~~Confidential~~

Helsinki, 06 May 2022

Addressees
Registrant(s) of JSO_Alcohols C9-11 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
22/09/2010

Registered substance subject to this decision ("the Substance")
Substance name: Alcohols, C9-11-branched and linear
EC number: 288-284-4

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***12 August 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. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: EU B.13/14. / OECD TG 471).

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

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 tests performed for the information requirement of Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. then: In vitro gene mutation study in mammalian cells is an information requirement under Annex VIII to REACH (Section 8.4.3.).

3. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.).

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

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

1. 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).

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 or 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 and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

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

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

Authorised[1] under the authority of 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 the weight of evidence adaptations

You have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation(s) under Annex XI, Section 1.2:

- 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.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- 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.)

For repeated dose and reproductive toxicity, you justify the weight of evidence as follows: "Based on the weight of evidence from all available studies, a 3 -generation dietary study in rats, repeated dose dietary studies of 90 -day and 2 year duration in rats and dogs, developmental toxicity studies by gavage in rats and rabbits, and a dietary study in rats covering the prenatal and complete gestation and parturition period in rats".

For mutagenicity,you justify the weight of evidence as follows: "The data available from standard in vitro and in vivo genetic toxicity assays for all related substances show no evidence of mutagenic potential."

Your weight of evidence adaptation raises the same decifiencies irrespective of the information requirement for which it is invoked. Accordingly, ECHA addressed these deficiencies in the present Appendix, before assessing the specific standard information requirements in the following appendices.

Annex XI, Section 1.2 states that there may be sufficient 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 approach.

In any weight of evidence justification, the integration of the sources of information is fundamental to support a robust conclusion on whether the Substance has a particular dangerous property. Three main aspects must be addressed: (1) Analysis of the extent to which the composition of the Substance is covered by the sources of information; (2) Analysis of the extent to which the hazard data obtained from the sources of information reliably cover the key aspects that is foreseen to be investigated by study normally required for the information requirement(s) where weight of evidence is invoked; and (3) Analysis of the residual uncertainty.

The Substance is a UVCB (unknown or variable composition, complex reaction products or of biological materials) substance composed of mainly linear but also branched C9-C11 alcohols.

The sources of information provided have mainly been conducted using mono- or multi constituent substances or UVCB substances. You have not explained to what extent each source of information covers the composition of the Substance.

Furthermore, you have not explained how the hazard data obtained with the sources of information, considering their relevance, reliability, coverage of investigations, consistency and results, can be brought together to reach a conclusion on whether or not the Substance has a particular dangerous property with regard each of the infromation requirement(s).

Moreover, you have not analysed the residual uncertainty associated with the weight of evidence conclusion for each infromation requirment.

Based on the above, ECHA concludes that you have not provided sufficient/adequate documentation to support a robust conclusions for your weight of evidence adaptations.

In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation.

Your weight of evidence approach has deficiencies that are common to all information requirements under consideration and also deficiencies that are specific for these information requirements individually. The common deficiencies are set out below, while the specific ones are set out under the information requirement concerned in the Appendices A to D.

1.1. Reliability of the provided information with analogue substances

ECHA understands that you use data obtained with analogue substances in a read-across approach as part of your weight of evidence adaptation. For this information to reliably contribute to the weight of evidence approaches, it would have to meet the requirements for Grouping of substances and read-across approaches.

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2] and related documents[3, 4].

Description of the grouping

In the CSR, you refer to a category of 'C6-24 Alcohols. Long Chain Alcohols (C6-24 primary aliphatic alcohols; linear and essentially linear)'. You identify the members of the category Table 1.1. of the CSR and provide a category justification document in Section 1.4. of the the CSR.

You define the the structural basis for the grouping as: a family of primary aliphatic alcohols within a carbon chain length range of C6-C24, limited to linear and essentially-linear alcohols.

ECHA understands that this is the applicability domain of the grouping and will assess your predictions on this basis.

Predictions for toxicological properties

You provide a read-across justification in the CSR.

[2] ECHA Guidance R.6
[3] Read-Across Assessment Framework (RAAF)
[4] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs

For toxicological properties you read-across to the Substance from the following source substances:

- octan-1-ol, EC No. 271-642-9;
- docosan-1-ol, EC No. 211-546-6;
- tetradecan-1-ol, EC No. 267-019-6;
- 2-ethylhexan-1-ol, EC No. 203-234-3;
- dodecan-1-ol, EC No. 203-982-0;
- hexan-1-ol, CAS No. 111-27-3;
- pentadecan -1-ol, EC No. 269-790-4;
- tetradecan-1-ol, EC No. 267-019-6; and
- alcohols, C7-11-branched and linear; EC No. 287-623-3.

You provide the following reasoning for the predictions of toxicological properties: the "hypothesis is that the long chain linear aliphatic alcohol family has at its centre an homologous series of increasing carbon chain length, which is associated with a consistency and predictability in the property data across the group, for the physicochemical, environmental, and toxicological property data sets. In addition, certain branched and unsaturated structures are considered to have such similar properties that their inclusion in the category is well justified."

You consider with respect to repeated dose and reproductive toxicity, that chronic and sub-chronic toxicity studies have shown that long chain alcohols (LCA) are of low toxicity. Furthermore, you note that combined repeated-dose studies with developmental endpoints, as well as reproductive and developmental studies showed no effects at the highest dose tested. Rather than having separate values for the three endpoints, one endpoint "systemic effects" has been used instead. As you consider that the NOAELs do not vary greatly across the category, you have chosen one key study as being representative of the whole category.

For mutagenicity, you further specify that "key studies were chosen from studies on closely related linear or branched alcohols of similar chain length".

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

ECHA notes the following shortcomings with regards to predictions of toxicological properties. They are common to all the information requirements for which you refer to read-across information, unless their limited application is indicated in the title:

> *Read-across hypothesis for repeated dose and developmental toxicity contradicted by existing data*

Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances". The Guidance on IRs and CSA, Section R.6.2.2.1.f., indicates that "it is important to provide supporting information to strengthen the rationale for the read-across". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the category members.

The observation of differences in the toxicological properties between the source substance(s) and the Substance would contradict the hypothesis that the properties of the Substance can be predicted from the data on category members. An explanation why such differences do not affect the read-across hypothesis must to be provided and supported by scientific evidence.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar category members cause the same type of effect(s) and that these effects are quantitatively similar.

However, the effects observed in the repeated dose toxicity studies including developmental toxicity studies vary among the category members from no effects to mortality.

Contrary to what you claim the reported NOAELs obtained from the sub-chronic toxicity (90 day) studies vary significantly among the category members; e.g. NOAEL 1200 mg/kg/day (Hexan-1-ol, diet); NOAEL 170 mg/kg/day (C14-16 Alcohols, diet); and NOAEL 125 mg/kg bw/day (2-EH; gavage).

The available data on the category members indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the Substance and category members cause the same type of effect(s) and that these effects are quantitatively similar. Therefore you have not demonstrated and justified that the properties of the category members are likely to be similar despite the observation of these differences.

Missing 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" (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). 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 must include bridging studies to compare properties of the category members.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). 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 that both substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

The Substance contains mainly linear but also branched alcohols. You have not provided supporting information addressing the impact on the toxicological properties of allowed variations in structural elements; i.e. linear alcohols, branched alcohols, and position of the branching within the alcohols. While there is information on the UVCB substances which may contain various linear and branched components, there are either no information on test substance composition to confirm the coverage of the constituents tested ('Missing information on the test material' below) or the test substance(s) are not covering the structural elements present in the target substance. You have not provided any supporting information to mitigate this fact.

ECHA also notes that you have provided additional summaries of information and data matricies in the CSR. As the information on these studies provided in the CSR is limited and not sufficient for an independent evaluation, this informaiton has not been further considered in this assessment of your adaptation.

For the reasons presented above, it is not possible to demonstrate that e.g. the toxicity profile of the Substance containing linear and branched components can be predicted from the source substances. There are no supporting information to explain why the structural differences do not influence toxicokinetics and toxicodynamics of the substances.

In the absence of such information, you have not established that the Substance and the source substance(s) are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

Missing information on the test material

Under Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must be adequate for the purpose of classification and labelling and/or risk assessment.

In order to predict the properties of the Substance, the test material used in the study on the source substance must be representative for the source substance (Article 10 and Recital 19 of REACH; Guidance on IRs and CSA, Section R.4.1.). Therefore, an unambiguous characterisation of the composition of the test material used to generate the source data is required to assess whether the test material is representative for the source substance.

For most of the studies provided, you have identified the test material by name and chemical identifiers, without further information on the composition of the test material.

In the absence of the information on the composition and impurities of the test material, you have not demonstrated that the test material is representative for the source substance. Therefore, the study is not adequate for the purpose of classification and labelling and/or risk assessment.

Conclusion on the reliability of the information on the analogue substances

Based on the above, the information from the analogue substances cannot reliably contribute to your weight of evidence adaptations.

2. Information provided in your comments on the draft decision regarding the environmental endpoints

In your comments to the initial draft decision, you do not agree to perform the requested studies for the following environmental endpoints:

- Short-term toxicity in aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study on algae (Annex VII, Section 9.1.2.)
- Short-term toxicity in fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity in aquatic invertebrates (Annex IX, Section 9.1.5.)

Long-term toxicity in fish (Annex IX, Section 9.1.6.)

Instead, you now indicate your intention to adapt the above mentioned standard information requirements by means of grouping and read-across according to Annex XI, Section 1.5, of the REACH Regulation.

In your proposed read-across adaptation, you refer to a C6-24 Alcohols Category, which consists of a family of primary aliphatic alcohols with carbon chain lengths in the range C6-C24. The category members have varied compositions and are linear or have a single short-chain alkyl side-branch at the 2-position in the alkyl chain (usually an α-methyl or α-ethyl group).

In the comments, you propose a strategy relying on the generation of further evidence to strengthen the category approach and for this you indicate your intention to first undertake a new programme of literature research and QSAR modelling. You indicate that you then intend to incorporate in the category data any new experimental data available for substances within the chain length of the category members. You will then reassess the selection of key studies.

You also indicate that you intend to do this "together with experimental work as necessary" and you further specify that "Short-term toxicity data may be generated (preferably for single constituent mono-branched alcohols) as needed, to ensure that sufficient relevant evidence

is available to justify the category approach for the ecotoxicity endpoints and for validation of QSARs". You do not specify which category members you intend to use in experimental testing other than your proposal to conduct OECD TG 210 tests in C6 and C14 linear saturated alcohols (Hexan-1-ol (EC 203-852-3) and Tetradecanol (EC 204-000-3)) within the category. You expect that these substances are at the extremes of the range where ecotoxicity effects may be observed.

In the comments, you further acknowledge that the category approach and the use of data for purposes of exposure assessment and risk characterisation could be documented more clearly and you commit to improve the documentation in the dossier update.

In the comments, you also foresee that validated QSAR predictions based on logKow are likely to be applicable since the mechanism of action for the category member alcohols is narcosis and a consistent trend in ecotoxicity correlated with carbon number is expected.

ECHA acknowledges your intention to generate additional information/data and your plans to refine the read-across approach.

However, as your strategy relies on a read-across hypothesis and on supporting information that needs to be fully described and justified, as well as on data/information which is yet to be generated for the proposed category members (including bridging studies and supporting information), no conclusion on the compliance of the proposed adaptation can be made. You remain responsible for complying with this decision by the set deadline.

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

1. In vitro gene mutation study in bacteria

An *in vitro* gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

1.1. Information provided for the information requirement

You have adapted this information requirement by using Weight of evidence based on the following experimental data with substances other than the Substance:

i. Bacterial reverse mutation assay (1996) conducted with octan-1-ol, EC No. 271-642-9.
ii. In vitro mammalian chromosome aberration test (2002) conducted with docosan-1-ol, EC No. 211-546-6.
iii. In vitro mammalian chromosome aberration test (1998) conducted with tetradecan-1-ol, EC No. 267-019-6.
iv. In vitro mammalian cell gene mutation test (1983) conducted with 2-ethylhexan-1-ol, EC No. 203-234-3.
v. Mammalian bone marrow chromosome aberration test (1983) conducted with 2-ethylhexan-1-ol, EC No. 203-234-3. 50 cells
vi. Mammalian erythrocyte micronucleus test (1992) conducted with dodecan-1-ol, EC No. 203-982-0.

1.2. Assessment of the information provided

You have adapted this information requirement using weight of evidence under Annex XI, Section 1.2.

As explained under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.1 at Annex VII include:

- Detection and quantification of gene mutations (base pairs, substitution, or frame shift) in cultured bacteria including data on the number of revertant colonies; and
- Data provided on 5 bacterial 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).

We have assessed the individual sources of information with regard to relevance and identified the following issue(s):

Sources of information (ii-vi) have not investigated gene mutation in bacteria. Consequently, these studies do not provide relevant information for this information requirement.

The source of information (i) provide information on gene mutations in bacteria. However, the study was performed with 4 strains. The fifth strain *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is missing. Consequently, the source of information provides partially relevant information on gene mutation in bacteria.

In addition, it has the following deficiency affecting its reliability:

Reliability of read-across predictions

As explained in Section 1.1. of the Appendix common to several requests, you have not demonstrated that you reliably can predict the properties of the Substance by using test results obtained with other substances.

Conclusion on the weight of evidence

As indicated above, only one source of infromation provide partially relevant information for the information requirement, as the 5th strain is missing. In addition, the reliability of this information is hampered by the use of read-across which increases the uncertainty of the conclusion for the Substance. In addition, as explained in the Annex common to several requests, you have not provided adequate documentation addressing how you integrate the evidence to reach a robust conclusion on the weight of evidence.

Therefore, it is not possible to conclude, based on any source of information alone or together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 471 test.

Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

In your comments on the draft decision, you agreed to conduct the test.

1.3. Information on study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471, 2020) is considered suitable.

2. Short-term toxicity testing on aquatic invertebrates

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

2.1. Information provided for the information requirement

You have provided the following information:

i. key study following "OECD 1981 and EEC 1979a" guideline equivalent or similar to OECD TG 202 with the substance Alcohols, C9-11-linear and branched (name of test material [redacted]) (1983, [redacted]).

ii. key study following test guideline by Ministry of Agriculture, Fisheries and Food, Burnham-on-Crouch, UK with the substance Alcohols, C9-11-linear and branched (name of test material [redacted]) (1991, [redacted].).

iii. supporting study following "test method identical to that used in Garforth 1983" with the substance Alcohols, C9-11-linear and branched ([redacted]) (1982, [redacted]).

2.2. Assessment of the information provided

We have assessed this information and identified the following issues:

2.2.1. To comply with the information requirement, the test material in a study must be representative for the Substance (Article 10 and Recital 19 of REACH; ECHA Guidance R.4.1).

For the studies (i-iii) above, you have identified the test material as "[redacted]", without further information. You have not provided the EC and/or CAS numbers of the test material and did not report any information on its composition.

In the absence of composition information on the test material, the identity of the test material and its impurities cannot be assessed, and you have not demonstrated that the test material is representative for the Substance.

2.2.2 To fulfil the information requirement, a study must comply with the OECD TG 202 and the requirements of the OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met: the concentrations of the test material are measured at least at the highest and lowest test concentration, at the beginning and end of the test.

Your Substance is considered as difficult to test, due to the reasons described below in section 2.3.

Your registration dossier provides two key studies (i-ii) and one supporting study (iii) showing the following: no analytical monitoring of exposure was conducted.

The fact that the test concentrations in the studies (i-iii) are not analytically monitored, despite the expected instability of the hydrophobic, surface active and readily biodegradable Substance in water, is considered a critical methodological deficiency resulting in the rejection of the study results.

On this basis, the studies are rejected and the information requirement is not fulfilled.

Your comments on the draft decision are addressed in the Appendix on Reasons common to several requests, section 2, above.

2.3. Study design

The Substance is difficult to test due to the high logKow (3.8-4.7), surface activity (surface tension 18-36 mN/m) and expected instability in water (readily biodegradable substance). OECD TG 202 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 202. 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.

3. Growth inhibition study aquatic plants

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

3.1. Information provided for the information requirement

You have provided the following information:

i. key study equivalent or similar to OECD TG 201 with the substance Alcohols, C9-11-linear and branched (name of test material [redacted]) (1982, [redacted]).

3.2. Assessment of the information provided

We have assessed this information and identified the following issues:

3.2.1. To comply with this information requirement, the test material in a study must be representative for the Substance (Article 10 and Recital 19 of REACH; ECHA Guidance R.4.1).

For the key study (i) above, you have identified the test material as "[redacted] You have not provided the EC and/or CAS numbers of the test material and did not report any information on its composition.

In the absence of information on the composition of the test material, the identity of the test material and its impurities cannot be assessed, and you have not demonstrated that the test material is representative for the Substance.

3.3.2. To fulfil the information requirement, a study must comply with the OECD TG 201 and the requirements of the OECD GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test (Article 13(3) of REACH). Therefore, the following specifications must be met: the concentrations of the test material are measured at least at the beginning and end of the test:

1) at the highest, and
2) at the lowest test concentration, and
3) at a concentration around the expected EC_{50}.

For unstable test substances, additional samplings for analysis at 24 hour intervals is required.

As already explained above, the Substance is difficult to test.

Your registration dossier provides an OECD TG 201 key study showing the following: no analytical monitoring of exposure was conducted.

The fact that the test concentrations in the study (i) are not analytically monitored, despite the expected instability of the hydrophobic, surface active and readily biodegradable Substance in water, is considered a critical methodological deficiency resulting in the rejection of the study results.

On this basis, the study is rejected, and the information requirement is not fulfilled.

Your comments on the draft decision are addressed in the Appendix on Reasons common to several requests, section 2, above.

3.3. Study design

The OECD TG 201 specifies that for difficult to test substances the 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.2.

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.).

1.1. Information provided for the information requirement

You have adapted this information requirement by using Weight of evidence based on the following experimental data with substances other than the Substance:

i. Bacterial reverse mutation assay (1996) conducted with octan-1-ol, EC No. 271-642-9.
ii. In vitro mammalian chromosome aberration test (2002) conducted with docosan-1-ol, EC No. 211-546-6.
iii. In vitro mammalian chromosome aberration test (1998) conducted with tetradecan-1-ol, EC No. 267-019-6.
iv. In vitro mammalian cell gene mutation test (1983) conducted with 2-ethylhexan-1-ol, EC No. 203-234-3.
v. Mammalian bone marrow chromosome aberration test (1983) conducted with 2-ethylhexan-1-ol, EC No. 203-234-3.
vi. Mammalian erythrocyte micronucleus test (1992) conducted with dodecan-1-ol, EC No. 203-982-0.

1.2. Assessment of the information provided

You have adapted this information requirement using weight of evidence under Annex XI, Section 1.2.

As explained under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.2. at Annex VIII includes:

- Detection and quantification of structural or numerical chromosomal aberrations in cultured mammalian cells including data on the cytotoxicity and the frequency of cells with chromosomal aberrations or micronuclei.

We have assessed the individual sources of information with regard to relevance and identified the following issue(s):

The sources of information (i) and (iv) have not investigated chromosomal aberrations in mammalian cells. Consequently, these studies do not provide relevant information.

The sources of information (ii), (iii), (v) and (vi) provide relevant information on chromosomal aberrations in mammalian cells.

However, they have the following deficiencies affecting their reliability:

Reliability of read-across predictions

As explained in Section 1.1. of the Appendix common to several requests, you have not demonstrated that you reliably can predict the properties of the Substance by using test results obtained with other substances.

Results obtained from studies (ii) and (iii) not fully reliable when compared to the OECD TG 473

Investigations/specifications in an *in vitro* mammalian chromosome aberration test (OECD TG 473) include that at least 300 well-spread metaphases must be scored per concentration.

In the sources of information (ii) and (iii), the following investigations/specifications are not to the requirements of OECD TG 473 as the studies scored 200 cells per concentration.

Based on the above, the reliability of the contribution of the results obtained from this study to the weight of evidence is limited. The lower statistical power of the studies introduce uncertainty in the results which must be considered.

Results obtained from study (v) is not fully reliable when compared to the OECD TG 475

Investigations/specifications in a Mammalian bone marrow chromosome aberration test (OECD TG 475) include:

a) 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.
b) 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.
c) At least 200 metaphases must be analysed for each animal for structural chromosomal aberrations including and excluding gaps.

In the source of information (v), the following investigations/specifications are not to the requirements of OECD TG 475:

a) The highest dose in the study correspond to about one fifth of the LD_{50}; this is well below the MTD.
b) >You provide a mitotic index, however you to have not explained how many cells were counted to calculate the index.
c) The study has counted 50 cells when 200 well spread metaphases should be analysed.

Based on the above, the reliability of the contribution of the results obtained from this study to the weight of evidence is limited. The lower statistical power of the study and the unclarity regarding how the results were obtained introduce uncertainty in the results which must be considered.

Results obtained from study (vi) is not fully reliable when compared to the OECD TG 474

Investigations/specifications in a Mammalian erytrocyte microneucleus test (OECD TG 474) include that the proportion of immature among total (immature + mature) erythrocytes must be determined for each animal (by counting a total of at least 2000 erythrocytes for peripheral blood).

In the source of information (vi), the following investigations/specifications are not to the requirements of the OECD TG 474 as the study has counted 1000 erythrocytes.

Based on the above, the reliability of the contribution of the results obtained from this study to the weight of evidence is limited. The lower statistical power of the study introduce uncertainty in the results which must be considered.

Conclusion on the weight of evidence

As indicated above, the sources of information provide relevant information for the information requirement. However, the reliability of this infromation is hampered by the use of read-across and issues related to how the results were obtained in the studies which increases the uncertainty of the conclusion for the Substance. In addition, as explained in

the Annex common to several requests, you have not provided adequate documentation addressing how you integrate the evidence to reach a robust conclusion on the weight of evidence.

Therefore, it is not possible to conclude, based on any source of information alone or together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in a OECD TG 473 or OECD TG 487 test.

Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

1.3. Information on 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.

In your comments on the draft decision, you agreed to conduct the test.

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.

The result of the requests for information in the Sections 1 of Appendix A and of this Appendix 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.

2.1. Information provided for the information requirement

You have adapted this information requirement by using Weight of evidence based on the following experimental data with substances other than the Substance:

i. Bacterial reverse mutation assay (1996) conducted with octan-1-ol, EC No. 271-642-9.
ii. In vitro mammalian chromosome aberration test (2002) conducted with docosan-1-ol, EC No. 211-546-6.
iii. In vitro mammalian chromosome aberration test (1998) conducted with tetradecan-1-ol, EC No. 267-019-6.
iv. In vitro mammalian cell gene mutation test (1983) conducted with 2-ethylhexan-1-ol, EC No. 203-234-3.
v. Mammalian bone marrow chromosome aberration test (1983) conducted with 2-ethylhexan-1-ol, EC No. 203-234-3. 50 cells
vi. Mammalian erythrocyte micronucleus test (1992) conducted with dodecan-1-ol, EC No. 203-982-0.

2.2. Assessment of the information provided

You have adapted this information requirement using weight of evidence under Annex XI, Section 1.2.

As explained under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.4.3 at Annex VIII includes similar information that is produced by the OECD TG 476/490 and OECD TG 488. This includes:

- Detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) including data on the frequency of mutant colonies in cultured mammalian cells (in vitro) or mutant frequency for each tissue in mammals (in vivo).

We have assessed the individual sources of information with regard to relevance and identified the following issue(s):

The sources of information (i) to (iii) and (v) to (vi) have not investigated gene mutation in mammalian cells. Consequently, these studies do not provide relevant information.

The source of information (iv) provides relevant information on gene mutation in mammalian cells.

However, there are deficiencies affecting its reliability:

Reliability of read-across predictions

As explained in Section 1.1. of the Appendix common to several requests, you have not demonstrated that you reliably can predict the properties of the Substance by using test results obtained with other substances.

Results obtained from study (iv) is not fully reliable when compared to the OECD TG 476

Investigations/specifications in an In vitro mammalian cell gene mutation tests using the Hprt and xprt genes (OECD TG 476) include:

a) 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.
b) Data on the cytotoxicity and the mutation frequency for the treated and control cultures must be reported.

In the source of information (iv), the following investigations/specifications are not to the requirements of the OECD TG 476:

a) You to not state which positive control was used nor do you provide data on the cytotoxicity and the mutation frequency for the positive control
b) You have not provided data on the cytotoxicity and the mutation frequency for the treated and control cultures.

Based on the above, the reliability of the contribution of the results obtained from this study to the weight of evidence is limited. The unclarity regarding how the results were obtained introduce uncertainty in the results which must be considered.

Conclusion on the weight of evidence

As indicated above, only one source provide relevant information for the information requirement. However, the reliability of this source of information is hampered by the use of read-across and issues related to how the results were obtained which increases the uncertainty of the conclusion for the Substance. In addition, as explained in the Annex common to several requests, you have not provided adequate documentation addressing how you integrate the evidence to reach a robust conclusion on the weight of evidence.

Therefore, it is not possible to conclude, based on any source of information alone or together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 476 or OECD TG 490 test.

Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

2.3. Information on 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.

In your comments on the draft decision, you agreed to conduct the test if the results of the In vitro bacterial mutagenicity (Appendix A, request 1) and In vitro mammalian cytogenicity (Appendix B, request 1) give negative results.

3. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII to REACH (Section 8.6.1.). This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII to REACH or a general adaptation rule under Annex XI to REACH.

3.1. Information provided for the information requirement

You have adapted this information requirement by using Weight of evidence based on the following experimental data with substances other than the Substance:

i. Combined Repeat dose and Reproductive/Developmental Toxicity Screening Test (1992) conducted with dodecan-1-ol, EC No. 203-982-0.
ii. Sub-acute toxicity study (7 days; 1970) conducted with octan-1-ol, EC No. 271-642-9.
iii. Sub-chronic toxicity study (90 days; 1966) conducted with hexan-1-ol, CAS No. 111-27-3.
iv. Sub-chronic toxicity study (90 days; 1978) conducted with pentadecan-1-ol, EC No. 269-790-4.
v. Sub-chronic toxicity study (90 days; 1993) conducted with 2-ethylhexan-1-ol, EC No. 203-234-3.
vi. Sub-acute toxicity study (28-days; 1999) conducted with tetradecan-1-ol, EC No. 267-019-6.

3.2. Assessment of the information provided

You have adapted this information requirement using weight of evidence under Annex XI, Section 1.2.

As explained under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.1. at Annex VIII includes similar information that is produced by the OECD TG 407. The following aspects of systemic toxicity are covered: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity.

We have assessed the individual sources of information with regard to relevance and identified the following issue(s):

Aspect 1) in-life observations

In-life observations must include information on survival, body weight development, clinical signs, functional observations, food/water consumption and other potential aspects of in life observations on the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory).

The sources of information (i) and (iii) to (vi) provide relevant information on aspect 1).

The source of information (ii) has not investigated any elements of aspect 1) apart from survival and cage side observations. Consequently, it provides partly relevant information on aspect 1).

However, these sources of information have deficiencies affecting their reliability:

Reliability of read-across predictions

As explained in Section 1.1. of the Appendix common to several requests, you have not demonstrated that you reliably can predict the properties of the Substance by using test results obtained with other substances.

Results obtained from study (ii) is not fully reliable when compared to the OECD TG 407

Investigations/specifications in a sub-acute toxicity study (OECD TG 407) include dosing of the Substance daily for a minimum of 28 days.

In study (ii), the following investigations/specifications are not to the requirements of OECD TG 408 as the study has an exposure duration of 7 days.

Based on the above, the reliability of the contribution of the results obtained from this study to the weight of evidence is limited. The shorter exposure duration introduce uncertainty in the results, which must be considered. This condition of exposure is essential because the effects observed over the longer exposure might be considerably more pronounced over a shorter study duration.

Aspect 2) blood chemistry

Information on blood chemistry must include haematological (full-scale) and clinical chemistry analysis (full-scale), and other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary).

The source of information (ii) has not investigated the elements of aspect 2). Consequently, it does not provide relevant information on aspect 2).

The source of information (iii) has not investigated the elements of aspect 2) apart from haematocrit, haemoglobin, total and differential leukocyte count. Consequently, it provides partly relevant information on aspect 2).

The sources of information (i) and (iv) to (vi) provide relevant information on aspect 2).

While the sources of information (i) and (iii) to (vi) provide (partly) relevant information with regard to aspect 2) their reliability is affected by the same issue related to read-across as identified for aspect 1) above.

Aspect 3) organ and tissue toxicity

Organ and tissue toxicity must include information on terminal observations on organ weights, gross pathology and histopathology (full-scale) and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory,

endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory).

The sources of information (i) and (iii) to (vi) provide relevant information on aspect 3).

The source of information (ii) has not investigated the elements of aspect 3) apart from histopathology of the gastro-intestinal tract. Consequently, it provides partly relevant information on aspect 3).

While the sources of information (i) to (vi) provide (partly) relevant information with regard to aspect 3) they have deficiencies affecting their relability.

Specifically, reliability issue related to read-across as identified for aspect 1) above also applies equally to this aspect. In addition, for the source of information (ii) the exposure duration issue as identified for aspect 1) above also applies equally to this aspect.

Conclusion on the weight of evidence

As indicated above, there are two types of reliability issues associated with your weight of evidence adaptation: unjustified use of read-across and issues related to how the results were obtained in the individual lines of evidence. In addition, as explained in the Annex common to several requests, you have not provided adequate documentation addressing how you integrate the evidence to reach a robust conclusion on the weight of evidence.

Therefore, it is not possible to conclude, based on any source of information alone or together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 407 study.

Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

3.2.1. Information on study design

The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days; see Appendix C, Section 1). According to Column 2 of Annex VIII, Section 8.6.1., and to prevent unnecessary animal testing, a Short-term toxicity study (28 days) does not therefore need to be conducted.

Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

In your comments on the draft decision, you agree to conduct a Sub-chronic toxicity study with the Substance. You may use the result of this study to adapt this information requirement.

4. Short-term toxicity testing on fish

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

4.1 Information provided for the information requirement

You have provided the following information:

i. OECD TG 203 key study with the substance Alcohols, C9-11-linear and branched (name of test material [redacted]) (1979, [redacted].
ii. supporting study following test guideline by Ministry of Agriculture, Fisheries and Food, Burnham-on-Crouch, UK, with the substance Alcohols, C9-11-linear and branched (name of test material [redacted]) (1991[redacted]).

We have assessed this information and identified the following issues:

4.2 Assessment of the information provided

4.2.1. To comply with this information requirement, the test material in a study must be representative for the Substance (Article 10 and Recital 19 of REACH; ECHA Guidance R.4.1).

For both studies (i and ii) above, you have identified the test material as "[redacted], without further information, including no information regarding EC and/or CAS numbers or composition.

In the absence of composition information on the test material, the identity of the test material and its impurities cannot be assessed, and you have not demonstrated that the test material is representative for the Substance.

4.2.2. To fulfil the information requirement, a study must comply with the OECD TG 203 and the requirements of the 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:

a) in static tests, if the concentrations of the test material are not expected to remain within ± 20 % of the nominal, then the test substance concentration is determined (in one replicate) in all concentrations at the beginning, at 48 hours and at the end of the test;
b) in semi-static tests, test concentrations are measured at least twice over one exposure period (before and after renewal of test solutions). If the concentrations of the test material are expected to decline by more than 20%, analytical monitoring is conducted on all test concentrations with an additional determination on the other exposure period(s);
c) at least 7 fish are used at each test concentration and in the control(s).

As already explained above, the Substance is difficult to test.

Your registration dossier provides one static key study (i) and one semi-static supporting study (ii) showing the following:

a) no analytical monitoring of exposure was conducted in static study (i);
b) no analytical moinitoring of exposure was conducted in semi-static study (ii);
c) only five fish were used at each test concentration in study (i).

The fact that the test concentrations in the studies (i) and (ii) are not analytically monitored despite the expected instability of the hydrophobic, surface active and readily biodegradable Substance in water is considered a critical methodological deficiency resulting in the rejection of the study results. Further, in study (i) the lower number of fish compared to the requirements of the OECD TG 203 reduces the statistical power in deriving the effect value.

On this basis, the studies are rejected, and the information requirement is not fulfilled.

Your comments on the draft decision are addressed in the Appendix on Reasons common to several requests, section 2, above.

4.3 Study design

The OECD TG 203 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.2.

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 under Annex IX to REACH.

1.1. Information provided for the information requirement

You have adapted this information requirement by using Weight of evidence based on the following experimental data with substances other than the Substance:

i. Combined Repeat dose and Reproductive/Developmental Toxicity Screening Test (1992) conducted with dodecan-1-ol, EC No. 203-982-0.
ii. Sub-acute toxicity study (7 days; 1970) conducted with octan-1-ol, EC No. 271-642-9.
iii. Sub-chronic toxicity study (90 days; 1966) conducted with hexan-1-ol, CAS No. 111-27-3.
iv. Sub-chronic toxicity study (90 days; 1978) conducted with pentadecan-1-ol, EC No. 269-790-4.
v. Sub-chronic toxicity study (90 days; 1993) conducted with 2-ethylhexan-1-ol, EC No. 203-234-3.
vi. Sub-acute toxicity study (28-days; 1999) conducted with tetradecan-1-ol, EC No. 267-019-6.

1.2. Assessment of the information provided

You have adapted this information requirement using weight of evidence under Annex XI, Section 1.2.

As explained under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.2. at Annex IX includes similar information that is produced by the OECD TG 408. The following aspects of systemic toxicity are covered: 1) in-life observations, 2) blood chemistry, 3) organ and tissue toxicity.

We have assessed the individual sources of information with regard to relevance and identified the following issue(s):

Aspect 1) in-life observations

In-life observations must include information on survival, body weight development, clinical signs, functional observations, food/water consumption and other potential aspects of in life observations on the relevant physiological systems (circulatory, digestive/excretory, integumentary, musculoskeletal, nervous, renal/urinary, and respiratory).

The sources of information (i) and (iii) to (vi) provide relevant information on aspect 1).

The source of information (ii) has not investigated the elements of aspect 1) apart from survival and cage side observations. Consequently, it provides relevant information on aspect 1).

However, these sources of information have deficiencies affecting their reliability:

Reliability of read-across predictions

As explained in Section 1.1. of the Appendix common to several requests, you have not demonstrated that you reliably can predict the properties of the Substance by using test results obtained with other substances.

Results obtained from study (i), (ii) and (vi) are not fully reliable when compared to the OECD TG 408

Investigations/specifications in a sub-chroni toxicity study (OECD TG 408) include:

a. At least 10 male and 10 female animals for each test and control group.
b. Dosing of the Substance daily for a minimum of 90 days.

In study (i), the following investigations/specifications are not to the requirements of OECD TG 408:

a. the study has an exposure duration of 41-54 days.

In study (ii), the following investigations/specifications are not to the requirements of OECD TG 408:

a. the study has 8 animals/sex/dose group
b. the study has an exposure duration of 7 days.

In study (vi), the following investigations/specifications are not to the requirements of OECD TG 408:

a. the study has 5 animals/sex/dose group
b. the study has an exposure duration of 28 days.

Based on the above, the reliability of the contribution of the results obtained from this study to the weight of evidence is limited. The lower statistical power and shorter exposure duration of the studies introduce uncertainty in the results which must be considered. This condition of exposure is essential because the effects observed over the longer exposure might be considerably more pronounced over a shorter study duration.

Aspect 2) blood chemistry

Information on blood chemistry must include haematological (full-scale) and clinical chemistry analysis (full-scale), and other potential aspects related to blood chemistry to address relevant physiological systems (circulatory digestive/excretory, endocrine, immune, musculoskeletal, and renal/urinary).

The source of information (ii) has not investigated the elements of aspect 2). Consequently, it does not provide relevant information on aspect 2).

The sources of information (i) and (iv) to (vi) provide relevant information on aspect 1.

The source of information (iii) has not investigated the elements of aspect 2) apart from haematocrit, haemoglobin, total and differential leukocyte count. Consequently, it provides partly relevant information on aspect 2).

While the sources of information (i) and (iii) to (vi) provide (partly) relevant information with regard to aspect 2) they have deficiencies affecting their relability.

Specifically,the reliability issue related to read-across as identified for aspect 1) above also applies equally to this aspect. In addition, for the sourcse of information (i), (ii) and (vi) the exposure duration issue identified for aspect 1) above also applies equally to this aspect.

Aspect 3) organ and tissue toxicity

Organ and tissue toxicity must include information on terminal observations on organ weights, gross pathology and histopathology (full-scale) and other potential aspects related to organ and tissue toxicity to address relevant physiological systems (circulatory, digestive/excretory,

endocrine, immune, integumentary, musculoskeletal, nervous, renal/urinary system, reproductive, and respiratory).

The sources of information (i) and (iv) to (vi) provide relevant information on aspect 3).

The source of information (ii) has not investigated the elements of aspect 3) apart from histopathology of the gatsro-intestinal tract. Consequently, it provides partly relevant information on aspect 3).

The source of information (iii) has not investigated all the elements of aspect 3); histopathology of thymus, peripheral nerve, muscle, spinal cord, eye plus optic nerve, pituitary or trachea are missing. Consequently, it provides partly relevant information on aspect 3).

However, all the sources have deficiencies affecting their reliability:

Specifically, the reliability issue related to read-across identified for aspect 1) above also applies equally to this aspect. In addition, for the source of information (i), (ii) and (vi) the exposure duration issue identified for aspect 1) above also applies equally to this aspect.

Furthermore, study (iii) is affected as follows:

Results obtained from study (iii) are not fully reliable when compared to the OECD TG 408

Investigations/specifications in a sub-chroni toxicity study (OECD TG 408) include:

a. At least 10 male and 10 female animals for each test and control group. Full histopathology as specified in paragraphs 47-49 of the test guideline.

In study (iii), the following investigations/specifications are not to the requirements of OECD TG 408:

a. the study had 10 animals/sex and dose group; however, histopathology as only been examined in 5 animals/sex and dose group

Based on the above, the reliability of the contribution of the results obtained from this study to the weight of evidence is limited. The lower statistical power of the study introduce uncertainty in the results which must be considered.

Conclusion on the weight of evidence

As indicated above, therere are sources of infromation (partially) relevant for the information requirement, the reliability of this information is hampered by the use of read-across and issues related to how the results were obtained in the studies which increases the uncertainty of the conclusion for the Substance. In addition, as explained in the Annex common to several requests, you have not provided adequate documentation addressing how you integrate the evidence to reach a robust conclusion on the weight of evidence.

Therefore, it is not possible to conclude, based on any source of information alone or together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 408 study.

Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

1.3. Information on study design

Following 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 of the Substance; Guidance on IRs and CSA, Section R.7.5.6.3.2.

According to the OECD TG 408, the rat is the preferred species.

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

In your comments on the draft decision, you agree to conduct the requested study with 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.

2.1. Information provided for the information requirement

You have adapted this information requirement by using Weight of evidence based on the following experimental data with other substances than the Substance:

(i) pre-natal developmental toxicity study (1997a) in rats conducted with the analogue substance Octan-1-ol; EC No. 203-917-6.
(ii) pre-natal developmental toxicity study (1997b) in rats conducted with the analogue substance Alcohols, C7-11-branched and linear; EC No. 287-623-3.
(iii) pre-natal developmental toxicity study (1997c) in rats conducted with the analogue substance 2-ethylhexan-1-ol; EC No. 203-234-3.
(iv) combined repeated dose and reproductive/developmental toxicity screening test (1992) in rats conducted with the analogue substance dodecan-1-ol; EC No. 203-982-0.

2.2. Assessment of the information provided

You have adapted this information requirement using weight of evidence under Annex XI, Section 1.2.

As explained under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

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

We have assessed the individual sources of information with regard to relevance and identified the following issue(s):

Aspect 1) pre-natal developmental toxicity

Pre-natal developmental toxicity includes information after pre-natal exposure on embryonic/foetal survivial (number of live foetuses; number of resorptions and dead foetuses, postimplantation loss), growth (body weights and size) and structural malformations and variations (external, visceral and skeletal).

The sources of information (i) and (iii) provide relevant information on aspect 1).

The source of information (iv) has investigated elements of survival and growth of the of the offspring. However, the study has not investigated skeletal and visceral malformations and variations. Consequently, the study provide partially relevant information on aspect 1).

However, these sources of information have deficiencies affecting their reliability:

Reliability of read-across predictions

As explained in Section 1.1. of the Appendix common to several requests, you have not demonstrated that you reliably can predict the properties of the Substance by using test results obtained with other substances.

Results obtained from study (iv) is not fully reliable when compared to the OECD TG 414

Investigations/specifications in a pre-natal developmental toxicity study (OECD TG 414) include:

a) each group should aim to have 20 female animals with implantation sites at necropsy. Groups with fewer than 16 animals with implantation sites may be inappropriate.
b) examination of the foetuses for sex and body weight; external, skeletal, and soft tissue alterations (variations and malformations); number of resorptions and or live foetuses; and measurement of anogenital distance in live rodent foetuses.

In study (iv), the following investigations/specifications are not to the requirements of the OECD TG 414:

c) the study started with 12 animals per group; no information on the number of animals with implantation sites.
d) the study has not investigated skeletal and soft tissue alterations (variations and malformations) nor measurement of anogenital distance in live rodent foetuses.

Based on the above, the reliability of the contribution of the results obtained from this study to the weight of evidence is limited. The lower statistical power of the study and unclairity on how the results were obtained introduce uncertainty in the results which must be considered.

Aspect 2) maternal toxicity and aspect 3) maintenance of pregnancy

Maternal toxicity includes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in dams.

Maintenance of pregnancy includes information on abortions and/or early delivery as a consequence of gestational exposure and other potential aspects of maintenance of pregnancy.

The sources of information (i) to (iv) provide relevant information on aspects 2) and 3).

However, these sources have deficiencies affecting their reliability. Specifically, the relaibility issue related to read-across identified for aspect 1) above also applies equally to these aspects.

In addition, the issues identified for aspect 1) related to low statistical power and how the investigations were obtained in the source of information (iv) equally affect aspects 2) and 3).

Conclusion on the weight of evidence

As indicated above, there are two types of reliability issues associated with your weight of evidence adaptation: unjustified use of read-across and issues related to how the results were obtained in the individual lines of evidence. In addition, as explained in the Annex common to several requests, you have not provided adequate documentation addressing how you integrate the evidence to reach a robust conclusion on the weight of evidence.

Therefore, it is not possible to conclude, based on any source of information alone or together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 414 study.

Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

2.2.1. Information on study design

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

In your comments on the draft decision, you agree to conduct the requested OECD TG 414 study in rats or rabbits as the first species.

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.).

3.1 Information provided for the information requirement

You have provided the following justification to omit the study "*In accordance with Section 1 of REACH Annex XI, the study does not need to be conducted because the needs associated with a sound understanding of long-term aquatic toxicity to invertebrates study (required in Section 9.1.5) are adequately met by the available data on constituents. For the purpose of risk assessment aquatic PNECs for individual constituents have been derived*".

3.2 Assessment of the information provided

We have assessed this information and identified the following issue:

Adapting the information requirement in accordance with the general rules for adaptation set out in Annex XI requires identifying clearly the specific legal basis of the adaptation invoked and complying with relevant conditions listed in the corresponding section of Annex XI. In all cases, adequate and reliable documentation must be provided, including relevant justification and study records.

You have not indicated any specific legal basis/section of Annex XI of REACH (e.g. 1.1. Use of existing data, or 1.2. Weight of Evidence, or 1.5. Grouping of substances and read-across approach) that you consider as a reason to adapt this information requirement. In addition, no relevant justification nor documentation (e.g. study record) is provided for this endpoint in the IUCLID dossier.

On this basis, your adaptation is rejected, and the information requirement is not fulfilled.

Your comments on the draft decision are addressed in the Appendix on Reasons common to several requests, section 2, above.

3.3 Study design

The 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.2.

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.).

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

4.1 Information provided for the information requirement

You have provided the following justification to omit the study "*In accordance with Section 1 of REACH Annex XI, the study does not need to be conducted because the needs associated with a sound understanding of long-term aquatic toxicity to fish study (required in Section 9.1.6) are adequately met by the available data on constituents. For the purpose of risk assessment aquatic PNECs for individual constituents have been derived*".

4.2 Assessment of the information provided

We have assessed this information and identified the following issue:

Adapting the information requirement in accordance with the general rules for adaptation set out in Annex XI requires identifying clearly the specific legal basis of the adaptation invoked and complying with relevant conditions listed in the corresponding section of Annex XI. In all cases, adequate and reliable documentation must be provided, including relevant justification and study records.

You have not indicated any specific legal basis/section of Annex XI of REACH (e.g. 1.1. Use of existing data, or 1.2. Weight of Evidence, or 1.5. Grouping of substances and read-across approach) that you consider as a reason to adapt this information requirement. In addition, no relevant justification nor documentation (e.g. study record) is provided for this endpoint in the IUCLID dossier.

On this basis, your adaptation is rejected the information requirement is not fulfilled.

Your comments on the draft decision are addressed in the Appendix on Reasons common to several requests, section 2, above.

4.3 Study design

The OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in 'Study design' under Appendix A.2.

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.

1.1. Information provided for the information requirement

You have adapted this information requirement by using Weight of evidence based on the following experimental data with the Substance:

(v) pre-natal developmental toxicity study (1997a) in rats conducted with the analogue substance Octan-1-ol; EC No. 203-917-6.
(vi) pre-natal developmental toxicity study (1997b) in rats conducted with the analogue substance Alcohols, C7-11-branched and linear; EC No. 287-623-3.
(vii) pre-natal developmental toxicity study (1997c) in rats conducted with the analogue substance 2-ethylhexan-1-ol; EC No. 203-234-3.
(viii) combined repeated dose and reproductive/developmental toxicity screening test (1992) in rats conducted with the analogue substance dodecan-1-ol; EC No. 203-982-0.

1.2. Assessment of the information provided:

You have adapted this information requirement using weight of evidence under Annex XI, Section 1.2.

As explained under Appendix on Reasons common to several requests, the weight of evidence adaptation must fulfil the information requirement based on relevant and reliable sources of information. These sources of information must provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

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

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 (two species taking the first species into account to address the potential species differences). The following aspects are covered: 1) prenatal developmental toxicity in two species, 2) maternal toxicity in two species, and 3) maintenance of pregnancy in two species.

1) Prenatal developmental toxicity: Prenatal developmental toxicity includes information after prenatal exposure on embryonic/foetal survivial (number of live foetuses; number of resorptions and dead foetuses, postimplantation loss), growth (body weights and size) and structural malformations and variations (external, visceral and skeletal) and other potential aspects of developmental toxicity due to *in utero* exposure. This information in two species should be covered to address the potential species differences.

2) Maternal toxicity: Maternal toxicity inlcudes information after gestational exposure on maternal survival, body weight and clinical signs and other potential aspects of maternal toxicity in the pregnant dam. This information in two species should be covered to address the potential species differences.

3) Maintenance of pregnancy: Maintenance of pregnancy includes information on abortions and/or early delivery as a consequence of gestational exposure.

We have assessed the individual sources of information with regard to relevance and identified the following issue(s):

All the sources of information have been conducted in the rat.

None of the sources of information provided have been generated in a species other than the rat. Information on PNDT properties in a second species is missing.

Therefore, it is not possible to conclude whether the Substance has or has not hazardous properties in relation to PNDT in two species.

Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

1.3. 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[6] administration of the Substance.

In your comments on the draft decision, you agree to conduct the requested OECD TG 414 study in rats or rabbits, depending on the species chosen for the first species.

[6] 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[7].

B. Test material

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

1. Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

a) the variation in compositions reported by all members of the joint submission,
b) the boundary composition(s) of the Substance,
c) 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

a) 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.
b) The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[8].

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

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

A. 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 05 Feburary 2021.

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

ECHA took into account your comments and did not amend the request(s).

Comments on the deadline to submit the requested information

In your comments you requested an extension of the deadline for providing the requested information from 24 months to 45 months. You argue that the extension is needed to perform sufficient studies to support read-across the toxicity information requirements of the larger category of C6-C24 alcohols of which the Substance is a member. In response, ECHA notes the following.

Your read-across testing strategy as explained in your comments refers to conducting tests on substances which are not addressed by this compliance check decision. In addition, the testing strategy covers information requirements which are not within the scope of this compliance check. However, for the calculation of the deadline ECHA can only take into account the requests in this decision.

Therefore, an extension of the deadline set in the decision to accommodate your intention to conduct a tentative testing strategy which may or may not result in compliance for the Substance is not considered justified.

The deadline set in this decision allows for generating the required data on the Substance as a result of incompliances identified in your registration. This deadline has already been set to allow sequential testing where appropriate.

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

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

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

Appendix H: List of references - ECHA Guidance[9] 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)[10]

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

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

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

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

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

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

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

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

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

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

OECD Guidance documents[12]

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

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

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

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

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

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

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

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

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.