~~Confidential~~

Helsinki, 25 February 2022

Addressees
Registrant as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
13/08/2015

Registered substance subject to this decision ("the Substance")
Substance name: Decene, hydroformylation products, low boiling
EC number: 938-875-4
CAS number: NS

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 in C.1. below by ***01 September 2023*** and all other information listed below by ***02 September 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. Skin sensitisation (Annex VII, Section 8.3.; test method:
   - *in vitro/in chemico* skin sensitisation information on inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (EU B.71/OECD TG 442E)(Annex VII, Section 8.3.1.); and
   - Only if the *in vitro/in chemico* test methods specified under point i.) are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);

2. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471)

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

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

2. If negative results are obtained in test performed for the information requirement of Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

3. Simulation testing on ultimate degradation in surface water also requested below

(triggered by Annex VIII, Section 9.2.)

4. Soil simulation testing also requested below (triggered by Annex VIII, Section 9.2.)

5. Sediment simulation testing also requested below (triggered by Annex VIII, Section 9.2.)

6. Identification of degradation products also requested below (triggered by Annex VIII, Section 9.2.)

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. 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)

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

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

5. 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. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

6. Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: EU C.23./OECD TG 307) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

7. Sediment simulation testing (Annex IX, Section 9.2.1.4.; test method: EU C.24./OECD TG 308) at a temperature of 12°C. Non-extractable residues (NER) must be quantified and a scientific justification of the selected extraction procedures and solvents must be provided.

8. 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) by oral route, in a second species (rat/rabbit)

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

- Appendix entitled "Reasons common to several requests";
- 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 Annexes VII to X to REACH, for registration at more than 1000 tpa.

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 are necessary for the PBT assessment. However, to determine the testing needed to reach the conclusion on the persistency of the Substance you should consider the sequence in which these tests are performed, potential alternative testing strategies 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 Mike Rasenberg, 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 information requirements for the following standard information requirements by grouping substances in the category and applying a read-across approach in accordance with Annex XI, Section 1.5:

- Skin sensitisation (Annex VII, Section 8.3)
- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Pre-natal developmental toxicity study in a second species (Annex X, Section 8.7.2.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

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

Grouping of substances and read-across approach

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 (addressed under 'Scope of the grouping'). 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[2,3].

A. Predictions for eco-/toxicological properties properties

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

You read-across between the structurally similar substances in the following list as source substances and the Substance as target substance.

Name	EC/List Number
Mineral Spirit	-
low aromatic white spirits	919-446-0
Undecane	214-300-6
Stoddard solvent	232-489-3

[2] 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)

[3] 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

Isooctene	234-294-9
Alkenes, C11-12, hydroformylation products, distn. residues, the Substance	292-427-6
Hydrocarbons, C9-C12, n-alkanes, isoalkanes, cyclics, aromatics (2-25%)	919-446-0
Hydrocarbons, C10-C13, n-alkanes, isoalkanes, cyclics, aromatics (2-25%)	
Hydrocarbons, C11-C14, n-alkanes, isoalkanes, cyclics, aromatics (2-25%)	925-653-7
Alkenes, C11-12, hydroformylation products, low boiling	932-235-8
White spirit (Naphtha (petroleum), hydrodesulfurized heavy)	
Hydrodesulfurized kerosene	
turbo fuel A	

Your reasoning for the prediction of eco-/toxicological properties is based on claimed structural similarity, overlaps in constituents ("*TAL 111 and Alchisor TAL 123 are predominantly comprised of material meeting the definition of C9-C14 aliphatics (2-25% aromatics) hydrocarbon solvents or 'Category 3 Hydrocarbons*"), similar "physico-chemical properties" and "*existing biodegradation data*" and "*acute aquatic invertebrate and algal exposure"* for Category 3 hydrocarbons and TAL 123. You conclude that both of these "*are readily biodegradable*" and "*TAL 123 is less toxic to invertebrates and algae than its Category 3 hydrocarbons*". You reference further information which, at the time of your dossier submission (2015), was not yet generated and has since not been included.

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 based on a worst-case approach.

ECHA notes the following shortcomings with regards to predictions of eco-/toxicological and environmental fate properties.

1. *No basis for prediction*

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference 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*". The constituent profile and composition can influence the overall toxicity/properties of the potential category members, including test materials.[4] Therefore, qualitative and quantitative information on the compositions of the test materials should be provided to allow assessment whether the attempted predictions are compromised by the composition and/or impurities.

The provided 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 other category members. Categories consisting of UVCB (Unknown or Variable

[4] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.4.1

composition, Complex reaction products or of Biological materials) substances need to include qualitative compositional information of the individual constituents of the test materials; 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.[5]

Your technical dossier contains limited compositional information for the source substances. It states that several source substances are UVCBs, such as substances with trivial names (Hydrodesulfurized kerosene, Turbo fuel A, Stoddard solvent, White spirits) as well as branched and linear alcohols, and hydrocarbons of certain carbon-chain lengths which contain n-alkanes, isoalkanes, cyclics, and aromatics (2-25%). The identification/naming information on test materials provided in your dossier is limited to the generic name of UVCB substance and/or numerical identifier.

The type of constituents are reported for some but not all studies. Their concentrations and exact composition of constituents (carbon chain length, branching, cyclicity, aromaticity, functional groups) are not provided for any test material that is a UVCB.

Without comprehensive reporting of all constituents present in the test material (including their identity and concentrations), no qualitative or quantitative comparative assessment between the compositions of the different substances as source substances/ test material on the one hand, and of the Substance on the other hand, can be completed. Therefore, is not possible to assess whether the attempted predictions are compromised by the composition of these UVCB test materials and their relation to the Substance.

2. *Supporting information*

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[6]. 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). Supporting information (1) must cover all constituents of a constituent-based read-across approach; (2) must confirm your claimed worst-case prediction; and (3) could be in the form of a bridging study with the Substance.

As indicated above, your read-across hypothesis is based on the assumption that the source substance constitutes a worst-case for the prediction of the property under consideration of the Substance. In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm a conservative prediction of the properties of the Substance from the data on the source substance(s). Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

You report the composition of the Substance with ranges of concentration (typical concentration) as

I. *Decane*: [redacted]
II. *Decene*: [redacted]
III. *Aromatics C10*: [redacted]
IV. *Undecan-1-ol, branched and linear*: [redacted]

[5] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.5.5
[6] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

V. *Undecane*: [redacted]
VI. *Undecene*: [redacted]
VII. *Dodecane*: [redacted]
VIII. *C10-C11 isoalkanes:* [redacted]
IX. *Napthalene:* [redacted]
X. *Unknown constituents*: [redacted]

In your dossier, you have provided the studies listed in the appendices on *reasons for the requests* **A-D**.

It does not appear that you have provided studies with source substances that are identified as constituents of the Substance (I-IV, VI-IX), and you have not provided information on *unknown constituents*. This constitutes [redacted] of your Substance for which there is no information to predict from. The source studies provided with UVCB substances are not reliable for reasons explained under issue "*1. No basis for prediction*", above. For several endpoints even the information provided does not cover the whole spectrum of constituents; e.g. alkenes or alcohols are not among the source studies for skin sensitisation, any of the *in vitro* genotoxicity endpoints, repeated dose toxicity, pre-natal developmental toxicity, long-term toxicity to aquatic invertebrates or fish.

In the comments to the draft decision you state your intention to improve the (eco)toxicological profile of the Substance and your plans to refine your read-across approach, including an OECD TG 422 study with the Substance in rats as bridging study.

In the absence of information for all constituents and/or a bridging study with the Substance, you have not established that any of the source substances constitute a worst-case for the prediction of the property under consideration of the Substance, or any basis for prediction. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. The acceptability of the adaptation will be conditional to the acceptability of the predicted properties. Please note that this decision does not consider 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). You remain responsible for complying with this decision by the set deadline.

The information provided is not sufficient to cover all constituents of the Substance, and not sufficient to conclude that the prediction of (eco-)toxicological properties are likely to constitute a worst-case.

3. Adequacy and reliability of studies

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across should:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).
- have adequate and reliable documentation of the applied method.

a. test material identity

The Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "if the test method is used for the testing of a [...] UVCB [...] sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents". Therefore, the unambiguous characterisation of the composition of the source substance and test material used to generate the source data is required to evaluate the reliability and uncertainty associated with predicting properties of substances with potential substantial compositional differences. The composition of the selected test material must be reported in the respective endpoint study record, under the test material section.

Your technical dossier contains limited compositional information for the source substances. It states that several source substances are UVCBs, such as substances with trivial names (turbo fuel A, Hydrodesulfurized Kerosene, Stoddard solvent, White spirit, Naphtha) as well as branched and linear alcohols, and hydrocarbons of certain carbon-chain lengths which contain n-alkanes, isoalkanes, cyclics, and aromatics (2-25%). The identification/naming information on test materials provided in your dossier is limited to the generic name of these UVCB substances and/or numerical identifier.

The type of constituents are reported for some but not all studies. The concentrations and exact composition of constituents (carbon chain length, position and length of branching, cyclic structures, aromatic structures, functional groups) are not provided for any test material that is a UVCB.

Without comprehensive reporting of all constituents present in the test material (including their identity and concentrations), no qualitative or quantitative comparative assessment between the compositions of the different substances as source substances/ test material on the one hand, and of the Substance on the other hand, can be completed.

ECHA is unable to confirm that the test materials which are UVCBs are relevant for the Substance and to all the registrants of the Substance. Therefore, ECHA concludes that it is not possible to assess whether the attempted predictions are compromised by the composition of these test materials. Consequently, the corresponding study results are not adequate for the purpose of classification and labelling and/or risk assessment.

b. Adequacy and reliability of studies – key parameters according to the test method regulation

Studies must be conducted in accordance with the corresponding test methods referred to in Article 13(3) and according to the provisions of the REACH Annexes. Additional issues of adequacy and reliability of studies submitted are identified and addressed in the relevant endpoint-specific reasons in appendices A-D.

Due to these shortcomings, ECHA concludes that the studies are unreliable.

B. Conclusions on the grouping of substances and 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.

2. Degradation testing

You have provided the following same adaptation for simulation testing on ultimate degradation in surface water, on soil and on sediment (Sections 9.2.1.2., 9.2.1.3. and 9.2.1.4. of Annex IX to REACH respectively):

i. An adaptation under Annex IX, Section 9.2., Column 2 with the following justification: "*Reliable studies show that the analogue substance, Alchisor TAL 123 and the constituent categories (Category 3 hydrocarbon solvents) of Alchisor TAL 111 (as justified in the Approach Justification Document in Section 13) are all readily biodegradable in water. Therefore Alchisor TAL 111 is also readily biodegradable in water. In accordance with REACH Annex IX column 2 exemption, the simulation testing in water and sediment does not need to be conducted as the test substance is readily biodegradable.*".

We have assessed this information and identified the following issue:

Under Sections 9.2.1.2., 9.2.1.3. and 9.2.1.4., Column 2 of Annex IX to REACH, the studies may be omitted if the substance is readily biodegradable.

You argue that the Substance is readily biodegradable, based on an OECD TG 301F study with the analogue substance: Alkenes, C11-12, hydroformylation products, low boiling, List number 932-235-8 (78% degradation after 28 days).

As explained in Appendix B, section 3, it is not possible to conclude whether the constituents of the Substance can be expected to be homogeneous in terms of their biodegradability. Any biodegradation observed in a ready biodegradability test performed with the Substance would not be sufficient to conclude that all the constituents of the Substance are readily biodegradable. Furthermore, the information available indicates that the Substance is a potential PBT/vPvB substance. As explained in ECHA Guidance R.11, in principle, degradation simulation studies performed in appropriate environmental media and at environmentally realistic conditions are the only tests that can provide a definitive degradation half-life that can be compared directly to the persistence criteria as defined in REACH Annex XIII.

Therefore, your adaption is rejected.

3. Degradation testing – based on the registrants' comments on the initial draft decision: Assessment of your adaptation under Annex XI, Section 2

In your comments to your initial draft decision, ECHA understands that you propose

An adaptation under Annex XI, Section 2 specifies the general rules for adapting the standard information requirement when testing is not technically possible.

For the following standard information requirements:

- Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.)
- Soil simulation testing (Annex IX, Section 9.2.1.3.)
- Sediment simulation testing (Annex IX, Section 9.2.1.4.)
- Identification of degradation products (Annex IX, 9.2.3.)

We have assessed this information and identified the following issues:

Annex XI, Section 2 specifies the general rules for adapting the standard information requirement when testing is not technically possible. The guidance on the technical limitations of the test method given in the test guideline itself or in relevant guidance complementing the test guideline must always be respected.

You have provided a list of general statements to indicate why you consider testing is not technically with no specific justification of these statements:

i. The testing of the complex UVCB is not technically possible
    a. Relevant constituents of the Substance cannot be determined
    b. Radiolabelling of this UVCB is not possible due to the manufacturing process and the complexity of the substance itself.

Therefore these remain unsupported hypotheses instead of justifications.

Therefore, your adaptation is rejected.

However, after the above adaptation, you have provided detailed screening assessment information with your comments on the initial draft decision covering different possibilities offered by ECHA R.11 guidelines and provided justification in this respect. ECHA understands that this screening assessment information is a Column 2 adaptation by you based on persistence, bioaccumulation and PBT assessment and as such it is addressed under the Appendix B, 3. and under Appendix C, 5. Simulation testing on ultimate degradation in surface water but it refers to all the Simulation testing requests in this decision.

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

1. Skin sensitisation

Skin sensitisation is an information requirement under Annex VII to REACH (Section 8.3.). Under Section 8.3., Column 1, the registrants must submit information allowing (1) A) a conclusion whether the substance is a skin sensitiser and B) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and (2) risk assessment, where required.

You have adapted this information requirement under Column 2 by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

You have provided the following information in the technical dossier, based on which you conclude that the Substance is not a skin sensitiser:

i) 1977 *in vivo* Guinea Pig Maximization test (OECD TG 406) with the source substance Hydrocarbons, C9-C12, n-alkanes, isoalkanes, cyclics, aromatics (2-25%), EC 919-446-0.

We have assessed this information and identified the following issues:

As explained in the Appendix on Reasons common to several requests your adaptation is rejected. The following endpoint-specific deficiencies have been identified in your read-across adaptation:

A. Non-compliant study

To be considered compliant and enable concluding whether the Substance causes skin sensitisation, a study has to meet the requirements of the EU Method B.6/OECD TG 406. The following key parameter(s) of this test guideline include

a) Dose level selection rationale
b) Positive controls to establish the sensitivity and reliability of the experimental technique (OECD TG 406, paragraph 11)

<u>OECD TG 406:</u>

In the provided study:

a) No dose level selection rationale was provided
b) No information on positive control group were provided.

Therefore the study does not fulfil the key parameters set in the EU method B.6/OECD TG 406 and does not allow to make a conclusion whether the Substance causes skin sensitisation.

Therefore, the information requirement is not fulfilled.

In your comments to the initial draft decision, you explained that because the Substance is a UVCB and does not have a very high water solubility, the currently available *in vitro*/*in chemico* methods are not applicable or reliable. More specifically, you stated that DPRA (OECD 442C) which relies on molecular interactions with skin proteins for skin sensitisation have not yet been sufficiently validated for UVCBs. Furthermore, Keratinosens method (OECD TG 442D) and h-CLAT method (OECD TG 442E) have known issues regarding solubility and potential false negative results. Finally, you propose to do an OECD TG 429 study only.

<u>OECD TG 442C</u>

The available methods included in the OECD TG 442C (Direct Peptide Reactivity Assay (DPRA), the Amino Acid Derivative Reactivity Assay (ADRA) and the kinetic Direct Peptide Reactivity Assay (kDPRA)) are not suitable for UVCBs.

OECD TG 442D

The OECD TG 442D (2018) contains currently two different methods i.e. keratinosens (Appendix IA) and Lusens (Appendix IB). For both of the test methods following statements are given in paragraph 4 of the respective Appendices "*In general mono constituent substances with a LogP above 7 may be insoluble in the exposure medium, however, if solubility or stable dispersion can be obtained and documented, testing may still be conducted*."
Based on the currently available methods, there are no LogP specific limitations, even if there are issues with solubility, but a stable dispersion can be obtained. If solubility limits are not met, or it not possible to obtain stable dispersion, positive results could still be validly used.

OECD TG 442E

The OECD TG 442E (2018) contains currently three methods i.e. Human Cell Line Activation test (h-CLAT), U937 cell line activation Test (U-SENS™), and Interleukin-8 Reporter Gene Assay (IL-8 Luc assay). For the h-CLAT method only there are LogP specific limitations, as the methods states in Annex I, paragraph 4 "*Test chemicals with a Log Kow greater than 3.5 tend to produce false negative results (14). Therefore negative results with test chemicals with a Log Kow greater than 3.5 should not be considered. However, positive results obtained with test chemicals with a Log Kow greater than 3.5 could still be used to support the identification of the test chemical as a skin sensitiser."* The other methods do not contain LogP specific limitations, however the substance needs to be solubilised at appropriate concentrations, or to form a stable dispersion, as specified in the individual methods, which you have not addressed.

Conclusion

The current *in chemico/in vitro* test guidelines OECD TGs 442D and E contain multiple methods in addition to the ones indicated by you in your comments to the draft decision. You have not demonstrated that these currently available *in vitro/in chemico* methods are not suitable for the Substance in the absence of any evidence, e.g. in the form of pre-tests with suitable vehicles as described in the corresponding test guidelines.

The OECD TG 442C is not suitable for UVCBs.

To fulfil the information requirement for the Substance for skin sensitisation, *in vitro/in chemico* studies (OECD TG 442D and 442E are considered suitable. In case *in vitro/in chemico* methods are not suitable for the Substance or the results cannot be used for classification and risk assessment an *in vivo* skin sensitisation study (OECD TG 429) must be performed.

2. In vitro gene mutation study in bacteria

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

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

You have provided *in vitro* bacterial gene mutation key studies and supporting studies in your dossier:

i. 1984 with the source substance *Hydrocarbons, C11-C14, n-alkanes, isoalkanes, cyclics, aromatics (2-25%)*, EC 925-653-7 and with the following strains, TA 1535, TA 1537, TA 1538, TA 98 and TA 100 which all gave negative results
ii. 1982 with the source substance *Stoddard Solvent*, EC 232-489-3 and with the following strains, TA 1535, TA 1537, TA 98 and TA 100 which all gave negative results
iii. 1984 with the source substance *White Spirit* and with unspecified strains

We have assessed this information and identified the following issue(s):

As explained in the Appendix on Reasons common to several requests your adaptation is rejected. The following endpoint-specific deficiencies have been identified in your read-across adaptation:

As stated in the Appendix on Reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case OECD TG 471[7] (1997). The key parameters of this test guideline include:

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)
b) The maximum dose tested must induce a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose must correspond to 5 mg/plate or 5 ml/plate.
c) At least 5 doses must be evaluated, in each test condition.
d) Triplicate plating must be used at each dose level.
e) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
f) The number of revertant colonies per plate for the concurrent negative control must be inside the historical control range of the laboratory.
g) The mean number of revertant colonies per plate must be reported for the treated doses and the controls.

The reported data for the studies you have provided did not include:

a) the required fifth strain, S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101). (i and ii)
b) a maximum dose of 5 mg/plate or 5 ml/plate or that induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. (ii)
c) the evaluation of at least 5 doses in each test condition.(i and ii)
d) triplicate plating at each dose level.(i and ii)
e) a positive control (ii)
f) a negative control with a number of revertant colonies per plate inside the historical control range of the laboratory. (ii)
g) data on the number of revertant colonies per plate for the treated doses and the controls.(i and ii)

The reported data for study iii) did not include any of the above listed key parameters neither are the strains used in the study reported.

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

Therefore, the information requirement is not fulfilled.

[7] ECHA Guidance R.7a, Table R.7.7–2, p.557

In your comments to the draft decision, you agree to perform the requested study.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

3. Growth inhibition study aquatic plants

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

You seek to adapt the standard information requirement for growth inhibition study with aquatic plants by applying a read-across approach in accordance with Annex XI, Section 1.5 and provided the following information:

i. OECD TG 201 key study (1997) with the analogue substance: Hydrocarbons, C9-C12, n-alkanes, isoalkanes, cyclics, aromatics (2-25%).
ii. OECD TG 201 key study (1996) with the analogue substance: Hydrocarbons, C10-C13, n-alkanes, isoalkanes, cyclics, aromatics (2-25%)
iii. OECD TG 201 key study (2005) with the analogue substance: Mineral spirits type 1A
iv. OECD TG 201 key study (2012) with the analogue substance: Alkenes, C11-C12, hydroformylation products, low boiling

We have assessed this information and identified the following issues:

As explained in the Appendix on Reasons common to several requests your adaptation is rejected. The following endpoint-specific deficiencies have also been identified in your read-across adaptation:

Reliability of studies (i. and ii.)

To fulfil the information requirement, a study must comply with OECD TG 201 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:

- If a solvent is used, its concentration is ≤ 100 µg/L;
- the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

Your registration dossier provides OECD TG 201 studies (i, ii and iv) showing the following:

- when acetone is used as a solvent, its concentration is not reported (study ii);

tabulated data on the algal biomass determined daily for each treatment group and
The Substance is difficult to test, due to its UVCB nature, low water solubility for most constituents (below 1 mg/l), volatility of some constituents, and high partition coefficient (log K_{ow} range 4.79-7.00), indicating high potential to adsorb.

Based on the above, there are critical methodological deficiencies resulting in the rejection of the study results (for studies i. and ii.). Specifically,

- You have not demonstrated that the concentration of acetone in the test solution is ≤ 100 µg/L:
- Due to the absence of data on the algal biomass determined daily for each treatment group and control, the reporting of the studies is not sufficient to conduct an independent assessment of its reliability.

Therefore, the requirements of OECD TG 201 are not met.

In the comments to the initial draft decision, you agree to perform the requested study.

On this basis, the information requirement is not fulfilled.

Study design

As already explained above, the Substance is difficult to test. OECD TG 201 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. 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 as described in OECD TG 201. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solutions.

For multi-constituents/UVCBs, the analytical method must be adequate to 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 constituents and/or groups of constituents).

If you decide to use the Water Accommodated Fraction (WAF) approach, in addition to the above, you must:

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (ECHA Guidance, Appendix R.7.8.1-1, Table R.7.8-3);
- 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.

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

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is an information requirement under Annex VIII to REACH (Section 8.4.2.).

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

You have provided a key study and supporting studies in your dossier:

i. 1984 an *in vitro* mammalian chromosome aberration test with the source substance *Hydrocarbons, C11-C14, n-alkanes, isoalkanes, cyclics, aromatics (2-25%)* EC: 925-653-7.

Furthermore you have provided the following supporting study and key study:

ii. 1984 *in vitro* sister chromatid exchange test with the source substance *White spirit* reported as similar to OECD 473;

iii. 1987 in vitro DNA damage and/or repair study/chromosome aberration assay with the source substance *Hydrodesulfurized kerosene*.

Furthermore you have provided the following *in vivo* tests:

iv. 1984 i*n vivo* chromosome aberration test with the source substance "White Spirit" with a modified protocol (Micronucleus assay, inhalation and i.p. route of administration);

v. 1982 *in vivo* chromosome aberration test with the source substance Stoddard Solvent, EC 232-489-3;

vi. 1994 *in vivo* Mammalian Erythrocyte Micronucleus test with the source substance turbo fuel A (CAS #64742- 47-8), CAS #8008-20-6

We have assessed this information and identified the following issues:

As explained in the Appendix on Reasons common to several requests your adaptation is rejected. The following endpoint-specific deficiencies have been identified in your read-across adaptation:

As stated in the Appendix on Reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case, an *in vitro* chromosomal aberration test or an *in vitro* micronucleus test, conducted in mammalian cells in accordance with OECD TG 473 or OECD TG 487, respectively[8]. The key parameter(s) of these test guidelines include:

a) The maximum concentration tested must induce 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest.
b) The response for the concurrent negative control must be inside the historical control range of the laboratory.
c) Data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures must be reported.

The reported data for the studies you have provided did not include:

a) a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 55+5% of cytotoxicity compared to the negative control, or the precipitation of the

[8] ECHA Guidance R.7a, Table R.7.7–2, p.557

tested substance.
b) a negative control with a response inside the historical control range of the laboratory.
c) data on the cytotoxicity and/or the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures.

The information provided does not cover key parameters required by OECD TG 473.

To fulfil the information requirement, a study must be an *in vitro* chromosomal aberration test or an *in vitro* micronucleus test, conducted in mammalian cells and comply with with the OECD TG 473 or OECD TG 487 (Article 13(3) of REACH and ECHA Guidance R.7, Table R.7.7-2).

Furthermore, study ii) and iii) are not *in vitro* cytogenicity studies in mammalian cells nor *in vitro* micronucleus studies. Therefore, the information provided does not cover the key parameters required by the OECD TG 473/487.

Therefore, the information requirement is not fulfilled.

Under Section 8.4.2., Column 2, first indent, Annex VIII to REACH, the study may be omitted "if *adequate data from an in vivo cytogenicity test are available*". ECHA Guidance[9] clarifies that the *in vivo* study must be either a micronucleus test or a chromosomal aberration test, performed according to OECD TG 474 or 475, respectively[10].

For the data from an *in vivo* cytogenicity test to be considered adequate, the *in vivo* study you submitted has to meet the requirements of OECD TG 475, and the specifications/conditions of this test guideline include:
a) Each group must have a minimum of 5 analysable animals (the test can be performed in either sex).
b) The highest dose studied must be the maximum tolerated dose (MTD), i.e. the highest dose that is tolerated without evidence of toxicity (e.g. body weight depression or hematopoietic system cytotoxicity, but not death or evidence of pain, suffering or distress necessitating humane euthanasia). The highest dose can also be a dose that produces toxicity in the bone marrow
c) The mitotic index must be determined as a measure of cytotoxicity in at least 1000 cells per animal for all treated animals (including positive controls), untreated or vehicle/solvent negative control animals.
d) The mitotic index and the mean number of cells with aberrations per group must be reported for each group of animals.
e) In order to provide a clear negative outcome, the data available must show that "*bone marrow exposure to the test Substance occurred*".

The reported data for the *in vivo* study/ies you submitted did not include:
a) a minimum of 5 animals per group(v)
b) a maximum studied dose that is a MTD or induces toxicity (iv and v)
c) the analysis of the adequate number of cells (iv and v)
d) data on the mitotic index and the mean number of cells with aberrations per group for each group of animals. (iv and v)
e) a demonstration that the systemic or target tissue (bone marrow) exposure to the Substance or its metabolites. (iv and v)

The information provided does not cover specifications/conditions required by OECD TG 475.

[9] ECHA Guidance R.7a, R.7.7.6.3, p.568
[10] ECHA Guidance R.7a, Table R.7.7–3, p.558

For these reasons, and for the reasons set in the Appendix on Reasons common to several requests, the requirements of Section 8.4.2., Column 2, first indent, Annex VIII to REACH are not met.

In your comments to the draft decision, you agree to perform the requested study.

Study design

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.) in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

i. Triggering of the study

Your dossier contains an adaptation for an *in vitro* gene mutation study in bacteria, and an adaptation for an in vitro cytogenicity study in mammalian cells or *in vitro* micronucleus study.

The information for the *in vitro* gene mutation study in bacteria and for the *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study provided in the dossier are rejected for the reasons provided in sections A.2. and B.1. of Appendices A and B, respectively.

The result of the requests for information in sections A.2. and B.1. of Appendices A and B respectively will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

ii. Assessment of information provided

You have provided a supporting study in your dossier:

i. 1982 *in vitro* mammalian cell gene mutation assay with the source substance Stoddard Solvent, EC 232-489-3.

As explained in the Appendix on Reasons common to several requests your adaptation is rejected. The following endpoint-specific deficiencies have been identified in your read-across adaptation:

As stated in the Appendix on Reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case OECD TG 476 or OECD TG 490[11]. The key parameter(s) of these test guidelines include:

a) Two separate test conditions must be assessed: in absence of metabolic activation and in presence of metabolic activation.
b) The maximum concentration tested must induce 80-90% of cytotoxicity compared to

[11] ECHA Guidance R.7a, Table R.7.7–2, p.557

the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration must correspond to 10 mM, 2 mg/mL or 2 µl/mL, whichever is the lowest.
c) At least 4 concentrations must be evaluated, in each test condition.
d) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the response compared with the concurrent negative control.
e) The response for the concurrent negative control must be inside the historical control range of the laboratory.
f) Data on the cytotoxicity and the mutation frequency for the treated and control cultures must be reported.

The reported data for the studies you have provided do not include:
a) two separate test conditions, but only in absence/presence of metabolic activation.
b) a maximum tested concentration of 10 mM, 2 mg/mL or 2 µl/mL, or that induced 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance.
c) the evaluation of at least 4 concentrations in each test condition.
d) one positive control
e) a negative control with a response inside the historical control range of the laboratory.
f) data on the cytotoxicity and the mutation frequency for the treated and control cultures.

The information provided does not cover key parameters required by OECD TG 476.

Therefore, the information requirement is not fulfilled.

Consequently, you are required to provide information for this endpoint, if the *in vitro* gene mutation study in bacteria / the *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study provides a negative result.

In your comments to the draft decision, you agree to perform the requested study.

Study design

To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

3. Simulation testing on ultimate degradation in surface water

Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if 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 potentially persistent or very persistent (P/vP) if it is not possible to conclude that the Substance, any of its constituent or impurity present in concentration ≥ 0.1% (w/w), or relevant transformation/degradation product is readily

biodegradable. In this regard, the OECD "*Guidelines for the Testing of Chemicals, Revised Introduction to the OECD Guidelines for Testing of Chemicals, Section 3 Part I: Principles and Strategies related to the Testing of Degradation of Organic Chemicals*"[12] indicates that ready biodegradability tests are intended for pure substances and are generally not applicable for complex compositions containing different types of constituents, typically UVCB and multiconstituent substances. For UVCB and multiconstituent substances, any observed biodegradation may indeed reflect the biodegradation only of some constituents. This OECD document further indicates that "*it is sometimes relevant to examine the ready biodegradability of mixtures of structurally similar chemicals*", but "*a case by case evaluation should however take place on whether a biodegradability test on such a complex mixture would give valuable information regarding the biodegradability of the mixture as such (i.e. regarding the degradability of all the constituents) or whether instead an investigation of the degradability of carefully selected individual components of the mixture is required*"

- 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);

Your registration dossier provides the following:

In relation to persistence assessment and bioaccumulation potential:

- The Substance is readily biodegradable (78% degradation after 28 days in OECD TG 301F, based on the study with the analogue substance: Alkenes, C11-12, hydroformylation products, low boiling, List number 932-235-8);
- Description of the Substance as a UVCB substance. Based on the information provided in the registration dossier, it contains constituents from various chemical classes (linear and branched alkanes, linear and branched alkenes, linear and branched alcohols, aromatic compounds).
- The Substance has a high potential to partition to lipid storage (log K_{ow} range 4.79-7.00 based on OECD TG 117);
- In the IUCLID dossier, section 2.3 and in the CSR, section 8, you indicated that "*According to Annex XIII of Regulation (EC) No 1907/2006 and to the Guidance on information requirements and chemical safety assessment Chapter R.11 (PBT Assessment, ECHA (2008)), a substance does not fulfil the criteria "bioaccumulative (B)" or "very bioaccumulative (vB)" if the bioconcentration factor (BCF) is below 2000 or 5000 respectively or if the log Kow is below 4.5. Standard tests for the bioaccumulation endpoint are intended for single substances. In the case of Alchisor TAL 111 and its analogue substance (Alchisor TAL 123) and category substances (C9-C14 aliphatics (2-25% aromatics)) the substance is a UVCB hydrocarbon and bioaccumulation testing is not appropriate for this complex substance. However, the bioaccumulation endpoint was predicted for representative hydrocarbon structures using the BCFWIN v2.16 model within EPISuite 3.12 or EUSES as input to the hydrocarbon block method incorporated into the PETRORISK model. The PETRORISK derivations are provided in Section 13 of the CSR. In addition, supporting information reported in CONCAWE's approach (Lampi et al., 2010), which is also included in Section 13 of the CSR, provides evidence of overestimation when BCF's are predicted through modelling approaches. PETRORISK model predictions for hydrocarbons ranged from 45.5 to 21,710… It is concluded by CONCAWE that based on available data, mono-aromatic hydrocarbons are neither bioaccumulative nor very bioaccumulative. Similar assessments for paraffins and branched (or iso-) paraffins concluded that C13 and C14 paraffins and C12-C16 branched paraffins may be bioaccumulative but not*

[12] https://www.oecd-ilibrary.org/docserver/9789264030213-en.pdf?expires=1634558948&id=id&accname=guest&checksum=3C5F4AAB82C23E11087C8CBE20195342

very bioaccumulative. These paraffins are longer than those found in Alchisor TAL 111 and it is anticipated that shorter carbon chain lengths will have a lower potential to bioaccumulate. In addition, due to the ready biodegradability of Alchisor TAL 111 it is concluded that there is a low potential for exposure and bioaccumulation in terrestrial organisms. Based on the evidence that Alchisor TAL 111 is readily biodegradable and predicted BCFs below the 2000 B-criterion the UVCB substance is not regarded as bioaccumulative in aquatic, sediment or terrestrial organisms. Alchisor TAL 111 does not fulfil the criteria "bioaccumulative (B)" or "very bioaccumulative (vB)". According to ECHA Guidance on information requirements and chemical safety assessment (May 2008), Chapter R.11, Figure 11-2: Integrated testing strategy for B-assessment, no further testing is required to conclude on the bioaccumulation criterion. "

- In the IUCLID dossier, section 5.3.1 you indicate that *"Alchisor TAL 111 is an alkenes C10 -C11, hydroformylation product, low boiling and can be characterised as a UVCB substance. As defined in the 'Read-Across Justification Document' section 13, data provided for the consitutent category substances, Category 3 hydrocarbon solvents, are representative of Alchisor TAL 111 and suitable for assessment purposes. However, standard tests for this endpoint are intended for single substances and are not appropriate for this complex substance. This endpoint has been calculated for representative hydrocarbon structures using the BCFWIN v2.16 model within EPISuite 3.12 as input to the hydrocarbon block method incorporated into the PETRORISK model. The predicted BCFs for hydrocarbons are generally overly conservative since biotransformation is not quantitatively taken into account. Therefore, indirect exposure and resulting risk estimates predicted by PETRORISK are likely to be overestimated. For the purposes of PBT assessment, measured bioaccumulation data for representative hydrocarbon constituents have been used as detailed in section 8 of the CSR."*
- No BCF values for individual constituents of the Substance, including documentation for the predictions.

In your comments on the initial draft decision, you have provided further screening information, QSARs, on the P and B properties of the Substance and further assessment of this information.

We have assessed this information and identified the following issues:

Persistence assessment

The Substance is an UVCB substance. It contains constituents with branched alkyl chains, but the exact composition, the degree and positions of branching, is not provided. The degree and positions of branching can affect differently the biodegradability of the different constituents of the Substance. Thus, the submitted information, a ready biodegradability on the Substance as a whole, is not appropriate to assess the biodegradability of the relevant individual constituents of the Substance. Therefore, it is not possible to conclude whether the constituents of the Substance can be expected to be homogeneous in terms of their biodegradability. Any biodegradation observed in a ready biodegradability test performed with the Substance would not be sufficient to conclude that all the constituents of the Substance are readily biodegradable.

Further, in your registration dossier, you have provided no study investigating the degradability of carefully selected individual constituents of the Substance which for example, would represent worst-case in respect of degradability.

In your comments on the initial draft decision, you have provided a PBT assessment based on single branched constituents reported as representative structures.

You have provided further description of your Substance but without any analytical information. As an example, you have reported that there is a certain percentage of unknowns in the Substance but without elaborating further.

You have concluded the Substance would not be a potential PBT/vPvB substance.

Without analytical information, it is not possible to assess any known variations of the constituents present in the composition of the Substance that may be relevant for PBT/vPvB assessment.

Without justification for the selection and without understanding of potential relevant variations of constituents, it is not possible to conclude that the selected single branched constituents are representative and to exclude constituents of higher concern for the PBT/vPvB assessment are present in the Substance, to avoid bias. In particular, considering that only the single branched constituents have been reported as representative structures, suggesting:

- that no constituents with more branching are present without substantiation.
- that no aromatics are present that are more branched than the constituents selected also without substantiation.

In your comments to the proposal for amendment you indicated that you will provide further explanation in a spontaneous dossier update, including the supporting analytical data, in particular demonstatrating that constituents with greater degrees of branching are not expected to be present in the Substance. However, such information was still not available when this decision was taken.

Therefore, the available information in your registration dossier and in your comments, does not rule out that the Substance, any of its constituents or relevant transformation/degradation products are potentially persistent or very persistent (P/vP).

Bioaccumulation potential

Furthermore, the Substance, any of its constituents, impurities or relevant transformation/degradation products are potentially bioaccumulative or very bioaccumulative (B/vB) as they have a high potential to partition to lipid storage.

In respect of feasibility of bioaccumulation testing, it should be noted that the trigger for simulation study is based on PBT/vPvB potential, and whether further bioaccumulation testing is feasible does not impact whether there is PBT/vPvB potential or not.

Furthermore, ECHA Guidance R.11 on PBT assessment explain about the integrated testing strategies (ITS) for the P, B and T assessments, including specifically for the complex UVCB substances. Presented approaches foresee testing not only of the whole substance, but also of various fractions, constituents. 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. It is not justified by you why PBT/vPvB assessment and necessary testing following approaches presented in the Guidance R.11 would not be feasible. Furthermore, you have not provided in the registration dossier BCF values of constituents of the Substance, including documentation for the predictions noted in the IUCLID dossier/CSR.

In your comments on the initial draft decision, you have provided a PBT assessment based on single branched constituents reported as representative structures.

You have provided further description of your Substance but without any analytical information. As an example, you have reported that there is a certain percentage of unknowns in the substance but without elaborating further.

You have concluded the Substance would not be a potential PBT/vPvB substance.

The information your provided in the comments does not change the assessment for bioaccumulation potential for the same reasons as described above under "persistence assessment".

Thus, all above considerations indicate that there is no sufficient information available to rule out bioaccumulation potential for the Substance, any of its constituents or relevant transformation/degradation products in line with principles of integrated testing strategy of PBT/vPvB assessment explained in ECHA Guidance R.11.

The information above indicates that the Substance is a potential PBT/vPvB substance.
Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix C.5.

4. Soil simulation testing

Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

This information requirement is triggered in case the chemical safety assessment (CSA) in your registration dossier indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4.).

As explained in the Appendix B, section 3 above, the information available for the Substance indicates that the Substance is a potential PBT/vPvB substance.

In addition, the Substance has low water solubility (below 1 mg/l for most constituents), high partition coefficient (log K_{ow} range 4.79-7.00), indicating high potential to adsorb to soil.

Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation. Based on the adsorptive properties of the Substance, soil represents a relevant environmental compartment.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix C.6.

Your comments on the initial draft decision and on the proposal for amendment for this endpoint have been addressed under Appendix C, Section 3.

5. Sediment simulation testing

Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4.).

As explained in the Appendix B, section 3 above, the information available for the Substance in your registration dossier indicates that the Substance is a potential PBT/vPvB substance.

In addition, the Substance has low water solubility (below 1 mg/l for most constituents), high partition coefficient (log K_{ow} range 4.79-7.00), indicating high potential to adsorb to sediment.

Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation. Based on the adsorptive properties of the Substance, sediment represents a relevant environmental compartment.

The examination of the available information or adaptations, as well as the selection of the requested test and the test design are addressed respectively in Appendix C.7.

Your comments on the initial draft decision and on the proposal for amendment for this endpoint have been addressed under Appendix C, Section 3.

6. Identification of degradation products

Further degradation testing must be considered if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance (Annex VIII, Section 9.2., Column 2).

This information requirement is triggered in case the chemical safety assessment (CSA) indicates the need for further degradation investigation (Annex I, Section 4; Annex XIII, Section 2.1), such as if the substance is a potential PBT/vPvB substance (ECHA Guidance R.11.4.).

As already explained in the Appendix B, section 3 above, the information available for the Substance in your registration dossier indicates that the Substance is a potential PBT/vPvB substance. Therefore, the chemical safety assessment (CSA) indicates the need for further degradation investigation.

The examination of the available information or adaptations, as well as further information on the selection of the approach to generate this information are addressed in Appendix C, section 8.

Your comments on the initial draft decision and on the proposal for amendment for this endpoint have been addressed under Appendix C, Section 3.

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

1. Sub-chronic toxicity study (90-day)

A Sub-chronic toxicity study (90 day) is a standard information requirement in 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 have provided the following studies:

i. 2013 oral route sub-acute (28-day) toxicity study (OECD TG 407) with the source substance TAL 123, EC 932-235-8;
ii. 1992 oral route combined repeated dose with screening for reproductive/ developmental toxicity study (pre-TG) with the source substance dodecan-1-ol, EC 203-982-0;
iii. 1966 oral route 90-day toxicity study (pre-TG) with the source substance hexan-1-ol, EC 203-852-3;
iv. 1984 oral route 30-day toxicity study with the source substance Hydrocarbons, C11-C14, EC 925-653-7;
v. 1980 inhalation route 90-daytoxicity study (pre-TG) with the source substance "low aromatic white spirits", EC 919-446-0;
vi. 1979 inhalation route 83-day toxicity study (pre-TG) with the source substance Hydrocarbons C9-C12, EC 919-446-0;
vii. 1975 inhalation route 90-day toxicity study (pre-TG) in rats and dogs with the source substance "Stoddard solvent", EC 232-489-3;
viii. 1971 inhalation route 90-day toxicity study (pre-TG) in guinea pigs with the source substance "Mineral spirit";
ix. 1997 dermal route 90-day study (OECD TG 411) with the source substance "Hydrodesulfurized kerosene".

We have assessed this information and identified the following issue(s):

As explained in the Appendix on Reasons common to several requests your adaptation is rejected. The following endpoint-specific deficiencies have been identified in your read-across adaptation:

As stated in the Appendix on Reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case OECD TG 408. The following key parameter(s) of this test guideline include, among others:

1. testing of at least three dose levels and a concurrent control;
2. highest dose level should aim to induce some systemic toxicity, but not death or severe suffering;
3. At least 10 female and 10 male animals should be used at each dose level (including control group);
4. dosing of the Substance daily for a period of 90 days until the scheduled termination of the study;
5. Clinical observations, ophthalmological examination, sensory reactivity to various stimuli and functional observations of the animals, Recording of body weight, hematology, clinical biochemistry, and pathology of sexual (male and female) organs, Full detailed gross necropsy and subsequent histopathology of both types tissues/ other.

The reported data for the studies you have provided do not include:

1. The studies (v, vi) you have provided were conducted with less than three dose levels, and therefore they do not fulfil the criterion set in OECD TG 408.
2. The highest dose level in the study (ix) did not induce any systemic toxicity. Therefore, the dose level selection was too low, and the study does not fulfil the criterion set in OECD TG 408.
3. The study you have provided (i, iv) was conducted with less than 10 animals per sex per test dose group. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of 20 animals (10 males + 10 females) for each test group set in OECD TG 408. The animal numbers were not reported in studies (vii, viii).
4. The studies you have provided (i, ii, iv) do not have the required exposure duration of 90 days as required in OECD TG 408, because you indicated an exposure duration of 28, 41-54 and 30 days, respectively.
5. The studies (iii, iv, v, vi, vii, viii) you have provided were not performed according to the criteria of the OECD TG 408, since the following key parameters are missing:
   iii) Clinical chemistry, ophthalmological findings, FOB, behavioural tests.
   iv) Information on organs other than kidney and liver.
   v) Behavioural observations, opthtalmology, urinalysis, behavioural tests.
   vi) Opthalmology, urinalysis, FOB, behavioural tests.
   vii) All key parameters from the TG.
   viii) Investigated organs, urinalysis, clinical chemistry, FOB, cage-side observations.

In the comments to the draft decision you reiterate your intention to adapt the information requirement according to Annex XI, Section 1.5. You present a strategy relying on the generation of additional information on the source substance Alkenes, C11-12, hydroformylation products, low boiling (EC No. 932-235-8).

ECHA acknowledges your intentions to improve the toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. Please note that this decision does not consider 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). You remain responsible for complying with this decision by the set deadline.

Based on the above, the information you provided in your dossier and with your comments on the draft decision do not fulfil the information requirement.

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 although the information indicate that human exposure to the Substance by the inhalation route is likely, potential inhalation-specific effects are already addressed by performing a qualitative assessment for inhalation, local effects.

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

2. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard 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.

In support of your adaptation, you have provided the following source of information:
(i) 1979 teratology study in rats (non-TG) with the source substance hydrocarbons C9-C12, EC 919-446-0;

We have assessed this information and identified the following issue(s):

As explained in the Appendix on Reasons common to several requests your adaptation is rejected. The following endpoint-specific deficiencies have been identified in your read-across adaptation:

According to the Appendix on Reasons common to several requests, a study must have adequate and reliable coverage of the key parameters of the corresponding test guidelines, in this case OECD TG 414. The key parameter(s) of this test guideline include:

- Dosing of the Substance from implantation until the day prior to scheduled caesarean section;
- Testing at least three dose levels and a concurrent control;

The source of information (i.) has exposure duration during gestation day 6-15, sacrifice was on gestation day 21 and only two dose levels were used.

Therefore, this source of information does not fulfil the above key parameter(s).

In the comments to the draft decision you reiterate your intention to adapt the information requirement according to Annex XI, Section 1.5. You present a strategy relying on the generation of additional information on the source substance Alkenes, C11-12, hydroformylation products, low boiling (EC No. 932-235-8).

ECHA acknowledges your intentions to improve the toxicological profile of the Substance and your plans to refine your read-across approach. As indicated in your comments, this strategy relies essentially on data which is yet to be generated, therefore no conclusion on the compliance can currently be made. Please note that this decision does not consider 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). You remain responsible for complying with this decision by the set deadline.

Therefore, the information requirement is not fulfilled.

Based on the above, the information you provided in your dossier and with your comments on the draft decision do not fulfil the information requirement.

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[13] administration of the Substance.

3. Long-term toxicity testing on aquatic invertebrates

Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

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

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5 and provided the following information:

i. OECD TG 211 key study with the analogue substance Mineral spirit type 1A
ii. Information on short-term toxicity to aquatic invertebrates

We have assessed this information and identified the following issues:

i. *Rejection of adaptation*

As explained in the Appendix on Reasons common to several requests your adaptation by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

ii. *Information on short-term toxicity*

Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has, or constituents have, a water solubility below 1 mg/l or below the detection limit of the analytical method of the test material (ECHA Guidance R.7.8.5).

You have provided information which indicates that the Substance includes constituents that are poorly water soluble.

Therefore, the short-term studies must be rejected and information on long-term toxicity on aquatic invertebrates must be provided.

In the comments to the initial draft decision, you agree to perform the requested study.

On this basis, the information requirement is not fulfilled.

Study design

OECD TG 211 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.3.

4. Long-term toxicity testing on fish

Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

You have adapted this information requirement based on Annex XI, Section 1.5.

You have provided the following information:

i. QSAR predicted no observed effect concentration(s) (NOECs) for fish with analogue substances.
ii. Information on short-term toxicity to fish

We have assessed this information and identified the following issues:

i. *Rejection of adaptation*

As explained in the Appendix on Reasons common to several requests your adaptation by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. is

rejected. The following endpoint-specific deficiencies have also been identified in your read-across adaptation:

As stated in the Appendix on Reasons common to several requests, if the grouping concept is applied then in all cases the results to be read across should:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).
- have adequate and reliable documentation of the applied method.

With regard to these conditions, we have identified the following issue(s):

a) Inappropriate measures of robustness of the model

Under ECHA Guidance R.6.1.3., a (Q)SAR model must fulfil the principles described in the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) to be considered scientifically valid. For that purpose, the fourth OECD principle requires that appropriate measures of the internal performance (i.e. goodness-of-fit and robustness using the learning data set) and predictivity (using a test data set) of the model are available.

You used the Petrotox tool to predict long term toxicity to fish. Reference is made to the report "Aquatic toxicity predictions obtained using the Petrotox model for hydrocarbons" by [redacted] from 2010. The report was however not attached to the information given in IUCLID. The Petrotox model is introduced as follows: "*Tha aquatic toxicity was estimated by a QSAR, the Petrotox computer model. This model combines a partitioning model used to calculate the aqueous concentration of hydrocarbon components with the Target Lipid Model used to calculate acute and chronic toxicity of non-polar narcotic chemicals. Petrotox computes toxicity based on the summation of the aqueous-phase concentrations of hydrocarbon block(s) that represent a hydrocarbon substance and membrane-water partition coefficients (KMW) that describe the partitionning of the hydrocarbons between the water and organism*.". The version of the model is not mentioned in the registration dossier.

The Petrotox model has a number of shortcomings in the target lipid model which likely lead to an underestimation of the (environmental) risk related to the production and use of petroleum products.[14] These shortcomings are not addressed in your justification.

On that basis, we conclude that the scientific validity of the model has not been established, and there is a risk of underestimating toxicity. Therefore, the information provided is not adequate for the purpose of classification and labelling and/or risk assessment.

b) Selection of the representative structure(s)

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 cumulative conditions is/are met:

- the composition of the substance is clearly defined, and
- representative structure(s) for the assessment are selected.

Your registration dossier provides the following information:

Four endpoint study records are provided in the registration dossier, differing in respect to the information given as test material. You provided Petrotox predictions for the following substances:

[14] https://echa.europa.eu/documents/10162/13628/review_environmental_physicochemical_methodol_en.pdf

- Hydrocarbons, C8-C12, n-alkanes, isoalkanes, cyclics, 2-25% aromatics. Key study: C8-C12 - LT Fish QSAR-Petrotox 2010 - R2, RS, K
- Hydrocarbons, C11-C14, n-alkanes, isoalkanes, cyclics, 2-25 %aromatics. Key study: C11-C14 aliphatics - LT Fish QSAR-Petrotox 2010 - R2, RS, K
- Hydrocarbons, C10-C13, n-alkanes, isoalkanes, cyclics, 2-25 %aromatics. Key study: C10-C13 Aliphatics - LT Fish QSAR-Petrotox 2010 - R2, RS, K
- Hydrocarbons, C9-C10, n-alkanes, isoalkanes, cyclics, 2-25 %aromatics. Key study: C9-C10 Aliphatics - LT Fish QSAR-Petrotox 2010 - R2, RS, K

You have considered these UVCB substances as representative structures. It is not clear how the predictions for these four UVCBs should be related to the toxicity of the Substance.

In absence of sufficient information, ECHA cannot establish that the predictions are adequate for the purpose of classification and labelling and/or risk assessment.

c) Lack of or ina*dequate 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 a QPRF. You provided documentation of the predictions that is limited to the input values and the end results. Therefore, you have not provided adequate and reliable documentation.

ECHA consider the information provided in the dossier insufficient.

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

ii. Information on short-term toxicity

As already explained in Appendix C.3, you have provided information which indicates that the Substance includes constituents that are poorly water soluble. As a result, the short-term tests does not give a true measure of toxicity for this type of substances and the long-term test is required.

Therefore, the short-term studies must be rejected and information on long-term toxicity on fish must be provided.

In the comments to the initial draft decision, you agree to perform the requested study.

On this basis, the information requirement is not fulfilled.

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 C.3.

5. 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 the following information:

i. an adaptation under Annex IX, Section 9.2., Column 2 with the following justification: *"Reliable studies show that the analogue substance, Alchisor TAL 123 and the constituent categories (Category 3 hydrocarbon solvents) of Alchisor TAL 111 (as justified in the Approach Justification Document in Section 13) are all readily biodegradable in water. Therefore Alchisor TAL 111 is also readily biodegradable in water. In accordance with REACH Annex IX column 2 exemption, the simulation testing in water and sediment does not need to be conducted as the test substance is readily biodegradable."*

We have assessed this information and identified the following issue:

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

In your comments to the initial draft decision, ECHA understands that you propose

1. An adaptation claiming that testing does not appear scientifically necessary because the Substance would not be a potential PBT substance.
2. An adaptation under Annex XI, Section 2 specifies the general rules for adapting the standard information requirement when testing is not technically possible.

Testing not scientifically necessary

We understand that you submit an adaptation under Column 2 of Section 9.2 of Annex IX according to which testing can be adapted if the chemical safety assessment does not indicate the need for further investigation.

However, this legal basis is a ground for requesting studies beyond the studies covered by the information requirements of Column 1. It is not a ground for adapting the latter studiese. Therefore, your adaptation is rejected.

Testing technically not possible

Regarding your adaptation under Annex XI, Section 2, we have assessed this information and as explained in Section 3 of the Appendix on Reasons common to several requests, it is rejected.

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.).

6. Soil simulation testing

Soil simulation testing is an information requirement under Annex IX to REACH (Section 9.2.1.3.) for substances with a high potential for adsorption to soil.

The Substance has low water solubility (below 1 mg/l for most constituents), high partition coefficient (log K_{ow} range 4.79-7.00), indicating high potential to adsorb to soil.

You have provided the following information:

i. an adaptation under Annex IX, Section 9.2., Column 2 with the following justification: "*Reliable studies show that the analogue substance, Alchisor TAL 123 and the constituent categories (Category 3 hydrocarbon solvents) of Alchisor TAL 111 (as justified in the Approach Justification Document in Section 13) are all readily biodegradable in water. Therefore Alchisor TAL 111 is also readily biodegradable in water. In accordance with REACH Annex IX column 2 exemption, the simulation testing in water and sediment does not need to be conducted as the test substance is readily biodegradable.*".

We have assessed this information and identified the following issue:

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

Therefore, the CSA indicates the need for further degradation investigation.

In your comments to the initial draft decision, ECHA understands that you propose

1. An adaptation claiming that testing does not appear scientifically necessary because the Substance would not be a potential PBT substance.
2. An adaptation under Annex XI, Section 2 specifies the general rules for adapting the standard information requirement when testing is not technically possible.

Testing not scientifically necessary

We understand that you submit an adaptation under Column 2 of Section 9.2 of Annex IX according to which testing can be adapted if the chemical safety assessment does not indicate the need for further investigation.

However, this legal basis is a ground for requesting studies beyond the studies covered by the information requirements of Column 1. It is not a ground for adapting the latter studiese. Therefore, your adaptation is rejected.

Testing technically not possible

Regarding your adaptation under Annex XI, Section 2, we have assessed this information and as explained in Section 3 of the Appendix on Reasons common to several requests, it is rejected.

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.

In accordance with the specifications of OECD TG 307, you must perform the test using at least four soils representing a range of relevant soils (*i.e.* varying in their organic content, pH, clay content and microbial biomass).

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 307.

In accordance with the specifications of OECD TG 307, 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 307; ECHA Guidance R.11.4.1.).

7. 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.

The Substance has low water solubility (below 1 mg/l for most constituents), high partition coefficient (log K_{ow} range 4.79-7.00), indicating high potential to adsorb to soil.

You have provided the following information:

i. an adaptation under Annex IX, Section 9.2., Column 2 with the following justification: "*Reliable studies show that the analogue substance, Alchisor TAL 123 and the constituent categories (Category 3 hydrocarbon solvents) of Alchisor TAL 111 (as justified in the Approach Justification Document in Section 13) are all readily biodegradable in water. Therefore Alchisor TAL 111 is also readily biodegradable in water. In accordance with REACH Annex IX column 2 exemption, the simulation testing in water and sediment does not need to be conducted as the test substance is readily biodegradable.*"

We have assessed this information and identified the following issue:

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

Therefore, the CSA indicates the need for further degradation investigation.

In your comments to the initial draft decision, ECHA understands that you propose

1. An adaptation claiming that testing does not appear scientifically necessary because the Substance would not be a potential PBT substance.
2. An adaptation under Annex XI, Section 2 specifies the general rules for adapting the standard information requirement when testing is not technically possible.

Testing not scientifically necessary

We understand that you submit an adaptation under Column 2 of Section 9.2 of Annex IX according to which testing can be adapted if the chemical safety assessment does not indicate the need for further investigation.

However, this legal basis is a ground for requesting studies beyond the studies covered by the information requirements of Column 1. It is not a ground for adapting the latter studiese. Therefore, your adaptation is rejected.

Testing technically not possible

Regarding your adaptation under Annex XI, Section 2, we have assessed this information and as explained in Section 3 of the Appendix on Reasons common to several requests, it is rejected.

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.

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.).

8. 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.

As explained in Appendix B, section 3, it is not possible to conclude whether the constituents of the Substance can be expected to be homogeneous in terms of their biodegradability. Any biodegradation observed in a ready biodegradability test performed with the Substance would not be sufficient to conclude that all the constituents of the Substance are readily biodegradable. Furthermore, the information available in the registration dossier indicates that the Substance is a potential PBT/vPvB substance.

Therefore, the CSA indicates the need for further degradation investigation.

In your comments to the initial draft decision, ECHA understands that you propose

1. An adaptation claiming that testing does not appear scientifically necessary because the Substance would not be a potential PBT substance.
2. An adaptation under Annex XI, Section 2 specifies the general rules for adapting the standard information requirement when testing is not technically possible.

Testing not scientifically necessary

We understand that you submit an adaptation under Column 2 of Section 9.2 of Annex IX according to which testing can be adapted if the chemical safety assessment does not indicate the need for further investigation.

However, this legal basis is a ground for requesting studies beyond the studies covered by the information requirements of Column 1. It is not a ground for adapting the latter studiese. Therefore, your adaptation is rejected.

Testing technically not possible

Regarding your adaptation under Annex XI, Section 2, we have assessed this information and as explained in Section 3 of the Appendix on Reasons common to several requests, it is rejected.

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 B and C, sections 3-5 and 5-7 respectively) 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 (Appendices B and C, sections 3 and 5 respectively) 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 studies] according to OECD TG 308 and 307 (Appendices B and C, sections 4-5 and 6-7 respectively) must be conducted at 12°C and at a test material application rates 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 standard information requirement mentioned above according to Annex XI, Section 1.2. of REACH (weight of evidence).

You have provided a waiver that concludes: "*The weight of evidence approach takes into consideration key factors identified below: [1] Commonality of functional group and metabolic fates across species (rodents and non-rodents) [2] Rats are sensitive indicators of developmental toxicity in other hydrocarbon substances (containing constituents not present in hydrocarbon solvents) [3] Results of selected developmental toxicity tests in hydrocarbon solvents are similar across species (rodents and non-rodents) A summary of the key factors identified is provided in the attached document (Prenatal Development 2nd Species Waiver) in section 13 of IUCLID.*".

In support of your adaptation, you have provided a document "*Prenatal Development 2nd Species Waiver*" in section 13 of IUCLID.

Annex XI, Section 1.2 states that there may be sufficient weight of evidence weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence adaptation.

You have provided a justification for the weight of evidence adaptation as follows:

1. Commonality of functional group and metabolic fates across species (rodents and non-rodents).
2. Rats are sensitive indicators of developmental toxicity in other hydrocarbon substances (containing constituents not present in hydrocarbon solvents).
3. Results of selected developmental toxicity tests in hydrocarbon solvents are similar across species (rodents and non-rodents).

While you have listed various risk-related aspects (1-4) to justify you adaptation, you have not included a justification with an assessment, integration and weighing of the individual sources of information for relevance, reliability, coverage, consistency and results, and subsequently decided whether they together provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Your adaptation is rejected because it lacks of adequate and reliable (concise) documentation for justification and the information requirement is not fulfilled.

Use always when go to evaluation of relevance and reliability of the information:

Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.7.2 at Annex X includes similar information that is produced by the OECD TG 414 on a second species. The following aspects are covered: 1) prenatal developmental toxicity, 2) maternal toxicity, and 3) maintenance of pregnancy.

You have not provided any source of information on a second species in your dossier. In addition, information on a first species is rejected as unreliable for the reasons explained in request C.2, above.

Therefore, you have provided no information on prenatal developmental toxicity, maternal toxicity and maintenance of pregnancy in a second species, while even the information provided on a first species is not reliable.

It is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 414 study in a second species as specified in this decision.

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

Based on the above, the information you provided do not fulfil the information requirement.

In your comments to the draft decision, you acknowledge that Pre-natal developmental toxicity study in two species is a standard information requirement for A.X registrations and that your technical dossier does not contain such a study. You agree to perform the study according to OECD TG 414 in second species with the source substance (EC#932-235-8).

Despite of accepting the legal requirement of the study, you however challenge the scientific justification for the request. In fact, you refer to several references in scientific literature (eg. RIVM, 2008; Janer et al, 2008; Hurrr et al, 2003; van Ravenzwaay et al, 2012) to question the added value of the rabbit and claiming the rabbit not being more sensitive than rats.

Furthermore, you refer to ECHA Guidance which concludes that the prenatal developmental test when performed on two species is usually sufficient for drawing a reliable conclusion on reproductive toxicity properties. Also you refer to the consultation phase of ECHA Guidance and note that despite of critical stakeholder comments, ECHA has not changed their position and a PNDT in two species is a standard information requirement in REACH Annex X.

Firstly, Pre-natal developmental toxicity study in two species is a legal information requirement at Annex X and your dossier has a data gap. Furthermore, ECHA Guidance aids the interpretation of the legal text. The major purpose of a PNDT study is to identify prenatal developmental hazard and if identified, classify accordingly following the criteria of the CLP Regulation.

Secondly, despite of some statements that for reviewed substances the added value of the rabbit was limited, the combination of rat and rabbit study will increase the probability of identifying developmental toxicity as compared to a single species study (Janer et al, 2008; Hurtt et al, 2003). Before conducting a study, one cannot know which species is more sensitive as no single species has been shown to be most predictive of a human teratogen

(Hurtt et al, 2003). This supports why the rabbit data may have added value when performing hazard assessment of individual substances and clarify their intrinsic properties and further, in weight of evidence approach when considering classification.

Information on study 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.2 in this decision).

The study shall be performed with oral[15] administration of the Substance.

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

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[16].

B. Test material

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 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

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[17].

[16] https://echa.europa.eu/practical-guides
[17] 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

Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. You must assess the PBT properties of each relevant constituent of the Substance present in concentrations at or above 0.1% (w/w) and of all relevant transformation/degradation products. Alternatively, you would have to justify why you consider these not relevant 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 and potential alternative testing strategies. 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. When determining the sequence of 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

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS. Similarly the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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 13 August 2020.

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

ECHA took into account your comments and amended the request for skin sensitisation.

The deadline to provide the requested information was amended to 30 months for most requests, to align with other decisions for related substances.

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 amendment(s) and referred the modified draft decision to the Member State Committee.

Your comments on the proposed amendment were taken into account by the Member State Committee.

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-77 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix H: List of references - ECHA Guidance[18] 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)[19]

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

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[20]
Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

[18] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[19] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[20] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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]

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.