Helsinki, 22 October 2020

Addressees
Registrant(s) of 701-314-7_JS_EM_LR as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
13/09/2019

Registered substance subject to this decision ("the Substance")
Substance name: Alkenes, C6-11 (branched), hydroformylation products, distn. residues, heavy cracked fraction
EC number: 701-314-7
CAS number: NS

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***30 January 2023***.

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

A. 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, with the Substance

2. Soil simulation testing (Annex IX, Section 9.2.1.3.; test method: EU C.23./OECD TG 307) at a temperature of 12 °C with the Substance

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

4. Identification of degradation products (Annex IX, 9.2.3.; test method: EU C.23/OECD TG 307 or EU C.24/OECD TG 308) with the Substance

B. 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)

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

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

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and

in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in 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.

Approved[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 for the requirements applicable to all the Registrants subject to Annex IX of REACH

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2)

A Sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX to REACH.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.2 of REACH (Weight of Evidence).

In support of your adaptation, you have provided the following sources of information:

(i) Supporting 28d RDT study ([redacted] 1990) according to EU Method B.7 (Repeated Dose (28 Days) Toxicity, Oral) with the Substance;
(ii) Reference to the U.S. EPA HPV Challenge Program Submission [redacted] 2003) of a substance with a similar compositional profile (CAS#68526-82-9), study equivalent or similar to OECD Guideline 413 (Subchronic Inhalation Toxicity: 90-Day Study (1987);
(iii) The OECD Guideline 473 (In vitro Mammalian Chromosome Aberration Test) and OECD Guideline 476 (In vitro Mammalian Cell Gene Mutation Test) studies;

Based on the presented sources of information, you argue that the available data gives sufficient information to conclude on the sub-chronic toxicity because: *"The overall weight of the evidence does not justify the additional use of animal testing."*.

Additionally, you have submitted an adaptation based on read-across in accordance with Annex XI, section 1.5. and to support your adaptation, you have provided the following source of information:

[redacted] Read-across adaptation of OECD Guideline 413 (Subchronic Inhalation Toxicity: 90-Day Study) based on analogue substance Alkenes, C6-10, hydroformylation products, high-boiling" (CAS#68526-82-9), [redacted]

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

A. Weight of evidence

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.

You have not included a justification for your weight of evidence adaptation, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

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

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 8.6.2 at Annex IX includes similar information that is produced by the OECD TG 408. At general level it includes information on repeated dose toxicity in live animals for comparable or longer exposure duration.

In more detail, sub-chronic repeated dose toxicity study (90 day) includes at least three dose levels, clinical observations, ophthalmological examination, haematology, clinical biochemistry, urinalysis, full detailed gross necropsy and subsequent histopathology and at least 20 animals per dose group and exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3), in this case 90 days.

The source of information (*i.*), 28d repeated dose toxicity study, provides relevant information on short term repeated dose toxicity on live animals. In more detail, it includes i.e. clinical and functional observations, body weight measurent, clinical biochemistry, histopathology, gross necropsy and organ weights in at least 10 animals per dose group.

The source of information (*ii.*), subchronic inhalation toxicity study with an analogue substance, provides relevant information on some key elements similar to OECD TG 408, such as similar exposure duration. In more detail, the study covers clinical observations, body weight measurements, clinical chemistry, gross necropsy and organ weights.

However the information provided on sub-chronic toxicity is limited and does not cover all relevant and essential aspects as defined above.

More in particular, the source of information (*i.*) does not have sufficient study duration and the number of animals does not meet the requirements as required in OECD TG 408.

The source of information (*ii.*) has particular attention to the respiratory tract and it does not cover all relevant and essential aspects as defined above. In particular, full histopathology, thyroid hormone level measurements, parameters related to spermatogenesis, sperm and oestrous cycle are missing. Finally, the oral route is the default one for sub-chronic toxicity studies as it is assumed that oral route of exposure maximises systemic availability (internal dose) of most substances.

The source of information (*iii.*) does not inform on repeated dose toxicity in live animals, as the OECD TG 473 and OECD TG 476 are *in vitro* studies on mammalian cells which only provide information on structural chromosomal aberrations in cultured mammalian somatic cells and mammalian cell gene mutations, respectively.

Taken together, the information that the relevant sources of information *(i.), (ii.)* and *(iii.)* provide can be summarised as following:

- Short-term repeated dose toxicity study (*i.*) provides information on clinical and functional observations, organ weights, histopathology and clinical biochemistry, but does not include sufficient exposure duration and number of animals.
- Subchronic inhalation toxicity study (*ii.*) provides information on clinical observations, body weight measurements, clinical chemistry, gross necropsy and organ weights with sufficient exposure duration. However, it does not cover all relevant information as described in OECD TG 408, such as full histopathology and hormone level measurements. Moreover, the oral route is the default one for sub-chronic toxicity studies.
- The *in vitro* studies (*iii.*) do provide information on mammalian cell mutagenicity but does not correspond to the information requirement of this endpoint.

Therefore, a significant amount of essential investigations are limited or totally lacking that would inform on sub-chronic repeated dose toxicity in order to conclude on these aspects.

It is not possible to conclude, based on any source of information alone or considered together, and taking into account the lack of proper justification for the WoE adaptation, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in an OECD TG 408 study. Therefore, your adaptation according to Annex XI, Section 1.2. is rejected and the information requirement is not fulfilled.

B. Read-across

Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must provide a justification for the read-across including a hypothesis, explanation of the rationale for the prediction of properties and robust study summaries of the source studies.[2]

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[3] and related documents[4, 5].

Predictions for properties

You have provided the following reasoning for the prediction of toxicological properties (in the IUCLID section 7.5.2): *"Several criteria justify the use of the read-across approach to fill a data gap for the registered substance "Alkenes C6-C11, hydroformylation products, distn. Residues, heavy cracked fraction" with the following substance "Alkenes, C6-10, Hydroformylation Products, High-Boiling". The read across substance has similar manufacturing process, similar composition and similar physic-chemical properties as the registered substance."* and *"The same types of molecules (alcohols, esters, and ethers) in*

[2] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.6.1

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

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

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

similar carbon ranges are present in both substances. Because the components have similar structures, they are metabolized by common pathways. Thus neither components nor metabolites with differentiating toxicological properties are expected in the two substances."

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 qualitatively and quantitatively equal to those of the source substance.

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

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*"[6]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on other category members.

Supporting information must include bridging studies to compare properties of the category members and to support your prediction, which is based on similarity of the relevant toxic properties.

As indicated above, your read-across hypothesis is based on the assumption that the similar composition of the target and source substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the target and source substance 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 for the target and the source substances.

The data set reported in the technical dossier does not include relevant, reliable and adequate information for the Substance to support your read-across hypothesis.

In the absence of such information, you have not established that the target and the source substances 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 formation of common compound

As indicated above, your read-across hypothesis is based on similar manufacturing process, similar composition and similar physico-chemical properties.

You have not provided any experimental data to document the presumed similar metabolisation of the target and the source substances.

In the absence of this information, you have not provided supporting evidence establishing the transformation of the Substance as assumed in your read-across hypothesis. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the

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

read-across.

As explained above, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. Therefore, your adaptation is rejected and it is necessary to perform testing on your Substance.

Route of exposure

As noted already under the WoE issue, oral route is the default one for subchronic toxicity studies because it is assumed to maximise systemic availability (internal dose) of most substances and the key investigations in OECD TG 408 are more comprehensive.

Based on the above, the information you provided does not fulfil the information requirement. Your adaptations according to Annex XI 1.2. and 1.5. are rejected and the information requirement is not fulfilled.

In your comments to the draft decision, you agree to conduct the requested OECD TG 408 study with the Substance.

Information on the design of the study to be performed

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity.

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

2. Soil simulation testing

and

3. Sediment simulation testing

Soil and sediment simulation testing are standard information requirements at Annex IX of REACH for substances with a high potential for adsorption to soil or sediment. The Substance has low water solubility (< 1 mg/L for most consituents) and high partition coefficient (Log Kow > 4.5 for most consituents), indicating high adsorptive properties.

You have sought to adapt these information requirements based on Annex IX, Section 9.2.1.3 and 9.2.1.4, Column 2.

We have assessed this information and identified the following issue:

Further testing on degradation is required if the CSA indicates the need for such investigations, for example if there are indications from screening or other information that the substance may have PBT or vPvB properties (Annex 1. Section 0.1; Annex IX, Section 9.2, Column 2, Annex XIII, Section 2.1)

Screening information demonstrating potential PBT or vPvB properties include (ECHA Guidance R.11, Sections R.11.4 and Annex XIII):

- The Substance is not readily biodegradable and thus potentially persistent, and
- The Substance has high potential for bioaccumulation (for instance log Kow > 4.5).

You justified the adaptation by stating that "[Simulation testing on soil and on sediment do] *not need to be conducted as the chemical safety assessment according to Annex I does not indicate the need to investigate further the degradation of the substance and its degradation products".*

However, screening information is provided in your dossier and this information indicates that the Substance may have PBT/vPvB properties (R.11.4):

- The Substance is not readily biodegradable and thus potentially P or vP (33 % in 28 days in OECD TG 301F), and
- The Substance has high potential for bioaccumulation as most of its constituents have log Kow > 4.5

Taking into account the above, no definitive conclusion can be reached for the P/vP, or B/vB assessments. Therefore, your CSA does not rule out the need to investigate further the degradation of the substance and its degradation products for the purpose of the PBT/vPvB assessment and your adaptation is rejected.

In your comments to the draft decision, you propose to adapt this standard information requirement by using data from Qualitative or quantitative structure-activity relationship (QSAR) in accordance with Annex XI, Section 1.3.

In support of your adaptation, you provide QSAR predictions for the representative constituents of the Substance.

Under Section 1.3., first paragraph, third indent of Annex XI to REACH, a study may be omitted if QSAR results are adequate for the purpose of classification and labelling and/or risk assessment, including PBT assessment. Results obtained from biodegradation (Q)SAR models are only regarded as screening information on P/vP properties (Annex XIII, Section 3.1.). As further explained in ECHA Guidance R.11.4.1.1.4., such information is not considered sufficient on its own to conclude on non-persistence and must supported by additional information (e.g. test data information, read-across).

You have provided the following QSAR prediction[s] in your comments to the draft decision:

- CATALOGIC Kinetic 301F model (v13.16):

1. alcohol C10 H22 O1, % BOD (28d)=81 Readily Degradable;
2. alcohol C9 H20 O1, % BOD (28d)=82 Readily Degradable;
3. ether C22 H46 O1, % BOD (28d)=73 Readily Degradable;
4. ether C20 H42 O1, % BOD (28d)=70 Readily Degradable;
5. ether C18 H38 O1, % BOD (28d)=68 Readily Degradable;
6. ether C16 H34 O1, % BOD (28d)=64 Readily Degradable;
7. ether alcohol C23 H48 O2, % BOD (28d)=82 Readily Degradable;
8. ether alcohol C21 H44 O2, % BOD (28d)=82 Readily Degradable;
9. ether alcohol C19 H40 O2, % BOD (28d)=83 Readily Degradable;
10. ether alcohol C17 H36 O2, % BOD (28d)=83 Readily Degradable;
11. acetal C33 H68 O2, % BOD (28d)=58 Inherently Degradable;
12. acetal C30 H62 O2, % BOD (28d)=57 Inherently Degradable;
13. acetal C27 H56 O2, % BOD (28d)=58 Inherently Degradable;
14. acetal C24 H50 O2, % BOD (28d)=58 Inherently Degradable.

In summary, calculated degradation half-lives for all the representative constituents listed above showing between <4.0 and 25,2 days in water and sediment and between < 1.0 and 6.29 days in soil.

Based on these QSAR results, you conclude that the Substance and its constituents are not persistent and that further simulation testing in soil and sediments are not necessary. You have not provided additional information to support this conclusion.

As explained above, the provided QSAR results alone does not provide a robust approach to to be used as assessment information, as defined in Section 3.2, Annex XIII of REACH, for the PBT/vPvB assessment. It is insufficient to conclude that the Substance does not meet the P/vP criteria and thus are not adequate for PBT assessment. Therefore, you adaptation is rejected.

Therefore, the information requirement is not fulfilled

Study design

Under Annex XIII, the information must be based on data obtained under conditions relevant for the PBT/vPvB assessment. Therefore:

- You must perform the OECD TG 308 test using two sediments. One sediment should have a high organic carbon content (2.5-7.5%) and a fine texture, the other sediment should have a low organic carbon content (0.5-2.5%) and a coarse texture.

- You must perform the OECD TG 307 test using five soils representing a range of relevant soils (*i.e.* varying in their organic content, pH, clay content and microbial biomass).

- You must perform the tests at the temperature of 12 °C, the average environmental temperature for the EU (ECHA Guidance R.16, Table R.16-8). Performing the tests at this temperature is in line with the applicable test conditions of the OECD TG 307 and TG 308.

Non-extractable residues (NER) must be quantified in all simulation studies. The reporting of results must include a scientific justification of the used extraction procedures and solvents. By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER. Such fractions could be regarded as removed when calculating the degradation half-life(s) (ECHA Guidance Chapter R.11).

Under Annex XIII, you must assess the PBT/vPvB properties of the relevant constituents of the Substance. Therefore, the persistence of each relevant constituent present in concentrations at or above 0.1% (w/w) or, if not technically feasible, in concentrations as low as technically detectable must be assessed. Alternatively, you would have to justify why you consider these not relevant for the PBT/vPvB assessment.

4. Identification of degradation products

Identification of the degradation products is a standard information requirement at Annex IX of REACH.

You have sought to adapt this information requirement based on Annex IX, Section 9.2, column 2.

We have assessed this information and identified the following issue:

> Under Section 9.2., Column 2 of Annex IX to REACH, this information may be omitted if the chemical safety assessment (CSA) does not indicate the need for further biotic degradation testing. In the context of the PBT/vPvB assessment (Annex I, Section 4) and the risk assessment (Annex I, Section 6) of the Substance, the CSA must address relevant transformation/degradation products (Annex XIII, 5th paragraph; ECHA Guidance R.11.4.1.).
>
> You have justified the adaptation by stating that CSA does not indicate the need to investigate further the degradation of the substance and its degradation products.
>
> However, screening information provided in your dossier indicates that the Substance is not readily biodegradable (33 % in 28 days in OECD TG 301F). Furthermore, you have not provided any information on the identity and PBT properties of the degradation products of the Substance.
>
> Based on the above, without information on relevant degradation products, no definitive conclusion can be reached for the PBT/vPvB assessment. Therefore, your CSA does not demonstrate that the risks of the Substance are adequately controlled and your adaptation is rejected.

In your comments to the draft decision, you provide information on the QSAR predictions on 14 representative structures of the Substance and 15 unique metabolites. In addition, you provide information on the metabolic pathways for 4 main classes of the constituents of the Substance. You indicated your intension to update the technical dossier with the identified metabolites obtained by the CATALOGIC 301F model.

Under Section 1.3., first paragraph, third indent of Annex XI to REACH, a study may be omitted if QSAR results are adequate for the purpose of classification and labelling and/or risk assessment, including PBT assessment. Under ECHA Guidance R.7.9.3.1., qualitative information on the identity of transformation/degradation products may be obtained from a number of models and databases (e.g. EAWAG Database, KEGG databases, CATALOGIC). However, the guidance specifies that this information may only contribute as part of a Weight of Evidence assessment if other data are available (e.g. information from biodegradation screening studies, information on analogue substances).

Your comments to the draft decision provide information on putative transformation/degradation products using the following QSAR model:

- CATALOGIC kinetic 301F model (v.13.16), identifying 15 unique metabolites listed in Table 5 in your Comments to the draft decision;
- Metabolic pathways obtained from CATALOGIC v5.11.19 Kinetic 3010F pathway model (V13.16) provided as Figure 1 in your comments to the draft decision.

You have not provided any other data to support the identification of the transformation/ degradation products of the Substance.

As explained above, the provided QSAR results alone are not adequate to conclude on the identity of transformation/degradation products and thus are not adequate for PBT assessment as defined in Section 3.2, Annex XIII of REACH, for the PBT/vPvB assessment.

Therefore, this information requirement is not fulfilled.

Study selection and design

Regarding appropriate and suitable test method, the methods will have to be substance-specific. Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported, when analytically possible. In addition, degradation half-life, log Kow and potential toxicity of the transformation/degradation may be investigated. You may obtain this information from the degradation simulation studies also requested in this decision (under section A.2 and A.3) or by some other measure. If the any other method than the requested degradation simulation studies is used for identification of the transformation/degradation products, you must provide a scientifically valid justification for the chosen method.

Appendix B: Reasons for the requirements applicable to all the Registrants subject to Annex X of REACH

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.,) 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 substance-tailored exposure-based adaptation for the second species according to the specific rules outlined in Annex XI 3.2 (a) of the REACH Regulation, and
- a dose-range finding study in rabbits as a supportive study.

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

A) In order to be considered compliant and enable assessing if the Substance is a developmental toxicant, the study has to meet the requirements of OECD TG 414.

The key parameter(s) of this test guideline include e.g.

- 20 female animals with implantation sites for each test and control group, and
- examination of the foetuses, skeletal and soft tissue alterations (variations and malformations).

The study was conducted with 5 pregnant females for each test group. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of 20 pregnant females for each test group set in OECD TG 414. Furthermore, key parameters such as skeletal and soft tissue alterations (variations and malformations) have not been examined as required in a pre-natal developmental toxicity study (OECD TG 414). Therefore, the provided study does not fulfil the information requirement.

In your comments to the draft decision, you clarify the status of the dose-range finding study as supportive data and note that this information was not intended to replace the information requirement for an OECD TG 414. ECHA takes note of the clarification provided in your comments and thereby considers that the dose-range finding study was submitted by you as supporting study not aiming to fulfil the required information for this endpoint.

B) As provided in Annex XI, Section 3.1., you may adapt the information requirement, based on the exposure scenarios developed in the Chemical Safety Report. According to Annex XI, Section 3.2., in all cases, adequate justification shall be based on a thorough and rigorous exposure assessment in accordance with section 5 of Annex I.

You report a variety of PROCs for industrial and professional uses in your registration dossier which could lead to significant exposures. You have not developed any exposure scenarios in your CSR and have not provided an exposure assessment. Consequently your substance-tailored exposure-driven testing argumentation cannot be accepted to omit the second species prenatal developmental toxicity study.

In your comments on the draft decision, you clarify that: "*the exposure assessment was developed for all of the industrial and professional uses registered and were submitted with the document demonstrating insignificant exposures (RCRs ranging from* [redacted]*) using*

the Inhalation Long Term DNEL (Derived No Effect Level): 76.9 mg/m³ and Dermal long term systemic DNEL: 137.7 mg/kg/day." [...] "*In addition, key quantitative information, which supports the substance-tailored exposure-driven testing for fulfilling the second species PNDT information requirement for the registered substance is present elsewhere in IUCLID (i.e., Section 7.8.2 and 7.8.3). A narrative interpretation and summary section is available, which is consistent with the final exposure scenario in the CSR*". Also, you have attached updated sections of your CSR to your comments.

We have assessed this information and identified the following issues:

Under Annex XI, 3.2(a), the first criterion requires "*absence of or no significant exposure in all scenarios of the manufacture and all identified uses*". In detail, the results of the exposure assessment covering all relevant exposures throughout the life cycle of the substance demonstrate the absence of or no significant exposure in all scenarios of the manufacture and all identified uses as referred to in Annex VI section 3.5.

As mentioned above, in Section 3.5 of your registration dossier, you report professional uses (e.g. widespread use by professional workers – use in coatings, use in cleaning agents) for the Substance. In your comments you clarify that: "the exposure assessment was developed for all of the industrial and professional uses registered".

The uses reported by you for the Substance include widespread uses by professional workers. These uses are, by definition, considered as widespread (ECHA Guidance R.12). Hence, you have not demonstrated that exposure throughout the life-cycle including waste stage of the Substance is absent or not significant.

Thus, in your comments to the draft decision you have not demonstrated no significant exposure.

Under Annex XI, Section 3.2(a), ii), a suitable DNEL can be derived from results of available test data for the Substance taking full account of the increased uncertainty resulting from the omission of the information requirement, and that DNEL is relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes. Furthermore, under Annex XI, Section 3.2(a), iii) the comparison of the derived DNEL with the results of the exposure assessment shows that exposures are always well below the derived DNEL.

In your comments to the draft decision, you have provided revised RCRs (from >0.1 to the highest being [redacted] in your updated section of your CSR.

Under (iii) of Annex XI, Section 3.2(a), the RCR should be "*well below*" the derived DNEL. ECHA notes that there is no threshold to determine "*well below*" hence individual considerations will be required to determine whether this criterion could be met. As a general rule, ECHA specifies that a RCR <<1 (meaning <0.1) (ECHA Guidance R.5: Adaptation of information requirements, page 15) based on a robust DNEL, and a rigorous exposure assessment, may be considered as acceptable. As part of the rigorous exposure assessment you should consider input parameters for exposure models that are representative of operational conditions, in addition to utilising higher tier exposure models and including representative workplace measurements in your exposure assessment when these are available.

The highest RCR is not well below 1.

Based on the information provided in your technical dossier and in your comments to the draft decision, the information requirement is not fulfilled. Therefore, ECHA did not amend request B.1.

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[7] administration of the Substance.

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

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

A. Test methods, GLP requirements and reporting

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

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

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[8].

B. Test material

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 boundary composition(s) of the Substance,
   b) 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.
Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[9].

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

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

A. Strategy for the PBT/vPvB assessment

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

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

B. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituens and, as indicated in ECHA Guidance R.11 (Section R.11.4.2.2), you are advised to consider the following approaches for persistency 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 synthetize its relevant constituents and/or fractions.

Appendix E: 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 02/10/2019.

The decision making followed the procedure of Article 51 of the REACH Regulation, as described below:

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).

Deadline to submit the requested information in this decision

The timeline indicated in the initial draft decision to provide the information requested was 27 months from the date of adoption of the decision.

In your comments on the draft decision, you requested an extension of the timeline to 33 months. However, after the expiry of the commenting period, you informed ECHA on 14 August 2020 that the extension of the deadline was no longer needed. Therefore ECHA did not modify the deadline of this decision.

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

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

Appendix F: List of references - ECHA Guidance[10] and other supporting documents

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

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

Read-across assessment framework (RAAF, March 2017)[11]

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

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

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

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

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

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

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

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

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

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

[10] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[11] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

OECD Guidance documents[12]
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.

[12] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix G: Addressees of this decision and the corresponding information requirements applicable to them

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

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

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