EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 04 June 2021

Addressees
Registrant(s) of JS_lanolin_alcohols as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
02/12/2014

Registered substance subject to this decision ("the Substance")
Substance name: Alcohols, lanolin
EC number: 232-430-1
CAS number: 8027-33-6

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***11 March 2024***.

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

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

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

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

1. Long-term toxicity testing on fish also requested below (triggered by Annex VIII, Section 9.1.3., Column 2)

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

1. 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 (rabbit)

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

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

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

- Appendices entitled "Reasons to request information required under Annexes VII to X of REACH", respectively.

Information required depends on your tonnage band

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

- the information specified in Annex VII to REACH, for registration at 1-10 tpa
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa
- the information specified in Annexes VII to 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 Christel Schilliger-Musset, Director of Hazard Assessment

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

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

1. Growth inhibition study aquatic plants

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

You have provided an OECD TG 201 key study (2001, [redacted]

We have assessed this information and identified the following issues:

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

- a reliable analytical method for the quantification of the test material in the test solutions with reported specificity, recovery efficiency, precision, limits of determination (*i.e.* detection and quantification) and working range must be available. Alternatively, a justification why the analytical monitoring of exposure concentrations is not technically feasible must be provided;

- the 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};

- the results can be based on nominal or measured initial concentration only if the concentration of the test material has been maintained within 20 % of the nominal or measured initial concentration throughout the test;

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

- a justification for, or validation of, the separation technique is provided, demonstrating that all reasonable efforts have been taken to achieve a saturation concentration. This is especially important if filtration is used, as it can cause losses due to adsorption onto the filter matrix.

Your registration dossier provides an OECD TG 201 study showing the following:

- One saturated stock solution was prepared and used as the highest test concentration. This saturated solution was diluted to create lower test concentration series of four dilution levels;

- The concentration of the test material was determined using a dissolved organic carbon (DOC) method. You did not provide performance parameters for this method, including limit of detection. While the performance of the method cannot be currently assessed based on the information submitted, the DOC is considered as a nonspecific method with low sensitivity. Therefore the DOC method used may not be reliable to measure the substance in test solution. You did not provide any justification why the substance specific analytical monitoring of exposure concentrations is not technically feasible;

- the concentration of the test material was determined only at the beginning of the test and only at the highest test concentration level;
- the results of the test (ErC50>2.5 mg DOC/L and NOEC 0.15 mg DOC/L) were based on nominal concentrations;
- test media preparation to achieve maximum dissolved concentration in the saturated stock solution included 24 h shaking and the use of filter (0.2 µm) as a separation method, and no justification for the use of this method was provided.

Your registration dossier also provides three EU Method A.6 studies and based on the results of these studies you conclude that the water solubility of the Substance falls within the range of 0.1 to 0.4 mg/L.

The Substance is difficult to test due to low water solubility and high adsorptive properties. These properties make it difficult to achieve maximum dissolved test substance concentration and to maintain dissolved concentrations during the test. Based on above, there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically you have not prepared WAFs separately for each dose level and you have not justified nor demonstrated that the method applied in test media preparation allowed achieving maximum dissolved concentration in the saturated stock solution. You have used a non-specific analysis method and you have analysed the DOC concentrations only at the beginning of the test and only at the highest test concentration level. You have also reported the study results based on nominal concentrations but due to lack of analytical monitoring at the end of the test and at lower concentrations, you have not demonstrated that the test concentrations have been maintained within 20% of the nominal or measured initial concentration.

Therefore, the requirements of OECD TG 201 and OECD GD 23 are not met.

On this basis, the information requirement is not fulfilled.

In your comments to the draft decision you agree with the deficiencies identified by ECHA and you agree to perform the requested test.
Study design

The Substance is difficult to test due to the low water solubility (0.1 - 0.4 mg/L), high lipophilicity (LogKow 6.73 – 10.79) and adsorptive properties (log Koc 3.67 – 6.78). OECD TG 201 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

For UVCBs, the analytical method must be adequate to monitor qualitative and quantitative changes in exposure to the dissolved fraction of the test material during the test (e.g. by comparing mass spectral full-scan GC or HPLC chromatogram peak areas or by using targeted measures of key components).

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

- use loading rates that are sufficiently low to be in the solubility range of most constituents (or that are consistent with the PEC value). This condition is mandatory to provide relevant information for the hazard and risk assessment (ECHA Guidance, Appendix R.7.8.1-1, Table R.7.8-3);
- provide a full description of the method used to prepare the WAF (including, among others, loading rates, details on the mixing procedure, method to separate any remaining non-dissolved test material including a justification for the separation technique);
- prepare WAFs separately for each dose level (i.e. loading rate) and in a consistent manner.

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

1. Long-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.). Long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

You have provided the following information:

- A key study according to OECD TG 203 (Fish, Acute Toxicity Test) on the Substance.
- You have adapted the information requirement on long-term toxicity on fish in your registration dossier.

We have assessed this information and identified the following issue:

Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (ECHA Guidance R.7b, Section 7.8.5).
In your dossier the solubility of the Substance in water was determined to be 0.1 – 0.4 mg/L.

Therefore, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

The examination of the information provided, as well as the selection of the requested test and the test design are addressed under section C.1. Your comments are also addressed under section C.1.

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

1. Long-term toxicity testing on fish

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

You have omitted this information and you provided the following justification:

You admit that no studies on the chronic toxicity to fish are available for the Substance, but you continue that the acute toxicity tests on fish and Daphnia showed no effects in the range of water solubility. You also state that it cannot be expected that a long-term test with fish will generate different results than the existing long-term test with aquatic invertebrates as there was no sign in the short-term tests that invertebrates are less sensitive than fish.

Furthermore, you refer to the *ECHA Guidance on information requirements and chemical safety assessment, Chapter R.7b (ECHA, 2012b),* which states that *"chronic fish toxicity testing is generally only necessary, when the P and B criteria are fulfilled",* and you conclude that the Substance is not P or B.

You also claim that chronic exposure of aquatic organisms is expected to be very low as only negligible releases into surface waters from sewage treatment plants are expected due to the high adsorption and low water solubility resulting in an effective removal in sewage treatment plants.

For the above reasons and to avoid unnecessary vertebrate tests, you conclude that long-term test with fish is not required for the Substance.

We understand that your adaptation is intended to refer to Annex IX, Section 9.1., Column 2 and you consider that the Chemical Safety Assessment does not indicate a need to investigate further the long-term toxicity in fish.

We have assessed this information and identified the following issues:

A registrant may only adapt this information requirement based on the general rules set out in Annex XI. It is noted that Column 2 of Annex IX, Section 9.1, does not allow omitting the need to submit information on long-term toxicity to fish under Column 1 (Decision of the Board of Appeal in case A-011-2018).

Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH.

Therefore, you have not demonstrated that this information can be omitted. Minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

Also, absence of short-term toxicity of a poorly soluble substance is not a legal ground for adaptation of long-term testing under the general rules of Annex XI. As already explained under Section B.1, poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests do not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (ECHA Guidance R.7.8.5).

We agree that the Substance is not having PBT/vPvB properties. Therefore, no further information is needed for the PBT assessment. However, long-term fish toxicity data are used to enable the environmental hazard assessment of the substance including, not only the PBT assessment, but also classification and labelling and derivation of PNECwater (*ECHA Guidance on* information requirements and chemical safety assessment, Chapter R.7b (ECHA, vers. 4.0. June 2017). Therefore, long-term fish toxicity data are needed for the environmental hazard assessment and the lack of P and B properties is not a legal ground for adaptation of long-term testing under the general rules of Annex XI.

For the sake of completeness, ECHA also evaluated your adaptation under Annex XI, Section 3.2(a)(Substance-tailored exposure-driven testing).

Under Annex XI, Section 3, this information may be omitted based on the exposure scenario(s) developed in the Chemical Safety Report. The justification must be based on a rigorous exposure assessment in accordance with Annex I, Section 5 and must meet the following criteria:

(a) It can be demonstrated that all the following conditions are met:
   i. the absence or no significant exposure in all scenarios of the manufacture and all identified uses referred to in Annex VI, Section 3.5., and
   ii. a PNEC can be derived from available data, which:
      - must be relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes and therefore must be based on reliable information on the hazardous properties of the substance on at least three trophic levels;
      - must take into account the increased uncertainty resulting from the omission of the information requirement, in this case by selecting an appropriate assessment factor (AF) as described in ECHA Guidance R.10.3.
   iii. the ratio between the results of the exposure assessment (PECs) and the PNEC are always well below 1

Your registration dossier does not provide an exposure assessment and risk characterisation for the freshwater/marine water compartments in your CSR.

In the absence of this information, the adaptation is not based on rigorous exposure assessment in accordance with Annex I, Section 5. Further, you have not demonstrated the absence or no significant exposure in all scenarios of the manufacture and all identified uses referred to in Annex VI and that for all exposure scenarios the PECs are well below the PNEC.

In your comments on the draft decision you have indicated that no effects were seen in an OECD 211 study with *Daphnia magna* using a Water Accomodated Fraction (WAF) method at single nominal loading rate of 100 mg/L, and you continue that "*Before conducting vertebrate testing it is proposed to update the chemical safety report to include an exposure assessment based on no effects being seen at the water solubility limit to determine if further information is needed.*".

ECHA understands that you first intend to update your chemical safety report by, e.g., including an exposure assessment and PNEC derivation based on currently available hazard data. ECHA also understands that you agree to conduct the requested study but only in case the updated chemical safety report indicates the need for further information.

As indicated above, you may only adapt this information requirement based on the general rules set out in Annex XI. Column 2 of Annex IX, Section 9.1, does not allow omitting the need to submit information on long-term toxicity to fish under Column 1 (Decision of the Board of Appeal in case A-011-2018).

In the absence of exposure scenario(s) in your current dossier, you have not demonstrated that no or no significant exposure to the Substance occurs in the context of the uses listed in your Chemical Safety Report. As regards the other conditions set in Annex XI, Section 3, you have not addressed the deficiency of the missing PNEC value and you have not demonstrated that the PEC/PNEC ratios are always well below one. PNEC value can be derived from data which must be relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes. As your substance is poorly water soluble, PNEC value must be derived from long-term aquatic toxicity data which provides reliable information on the hazardous properties of such substances.

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

Study design

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

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

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

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

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

You have provided a PNDT study in a first species (rats; [redacted] 2014) and the following justification for an adaptation of the PNDT study in a second species: "*In accordance with Column 1, Section 8.7.2. of Annex IX of the REACH regulation, a prenatal developmental toxicity study has to be performed in one species, considering the most appropriate route of administration, and having regard to the likely route of human exposure. Furthermore, in accordance with Column 2, Section 8.7.2 of Annex IX of the REACH regulation, the study shall be initially performed in one species. A decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available data. One prenatal developmental toxicity study was recently performed in the standard species rat with the test material Lanolin Alcohols. No effects on developmental endpoints or teratogenicity up to the limit dose tested were observed. Thus, to account for animal welfare, the conduct of further developmental toxicity studies in a second species according to Annex IX of the REACH regulation with Lanolin Alcohols would be scientifically unjustified.*".

ECHA understands that you refer to an adaptation of Annex IX, Section 8.7.2., Column 2, "*A decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available data.*"

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

In order to be compliant and enable concluding if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in two species.

A pre-natal developmental toxicity study in a second species is a standard information requirement at Annex X unless one or more of the adaptations in Section 8.7 of Annex X or Annex XI apply, taking into account the results of the test in the first species or any other relevant avalable information.

Your adaptation refers to the provisions of Annex IX, Column 2, Section 8.7.2. Since your Substance is registered at more than 1000 tpa, the information requirement of Annex X, 8.7.2 for a PNDT study in a second species applies. This standard information requirement cannot be adapted according to Annex IX, Column 2, Section 8.7.2.

In your comments on the draft decision you have further indicated that you consider that a second PNDT study is not necessary "*because the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available) . The substance did not show any evidence of genotoxicity or mutagenicity in the studies reported in section 7.6 (OECD 471, OECD 473 and OECD 476). No adverse treatment related effects were seen at doses up to and including the limit dose (1000mg/kg) in the OECD 408 study reported in section 7,5. This study included examination of the reproductive organs. No adverse effects were seen; up to and including the limit dose (1000mg/kg), in either the mother or the offspring in the OECD 414 study conducted in rats reported and reported in section 7.8*"

ECHA understands that you refer in your comments to an adaptation of the information requirement of Annex X, 8.7.2 for a PNDT study in a second species according to Annex X, Section 8.7., Column 2, third indent.

According to Annex X, Section 8.7., Column 2, third indent, the study does not need to be conducted if three concomitant criteria are fulfilled, two of them being:

i. that it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure; and
ii. that there is no or no significant human exposure.

The criterion i. listed above requires the demonstration that no systemic absorption occurs. You have not provided toxicokinetic data on the Substance. Instead, you conducted a qualitative assessment of the available substance specific data on physico-chemical and toxicological properties. In section 5.1.3 of your Chemical Safety Report, you concluded on this basis that *"based on molecular weight and physico-chemical characteristics, the oral absorption rate of Lanolin alcohols is anticipated to be low. However, the absorption rate may be higher if the substance undergoes micellar solubilisation as described for cholesterol"*.

The criterion ii. listed above refers to the absence of human exposure or of significant human exposure. According to the information provided in your dossier, you report uses of the Substance at industrial sites, widespread uses by professional workers and consumer uses. Your dossier does not include an exposure assessment.

In the absence of toxicokinetic data, you have not established that no systemic absorption occurs via the relevant routes of exposure. Similarly, in the absence of an exposure assessment, you have not demonstarted that no or no significant exposure to the Substance occurs in the context of the uses listed in your Chemical Safety Report.

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

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

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 species. The test in the first species was carried out by using a rodent species (rat). Therefore, a PNDT study in a second species must be performed in the rabbit as preferred non-rodent species.

The study shall be performed with oral[2] administration of the Substance.

2. Extended one-generation reproductive toxicity study

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

You have provided the following justification for an adaptation of the EOGRT study: *"In accordance with Column 1, Section 8.7.3 of Annex IX of the REACH regulation, a two-generation reproductive toxicity study has to be performed in one species, male and female, considering the most appropriate route of administration, and having regard to the likely route of human exposure, if the 28-day or 90-day study indicates adverse effects on reproductive organs or tissues. Furthermore, in accordance with Column 2 of Annex IX of the REACH regulation, the study shall be initially performed in one species. A decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available date. The available 90-day repeated*

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

dose toxicity study in rats revealed no effects on female and male reproductive organs or tissues up to the limit dose tested. Furthermore, a prenatal developmental toxicity study performed according to OECD 414 and tested up to the limit dose in rats showed no substance-related effects on developmental toxicity endpoints. Thus, to account for animal welfare, the conduct of further reproduction toxicity studies according to Annex IX of the REACH regulation with Lanolin Alcohols would be scientifically unjustified".

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

In order to be compliant and enable concluding if the Substance is a reproductive toxicant, information provided has to meet the requirements of OECD TG 443.

The basic test design of an Extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is a standard information requirement under Annex X to REACH unless one or more of the adaptations in Section 8.7 of Annex X or Annex XI apply. Furthermore Column 2 of Section 8.7.3. defines when the study design needs to be expanded.

We understand that with reference to the provisions of Annex IX, Column 2, Section 8.7.3 you consider that the EOGRT study is not triggered based on the results of the available 90-day repeated dose toxicity study and prenatal developmental toxicity study. However, since your Substance is registered at more than 1000 tpa, the information requirement of Annex X, 8.7.3 for an Extended one-generation reproductive toxicity (EOGRT) study applies. This standard information requirement cannot be adapted according to Annex IX, Column 2, Section 8.7.3 and does not have as a requirement that the available repeated-dose studies indicate adverse effects or concerns related to reproductive toxicity.

Furthermore, in your comments on the draft decision you have referred to the provisions of Annex X, 8.7.3, column 2 a) and b) and reported that you "*consider that this end point is not necessary since there is no information to suggest that any of the criteria in part b are met*". You specify that the Substance "*did not show any evidence of genotoxicity or mutagenicity in the studies reported in section 7.6 (OECD 471, OECD 473 and OECD 476)*" and that in the subchronic toxicity study on the Substance, "*no adverse treatment related effects were recorded and there is no indication of endocrine disruption*". The provisions of Annex X, 8.7.3, column 2 a) and b) present the criteria warranting the extension of the cohort 1B to include the F2 generation. These provisions do not constitute a basis for adapting the standard information requirement of Annex X, 8.7.3 for an EOGRT study.

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

The specifications for the study design

Premating exposure duration and dose-level setting

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

Ten weeks premating exposure duration is required to obtain results adequate for classification and labelling and /or risk assessment. There is no substance specific information in the dossier supporting shorter premating exposure duration.[1]

Therefore, the requested premating exposure duration is ten weeks.

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

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

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

Cohorts 1A and 1B

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

Species and route selection

The study must be performed in rats with oral[3] administration.

Further expansion of the study design

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and/or Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if relevant information becomes available from other studies or during the conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance[4].

[3] ECHA Guidance R.7a, Section R.7.6.2.3.2.
[4] ECHA Guidance R.7a, Section R.7.6.

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

A. Test methods, GLP requirements and reporting

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

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

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[5].

B. Test material

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

1. Selection of the Test material(s)

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

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

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

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[6].

[5] https://echa.europa.eu/practical-guides
[6] 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

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 16 July 2020.

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

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

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

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

Appendix H: List of references - ECHA Guidance[7] 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)[8]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[8]

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[9]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

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

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

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

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

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

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

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

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