EUROPEAN CHEMICALS AGENCY

Helsinki, 22 November 2019

Addressee: [redacted]

Decision number: TPE-D-2114489554-35-01/F
Substance name: 4,4'-Isopropylidenediphenol, ethoxylated
EC number: 500-082-2
CAS number: NS
Registration number: [redacted]
Submission number: [redacted]
Submission date: 09/02/2018
Registered tonnage band: 100-1000 (Lead) and over 1000 (Joint registration)

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation ((EC) No 1907/2006) (the REACH Regulation), ECHA examined your testing proposal(s) and decided as follows.

Your testing proposal is modified and you are requested to carry out:

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408) in rats using the registered substance modified to include urinalysis and a full histopathological examination which is to include immunohistochemical investigation of renal pathology to determine if the pathology is mediated by alpha-2u globulin nephropathy.**

Your testing proposals are accepted and you are requested to carry out:

2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) in a first species (rat or rabbit), oral route using the registered substance.**
3. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rabbit or rat), oral route using the registered substance.**
4. **Effects on soil micro-organisms (Annex IX, Section 9.4.2.; test method: Soil microorganisms: nitrogen transformation test, EU C.21./OECD TG 216) using the registered substance.**
5. **Long-term toxicity on terrestrial invertebrates (Annex X, Section 9.4.4.; test method: Earthworm reproduction test, OECD TG 222) using the registered substance.**

You are required to submit the requested information in an updated registration dossier by ***29 November 2021*** except for the information requested under points *1, 4 and 5* for a Sub-chronic toxicity study (90-day), Effects on soil micro-organisms, and Long-term toxicity on terrestrial invertebrates which shall be submitted in an updated registration dossier by ***30 November 2020***. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons for this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

This decision does not address the information requirement of the Extended one-generation reproductive toxicity study according to Annex X, Section 8.7.3. of the REACH Regulation. The results of the Sub-chronic toxicity study (90-day) will be used, among other relevant information, to decide on the study design of the Extended one generation reproductive toxicity study. Therefore, your testing proposal for Extended one-generation reproductive toxicity study will be addressed after having received the results of the Sub-chronic toxicity study (90-day).

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Claudio Carlon, Head of Unit, 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 1: Reasons

The decision of ECHA is based on the examination of the testing proposals submitted by you.

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

Pursuant to Article 40(3)(b) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test under modified conditions.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to OECD TG 408.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Sub-chronic toxicity (90-day): oral. ECHA notes that you provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

You proposed testing by the oral route. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA agrees that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of very low vapour pressure and no uses with spray application are reported that could potentially lead to aerosols of inhalable size. Hence, the test shall be performed by the oral route using the test method OECD TG 408.

Therefore, ECHA considers that the proposed study performed by the oral route with the registered substance is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation.

You proposed testing in rats. According to the test method OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

In the "Combined repeated dose toxicity study with the reproduction/developmental screening test" according to OECD TG 422 present in your registration dossier, adverse effects (slight to moderated histopathological changes at the highest dose level of 1000 mg/kg bw/day) were observed in the kidneys of male rats and not in female rats. Also relative kidney weight increased at the highest dose level, but it was associated with decreased weight gain. You did not provide any further information on these histopathological findings directly in the study summary. However, you provided also a study report (mainly in Japanese, but most of the result tables and figures are in English) as an attachment in the IUCLID Section 7.5.1. According to the report, basophilic tubule was the main histopathological finding in the kidneys of male rats. The fact that these effects were only observed in male rats may indicate that the registered substance may induce

alpha-2u-globulin-mediated nephropathy. ECHA accordingly considers that the kidney is a target organ of the registered substance, although the observed kidney effects were not observed in the recovery group of male rats. Since humans do not excrete alpha-2u-globulin and this mode of action is not relevant to humans, determining whether alpha-2u-globulin is involved in the kidney effects is a key parameter for establishing the relevance of the kidney effects for risk assessment. Indeed, where there are no indications of involvement of alpha-2u globulin in the observed kidney effects, the kidney findings in rats are considered to be relevant also for humans and risk assessment. For these reasons, ECHA considers that urinalysis is required to investigate kidney function (which is referred to in paragraphs 3 and 37 of OECD TG 408). Additionally, a full histopathological examination (paragraphs 3, 45 and 47 of OECD TG 408), which is to include immunohistochemical investigation of renal pathology to determine if the pathology is indeed mediated by alpha-2u globulin.

In your comments on the draft decision, you indicated that the test substance for 90-day subchronic study may differ from the ones previously investigated for their short-term repeated-dose toxicity via oral route and their toxicity to reproduction (screening test). Therefore, it may require the addition of a Dose-Range Finding (DRF) study to confirm the doses to use during the subchronic toxicity study via the oral route. You also stated in your comments that the reversibility of some adverse effects was observed in previous studies. Therefore, you proposed to include recovery groups as part of this study. You also stated that inclusion of DRF study and recovery groups would involve additional animal testing.

ECHA notes that according to OECD TG 408 dose levels may be based on the results of repeated dose or range finding studies and should take into account any existing toxicological and toxicokinetic data for the test compound or related materials. ECHA also notes that the test substance for the requested 90-day study may differ from the previously investigated substance(s) for other repeated-dose toxicity studies. In addition, OECD TG 408 allows for the inclusion of an additional satellite group for observation after the treatment period for the potential reversibility or persistence of any toxic effects. Hence, both dose range finding study and recovery groups can be included in the 90-study.

Grade of substance to be tested for toxicological studies

In your comments on the draft decision, you provided a rationale to use the grade 4 of BPA EO in the OECD 408 and 414 studies. In addition, you requested if ECHA could confirm the grade of BPA to be used in each of the studies.

You consider the results of two studies conducted according to OECD TG 422 in order to select the most relevant grade of BPA for the purpose of the human health toxicity testing. One OECD TG 422 study is available on Grade 5 of BPA EO and the other on mono-constituent BPA 2EO. You state that both substances caused similar adverse effects at the doses investigated. However, Grade 5 of BPA EO also induced basophilic tubule in male rats. This effect was not seen in the study with mono-constituent BPA 2EO.

You consider that the observed kidney effects could be related to the higher degree of ethoxylation of the constituents within Grade 5 of BPA EO. You also state that it is paramount to select for the toxicity studies a test substance that will induce this effect in order to properly investigate it as additional investigation on kidney effects has been requested in the draft Decision. Therefore, you propose to conduct the human health studies on Grade 4 of BPA EO.

ECHA notes that the study with mono-constituent BPA 2EO is not available in the dossier. Therefore, ECHA is not able to evaluate it and make a comparison between the two studies considered by you to select the most relevant grade of BPA for human health toxicity testing. ECHA also notes that mono-constituent BPA EO represents only one consituent present in the registered substance, BPA 1 – 4.5 EO. You state that commercially available grades of the registered substance are BPA 2EO, BPA 3EO and BPA 4EO. No toxicity data is provided for these grades which all have different composition, i.e. the degree of ethoxylation of the constituents varies with different grades of the substance.

Therefore, ECHA cannot conclude which is the most relevant grade of BPA EO for the purpose of the human health toxicity testing. However, ECHA reminds you that the sample tested should fall within the specification of the registered substance. Furthermore, you should decide which grade to test. ECHA recommends you to provide a justification in the updated dossier for the choice of sample and include information on the composition of the batch tested.

Therefore, pursuant to Article 40(3)(b) of the REACH Regulation, you are requested to carry out the modified study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: OECD TG 408) modified to include urinalysis and a full histopathological examination which is to include immunohistochemical investigation of renal pathology to determine if the pathology is mediated by alpha-2u globulin nephropathy.

Notes for your considerations:

You submitted a testing proposal for an Extended one-generation reproductive toxicity study (Annex X, 8.7.3.). However, this testing proposal is not addressed in this decision because the results of the Sub-chronic toxicity study (90-day) are considered crucial to inform on the study design of the Extended one-generation reproductive toxicity study. Therefore, you are required to perform the Sub-chronic toxicity study (90-day) first, and submit the results by the deadline indicated above.

Together with providing the results for the requested Sub-chronic toxicity study (90-day), you may also consider updating your testing proposal for the Extended one-generation reproductive toxicity study. The updated testing proposal should include a justification for the design of the Extended one-generation reproductive toxicity study following ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017), taking into account the results of the Sub-chronic toxicity study (90-day).

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a pre-natal developmental toxicity study in rats according to OECD TG 414.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (pre-natal developmental toxicity). ECHA notes that you provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

ECHA considers that the proposed study performed with the registered substance is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

You proposed testing with the rat as a first species. According to the test method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with the rat or the rabbit as a first species.

You did not specify the route for testing.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

In your comments on the draft decision, you provided a rationale to use the grade 4 of BPA EO in the OECD 414 study. Our response is given above under Appendix 1, section 1, of the decision.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in a first species (rat or rabbit), oral route (test method: OECD TG 414).

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017), Chapter R.7a, Section R.7.6.2.3.2.

3. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

Pre-natal developmental toxicity studies on two species are part of the standard information requirements for substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a pre-natal developmental toxicity study in a second species (rabbits) according to EU OECD TG 414 by the oral route.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (pre-natal developmental toxicity). ECHA notes that you provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

ECHA considers that the proposed study performed with the registered substance is appropriate to fulfil the information requirement of Annex X, Section 8.7.2. of the REACH Regulation.

You proposed testing with the rabbit as a second species. According to the test method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with the rabbit or the rat as a second species, depending on the species tested in the first pre-natal developmental toxicity study.

You proposed testing by the oral route.

ECHA agrees that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

In your comments on the draft decision, you provided a rationale to use the grade 4 of BPA EO in the OECD 414 study. Our response is given above under Appendix 1, Section 1, of the decision.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are thus requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in a second species (rabbit or rat), oral route (test method: OECD TG 414).

Before performing a pre-natal developmental toxicity study in a second species you should consider the specific adaptation possibilities of Annex X, Section 8.7.2., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species or any other new information enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement and underlying scientific justification.

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017), Chapter R.7a, Section R.7.6.2.3.2.

4. Effects on soil micro-organisms (Annex IX, Section 9.4.2.)

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX, Section 9.4. of the REACH Regulation. The Registrant must address the standard information requirements set out in Annex IX, Section 9.4., for different taxonomic groups: short-term toxicity testing on invertebrates (Annex IX, Section 9.4.1.), effects on soil micro-organisms (Annex IX, Section 9.4.2.), and short-term toxicity testing on plants (Annex IX, Section 9.4.3.).

The information on "effects on soil micro-organisms" is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a nitrogen transformation test (OECD TG 216) with the following justification: '*In addition, for substance which are not in the soil hazard category 1, it is considered that soil microorganisms are not covered by EPM. Therefore, a study according to OECD 216 guideline is proposed.*' ECHA concludes that the effects on soil microorganisms need to be ascertained by performing a relevant test.

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, Chapter R.7c of the ECHA Guidance on information requirements and chemical safety assessment (version 3.0, June 2017), ECHA considers the nitrogen transformation test (EU C.21/OECD TG 216) suitable for non-agrochemicals. ECHA notes that the strategy pursued by you is based on this approach.

Grade of substance to be tested in ecotoxicological studies

In your comments on the draft decision, you provided a rationale to use the grade 4 of BPA EO in the OECD 216 and 222 studies.

You state (a) that grade 2 of BPA EO showed a higher acute toxicity to fish, Daphnia and algae than grades with higher ethoxylation, but that (b) this has no bearing on choosing a grade for soil organism testing as toxicity in soil may be driven by other factors.

ECHA cannot assess statement (a) from the registration dossier in the absence of information on the composition of the samples tested, but it is not necessary to provide such information because ECHA agrees with your statement (b).

You argue that conducting the soil organism studies on the most ethoxylated grade 4 of BPA EO will represent a 'worst case', because this grade will contain a predominance of more ethoxylated constituents that will be more persistent in soil due to their physico-chemical properties. You argue that hydrophobicity & logKow increase with higher ethoxylation. However, you have not explained why higher hydrophobicity would necessarily result in a worst-case assessment as regards toxicity to soil microorganisms & earthworms. Therefore ECHA cannot assess your assertion.

Furthermore, ECHA considers that there is conflicting evidence on the effect of increasing the degree of ethoxylation of BPA:

- Your QSAR estimates show that logKow, logKoc (by MCI method) & logKoc (by Kow method) all decrease for higher ethoxylation.
- The two OECD 117 studies in the registration dossier are on unspecified grades, showing many peaks in the hlpc. There is no definitive assignment of peaks with structure, but based on the distribution of early major peaks with a 'tail' they both

can be interpreted as logKow increasing with higher ethoxylation.

- You state '[redacted] *(1987) showed that both ethoxylated alcohols and ethoxylated sulfonates exhibited increased adsorption and hydrophobicity when their degree of ethoxylation increases. This is because their logKow increases with the degree of ethoxylation. Similar pattern can be expected for BPA EO'*. ECHA disagrees with this interpretation because [redacted] were investigating surfactants, whereas the registered substance is not surface active. Nevertheless, their conclusions for ethoxylated alcohols would be more likely to apply to the registered substance than their findings for ethoxylated suplfonates: in their conclusion, [redacted] state that 'Increasing the degree of ethoxylation increases the hydrophobicity of ethoxylated supfonates but decreases the hydrophobicity of ethoxylated alcohols.'

Therefore ECHA cannot conclude which grade is a 'worst case' for the soil studies. However your are reminded that the sample tested should fall within the specification of the registered substance. Furthermore you should decide which grade to test and we recommend you to provide the justification in the updated dossier and include information on the composition of the batch tested.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study using the registered substance subject to the present decision:

- Soil microorganisms: nitrogen transformation test, EU C.21/OECD TG 216

5. Long-term toxicity to terrestrial invertebrates (Annex IX, Section 9.4.1., column 2 and Annex X, Section 9.4.4.)

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex IX and X, Section 9.4. of the REACH Regulation. The Registrant must address the standard information requirements set out in Annex IX and X, Section 9.4., for different taxonomic groups: short-term toxicity testing on invertebrates (Annex IX, Section 9.4.1.), long-term toxicity testing on invertebrates (Annex X, section 9.4.4.), short-term toxicity testing on plants (Annex IX, section 9.4.3.) and long-term toxicity testing on plants (Annex X, section 9.4.6.).

The information on "long-term toxicity to invertebrates" is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a long-term toxicity test to invertebrates (Earthworm reproduction test, OECD TG 222) with the following justification*: 'Indirect exposure of BPA (1 -4.5 EO) to soil cannot be excluded. Therefore, according to column 2 of annex IX of Reach regulation, "in the absence of toxicity data for soil organisms, the equilibrium partitioning method may be applied to assess the hazard to soil organisms". ECHA's guidance on information requirements and chemical safety assessment, chapter R.7c (v4.0 ; June 2017 ; pp.158 -159) explains how EPM should be used. In the absence of any soil toxicity data, a soil hazard category must be assigned to the substance. BPA- (1 - 4.5 EO) is not readily biodegradable but not H400/H410. It falls therefore within the scope of soil hazard category 3. In this category, it is demanded to conduct one confirmatory long-term soil testing. It is our understanding that invertebrate testing is preferred to plant*

testing in a first approach (ECHA's guidance R.7c; v4.0 ; June 2017 ; p. 149, fourth paragraph). Therefore a study according to OECD 222 guideline is proposed.' According to Section R.7.11.5.3., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), substances that are ionisable or have a log K_{ow}/K_{oc} >5 are considered highly adsorptive, whereas substances with a half-life >180 days are considered very persistent in soil. According to the evidence presented within the Registration dossier, the substance is considered very persistent which is the default setting for not readily biodegradable substances, when the value of the half-life in soil is not available. Therefore ECHA agrees that a long-term testing is indicated and the proposed test is appropriate to fulfil the information requirement of Annex IX, Section 9.4.1., column 2.

Furthermore, based upon the available aquatic toxicity information and the physico-chemical properties of the substance, and in relation to Section R.7.11.6., Chapter R.7c of the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, June 2017), ECHA considers that the substance would fall into soil hazard category 3. In the context of an integrated testing strategy for soil toxicity, the Guidance advocates performing an initial screening assessment based upon the Equilibrium Partitioning Method (EPM), together with a confirmatory long-term soil toxicity test. The PNECscreen is calculated through EPM on the basis of aquatic toxicity data only. ECHA notes that the strategy pursued by you is based on this approach.

In your comments on the draft Decision, you provided a rationale to use the grade 4 of BPA EO in the OECD 222 study. Our response is given above under Appendix 1, section 4, of the decision.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study using the registered substance subject to the present decision:

- Earthworm reproduction test (OECD TG 222)

Deadline to submit the requested information under point 1 of the decision

The timeline indicated in the draft decision to provide the information requested under point 1 (Sub-chronic toxicity study (90-day)) is 12 months from the date of adoption of the decision. In your comments on the draft decision, you indicated that it may not be possible to submit the results within the requested deadline of 12 months due to the limited capacity of testing providers and the various analysis and examinations that are required for the study, including the DRF and recovery groups. Following your comments ECHA requested you on 17 May 2019 to submit documentary evidence in order to justify why an extension to the stated deadline of 12 months is required. You did not, however, provide any further information to support the extension of the given deadline. Furthermore, ECHA notes that the timeline already allows for the inclusion of a DRF study. Therefore, ECHA has not modified the deadline.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 9 February 2018.

ECHA notes that the tonnage band for one member of the joint submission is 1 000 tonnes or more per year.

ECHA held a third party consultation for the testing proposals from 21 May 2018 until 5 July 2018. ECHA received information from third parties. The information received concerned only testing proposal for the Extended one-generation reproductive toxicity study. However, this testing proposal is not addressed in this decision because the results of the Sub-chronic toxicity study (90-day) are considered crucial to inform on the study design of the Extended one-generation reproductive toxicity study.

This decision does not take into account any updates after **6 March 2019**, 30 calendar days after the end of the commenting period.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

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

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

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

Appendix 3: Further information, observations and technical guidance

1. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for the start of substance evaluation in 2021.

2. This decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

3. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.

4. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.