also reach marine waters, at least one of the water-sediment systems should be of marine origin.

The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 308.

In accordance with the specifications of OECD TG 308, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents (ECHA Guidance R.7.9.4.1.). By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (ECHA Guidance R.11.4.1.1.3.). Further recommendations may

be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website.

Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 308; ECHA Guidance R.11.4.1.).

6. Identification of degradation products

Identification of degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).

> You have provided no information on the identity of transformation/degradation products for the Substance.
>
> Therefore, this information requirement is not met.
>
> This information is required for the purpose of the PBT/vPvB assessment (Annex I, Section 4) and the risk assessment (Annex I, Section 6) of the Substance.

In your comments to the draft decision, you have provided the same comment as in sections C.2 and C.3. As stated above, the CSA does indicate the need for further biotic degradation testing (Annex I, Section 4; Annex XIII, Section 2.1) since the substance is considered as a potential PBT/vPvB substance (ECHA Guidance R.11.4).

On this basis, the information requirement is not fulfilled.

Study design

Regarding the selection of appropriate and suitable test method(s), the method(s) will have to be substance-specific. Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported, when analytically possible. In addition, degradation half-life, log K_{ow} and potential toxicity of the transformation/degradation may need to be investigated. You may obtain this information from the degradation studies requested in Appendices C.4 and C.5 or by some other measure. If any other method is used for the identification of the transformation/degradation products, you must provide a scientifically valid justification for the chosen method.

To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (Appendix C.4) must be conducted at 12°C and at a test concentration < 100 µg/L. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline, *e.g.* 20°C) and at higher application rate (*i.e.* > 100 µg/L).

To determine the degradation rate of the Substance, the requested study according to OECD TG 308 (Appendix C.5) must be conducted at 12°C and at a test material application rate reflecting realistic assumptions. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline) and at higher application rate (*e.g.* 10 times).

Appendix D: Reasons to request information required under Annex X of REACH

1. Pre-natal developmental toxicity study in a second species

Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is a standard information requirement under Annex X to REACH.

You have adapted the information requirement according to Annex XI, Section 1.5. In support of your adaptation, you provided the following studies with the analogue substance vinyl neononanoate, EC no. 259-160-7:

i. Developmental toxicity study in rats, OECD TG 414, oral route, ([redacted], 2013);
ii. Developmental toxicity study in rabbits, OECD TG 414, oral route, ([redacted], 2017).

You also provided the following study with the Substance:

iii. Combined Repeated dose Toxicity with the Reproduction / Developmental Toxicity Screening Test, OECD TG 422, oral route, ([redacted], 2005).

For the reasons already explained under Appendix C.1, none of the studies submitted fulfils the information requirement. In the comments to the draft decision you inform on your intention to update the read across justification to address the current deficiencies.

Test design

A PNDT study according to the OECD TG 414 study should be performed in the rabbit or rat as the preferred second species, depending on the species tested in the first PNDT study (request C.1 in this decision).

The study shall be performed with oral[6] administration of the Substance.

2. Extended one-generation reproductive toxicity study

The basic test design of an Extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is an information requirement under Annex X to REACH. Furthermore Column 2 of Section 8.7.3. defines when the study design needs to be expanded.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. To support your adaptation you provided the following justification:

> *"It is intended that data will be read across from vinyl neononanoate to vinyl neodecanoate. […] The results of this testing will be evaluated in conjunction with existing data for this substance, and read-across will be applied to vinyl neodecanoate if the study data is not inconsistent […]"*

We have assessed this information and identified the following issues:

Under Article 10 (a)(vii) and (ix) in conjunction of Articles 13 and 40 of the REACH Regulation, to fulfil an information requirement registrants must provide either one of the following pieces of information:

- A robust study summary compliant study, performed according to the relevant test method (EU test method or OECD test guideline) and fulfilling its validity criteria; or
- A valid adaption foreseen either in column 2 of the relevant Annex and section of REACH or in Annex XI, including a well-documented justification and relevant supporting

[6] ECHA Guidance R.7a, Section R.7.6.2.3.2.

information; or
- A proposal for further testing, when the registrant identifies a data gap which is relevant to information required from Annex IX and/or X.

However:
- the information you provided is not a robust study summary;
- you invoke a read-across hypothesis without providing any EOGRTS study perfomed on an analogue substance and from which the property of the Substance could be predicted.
- the information you provided is not a proposal for testing, but a statement that a future test will be submitted. Therefore, ECHA cannot examine this information as a testing proposal under Article 40.

Therefore, the information requirement is not fulfilled. In the comments to the draft decision you inform on your intention to update the read across justification to address the current deficiencies.

The specifications for the study design

i. Premating exposure duration and dose-level setting

The length of premating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required to obtain results adequate for classification and labelling and /or risk assessment. There is no substance specific information in the dossier supporting shorter premating exposure duration (ECHA Guidance R.7a, Section R.7.6.). Moreover, in this specific case ten weeks exposure duration is supported by the lipophilicity of the Substance (logKow = 4.9 at 20°C) to ensure that the steady state in parental animals has been reached before mating.

Therefore, the requested premating exposure duration is ten weeks.

In order to be compliant and not to be rejected due to too low dose levels, the highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects. A descending sequence of dose levels should be selected in order to demonstrate any dose-related effect and to establish NOAELs.

If there is no relevant data to be used for dose level setting, it is recommended that range-finding results are reported with the main study.

You have to provide a justification with your study results that demonstrates that the dose level selection meets the conditions described above.

ii. Cohorts 1A and 1B

Cohorts 1A and 1B belong to the basic study design and must be included.

Species and route selection

The study must be performed in rats with oral[7] administration.

[7] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Further expansion of the study design

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and/or Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if relevant information becomes available from other studies or during the conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance[8].

[8] ECHA Guidance R.7a, Section R.7.6.

Appendix E: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

1. Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

2. Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[9].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[10].

[9] https://echa.europa.eu/practical-guides
[10] https://echa.europa.eu/manuals

Appendix F: General recommendations when conducting and reporting new tests for REACH purposes

A. Strategy for the PBT/vPvB assessment

You are advised to consult ECHA Guidance R.7b (Section R.7.9.), R.7c (Section R.7.10) and R.11 on PBT assessment to determine the sequence of the tests needed to reach the conclusion on PBT/vPvB. The guidance provides advice on 1) integrated testing strategies (ITS) for the P, B and T assessments and 2) the interpretation of results in concluding whether the Substance fulfils the PBT/vPvB criteria of Annex XIII.

In particular, you are advised to first conclude whether the Substance fulfils the Annex XIII criteria for P and vP, and then continue with the assessment for bioaccumulation. When determining the sequence of simulation degradation testing you are advised to consider the intrinsic properties of the Substance, its identified uses and release patterns as these could significantly influence the environmental fate of the Substance. You must revise your PBT assessment when the new information is available.

B. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in ECHA Guidance R.11 (Section R.11.4.2.2), you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

Appendix G: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 06 March 2020.

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

ECHA took into account your comments and did not amend the requests.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments and referred the modified draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee unanimously agreed on the draft decision in its MSC-75 written procedure. ECHA adopted the decision under Article 51(6) of REACH.

Appendix H: List of references - ECHA Guidance[11] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[12]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[13]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[14]

[11] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[12] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[13] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[14] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix I: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.