EUROPEAN CHEMICALS AGENCY

Helsinki, 24 June 2019

Addressee: [redacted]

Decision number: CCH-D-2114471560-52-01/F
Substance name: 2-ethylhexyl diphenyl phosphate
EC number: 214-987-2
CAS number: 1241-94-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 11/08/2015
Registered tonnage band: Over 1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Composition of the substance (Annex VI, Section 2.3.) of the registered substance;**
   - **Concentration values**
2. **Spectral data (Annex VI, Section 2.3.5.);**
   - **Nuclear magnetic resonance or mass spectrum**
   - **Ultra-violet spectrum**
3. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rabbit), oral route with the registered substance;**
4. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route with the registered substance specified as follows:**
   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce systemic toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
   - **Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation; and**
   - **Cohort 3 (Developmental immunotoxicity).**
5. **Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test**

method: Alga, growth inhibition test, EU C.3./OECD TG 201) with the registered substance;

6. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: Daphnia magna reproduction test, EU C.20./OECD TG 211) with the registered substance;**

7. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI to the REACH Regulation. To ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by **3 January 2022**. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of 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.

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

1. Composition of the substance (Annex VI, Section 2.3.)

In accordance with Article 10(a)(ii) of the REACH Regulation, the technical dossier must contain information on the identity of the substance as specified in Annex VI, Section 2 to the REACH Regulation. In accordance with Annex VI, Section 2 the information provided has to be sufficient to enable the identification of the registered substance.

Annex VI, section 2.3. of the REACH Regulation requires that each registration dossier contains sufficient information for establishing the composition of the registered substance and therefore its identity.
In that respect, according to chapter 4.2 of the Guidance for identification and naming of substances under REACH and CLP (Version: 2.0, December 2016) – referred to as the "SID Guidance", you shall note that, for well-defined substances, for each constituent (i.e. main constituents, impurities, etc.), the typical, minimum and maximum concentration levels shall be specified regardless of the substance type. In addition, as a general rule, the compositional information should be completed up to 100%.

In the present dossier, you identified the registered substance as a well-defined mono-constituent substance. In IUCLID section 1.2 you have reported 2-ethylhexyl diphenyl phosphate as the main constituent with a typical concentration [redacted] but without providing the concentration ranges. Similarly, the impurities bis(2-ethylhexyl) phenyl phosphate and triphenyl phosphate were reported with the typical concentrations values [redacted] and [redacted] respectively), but without providing the concentration ranges.

As the concentration ranges are missing, ECHA concludes that the compositional information has not been provided to the required level of detail. Additionally, the sum of the typical concentration of the main constituent and the impurities do not add up to 100%.

Consequently, you will need to provide a complete compositional information where the main constituent and the relevant impurities are reported with their typical, minimum and maximum concentration levels. The compositional information of the substance should be completed up to 100%.

In your comments on the draft decision, you agreed to provide the requested additional information on the composition of the registered substance.

The requested information shall be included in section 1.2 of the registration dossier.

2. Spectral data (Annex VI, Section 2.3.5.)

In accordance with Article 10(a)(ii) of the REACH Regulation, the technical dossier must contain information on the identity of the substance as specified in Annex VI, Section 2 to the REACH Regulation. In accordance with Annex VI, Section 2 the information provided has to be sufficient to enable the identification of the registered substance.

"Spectral data" (ultra-violet, infra-red, nuclear magnetic resonance or mass spectrum) is an information requirement as laid down in Annex VI, Section 2.3.5. of the REACH Regulation. Adequate information needs to be present in the technical dossier for the registered substance to meet this information requirement.

Your registration dossier does not contain the full set of analytical data for the registered substance. You have provided only an infra-red (IR) spectrum. No ultra-violet (UV) spectrum and nuclear magnetic resonance (NMR) spectrum or, alternatively, a mass spectrum (MS)) have been submitted. Moreover, a scientifically based justification for not including this information has not been provided.

ECHA considers that the IR spectrum alone is not sufficient to identify the substance, and considers that the full set of analytical data is necessary for the identification of the registered substance.

Therefore, you are requested to submit a UV spectrum and an NMR spectrum or, alternatively to the NMR, a MS spectrum generated on the substance subject to the present decision. You shall ensure that the description of the analytical methods used for recording the spectra is specified in the dossier in sufficient details to allow the methods to be reproduced, in line with the requirements under Annex VI Section 2.3.7 of the REACH Regulation. You shall ensure that the information is consistent with the information provided throughout the dossier.

In your comments on the draft decision, you agreed to provide a UV spectrum and an NMR spectrum or a MS spectrum generated on the registered substance.

Regarding how to report the spectral data, the information shall be attached in section 1.4 of the IUCLID dossier.

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Pre-natal developmental toxicity studies (test method OECD TG 414) on two species are part of the standard information requirements for a 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).

a) The information provided

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.2., weight of evidence. Hence, ECHA has evaluated your adaptation with respect to this provision.

In the technical dossier you provided the following justification for the adaptation "*A developmental toxicity study in a second species can be waived because in the Guidance Document on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance is indicated that the study does not need to performed, because the developmental toxicity study and the one-generation reproduction study in rats do not indicate the substance to cause developmental effects, and there are no indications that the*

substance may be toxic to reproduction in the 90-day repeated dose toxicity studies."

ECHA understands that you conclude that the registered substance does not have a dangerous (hazardous) property with respect to developmental toxicity. However, you have not provided an explanation or justification on how the sources of information/studies, which you have provided enable such assumption or conclusion.

b) ECHA's evaluation and conclusion of the information provided

Evaluation approach/criteria:

An adaptation pursuant to Annex XI, Section 1.2. requires sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion.

Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to a pre-natal developmental toxicity study (OECD TG 414) with a second species. Relevant elements are in particular, information on a second species (information on species differences), exposure route, duration and levels, sensitivity and depth of investigations to detect pre-natal developmental toxicity (including growth, survival, external, skeletal and visceral alterations) and maternal toxicity.

Evaluation of the provided information:

Your main argument to waive the pre-natal developmental toxicity study is "*because the developmental toxicity study and the one-generation reproduction study in rats do not indicate the substance to cause developmental effects"* with a reference to ECHA Guidance Chapter R.7a[2]. However, there is no such statement in ECHA Guidance to allow an adaptation for information on prenatal developmental toxicity on a second species.

ECHA notes that in the technical dossier there is only information for developmental toxicity on one species (the rat), hence information on a second species is missing. Secondly, the one-generation reproductive toxicity study refers to toxicity to reproduction and it does not specifically address the key parameters which are investigated in the prenatal developmental toxicity endpoint (for example, examinations of foetuses for skeletal and visceral alterations).

Additionally, you state that "*there are no indications that the substance may be toxic to reproduction in the 90-day repeated dose toxicity studies*". However, the repeated-dose toxicity study may indicate concerns in relation to fertility, not to (prenatal) developmental toxicity which is a separate information requirement. Thus, results from a 90-day study do not influence on the evaluation of potential hazardous properties for (prenatal) developmental toxicity.

[2] ECHA Guidance Document on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance (version 6.0, July, 2017).

c) Conclusion

As indicated above, essential information addressing the key parameters on (pre-natal) developmental toxicity on a second species is missing, which does not allow assessing the potential hazard with adequate confidence. Hence, the sources of information you provided, do not allow to assume/conclude on the dangerous (hazardous) property of the registered substance with respect to the information requirement for Annex X, Section 8.7.2.

Therefore, the general rules for adaptation laid down in Annex XI, Section 1.2. of the REACH Regulation are not met and your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The test in the first species was carried out by using a rodent species (rat). According to the test method OECD TG 414, the rabbit is the preferred non-rodent species. On the basis of this default assumption, ECHA considers that the test should be performed with rabbit as a second species.

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 indicate that after consulting the members of the joint submission, all registrants intend to downgrade the tonnage band of their registration to 100-1000 tonnes per year. Accordingly, the information requirement for a pre-natal developmental toxicity study in a second species would not apply, as this is an information requirement set out in Annex X of the REACH Regulation (i.e. for substances imported or manufactured at over 1000 tonnes per year).

ECHA invited you in the separate communication CCH-C-2114438246-49-01/F to provide further details (tonnage volumes for the three preceding calendar years) to establish if the tonnage band downgrade can be taken into account in the ongoing decision making process. Based on the information you provided in response to this communcation, ECHA established that the average volume subject to the registration for the three calendar years preceding the end of the 30-day commenting period for the CCH draft decision is > 1000 tonnes per year. Accordingly, ECHA concluded that you are responsible for the Annex X standard information requirements as already addressed in the CCH draft decision. ECHA also notes that there is another registrant in the joint submission subject to the information requirement of Annex X of the REACH Regulation (i.e. tonnage subject to full registration > 1000 tonnes per year).
This information was communicated to you on 19 December 2018 (communication number CCH-C-2114455685-38-01/F) in response to your enquiry number INC000000245132.

d) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the

present decision: Pre-natal developmental toxicity study (test method: OECD TG 414) in a second species (rabbit) by the oral route.

4. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

The basic test design of an extended one-generation reproductive toxicity study (test method OECD TG 443 with Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Further detailed guidance on study design and triggers is provided in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

a) The information provided

You have not provided any study record of an extended one-generation reproductive toxicity study in the dossier that would meet the information requirement of Annex X, Section 8.7.3.

In the technical dossier you have provided a study record for a one-generation reproductive toxicity study ([redacted] 1992), in rats by the oral route, with the registered substance (reliability score of 2). Hence, ECHA has evaluated your adaptation according to Annex XI, Section 1.1.2 (Use of existing information).

Additionally, while you have not explicitly specified an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.2., weight of evidence. Hence, ECHA has evaluated your adaptation also with respect to this adaptation.

In the technical dossier you provided the following justification for the adaptation "*A two-generation reproduction study can be waived because in the Guidance Document on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance is indicated that the study does not need to performed, because the developmental toxicity study and the one-generation reproduction study in rats do not indicate the substance to cause developmental and reproductive effects, and there are no indications that the substance may be reproductive toxic in the 90-day repeated dose toxicity studies.*"

To support your weight of evidence adaptation you have provided the above mentioned one-generation reproductive toxicity study and you also refer to information from developmental toxicity studies and 90-day toxicity studies, all in the registration dossier.

ECHA understands that you conclude that the registered substance does not have a dangerous (hazardous) property with respect to sexual function and fertility. However, you have not provided an explanation or justification on how the sources of information/studies, which you have provided enable such assumption or conclusion.

b) ECHA's evaluation and conclusion of the information provided

Evaluation approach/criteria:

ECHA has evaluated the information from the one-generation reproductive toxicity study as an adaptation according to criteria of Annex XI, Section 1.1.2. (Use of existing data). Additionally ECHA has considered this study as a piece of evidence according to Annex XI, Section 1.2 adaptation (Weight of evidence) along with your adaptation justification.

An adaptation pursuant to Annex XI, Section 1.2. requires sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion. Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to an extended one-generation reproductive toxicity study (OECD TG 443) as requested in this decision. ECHA considers that this study provides, in addition to information to general toxicity, information in particular on two aspects, namely on sexual function and fertility in P0 and F1 generations (further referred to as 'sexual function and fertility') and on development and toxicity of the offspring from birth until adulthood due to pre- and postnatal and adult exposure in the F1 generation and F2 generation until weaning (further referred to as 'effects on offspring').

Relevant elements for 'sexual function and fertility' are in particular functional fertility (oestrous cycle, sperm parameters, mating behaviour, conception, pregnancy, parturition, and lactation) in the P0 and F1 parental generations after sufficient pre-mating exposure duration and histopathological examinations of reproductive organs in both P and F1 generations. Relevant elements for 'effects on offspring' are in particular peri- and post-natal investigations of the F1 generation up to adulthood including investigations to detect certain endocrine modes of action, sexual development, investigations on developmental immunotoxicity and postnatal development of F2 generation. Also the sensitivity and depth of investigations to detect effects on 'sexual function and fertility' and 'effects on offspring' needs to be considered.

Furthermore, the relative values/weights of different pieces of the provided information needs to be assessed as indicated in ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.4., Section 4.4 (version 1.1, December 2011). In particular relevance, reliability and consistency of results/data and coverage (completeness) need to be considered.

Evaluation of the provided information:

Adaptation according to Annex XI, Section 1.1.2: The one-generation reproductive toxicity study does not provide the information required by Annex X, Section 8.7.3. because of limited postnatal exposure duration and inadequate coverage of key aspects/parameters (for further details see below the evaluation under the weight of evidence). Therefore this

study fails to meet the requirement of Annex XI, Section 1.1.2., as the data provided is not considered as being equivalent to the data generated by the corresponding test method referred to in Article 13(3). Therefore, your adaptation of the information requirement is rejected.

Adaptation according to Annex XI, Section 1.2: ECHA highlights that two-generation reproductive toxicity study is no longer an information requirement at Annex X, Section 8.7.3. It has been replaced by the extended-one generation reproductive toxicity study. In your justification you refer to ECHA Guidance Chapter R.7a[3] which, however, does not allow an adaptation of extended one-generation reproductive toxicity study based on no indication of reproductive toxicity from one-generation reproductive toxicity study, developmental toxicity study and 90-day study. Thus, you reference to ECHA Guidance is invalid.
Your main argument to adapt the information requirement for an extended one-generation reproductive toxicity study is "*because the developmental toxicity study and the one-generation reproduction study in rats do not indicate the substance to cause developmental and reproductive effects, and there are no indications that the substance may be toxic to reproduction in the 90-day repeated dose toxicity studies.*"

As indicated above, comparing to the criteria, the one-generation reproductive toxicity study fails to provide information on various elements on reproductive toxicity, such as extensive evaluation of F1 generation up to adulthood including the sexual maturation and functional fertility, and including investigations to detect certain endocrine modes of action, sexual development, investigations on developmental immunotoxicity and postnatal development of F2 generation.

The pre-natal developmental toxicity study provides a focused evaluation of potential effects on prenatal development, however, it does not provide information on postnatal development. The information related to sexual function and fertility is limited to maintenance of pregnancy. The 90-day study can provide information only on histopathology on reproductive organs and general toxicity but not on functional fertility or on F1 generation.

Furthermore, an extended one-generation reproductive toxicity study is a standard information requirement at Annex X and is not triggered based on a concern such as indication of reproductive toxicity in other studies.

Currently there is no information available on mating, fertility and reproductive performance of the F1 animals, postnatal development of F2 generation and on developmental immunotoxicity. As explained hereunder, under the sub-headings of *Extension of Cohort 1B* and *Cohort 3*, there are concerns with the registered substance that need to be further investigated.

Thus, ECHA considers that the information provided, alone or together, is not sufficient to allow to conclude on reproductive toxicity and your adaptation according to Annex XI, Section 1.2 is rejected.

[3] ECHA Guidance Document on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance (version 6.0, July, 2017).

c) Conclusion

The one-generation reproductive toxicity study does not provide the information required by Annex X, Section 8.7.3., and the study fails to meet the requirement of Annex XI, Section 1.1.2., Therefore, your adaptation of the information requirement is rejected.

Essential information is missing, which does not allow assessing the potential hazard. Hence, the sources of information you provided, together with your justification for the adaptation, do not allow to assume/conclude that the substance does not have a particular dangerous (hazardous) property with respect to the information requirement for Annex X, Section 8.7.3.

Therefore, the general rules for adaptation laid down in Annex XI, Section 1.2. of the REACH Regulation are not met and your adaptation of the information requirement is rejected.

Hence, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint. Thus, an extended one-generation reproductive toxicity study according Annex X, Section 8.7.3. is required. The following refers to the specifications of this required study.

d) The specifications for the study design

Premating exposure duration and dose-level setting

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required if there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017). In this specific case ten weeks exposure duration is supported by the lipophilicity of the substance (log Kow 5.87) to ensure that the steady state in parental animals has been reached before mating.

The highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

If there is no existing relevant data to be used for dose level setting, it is recommended that results from a conducted range-finding study (or range finding studies) are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

Extension of Cohort 1B

If the column 2 conditions of 8.7.3., Annex X are met, Cohort 1B must be extended, which means that the F2 generation is produced by mating the Cohort 1B animals. This extension provides information also on the sexual function and fertility of the F1 animals. The extension is inter alia required, if the use of the registered substance is leading to significant exposure of consumers or professionals (column 2, first paragraph, lit. (a) of section 8.7.3., Annex X) and if there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure (column 2, first paragraph, lit. (b), second indent of section 8.7.3., Annex X).

The use of the registered substance in the joint submission is leading to significant exposure of consumers and professionals because the registered substance is used by professionals in the application of coatings, paints, thinners, paint removers, leather tanning, dyes, finishes, adhesives, sealants, fillers, putties, plasters, polymer preparations and compounds (PROCs 10 and 19). Moreover, the substance is used by consumers as coatings, paints, thinners and paint remover.

Furthermore, there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure. According to the technical dossier, the log Kow for the registered is 5.87. According to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Appendix R.7.6-2 (version 6.0, July 2017), this value is above the threshold value indicating that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure.

Therefore, ECHA concludes that Cohort 1B must be extended to include mating of the animals and production of the F2 generation because the uses of the registered substance are leading to significant exposure of professionals and consumers and there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure.

Cohort 3

The developmental immunotoxicity Cohort 3 needs to be conducted in case of a particular concern on (developmental) immunotoxicity as described in column 2 of 8.7.3., Annex X.

ECHA notes that existing information on the registered substance itself derived from an available *in vivo* study, a one-generation reproductive toxicity study, in rats by the oral route, ([redacted] 1992) (reliability score of 2), shows evidence of toxicity in the spleen in the parental generation and the offspring. More specifically, in the study report by [redacted] (1992), there is no information reported on the absolute organ weights and there is no tabulated data with the organ weight measurements. However, according to the information provided, a significant decrease in the relative spleen weight was observed in the P0 females at the mid- and high-dose groups. The F1 offspring was sacrificed at 21 days of age; at this time, there was a significant decrease in the relative spleen weight in the male offspring at the mid- and high-dose groups while in the female offspring it was noted in all dose groups. It must be noted that the post-natal survival until day 21 was decreased in the high-dose group by 26.6%, when compared to the control group. ECHA also notes that no histopathology was performed in this study. ECHA notes that according to ECHA's *Guidance*

on information requirements and chemical safety assessment Chapter R.7a, Section R.7.6 (version 6.0, July 2017), "*one severe statistically and/or biologically significant organ weight organ weight or histopathological finding related to an immunology organ*" is considered as a specific finding that may indicate a particular concern justifying the inclusion of the developmental immunotoxicity cohort. In this case a statistical significant decrease was observed in the relative spleen weight, not only in the female parental generation but also in the F1 offspring. Hence, this specific finding alone triggers concern for developmental immunotoxicity.

As a consequence, ECHA concludes that the developmental immunotoxicity Cohort 3 needs to be conducted because there is a particular concern on (developmental) immunotoxicity based on the results from the above-identified *in vivo* study on the registered substance itself.

Species and route selection

According to the test method OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in rats.

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 indicate that after consulting the members of the joint submission, all registrants intend to downgrade the tonnage band of their registration to 100-1000 tonnes per year. As already explained under request 3, ECHA has reviewed the updated tonnage information provided by you and concluded that the information requirement set out in Annex X of the REACH Regulation applies.

You also state that you are currently reviewing the information from a member registrant that recently joined the joint registration following the application of the One Substance One Registration principle. You foresee that the registrant dossier may include further information on the study by Worrell (1992). You consider that it may address some (or all) of the specific questions/issues identified by ECHA. However, ECHA notes that this new information was not included in the registrant comments on the draft decision and it could not have been assessed.

e) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce systemic toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to

produce the F2 generation; and
- Cohort 3 (Developmental immunotoxicity).

Notes for your consideration

No triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) were identified. However, you may expand the study by including Cohorts 2A and 2B if new information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the new information shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017). You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented. The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented.

5. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Growth inhibition study aquatic plants" is a standard information requirement as laid down in Annex VII, Section 9.1.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.2., weight of evidence. Hence, ECHA has evaluated your adaptation with respect to this provision.

a) The information provided

To support your weight of evidence adaptation you have provided the following sources of information in your IUCLID dossier:

- Supporting study: [redacted] based on the US EPA (1971) [redacted] with the registered substance (the test material is reported as S-141, which is claimed by you to be identical to the registered substance), [redacted] 1979 (study report), reliability score of 3,
- Supporting study: [redacted] based on a method similar to OECD Guideline 201 with the registered substance, [redacted] 1994 (study report), reliability score of 3,
- Supporting study: [redacted] based on a method similar to EU Method C.3 and OECD Guideline 201 with the registered substance, [redacted] 1995 (study report), reliability score of 3,

- Weight of evidence: [redacted] based on a method similar to EU Method C.3 and OECD Guideline 201 with the registered substance, [redacted] 1995 (study report), reliability score of 4.

b) ECHA's evaluation and conclusion of the information provided

An adaptation pursuant to Annex XI, Section 1.2. requires sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion.

Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to the study of growth inhibition of aquatic plants (EU C.3/OECD TG 201). Relevant elements are in particular duration and levels of exposure, sensitivity and specific data on the growth rate determined over the course of the experiment.

Evaluation of the provided information

Reliability and relevance of individual information

With regard to quality and relevance, ECHA has observed several deficiencies:

- All provided studies have been assigned with reliability 3 or 4. ECHA agrees with your conclusions as detailed below.
- In the studies of [redacted] (1979) and [redacted] (1994), the test concentrations were mostly above the water solubility of the substance and no analytical monitoring was performed. Considering the characteristics of the test substance (poor solubility, adsorptive properties, potential instability in water), experimental exposure levels are uncertain and the results obtained from these studies have limited reliability to evaluate the toxicity of the registered substance towards aquatic algae and cyanobacteria.
- In the studies by [redacted] (1995), the 72h EC50 for *D. subspicatus* and *P. subcapitata* was determined to be 120 and 226 µg/L (based on biomass), respectively. No 72h EC50 or 72h NOEC based on growth rate were derived. However, according to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b, Section R.7.8.4.1* (version 4.0, June 2017), effect values based on biomass should not be used for the purpose of chemical safety assessment.

Consistency of provided information

ECHA has observed relevant inconsistencies in the information you have provided:

- In the studies of [redacted] (1995), the effects of the substance were tested on *Desmodesmus subspicatus* and *Pseudokirchnerella subcapitata*. You provided the study on *D. subspicatus* as supporting information (reliability score of 3) in both your CSR and the IUCLID dossier. However, ECHA notes that there is an inconsistency between the information provided in your CSR and in the IUCLID dossier for the study on *P. subcapitata*. While the study is provided as part of the

weight of evidence in the IUCLID dossier (reliability score of 4), it is provided as supporting information (reliability score of 3) in your CSR.

Conclusion on the provided information

You have concluded that the information provided *"may be considered generally supportive of the conclusion that 2EHDPP is not toxic to aquatic organisms in short or long term tests at or below the water solubility".*

However, as explained above, the information you provided is not sufficient to support your conclusion as no reliable study is included in you dossier.

In addition, the results reported in [redacted] (1995) do not support the conclusion that the registered substance is not toxic to algae at concentrations below the water solubility. First, the effect concentrations reported in the robust study summaries (RSSs) are based on measured concentration at test initiation. However, according to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b, Section R.7.8.4.1* (version 4.0, June 2017), if measured concentrations fall below 80% of nominal concentration, effect values should be calculated as the geometric mean of measured concentrations. For both algae species, a NOEC based on cell number of 72 µg/L is reported (corresponding to a nominal concentration of 237 µg/L) based on measured test item concentration at t0. ECHA notes that the measured concentration at the end of the test (i.e. 72h) was 31 µg/L. Accordingly, the NOEC based on biomass is 47.2 µg/L, which is below the water solubility limit of the registered substance (i.e. 50.6 µg/L). Then, ECHA notes that test results are attached to the RSS of the study conducted on *D. subspicatus*. It appears that a 14.6% decrease in growth rate was observed at 35.3 µg/L (calculated as the geometric mean of measured concentrations at 0 and 72h), which corresponds to the lowest nominal test concentration (i.e. 158 µg/L). This result indicates that the NOErC 72h is < 35.3 µg/L and that toxic effects may occur below the solubility limit of the registered substance.

c) Conclusion

Hence, the sources of information you provided, do not allow to assume/conclude that the substance does not have a particular dangerous (hazardous) property with respect to the information requirement for Annex VII, Section 9.1.2.
Therefore, the general rules for adaptation laid down in Annex XI, Section 1.2. of the REACH Regulation are not met and your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017), Algae growth inhibition test (test method EU C.3. / OECD TG 201) is the preferred test to cover the standard information requirement of Annex VII, Section 9.1.2.

d) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Algae growth inhibition test, EU C.3./OECD TG 201).

In your comments on the draft decision, you agreed to perform the requested study.

Note for your consideration

Due to the poor solubility of the substance in water and its adsorptive properties, you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s). You should also ensure that the information provided in the IUCLID dossier and in your CSR for the registered substance are consistent (e.g. type of information and reliability score assigned to reported studies).

6. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.2., weight of evidence. Hence, ECHA has evaluated your adaptation with respect to this provision.

a) Information provided

To support your weight of evidence adaptation you have provided the following sources of information in your IUCLID dossier:

- Key study: [redacted] based on an in-house protocol from EG&G Bionomics with the registered substance (the test material is reported as S-141, which is claimed by you to be identical to the registered substance), [redacted] 1979 (study report), reliability score of 2,
- Weight of evidence: Short-cut toxicity estimates using Daphnia magna, Adams & Heidolph, 1985 (publication) and referring to the results from [redacted] (1979) listed above, reliability score of 4,
- Supporting study: Short-cut toxicity estimates using *Daphnia magna*, Adams &

Heidolph, 1985 (publication), reliability score of 2.

ECHA notes that the three study records refer to the same study by Wilson & Leblanc (1979).

b) ECHA's evaluation and conclusion of the information provided

An adaptation pursuant to Annex XI, Section 1.2. requires sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion. Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.). Relevant elements are in particular duration and levels of exposure, sensitivity and specific data on reproduction determined over the course of the experiment.

Evaluation of the provided information

Reliability and relevance of individual information

With regard to quality and relevance, ECHA has observed several deficiencies:

- Regarding the study of [redacted] (1979), you state in your CSR that *"A flow-through test design was employed that exposed a range of concentrations (0 to 0.15 mg/L) to daphnids beginning with <24-h old neonates through adult reproduction. Endpoints included survival throughout the 21-day test and cumulative young produced per female during reproduction"*. You then add that *"Egg production was reported to be reduced at the nominal concentration of 0.075 mg/L that exceeds the water solubility (mean measured 0.043 mg/L)"*, which would trigger setting the NOEC for reproduction at 18 µg/L (corresponding to a nominal concentration of 38 µg/L). However, you considered the study results unreliable (reliability score 4) as you state that *"Entrapment of daphnids noted at 0.036 mg/L during the range-finding study. This indicates the presence of undissolved test material and suggests that the solubility in water may be even lower than the measured value of 0.0506 mg/L"*. ECHA notes that the relevance of this information to interpret the definite study is unclear considering that the NOEC related to mortality was determined to be 0.043 mg/L in the chronic study.
- In the IUCLID dossier you state that high mortality (20%) was observed in the solvent control and you did not report any information on the test results apart from the NOEC estimates, water quality parameters and the results of the analytical monitoring.

Consistency of provided information

ECHA has observed relevant inconsistencies in the information you have provided:

- In your IUCLID dossier you included three study reports which appear to refer to the same study report by [redacted] (1979). The same piece of information is considered as a key study with a reliability score of 2, a weight of evidence with a reliability score of 4 or a supporting information with a reliability score of 2

depending on the study record considered. In your CSR, the information reported in [redacted] (1979) is reported as "[redacted] *(1979), also cited in Adams & Heidolph (1985)*" and is considered to be part of a weight of evidence with a reliability score of 4.
Conclusion on the provided information

You have concluded in your CSR that the information provided support the fact that "*2EHDPP is not toxic to daphnids at or below the water solubility*".
However, as explained above, the information you provided is not sufficient to support your conclusion as:

- a weight of evidence should rely on several independent sources of information. However, while you report three study records in your technical dossier, all reported data refer to the same original study by [redacted] (1979). In addition, the reliability you assigned to this piece of information is unclear due to inconsistencies in your IUCLID dossier and in your CSR,
- ECHA considers that the reliability of the test results by [redacted] (1979) is insufficient considering that high mortality was observed in the control condition. Accordingly, as no reliable information is provided it cannot support your assumption/conclusion.

c) *Conclusion*

Hence, the sources of information you provided, do not allow to assume/conclude that the substance does not have a particular dangerous (hazardous) property with respect to the information requirement for Annex IX, Section 9.1.5.

Therefore, the general rules for adaptation laid down in Annex XI, Section 1.2. of the REACH Regulation are not met and your adaptation of the information requirement is rejected.

In addition, you have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a *Daphnia magna* reproduction test (OECD TG 211) with the analogue substance Isodecyl Diphenyl Phosphate (EC no 249-828-6).

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). ECHA considers that the generation of information by such alternative means should offer equivalence to prescribed tests or test methods.

Based on the above, a read-across hypothesis needs to be provided. This hypothesis establishes why a prediction for a toxicological or ecotoxicological property is reliable and should be based on recognition of the structural similarities and differences between the source and registered substances[4]. This hypothesis explains why the differences in the

[4] Please see for further information ECHA *Guidance on information requirements and chemical safety assessment* (version 1, May 2008), Chapter R.6: QSARs and grouping of chemicals.

chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

The read-across approach must be justified scientifically and documented thoroughly, also taking into account the differences in the chemical structures. There may be several lines of supporting evidence used to justify the read-across hypothesis, with the aim of strengthening the case.

Due to the different nature of each endpoint and consequent difference in scientific considerations (e.g. key parameters, biological targets), a read-across must be specific to the endpoint or property under consideration. Key physicochemical properties may determine the fate of a compound, its partitioning into a specific phase or compartment and largely influence the availability of compounds to organisms, e.g. in bioaccumulation and toxicity tests. Similarly, biotic and abiotic degradation may alter the fate and bioavailability of compounds as well as be themselves hazardous, bioaccumulative and/or persistent. Thus, physicochemical and degradation properties influence the human health and environmental properties of a substance and should be considered in read-across assessments. However, the information on physicochemical and degradation properties is only a part of the read-across hypothesis, and it is necessary to provide additional justification which is specific to the endpoint or property under consideration.

The ECHA Read-across assessment framework foresees that there are two options which may form the basis of the read-across hypothesis[5]- (1) (Bio)transformation to common compound(s)- the read-across hypothesis is that different substances give rise to (the same) common compounds to which the organism is exposed and (2) Different compounds have the same type of effect(s)- the read-across hypothesis is that the organism is exposed to different compounds which have similar (eco)toxicological and fate properties as a result of structural similarity (and not as a result of exposure to common compounds).
Finally, Annex XI, Section 1.5. lists several additional requirements, which deal with the quality of the studies which are to be read-across.

You consider to achieve compliance with the REACH information requirements on the long term toxicity testing on invertebrates for the registered substance 2-Ethylhexyl Diphenyl Phosphate using data of Isodecyl Diphenyl Phosphate (EC no 249-828-6) (hereafter the 'source substance') that you claim to be a structural analog.

You have provided documentation of the read-across adaptation attached to section 13 of your IUCLID dossier. The documentation is limited to an image file showing the chemical structure of the target and source substances, some basic physic-chemical properties (molecular weight, water solubility and Log Kow) and a statement on the chemical nature of the two substances. However, the documentation that you provided in your dossier does not contain any specific justification why relevant environmental properties of the registered substance may be predicted from data for the source substance. Specifically, your dossier does not address why such prediction would be possible and how structural differences, impurity profiles and difference physico-chemical properties (e.g., water solubility) may impact the prediction.

[5] Please see ECHA's Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across).

In the absence of this information, ECHA cannot verify that the properties of the registered substance can be predicted from the data on the source substance.
Hence, you have not established that relevant properties of the registered substance can be predicted from data on the analogue substance. Since your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5., it is rejected.
Accordingly, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment,* (version 4.0, June 2017), Chapter R.7b, *Daphnia magna* reproduction test (test method EU C.20. / OECD TG 211) is the preferred test to cover the standard information requirement of Annex IX, Section 9.1.5.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Daphnia magna reproduction test (test method: EU C.20./OECD TG 211).

In your comments on the draft decision, you acknowledged your agreement to perform the requested study.

Note for your consideration:

Once results of the test on long-term toxicity to invertebrates are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation. Due to the poor solubility of the substance in water and its adsorptive properties, you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

7. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.) needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for a toxicity study of Santicizer 141 to early life stages of Rainbow Trout (*Salmo gairdneri*) based on the proposed new standard practice for conducting toxicity tests with the early life stages of fishes Draft No. 3 published by ASTM (1980). However, this study does not provide the information required

by Annex IX, Section 9.1.6.1 / 9.1.6.2 / 9.1.6.3., because it is not considered as reliable, as explained below.

In your chemical safety report, you provided the following statement: "*For fish, a 71-day early life stage test was conducted with rainbow trout. A flow-through test design was employed that exposed a range of concentrations (0 to 0.60 mg/L nominal) to eggs and fry over the course of the test. Endpoints were based on measured concentrations was found to be 21.1 ug/l and the LOEC 71d- LOEC based on reduced survival and abnormal behaviour is 50.8 ug/l. The test concentrations ranged from 21.2 to 245 ug/l, which nearly all exceed the water solubility value of 50.6 ug/L. For this reason the Klimish score assigned is 4. The study may be considered generally supportive of the conclusion that 2EHDPP is not toxic to aquatic organisms in short or long term tests at or below the water solubility.*"

ECHA notes that reduced survival rates were observed at 50.8 µg/L (mean measured concentration). At this concentration, exposure to the substance also induced a reduction in the length and mean weight of surviving animals (the statistical significance of this result was not reported). In addition, ECHA notes that you did not provide any evidence to support that the water solubility of the substance is significantly reduced at 12 °C. Effects were observed at 50.8 µg/L, a concentration equivalent to the water solubility of the substance at 23.5 °C. however, considering that the reduced temperature of the test (12 °C) might have impacted the water solubility of the substance, ECHA agrees that, based on the information provided, the study is inadequate for the purpose of classification and labelling and/or risk assessment as the long-term NOEC on fish cannot be reliably determined.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently, there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 4.0, June 2017) fish early-life stage (FELS) toxicity test (test method OECD TG 210), fish short-term toxicity test on embryo and sac-fry stages (test method EU C.15. / OECD TG 212) and fish juvenile growth test (test method EU C.14. / OECD TG 215) are the preferred tests to cover the standard information requirement of Annex IX, Section 9.1.6.

However, the FELS toxicity test according to OECD TG 210 is more sensitive than the fish, short-term toxicity test on embryo and sac-fry stages (test method EU C.15 / OECD TG 212), or the fish, juvenile growth test (test method EU C.14. / OECD TG 215), as it covers several life stages of the fish from the newly fertilized egg, through hatch to early stages of growth (see ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2018), *Chapter R7b, Figure R.7.8-4).*

Moreover, the FELS toxicity test is preferable for examining the potential toxic effects of substances which are expected to cause effects over a longer exposure period, or which require a longer exposure period of time to reach steady state (ECHA *Guidance Chapter R7b,* version 4.0, June 2017). This is the case for poorly water soluble with high adsorption potential, such as the registered substance.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).

In your comments on the draft decision, you agreed to perform the requested study.

Note for your consideration:

Once results of the test on long-term toxicity to fish are available, you shall revise the chemical safety assessment as necessary according to Annex I of the REACH Regulation. ECHA notes that there are no reliable data to support the fact that fish may be less sensitive than invertebrates. Therefore the Integrated testing strategy (ITS) outlined in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b (Section R.7.8.5 including Figure R.7.8-4), is not applicable in this case and the long-term studies on both invertebrates and fish are requested to be conducted.

Due to the poor solubility of the substance in water and its adsorptive properties, you should consult OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, ENV/JM/MONO (2000)6 and ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, June 2017), Chapter R7b, Table R.7.8-3 summarising aquatic toxicity testing of difficult substances for choosing the design of the requested ecotoxicity test(s) and for calculation and expression of the result of the test(s).

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 11 August 2017.

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.

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

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

ECHA received proposal(s) for amendment and did not modify the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

In addition, you provided comments on the draft decision. These comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-64 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

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Appendix 3: Further information, observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

2. 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 your Member State.

3. 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.