~~Confidential~~

Helsinki, 15 October 2020

Addressees
Registrants of HX_202-297-4 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
30/07/2018

Registered substance subject to this decision ("the Substance")
Substance name: Vinyl 2-ethylhexanoate
EC number: 202-297-4
CAS number: 94-04-2

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 ***21 July 2022***.

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. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. /OECD TG 471) using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102

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

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

2. Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4.; test method: EU C.11/ OECD TG 209)

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

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

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)

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

- Appendices entitled "Reasons to request information required under Annexes VII to IX 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 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.

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".

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

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

- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Acute aquatic invertebrate toxicity (Annex VII, Section 9.1.2)
- Acute fish toxicity (Annex VIII, Section 9.1.3)
- Toxicity to microorganisms (Annex VIII, Section 9.1.4)

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[2] and related documents[3, 4].

Predictions of toxicological and ecotoxicological properties

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

You read-across between the structurally similar substances, vinyl neononanoate CAS No. 54423-67-5, vinyl neodecanoate EC No. 256-905-8 (CAS No. 51000-52-3) / as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological and ecotoxicological 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. This confirms that the 'active' function group in the esters produce the same effects (or no effects) and that the carbon difference in one of the alkyl chains does not significantly affect the toxicological properties of the vinyl esters.

We conclude that 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

[2] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9

[3] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

[4] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

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.

ECHA notes the following shortcomings with regards to the predictions of the properties of the substance.

1) Common deficiency for the predictions of toxicological and ecotoxicological properties

Annex XI, Section 1.5 of the REACH Regulation provides that "*substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group.*"

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*". The purity profile and composition can influence the overall toxicity/properties of the Substance and of the source substance(s).[5] 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 category members 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.[6]

However, your read-across justification document does not contain compositional information for the source substances which are UVCB substances.

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) Deficiency on the predictions of toxicological properties

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. The ECHA Guidance[7] 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

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

is a warning sign. An explanation for such a difference resulting in a contradiction between the similarities in properties claimed in the read-across hypothesis and the observation of different properties needs to be provided and supported by scientific evidence.

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).

However, the results of the information on repated dose toxicity obtained with the source substances and target vary. Specifically, you stated that:

"The results in all three studies for these three vinyl esters suggest similar 'biological effects". A weight-of-evidence assessment approach suggests that the liver enlargement is an adaptive normal "biological" response, and not a toxic effect. In addition, both neodecanoate and the neononanoate vinyl esters exhibited renal effects characteristic of "male rat nephropathy". The NOAEL for both vinyl 2-ethylhexanoate and vinyl neononanoate in similar 14-day oral rat studies is 200 mg/kg/day based on increased mean liver weights at the higher doses.

While we believe that neither the compensatory effects in the liver nor the male rat nephropathy are indicative of a human health hazard, the similarity of 'biological effects' produced by the neodecanoate and the neononanoate vinyl esters, as well as the lack of any significant toxic findings, strongly supports that these two substances can be 'read-across' for other toxicological endpoints. "

The available set of data on the target and source substances indicates differences in the toxicological properties of the substances. Specifically, the different types of effects were:

- hyaline droplets and karyomegaly in the renal cortex in high dose males treated with Vinyl neononanoate for 28-d, and only significantly elevated group mean male kidney weights at 1000 mg/m3 (not supported by clinical chemistry or histopathology) after 90-d treatment with Vinyl neodecanoate,
- significant evidence of hematotoxicity in males and females (anemia i.e) at 1000 mg/kg bw/d after 14-d treatment with the substance while no signifcant reduction in red blood cells in the OECD 408 with Vinyl neononanoate (the reduction observed was within the historical cotrol range) nor in the OECD 422 with Vinyl neodecanoate. No hematotoxicity was observed in any of the inhalation studies.
- effects on the nervous system at 1000 and 2000 mg/kg/bw/d in the 14-d study with the substance. No effects on the nervous system in any of the studies provided for the source substances.
- the substance caused developmental effects at 750 mg/kg bw/d in the absence of maternal toxicity while no developmental effects effects were seen in a screening study with Vinyl Neodecanoate at 1000 mg/kg bw/d.

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.

3) Source studies deficient for aquatic toxicity

Annex XI, section 1.5. requires that in all cases results should have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3) of REACH.

As detailed below under the respective information requirements some of the source studies provided have criticial deficiencies and are not adequate to meet the information requirement.

A. 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 substance. 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.

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

1. *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)

An *in vitro* gene mutation study in bacteria is a standard information requirement in Annex VII to REACH.

You have provided a key study in your dossier:

i. OECD Guideline 471 (Bacterial Reverse Mutation Assay) ([redacted] 1991) with the following strains, TA 1535, TA 1537, TA 98 and TA 100 which all gave negative results.

We have assessed this information and identified the following issue:

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471 (1997). One of the key parameters of this test guideline includes:

a) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101)

However, the reported data for the study you have provided did not include results for the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101).

The information provided does not cover one of the key parameters required by OECD TG 471.

Therefore, the information requirement is not fulfilled.

In your comments to the draft decision you agreed to perform the study.

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

Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1) is a standard information requirement in Annex VII to REACH.

You have adapted this information requirement under Section 1.5, Annex XI to REACH by providing a key study ([redacted] 2000) conducted according to OECD Guideline 202 using the analogue substance vinyl neodecanoate EC No. 256-905-8 (CAS No. 51000-52-3):

We have assessed this information and identified the following issues:

1) For the reasons explained in section "Appendix on Reasons common to several requests", your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5 (read-across).

2) *Inadequate source study*

Annex XI, section 1.5. requires that in all cases results should have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3) of REACH, in this case OECD TG 202. Therefore, the following requirements must be met:

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;
- The effect values can only be based on nominal or measured initial concentration if the concentration of the test material has been satisfactorily maintained within 20 % of the nominal or measured initial concentration throughout the test (see also ECHA Guidance R.7b, Section R.7.8.4.1);

Reporting of the methodology and results

- The number of immobilised daphnids is determined at 24 and 48 hours. Data are summarised in tabular form, showing for each treatment group and control, the number of daphnids used, and immobilisation at each observation;
- Adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided;

In your registration dossier you report:

- Analysis of treatment media was conducted by HPLC with UV-detection after dilution of SPE.
- Effect concentrations based on the measured concentrations of vinyl neodecanoate (EC: 256-905-8; CAS: 51000-52-3) without specifying the measured constituents and impurities of the test substance;
- The number of immobilised daphnids at the end of the test, i.e. after 48 hours of exposure;
- The analytical method having the recovery of dilution method of 80 -101% and the recovery of SPE method 48-85% (mean 67%) and hence a correction was used on measured concentrations.

The submitted information on the Short-term toxicity test on aquatic invertebrates (i) did not contain details on the used analytical method and detailed results of the analytical monitoring as required by the OECD TG 202. Futher, the substance tested is a UVCB and its constituents have a range of water solubility and the study was conducted using the water accommodated fractions (WAFs) method. While analytical monitoring to verify the presence of the dissolved fraction took place, the identity of the constituents and their concentration in this fraction is not reported. Based on this it is not clear which constituents of the test substance were used to define the reported effect concentrations. In addition the data was not reported as required, i.e. in tabular form, showing results for each treatment group and control, the number of daphnids used, and immobilisation at each observation during the course of the study. As a result, the reported study (i) is not considered as valid.

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

3. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is a standard information requirement in Annex VII to REACH (Section 9.1.2).

You have provided the following key study conducted with the Substance:

i. 96-hour Algal Inhibition to the Freshwater Algae *Selenastrum capricornutum*, EPA OPPTS 850.5400/OECD TG 201 ([redacted] 2004).

We have assessed this information and identified the following issues:

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

Validity criteria

- Exponential growth in the control cultures is observed over the entire duration of the test;
- At least 16-fold increase in biomass is observed in the control cultures by the end of the test;
- 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%;
- 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* (previously named as *Selenastrum capricornutum)*.

Technical specifications impacting the sensitivity/reliability of the test

- The test duration is 72 hours. However, for slow-growing species (*i.e.* specific growth rate < 0.92 day^{-1} in the control), the test duration must be extended until the biomass in the control cultures increases by at least 16-fold;
- Three replicates at each test concentration and at least three replicates for controls (including solvent controls, if applicable) are included;
- 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;

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. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;
- The test media prepared specifically for analysis of exposure concentrations during the test is treated identically to those used for testing (*i.e.* inoculated with algae and incubated under identical conditions);
- 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}.

  For volatile, unstable or strongly adsorbing test substances, additional samplings for analysis at 24 hour intervals is required.
- If the concentration of the test material has not been maintained within 20 % of the nominal or measured initial concentration throughout the test, results must be based on the geometric mean of measured concentrations during exposure or on a model describing the decline of the concentration of the test material.

Reporting of the methodology and results

- The test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);
- The test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);
- 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 must at least daily during the test period are reported in a tabular form;
- Microscopic observation performed to verify a normal and healthy appearance of the inoculum culture are reported. Any abnormal appearance of the algae at the end of the test is reported;
- Adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided;

In your registration dossier under key study (i):

Validity criteria
- Section-by-section growth rates were not reported;
- The initial biomass and the biomass at the end of the test were not reported;
- The mean coefficient of variation for section-by-section specific growth was not reported;
- The coefficient of variation of average specific growth rates during the whole test period in replicate control cultures was not reported;

Technical specifications impacting the sensitivity/reliability of the test
- The number of replicates was not reported;
- The test medium is described as freshwater. You have not provided a justification as why you did not use one of the two alternative growth media of OECD TG 201;

Characterisation of exposure
- You have not provided performance parameters of the analytical method (reported specificity, recovery efficiency, precision, limits of determination);
- The concentration of the test material was determined only as the verification of the nominal dose (i.e. concentration) and not in the test vessels during the course of the test;
- The test media prepared specifically for analysis of exposure concentrations was not inoculated with algae;

Reporting of the methodology and results
- On the test design, you have not specified number of replicates and test vessel size or volume;
- On the test procedure, you have not specified culturing apparatus and light intensity and quality (source, homogeneity);
- Tabulated data on the algal biomass determined daily for each treatment group and control are not reported;
- Algal biomass is not reported;

Additionally, in your comments to the draft decision you state the following: "*Additional testing outside the algae test would need to be conducted to support the retention of test material in the test system. This cannot be done in the official algae test due to the nature of the test system. It Is not the standard procedure to ever take samples from test solutions during the test for algae tests, nor is it recommended per guidelines to take termination samples for dose verification due to the nature of algal cells and their disruption in chemical analysis.*"

ECHA notes that according to the OECD TG 201 the characterisation of the exposure should be performed in the test media prepared specifically for analysis of exposure concentrations during the test and treated identically to those used in for testing, i.e. they should be inoculated with algae and incubated under identical conditions. This means that

parallel test vessels for chemical analyses are part of the test design. Furthermore, concentrations in the test media should be provided at least at the beginning and at the end of the algae test. Therefore, according to the OECD TG 201 you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. The OECD TG 201 also requires that, if it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values.

Based on the above, the validity criteria of OECD TG 201 are not met due to critical methodological deficiencies resulting in the rejection of the study results. More specifically exponential growth, at least 16-fold increase in biomass, section-by-section specific growth rates and coefficient of variation of average specific growth rates during the whole test period in controls were not reported. Without this information normal growth and variability in the test system cannot be verified. In addition, characterisation of the test exposures, i.e. reliable analytical method, test media prepared specifically for analysis of exposure concentrations and measurement of the test substance concentration at the beginning and end of the study were not reported. As a result, the reported test concentrations may not reflect the actual test substance concentrations in the test media and therefore the reported effect concentrations (EC50 and NOEC) are not reliable measures of effects. In addition, missing information on the test method does not allow independant assessment of the reliability of the applied test methods and whether the requirements of the OECD TG 201 were followed. Also the reporting detail of the results is not sufficient to conduct an independent assessment of some validity criteria (e.g. growth).

Therefore, the information requirement is not fulfilled.

In your comments to the draft decision you agreed to add missing information to the robust study summary. You also stated that in some cases the specific test requirement is met. In order to prove this statement, ECHA wants to highlight that such information should also be added to the robust study summary.

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

1. Short-term toxicity testing on fish

Short-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex VII to REACH.

You have adapted this information requirement under Section 1.5, Annex XI to REACH by providing a key study ([redacted] 2000) conducted according to OECD Guideline 203 using the analogue substance vinyl neodecanoate EC No. 256-905-8 (CAS No. 51000-52-3):

We have assessed this information and identified the following issues:

1) For the reasons explained in section "Appendix on Reasons common to several requests", your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5 (read-across).

2) *Inadequate source study*

Annex XI, section 1.5. requires that in all cases results should have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3) of REACH, in this case OECD TG 203. Therefore, the following requirements must be met:

Validity criteria
- The analytical measurement of test concentrations is conducted;

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 is available;
- In semi-static tests, test concentrations are measured at least twice over one exposure period (before and after renewal of test solutions). If the concentrations of the test material:

  a) are expected to remain within ± 20 % of the nominal, then the test substance concentration is determined in the highest and lowest test concentrations, and a concentration around the expected LC50.
  b) are expected to decline by more than 20%, analytical monitoring is conducted on all test concentrations with an additional determination on the other exposure period(s);

Reporting of the methodology and results
- Adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations are provided;

In your registration dossier under the key OECD TG 203 study:

Validity criteria
- The analytical measurement of test concentrations were reported only at the beginning of the test. In addition, the test substance is a UVCB and there is no information on which constituents were analysed and reported;

Characterisation of exposure

- Analytical method "HPLC with UV-detection subsequent to either dilution or concentration by solid phase extraction (SPE)" was reported, no further details on 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 were included;
- Test substance concentrations were measured in the diluted stock solutions only, not as recommended in the test guideline (i.e. at least twice over one exposure period, before and after renewal of test solutions).

Reporting of the methodology and results

- Adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations were not reported;

Based on the above, the validity criteria of OECD TG 203 are not met. There are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the analytical measurement of test concentrations were performed only at the beginning of the test, not before and after the renewal as required in the test guideline. In addition, no further details on the quantification method of the test material in test media or performance parameters of the analytical method were reported. Futher, the test substance is a UVCB and there is no information on which constituents were analysed and included in the reported test concentrations. As a result, the reported test concentrations may not reflect the actual test substance concentrations in the test media throughout the test and therefore the reliability of the reported effect concentrations (EC50 and NOEC) cannot be independently assessed.

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

In your comments to the draft decision you agreed to perform the study.

2. Activated sludge respiration inhibition testing (Annex VIII, Section 9.1.4)

Activated sludge respiration inhibition testing is a standard information requirement in Annex VII to REACH.

You have adapted this information requirement under Section 1.5, Annex XI to REACH by providing a key study ([redacted] 2010) conducted according to OECD Guideline 209 using the analogue substance vinyl neodecanoate EC No. 256-905-8 (CAS No. 51000-52-3):

1) For the reasons explained in section "Appendix on Reasons common to several requests", your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5 (read-across).

Therefore, the provided study is rejected and the information requirement is not fulfilled.

In your comments to the draft decision you agreed to perform the study.

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

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 in Annex IX to REACH.

You have provided the following adaptation according to Annex XI, Section 1.5.:

"A test proposal for an OECD 408 90-day repeat dose toxicity study has been submitted in the Registration dossier for vinyl neononanoic acid and the results of the study will be entered here once the study has been approved and completed. In accordance with section 1.5 of REACH Annex XI, similarity "(1) a common functional group" the study does not need to be conducted this substances', vinyl 2-ethylhexanoate, physicochemical, toxicological and ecotoxicological properties of vinyl 2-ethylhexanoic acid are similar to that of vinyl neononanoate and follow a regular pattern as a result of structural similarity and therefore may be considered as a group."

In addition you also provided in the dossier the following supporting studies:

- An OECD 422 performed with the analogue vinyl neodecanoate / 51000-52-3 / 256-905-8
- An OECD Guideline 413 (Subchronic Inhalation Toxicity: 90-Day Study) with analogue vinyl neodecanoate / 51000-52-3 / 256-905-8
- A 14-day oral range finder for a rat developmental toxicity study with the Substance

We have assessed this information and identified the following issues:

For the reasons explained in section "Appendix on Reasons common to several requests", your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5 (read-across).
Based on the above, the information you provided do not fulfil the information requirement.

Information on the design of the study to be performed (route/ species/ strain)

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the substance is a liquid with a low vapour pressure.

Therefore the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

Additional parameters

The studies you submitted showed that adverse effects such as hyaline droplets and karyomegaly in the renal cortex in high dose males treated with Vinyl neononanoate were observed in the kidneys of male rats but not in male control rats or in any exposed/control female rats.

This indicates that the kidney is a target organ of the Substance which may induce alpha-2u-globulin-mediated nephropathy. Since this mode of action is considered not relevant to humans, the involvement of alpha-2u-globulin in the kidney effects is a key parameter for establishing the relevance of the kidney effects for risk assessment.

Therefore, although optional (as per paragraph 37 of OECD TG 408), a urinalysis is required to investigate further the kidney function after administration of the Substance. Additionally, a full histopathological examination including immune-histochemical investigation of renal pathology is required to determine if the pathology is mediated by alpha-2u globulin.

In your comments to the draft decision you agreed to perform the study.

2. Long-term toxicity testing on aquatic invertebrates and 3. Long-term toxicity testing on fish

Long-term toxicity testing on aquatic invertebrates and on fish are standard information requirements in Annex IX to the REACH Regulation, unless already provided as part of Annexes VII and VIII requirements, respectively.

You have adapted this information requirement based on Annex IX, Section 9.1.5 and 9.1.6., Column 2 with the following Justification:

- *"In accordance with column 2 REACH Annex IX, the long-term toxicity testing on invertebrates (required in section 9.1.5) does not need to be conducted as the chemical safety assessment according to Annex I does not indicate the need to investigate further the effects on aquatic organisms."* and
- *"In accordance with column 2 REACH Annex IX, the long-term toxicity testing on fish (required in section 9.1.6) does not need to be conducted as the chemical safety assessment according to Annex I does not indicate the need to investigate further the effects on aquatic organisms."*

We have assessed this information and identified the following issue:

As specified in Annex IX, Section 9.1., Column 2, a long-term toxicity study on aquatic invertebrates and/or fish must be performed unless the Chemical Safety Assessment (CSA) demonstrates that risks towards the aquatic compartment arising from the manufacture and use of the Substance are controlled (Annex I, Section 0.1). The justification must be documented in the Chemical Safety Report (CSR).

In particular, the CSA must take into account the following elements to support that long-term aquatic toxicity testing is not required:

- all relevant hazard information from your registration dossier, and
- the outcome of the risk characterisation in relation to the manufacture and/or uses of the Substance.

The risk characterisation consists of a comparison of the predicted environmental concentrations in each environmental sphere with the PNECs (Annex I, Section 6.3).

According to ECHA Guidance, Chapter R.7b, for the derivation of Predicted No Effect Concentration (PNEC) for water compartment "*The information should at least cover species of three trophic levels: algae/aquatic plants, invertebrates (Daphnia preferred), and fish.*"

In your dossier, in support of your justification that the CSA demonstrates that risks towards the aquatic compartment are controlled, you refer to four studies:

- a short-term aquatic toxicity data with analogue substance vinyl neodecanoate EC No. 256-905-8 for aquatic invertebrates;
- a short-term aquatic toxicity data with analogue substance vinyl neodecanoate EC No. 256-905-8 for fish;
- an activated sludge respiration inhibition testing test performed with analogue substance vinyl neodecanoate EC No. 256-905-8; and

- An algae growth inhibition test study performed with your Substance.

Based on these studies, you argue that they have similar effects so they are of low toxicity. Hence the PNEC and further derived RCRs show that there are no risks for the environment using these studies.

As specified in sections 2 and 3 of Appendix A, as well as sections 1 and 2 of Appendix B, none of the short-term aquatic toxicity tests you provided complies with the information requirements. Such information includes reliable data on short-term toxicity on at least three trophic level or on long-term toxicity on at least one trophic level (fish or Daphnia) if it has been generated from that showing the lowest L(E)C50 of the short-term tests. Hence, a reliable PNEC cannot be derived. Therefore, your adaptation is rejected.

Without compliant information, your CSA does not demonstrate that the risks of the Substance are adequately controlled for the aquatic compartment. As a consequence, your adaptation is rejected as it does not meet the specific rules for adaptation of Annex IX, Section 9.1., Column 2.

On this basis, the information requirement is not fulfilled.

In your comments to the draft decision you propose for both endpoints to *"perform the necessary study if the results of the chemical safety assessment warrant the additional information. This will be known after the short term studies have been completed".*

ECHA notes that currently the available aquatic toxicity tests are not valid and therefore, there is no reason to modify the rationale or requirements of the draft decision based on aquatic toxicity considerations.

Appendix D: 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[8].

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[9].

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

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

1. Testing strategy for aquatic toxicity testing

You are advised to consult ECHA Guidance R.7b, (Section R.7.8.5) which describes the Integrated Testing Strategy, to determine the sequence of aquatic toxicity tests and testing needed.

Appendix F: 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 03 September 2019.

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 or the deadline.

The timeline indicated in the draft decision to provide the information requested is 18 months from the date of adoption of the decision. In your comments to the draft decision, you requested an extension of the timeline to 24 months. You justified your request stating that after performing the 90-day repeated dose toxicity study, i.e. after 12 months, you need another 6 to 9 months to perform the 2 long-term aquatic tests, and some additional months for contingency; hence you suggest 24 months.

ECHA notes that you have not substantiated the request for deadline extension with documentary evidence. Consequently, there is no objective reason to consider that the 18 months period is not sufficient for the performance of the studies.

Therefore, ECHA has not modified the deadline of the decision.

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

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix G: List of references - ECHA Guidance[10] 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)[11]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[11]

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[12]

[10] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[11] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[12] 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 H: Addressees of this decision and the corresponding information requirements applicable to them

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]

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.