~~Confidential~~

Helsinki, 21 October 2021

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

Date of submission of the dossier subject to this decision
20/06/2019

Registered substance subject to this decision ("the Substance")
Substance name: 3a,4,5,6,7,7a-hexahydro-4,7-methano-1H-indenyl propionate
EC number: 272-805-7
CAS number: 68912-13-0

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 ***26 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. 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)

2. Long-term toxicity testing on terrestrial invertebrates (triggered by Annex IX, Section 9.4.1., column 2; test method: OECD TG 222 or 220 or 232)

   Or

   Long-term toxicity to terrestrial plants (triggered by Annex IX, Section 9.4.3., column 2; test method: OECD TG 208 with at least six species or ISO 22030)

3. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: EU C.21./OECD TG 216)

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

- Appendix entitled "Reasons common to several requests";
- Appendix entitled "Reasons to request information required under Annex IX of REACH".

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, VIII and IX to REACH, for registration at 100-1000 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". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

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

Failure to comply

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

Authorised[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

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

Appendix on Reasons common to several requests

1. **Assessment of your read-across approach under Annex XI, Section 1.5.**

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

- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)
- Long-term toxicity testing on terrestrial invertebrates (triggered by Annex IX, Section 9.4.1., column 2)
- Effects on soil micro-organisms (Annex IX, Section 9.4.2.)
- Long-term toxicity to terrestrial plants (triggered by Annex IX, Section 9.4.3., column 2).

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

Grouping of substances and read-across approach

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

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

A. Predictions of ecotoxicological and toxicological properties

You have provided a read-across justification in the endpoint sections of the CSR and/or IUCLID registration dossier only for selected source substances.

You propose to read-across between the structurally similar substances,

1. Reaction mass of 3a,4,5,6,7,7a-hexahydro-4,7-methanoinden-5-yl acetate and 3a,4,5,6,7,7a-hexahydro-4,7-methanoinden-6-yl acetate (Cyclacet) EC 911-369-0
2. Cis-2-tert-butylcyclohexyl acetate (Verdox) CAS 20298-69-5, EC 243-718-1

as source substances, and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties from the source substances: "*Absence of developmental toxicity based on read across from Verdox in a dietary OECD TG 414 study in which the NOAEL≥444 mg/kg bw/day was derived. In addition, no developmental toxicity is seen in a reproduction/developmental toxicity screening*

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

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

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

study (rats, oral gavage, OECD TG 421) with Cyclacet." and "*Cyclaprop has the same developmental toxicity as Verdox based on structural, repeated and reproductive toxicity similarity using Cyclacet as a bridging substance."*

You have provided the following reasoning for the prediction of the toxicity to soil organisms from the source substance: "*Cyclaprop's terrestrial EC10/NOEC values can be derived from Verdox based on structural similarity and similarity in environmental fate and aquatic toxicity […] Verdox long-term terrestrial toxicity is available resulting in EC10/NOECs of 45, 44 and 100 mg/kg dw soil for earthworm, plants and micro-organisms, respectively. This effect levels can be used for Cyclaprop without conversion because the log Kow values are sufficiently similar.".*

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 ecotoxicological and toxicological properties.

a. Shortcomings with regards to predictions of toxicological and ecotoxicological properties

1. Adequacy of the source data

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across should have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

Specific deficiencies of the studies with the analogue substance are addressed, where relevant, in the endpoint-specific sections of the next two appendices.

2. Supporting information - Missing information to compare properties of the substances

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*"[5]. 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 Substance and source substances.

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 substance 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).

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

Pre-natal developmental toxicity
You have provided a screening for reproductive/developmental toxicity study (OECD TG 421, 2010) with the source substance Cyclacet and a pre-natal developmental toxicity study (OECD TG 414) in a first species with the source substance Verdox. You have not provided any study with the Substance. Furthermore, you have provided a comparison of study results for repeated dose toxicity between the source substances in the endpoint summary for reproductive toxicity, without providing robust study summaries in the technical dossier.

The source study OECD TG 414 with the source substance Verdox is unreliable for the reasons specified in Appendix A Section A.1 and therefore it cannot be used as a source study for comparison of effects and prediction of properties. You have not addressed the difficulty of using a screening study OECD TG 421 with the source substance Cyclacet as a bridging study for the PNDT endpoint in so far as the screening study addresses developmental toxicity *post* parturition while the PNDT investigates *pre*-natal effects. Secondly, this study was not performed with the Substance, but instead with another source substance. For that reason this study cannot be used as a bridging study.

The comparison of repeated dose toxicity between the source substances does not inform on similarities in developmental toxicity. Furthermore, you have not provided this information as robust study summaries and we cannot independently assess the reliability of that information since there is no information on study design, investigations performed and results corresponding to each of those investigations.

Toxicity to soil organisms
In the registration dossier you have noted that "*For Cyclaprop no terrestrial toxicity information is available, but for the related analogue Verdox long-term terrestrial toxicity is available and read across can be applied.*"

Thus, the data set reported in the technical dossier does not include relevant, reliable and adequate information on toxicity to soil organisms, for example, from bridging studies of comparable design and duration for the Substance and of the source substances to support your read-across hypothesis.

In the absence of such bridging 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.

b. Shortcomings with regards to predictions of toxicological properties

1. Read-across hypothesis 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 ECHA Guidance[6] indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s). The observation of differences in the toxicological properties between these different analogue substances, source substances as well as the Substance, would contradict the hypothesis that the

[6] Guidance on information requirements and chemical safety assessment (version 6.0, July 2017), Chapter R.6, Section R.6.2.2.1.f

properties of the Substance can be predicted from data on the source substances. An explanation why such differences do not affect the read-across hypothesis needs to be provided and supported by scientific evidence. As indicated above, your read-across hypothesis is based on the assumption that the structurally similar target and source substances cause the same type of effect(s).

Your information submitted with the technical dossier demonstrates inconsistencies in effects between the source substances:

1) The provided screening for reproductive/developmental toxicity study (OECD TG 421, 2010) and repeated dose toxicity studies indicate differences in toxicological profiles between the source substances: Adrenal effects confirmed by histopathology have been observed only with Cyclacet, while relative uterus weights were increased up to 77% only with Verdox in the high dose group of a 90-day repeated dose toxicity study.
2) The Substance and the source substance Cyclacet are both [redacted], whereas the source substance Verdox is a [redacted] which is structurally more different to the other two analogues. You have not provided an explanation how these differences in structural features between the different source substances impact the prediction of properties of the Substance; in particular:
    a. [redacted], which is structurally more rigid compared to the [redacted];
    b. effect on the 3D-structure / potential receptor-binding properties of the Substance by the [redacted];
    c. presence of [redacted] of the Substance and their impact on the 3D-shape;
    d. effect of the [redacted] on metabolism other than hydrolysis of the [redacted].

We observe differences between the source substances, and also towards the Substance, in the toxicity profiles with relevance to the endpoint pre-natal developmental toxicity. In your justification you have not addressed these differences, which may result from the specific 3D shape of the [redacted]. You have not explained the impact of these differences in structure on the prediction of properties, in particular in relation to the differences in toxicity described above. We observe that Verdox's substructure has more degrees of freedom in how its (receptor-specific) 3D shape is formed, and the Substance is a worst case in comparison of conformational rigidity. This is particularly important in the prediction of pre-natal developmental toxicity, which investigates the effect of a substance on receptors and targets of developing embryos and fetuses.

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

c. Shortcomings with regards to predictions of ecotoxicological properties

1. Read-across hypothesis for toxicity to soil organisms

According to Annex XI, Section 1.5., two conditions shall be necessarily fulfilled. 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 (read-across approach).

A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the source substance(s) and your Substance[7]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

Your read-across hypothesis is that the similarity between chemical structures, similar bioavailability and presence of the same functional group ([redacted]) leading to the same toxicity mode of action between the source substance Verdox and your Substance is a sufficient basis for predicting the properties of your Substance for toxicity to soil organisms.

In the registration dossier you explain the following:
"Structural similarities and differences: Cyclaprop and Verdox have a [redacted] The difference is that Cyclaprop has [redacted], while Verdox has a [redacted]. In addition, Verdox is an [redacted] while Cyclaprop is a [redacted].
Bioavailability: Cyclaprop (target) and Verdox (source) have similar bioavailability based on the similarity in chemical structure, molecular weight and log Kow values.
Environmental fate: Cyclaprop and Verdox are both not readily biodegradable and have the same adsorption potential: Log Koc is 3.1.
Mode of action (MoA): Cyclaprop and Verdox have both a [redacted] and therefore the MoA is the considered the same. As the difference in log Kow between Cyclaprop and Verdox is below 0.5 (4.4 and 4.75, respectively) and log Koc values are 3.1 no conversion of effect levels is needed."

There is no specific explanation how the differences in structural features between the Substance and the source substance Verdox impact the prediction of the specific property, i.e. toxicity to soil organisms. Furthermore, the specific mode of toxicity action to soil organisms for the Substance and source substance Verdox is not specified and it is not explained how structural differences between these two substances were considered to conclude on the "same" mode of toxicity action to soil organisms.

Thus, you have not provided a well-founded hypothesis to establish a reliable prediction for an ecotoxicological property, based on recognition of the structural similarities and differences between the source substance(s) and your Substance.

2. *Relevance of the supporting information for toxicity to soil organisms*

According to the ECHA Guidance[8] "*it is important to provide supporting information to strengthen the rationale for the read-across approach. Thus, in addition to the property/endpoint being read-across, it is also useful to show that additional properties, relevant to the endpoint, are also (qualitatively or quantitatively) similar between the source and target chemicals*".

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

In order to support your claim that your Substance and source substance(s) have similar properties for the terrestrial toxicity endpoints under consideration in the read-across approach, you refer to their *"aquatic effect levels, which are similar between Cyclaprop and Verdox"*.

Whilst this data set suggests that the substances may have similar properties for aquatic toxicity, these aquatic toxicity studies do not inform on the toxicity to soil organisms of the target and source substances. Accordingly, these information are not considered as relevant to support prediction of all the endpoints under consideration.

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

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

1. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

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

i. a screening for reproductive / developmental toxicity test (OECD TG 421) with the source substance Cyclacet (EC 911-369-0),
ii. a pre-natal developmental toxicity study (OECD TG 414) with the source substance Verdox (EC 243-718-1).

As explained in the Appendix on general considerations your adaptation is rejected. In addition, the following endpoint-specific deficiencies have been identified in your read-across adaptation:

Relevance of source study (i.)

The provided adaptation must provide the information equivalent to an OECD TG 414 study, as explained in the Appendix on reasons common to several requests, section **A.a**. A "reproduction/ developmental toxicity screening test" (OECD TG 421) does not inform on skeletal and visceral malformations and variations as required by OECD TG 414. Therefore, this study does not fulfil the information requirement.

Adequacy and reliability of source study (ii.)

The provided adaptation must provide the information equivalent to an OECD TG 414 study, as explained in the Appendix on reasons common to several requests, section **A.a**. The key parameter(s) of this test guideline include e.g.

- highest dose level should aim to induce some developmental and/or maternal toxicity.

  You have justified the lower dose levels used in the OECD TG 414 study based on data obtained from a 14-day dose-range finding study (OECD TG 422) with the source substance. You concluded that "*the reduced food intake and the accompanying lower body weights in the high-dose group are considered to be due to reduced palatability rather than to the test substance per se, and are not considered to be adverse*", and "*the 7500 mg/kg diet* [= 444 mg/kg bw/d] *was sufficiently high to present* (absence of adverse) *effects for the OECD TG 414 study.*"

The highest dose level in the study did not induce any developmental and/or maternal toxicity and you have not shown that the aim was to induce toxicityThe non-adverse liver effects observed in *male* rats only in the OECD 422 study is not relevant for a dose selection for the OECD 414 for *pregnant* females.

Furthermore, the pre-natal developmental toxicity study was conducted via feed despite the known issues with the palatability of the test material, which was observed in the 14-days dose range finding study and was attributed to the odorous character of the test material. You have not justified in your dossier why dosing via gavage was not performed to overcome the known palatability issues.

Therefore, the dose level selection was too low, and the study does not fulfil the criterion set in OECD TG 414.

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

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[9] administration of the Substance.

2. Long-term toxicity on terrestial invertebrates or Long-term toxicity to terrestrial plants

Short-term toxicity testing on invertebrates and plants are information requirements under Annex IX to REACH (Section 9.4.1. and 9.4.3. respectively). Long-term toxicity testing on invertebrates and plants must be considered (Section 9.4., Column 2) if the substance has a high potential to adsorb to soil or is very persistent.

According to ECHA Guidance R.7c, Section R.7.11.6.3. substances that are ionisable or have a log Kow/Koc >5 are considered highly adsorptive and substances with a half-life >180 days (default setting that it is very persistent in the absence of soil data, unless classified as readily biodegradable) are considered very persistent.

You have provided an OECD TG 301F study showing 15% degradation after 28 days but no information on half-life of the Substance in soil.

On this basis, the Substance is not readily biodegradable but is considered very persistent in soil and long-term toxicity testing on invertebrates and/or plants is necessary.

You have adapted these information requirements by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. In support of your adaptation you provided in the IUCLID registration dossier a long-term toxicity studies on invertebrates (OECD TG 222) and on plants (OECD TG 208 with six species), both with an analogue substance.

Furthermore, in the chemical safety report (CSR) you provided the adaptation according to Annex IX, Section 9.4., Column 2 with the following justification: "*No studies on the toxicity of Cyclaprop to soil macro-organisms, terrestrial arthropods, terrestrial plants and soil micro-organisms are available. According to column 2 of REACH (Regulation 1907/2006/EC) Annex IX, in the absence of data for soil organisms, the equilibrium partitioning method may be applied to assess the hazard to soil organisms. The choice of the appropriate tests depends on the outcome of the chemical safety assessment.*

Using the available information for Cyclaprop and a PNECsoil derived by equilibrium partitioning, the chemical safety assessment does not reveal a need for further investigation (the environmental risk assessment for all intended uses shows that the risk is controlled). Therefore, studies on the short and long-term effects on soil macro-organisms are waived."

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

a) Rejection of adaptation according to Annex XI, Section 1.5

As explained in the Appendix on reasons common to several requests your adaptation according to Annex XI, Section 1.5 is rejected.

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

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

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

- be adequate for the purpose of classification and labelling and/or risk assessment.

As explained in ECHA Guidances R.7c, Section R.7.11.5.3 (p.153) and R.10, Sections R.10.6.3 (p. 41) and R.10.3.1.3 (p. 21-22) 'averaging' of data to a single value of (no-) effect concentration could be applied when multiple data for one species and same endpoint are available.

In the registration dossier, as the key value for the chemical safety assessment (including risk assessment) you reported effect concentration which is an average of effect concentrations for six different plant species tested.

As explained above, averaging of effect concentrations from various species should not be done and the lowest (or if relevant averaged for the same endpoint) effect concentration from the single species should be be used for the chemical safety assessment. Thus, your key value for the chemical safety assessment is not adequate for the purpose of risk assessment.

b) Rejection of adaptation according to Annex IX, Section 9.4., Column 2

According to Annex IX, Section 9.4., Column 2 in the absence of toxicity data for soil organisms, the equilibrium partitioning method (EPM) may be applied to assess the hazard to soil organisms. According to ECHA Guidance R.7c, Section R.7.11.6, where there are adequate data available to derive a PNEC for aquatic organisms, this PNEC can be used in a screening assessment of risks for soil through the use of the EPM approach. In the context of an integrated testing strategy for soil toxicity under the Guidance R.7c, Section R.7.11.6, an initial screening assessment based upon the EPM, together is to be performed with a confirmatory long-term soil toxicity test (either with invertebrates or plants) for the substances falling into soil hazard category 3, i.e., meeting criteria related to the following: very persistent and not very toxic to aquatic organisms.

According to ECHA Guidance R.7c, Section R.7.11.6.3., substances with a half-life >180 days (default setting is that it meets the criterion in the absence of soil data, unless classified as readily biodegradable) are considered very persistent in soil and substances with EC/LC50 < 1 mg/L for algae, daphnia or fish are considered very toxic to aquatic organisms.

In the CSR, predicted no-effect concentration (PNEC) for soil was derived by you by using EPM from the PNEC for aquatic organisms and used to prove safe use of the Substance for soil compartment.

You also have provided the following results: (1) EC/LC50 >1 mg/L for algae, daphnia and fish and (2) 15% degradation after 28 days was detected in the key study performed according to OECD TG 301F, without half-life of the Substance in soil.You have provided no further justification for excluding a confirmatory long-term soil toxicity test.

Based on the criteria given in ECHA Guidance R.7c, Section R.7.11.6 and information available in the registration dossier the Substance is considered as not very toxic to aquatic organisms () and as very persistent in soil (the Substance is not readily biodegradable). Thus, the Substance would fall into soil hazard category 3.

Therefore, your adaptation is rejected.

On this basis, the information requirements are not fulfilled.

Study design

Based on its properties, the Substance falls into soil hazard category 3 (see above) and a confirmatory long-term soil toxicity test is needed.

The earthworm reproduction test (OECD TG 222), Enchytraeid reproduction test (OECD TG 220), and Collembolan reproduction test (OECD TG 232) are each considered capable of generating information appropriate for the fulfilment of the information requirement for long-term toxicity testing on terrestrial invertebrates.

ECHA notes that when log Kow >5 or log Koc >4, the test OECD 232 is not appropriate as the dominant route of exposure for Collembolans is via pore water.

OECD TG 208 (Terrestrial plants, growth test) considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing shall be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208 guideline. You should consider if testing on additional species is required to cover the information requirement.

Terrestrial plants, growth test (OECD TG 208 with at least six species) and Soil Quality – Biological Methods – Chronic toxicity in higher plants (ISO 22030) are each considered capable of generating information appropriate for the fulfilment of the information requirement for long-term toxicity testing on terrestrial plants.

ECHA is not in a position to determine the most appropriate test protocol, since such determination is dependent upon species sensitivity and substance properties. You are to apply the most appropriate and suitable test guideline among those listed above.

3. Effects on soil micro-organisms

Effects on soil micro-organisms is an information requirement under Annex IX to REACH (Section 9.4.2.).

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. In support of your adaptation you provided in the IUCLID registration dossier a toxicity study with soil micro-organisms (OECD TG 216) with an analogue substance.

Furthermore, in the chemical safety report (CSR) you provided the adaptation according to Annex IX, Section 9.4., Column 2 with the following justification: *"No studies on the toxicity of Cyclaprop to soil micro-organisms are available. According to column 2 of REACH (Regulation 1907/2006/EC) Annex IX, in the absence of data for soil organisms, the equilibrium partitioning method may be applied to assess the hazard to soil organisms. The choice of the appropriate tests depends on the outcome of the chemical safety assessment. Using the available information for Cyclaprop and a PNECsoil derived by equilibrium partitioning, the chemical safety assessment does not reveal a need for further investigation (the environmental risk assessment for all intended uses shows that the risk is controlled). Therefore, studies on the short and long-term effects on soil macro-organisms are waived."*

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

a) Rejection of adaptation according to Annex XI, Section 1.5

As explained in the Appendix on reasons common to several requests your adaptation according to Annex XI, Section 1.5 is rejected.

b) Rejection of adaptation according to Annex IX, Section 9.4., Column 2

ECHA emphasises that the intrinsic properties of soil microbial communities are not addressed through the EPM extrapolation method and therefore the potential adaptation possibility outlined for the information requirement of Annex IX, Section 9.4., Column 2 does not apply for the information requirement under Annex IX, Section 9.4.2.

Consequently, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

To address this endpoint, either a nitrogen transformation test (test method: EU C.21/OECD TG 216) or a carbon transformation test (test method: EU C.22/OECD TG 217) could be performed. According to Section R.7.11.3.1 of ECHA Guidance R.7c, ECHA considers the nitrogen transformation test (EU C.21/OECD TG 216) suitable for non-agrochemicals. For agrochemicals the carbon transformation test (EU: C.22/OECD TG 217) is also required.

The uses identified in the registration dossier do not indicate agrochemical uses, therefore, EU C.21/OECD TG 216 is the most suitable.

Appendix B: 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[10].

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[11].

[10] https://echa.europa.eu/practical-guides
[11] https://echa.europa.eu/manuals

Appendix C: 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 15 May 2020.

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

ECHA did not receive any comments within the commenting period.

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 D: List of references - ECHA Guidance[12] 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)[13]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[14]

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[15]

[12] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[13] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[14] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[15] 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 E: 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]

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.