ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 24 April 2019

Addressee: [redacted]

Decision number: CCH-D-2114460639-38-01/F
Substance name: Reaction mass of 2-ethylpropane-1,3-diol and 5-ethyl-1,3-dioxane-5-methanol and propylidynetrimethanol
EC number: 904-153-2
CAS number: NS
Registration number: [redacted]
Submission number: [redacted]
Submission date: 11/09/2013
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. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408) in rats with the registered substance;**

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 with the registered substance;**

3. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rat or rabbit), oral route 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 are required to submit the requested information in an updated registration dossier by **3 May 2021** except for the information requested under point 1. for a Sub-chronic toxicity study (90-day) which shall be submitted in an updated registration dossier by **4 May 2020.** For each deadline, you shall also update the chemical safety report, where relevant. The deadlines have 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.

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.

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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, **Wim De Coen**, Head of Unit, Hazard Assessment NC2

[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

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 IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

0. Grouping of substances and read-across approach

You have sought to adapt information requirements by applying a read-across approach in accordance with Annex XI, Section 1.5, for the endpoints:

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)
2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species.

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[2]. This hypothesis explains why the differences in the 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

[2] 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.

may form the basis of the read-across hypothesis[3]- (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 for the registered substance Reaction mass of 2-ethylpropane-1,3-diol and 5-ethyl-1,3-dioxane-5-methanol and propylidynetrimethanol, (EC number: 904-153-2) using data of structurally similar substances TMP (propylidynetrimethanol), DMP (2-ethylpropane-1,3-diol) and CTF (5-ethyl-1,3-dioxane-5-methanol) (EC Numbers not indicated) hereafter the 'source substances', which are the constituents of the registered/target substance.

i. Description of the grouping and read-across approach proposed by you

You consider to achieve compliance with the REACH information requirements for the registered substance Reaction mass of 2-ethylpropane-1,3-diol and 5-ethyl-1,3-dioxane-5-methanol and propylidynetrimethanol (Polyol TD, a reaction mass), EC number: 904-153-2 using data of structurally similar substances TMP (propylidynetrimethanol; typical concentration in the target substance [redacted]), DMP (2-ethylpropane-1,3-diol; typical concentration in the target substance [redacted]) and CTF (5-ethyl-1,3-dioxane-5-methanol; typical concentration in the target substance [redacted]) (EC Numbers not indicated) hereafter the 'source substances'.

You have provided a read-across documentation as a separate attachment in your dossier.

You use the following arguments to support the prediction of properties of the registered substance from data for source substances within the group:

"*It is proposed to address the toxicity of the multi-constituent substance according to the REACH data requirements largely through the provision of data for the individual constituents. Testing in higher tier toxicological studies (90-day repeated dose oral toxicity study, pre-natal developmental toxicity study) is therefore proposed with TMP and CTF. Read-across is proposed from studies with TMP to DMP to address the toxicity of this constituent. This read-across approach is justified on the basis of the similar chemical structure, physicochemical properties and toxicological properties of DMP and TMP.*"
However, ECHA notes that these testing proposals referred to above are not available in the current dossier.

Furthermore you have claimed in your read-across justification document (December 2012) that "*The two substances DMP and TMP are considered to be comparable in terms of chemical structure and physicochemical properties. TMP is shown to be of generally low toxicity in studies of acute and repeated dose toxicity; toxicological data are more limited for DMP but the available data similar indicate low toxicological activity. The toxicokinetics*

[3] 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).

of the two substances are predicted to be comparable, with extensive and rapid absorption, rapid metabolism and urinary excretion."

As an integral part of this prediction, you propose that the source and registered substances have similar properties for the above-mentioned information requirements. ECHA considers that this information is your read-across hypothesis.

ii. ECHA analysis of the grouping and read-across approach in light of the requirements of Annex XI, 1.5.

With regard to the proposed predictions ECHA has the following observations:

a) Explanation on why and how the structural similarities allow predictions

In order to meet the provisions in Annex XI, Section 1.5. to predict human health effects from data for a reference substance within the group by interpolation to other substances in the group, ECHA considers that structural similarity alone is not sufficient. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. In particular, the structural similarities must be linked to a scientific explanation of how and why a prediction is possible.

ECHA notes the following observations:

1. The registered substance, the target substance, is Reaction mass of 2-ethylpropane-1,3-diol and 5-ethyl-1,3-dioxane-5-methanol and propylidynetrimethanol (**Polyol TD**) and it consists of three components
   - **DMP** (2-ethylpropane-1,3-diol; typical composition [redacted])
   - **CTF** (5-ethyl-1,3-dioxane-5-methanol; typical composition [redacted])
   - **TMP** (propylidynetrimethanol; typical composition [redacted])

2. All human health data, subject to read-across adaptation, has been obtained from studies with TMP. TMP is chemically and structurally different from the target substance, e.g. because the target has a constituent with a dioxane group in it (CTF).
3. DMP and TMP are structurally simple short-chain aliphatic alcohols containing short side chains and multiple hydroxy- groups. However, TMP contains an additional hydroxymethyl sidechain, which is not present in DMP.

[redacted]Chemical structures of the components do not support proposed read across. 1,3-dioxane group in CTF and 2-methoxymethoxy group in the impurity 2 [redacted] and methoxy-group on impurity 3 ca. [redacted] metabolism and toxic properties can be expected to differ from the hydroxylated components like TMP. Impurities 2 and 3 are present in ca. [redacted] in the composition. In addition there are unknown impurities ca. [redacted]

ECHA concludes that you have not addressed the obvious structural differences between the source substances and the target substance and did not explain why those differences would not lead to differences in the toxicity profile of target and source substances. The provided explanation is not considered as valid to establish a scientific credible link between the structural similarity and the prediction. In particular, the dioxane group, which is

presents in the target substance, is not present in TMP (propylidynetrimethanol) that has been used in all studies, subject to the read-across adaptation.

c. Support of a similar or regular pattern as a result of structural similarity

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances.* One prerequisite for a prediction based on read-across therefore is that the substances involved are structural similar and are likely to have similar properties. One important aspect in this regard is the analysis of the data matrix to compare the properties of source and target substances and to establish whether indeed they are similar or follow a regular pattern.

ECHA notes the following observations:

1. While you claim that "*DMP and TMP are considered to be comparable in terms of chemical structure",* you have not demonstrated with experimental data that these two substances share similar toxicological properties, since no human health studies subject to the read-across adaptation have been provided for both substances, and no bridging studies have been provided for DMP.

2. For CTF, which is structurally different from the two other constituents, no human health study on the relevant standard information requirements, except for genotoxicity, has been provided in the dossier of the target substance.

3. Earlier you have submitted testing proposals on sub-chronic and pre-natal developmental toxicity for CTF (one of the constituents), but these testing proposals are not available in the dossier of the target substance. Therefore, similar toxicological properties of CTF, and of the target substance, cannot be demonstrated, based on the available information.

4. All human health studies referred to in the read-across adaptation, except genotoxicity, has been obtained from studies with TMP. Two other constituents DMP and CTF have not been tested. Neither has the target substance been tested, which is constituted of these three compounds. Because the target substances contains two other substances in addition to TMP, ECHA therefore notes that you have not demonstrated that toxicological properties of the source substance TMP and the target substance are similar.

5. Furthermore, you claim that "*The existing dataset shows that TMP is of low toxicity following single and repeated administration and is of low irritancy potential*. " However, the results of the sub-chronic and sub-acute toxicity studies do not support this claim, because effects on hematology and signs of hepatotoxicity and renal toxicity were observed in these studies.

ECHA furthermore notes that you have not provided a data matrix, which would support a similar or regular pattern of toxicity as a result of structural similarity. Therefore it cannot be verified that the proposed analogue substances can be used to predict properties of the registered substance.

d. Toxicokinetics

One important aspect in establishing that substances have similar effects or follow a regular pattern is the comparison of absorption, distribution, metabolism and elimination of source and target substances. This allows assessing the qualitative and quantitative internal systemic exposure of the test organism when exposed to source and target.

ECHA notes the following observations:

a. Concerning the toxicokinetics you have stated that "*No experimental toxicokinetic data are available for these substances; however a theoretical assessment of the likely toxicokinetic properties of the substances can be made.*"

b. Instead, you have provided assessments and prediction, which are partly based on the physico-chemical properties of the subtances, on absorption and metabolism of the three constituents of the registered substance. ECHA considers that these predictions are poorly documented. For example training set and the domain of these modelling tools and the exact identity of the metabolites have not been reported in the registration dossier.

c. Furthermore, on metabolism you point out that "*Metabolism of TMP and DMP is predicted (OECD QSAR Toolbox) via sequential oxidation of an alcohol group; by hydroxylation of the terminal carbon of the ethyl group to form a substance with four alcohol groups and subsequent oxidation; or via hydroxylation of the non-terminal carbon of the ethyl group.*" However, ECHA notes that the metabolites of the third constituent CTF have not been identified.

ECHA concludes that you did not adequately address important aspects such as the toxicokinetics of the parent substance and their metabolic fate / (bio)transformation and the resulting possible difference in the metabolite profile. In the absence of such information there is not an adequate basis for predicting the properties of the registered substance from the data obtained with the source substance.

iv. Conclusion on the read-across approach

The adaptation of the standard information requirements

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)
2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

The technical dossier is based on the proposed read-across approach examined above. ECHA does not consider the read-across justification to be a reliable basis to predict the properties of the registered substance for the reasons set out above. Thus, the adaptation does not comply with the general rules of adaptation as set out in Annex XI, 1.5. Therefore, ECHA rejects all adaptations in the technical dossier that are based on Annex XI, 1.5.

In your comments to the draft decision, you have provided data on the composition of the registered substance as well as on the three main constituents of it. Furthermore, you

provided data matrices that cover physico-chemical, ecotoxicological and toxicological properties of these four substances. ECHAs notes that a constituent-based or "many-to one" read-across requires that all the main constituents are covered for the studies that are required for the target substance of the read-across. However, in this case for one constituent (DMP) and for the registered substance, both the 90 day study and the developmental toxicity study have not been provided. Furthermore, ECHA notes that there is neither a 28 day nor a screenings study reported for this constituent (DMP). In conclusion, the read-across documentation remains incomplete, because the toxicity of the main constituent of the target substance is unknown. Therefore, your read-across approach does not allow prediction of the respective toxic properties of the target 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 and it is necessary to perform testing on the registered substance.

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

A "sub-chronic toxicity study (90 day)" is a standard information requirement as laid down in Annex IX, Section 8.6.2. 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.

You have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing the following study records
1. An old 90-day oral study "similar to" OECD 408, (1969) with read-across substance trimethylpropane (TMP); in rats, via feed, rel 2, no GLP. The doses were 0.03, 0.1, 0.3 and 1.0%.
2. In addition a screening study OECD 422, (1994) with read-across substance trimethylpropane; in rats, gavage, rel 1, GLP yes. The doses were 12.5, 50, 200, 800 mg/kg
3. Also an old 28-day oral study "similar to" OECD 407, (1969) with read-across substance trimethylpropane; in rats, via feed, rel 2, no GLP. The doses were 0.3, 1.0, 2.0 and 4.0%

However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

Concerning the last two studies, ECHA also has the following comments:

Concerning the "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test", test method OECD TG 422, with read-across substance TMP (trimethylpropane), ECHA furthermore notes that, this study does not provide the information required by Annex IX, Section 8.6.2., because the exposure duration is less than 90 days and the number of animals examined per dose group for histopathology and clinical chemistry is significantly lower than in the 90 day sub-chronic toxicity study (OECD TG 408).

Concerning the "repeated dose 28-day oral toxicity study", test method was "similar to" OECD 407, with read-across substance *trimethylpropane*; ECHA notes that this study does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days and the number of animals per dose group is significantly lower than in the 90 day sub-chronic toxicity study (OECD TG 408) . Therefore, the sensitivity of a 28-day study is much lower than that of a 90-day study.

You also refer to an adaptation making reference to the testing proposal made for oral 90-day study with an analogue substance Cyclic Trimethylolpropane Formal (CTF, 5-ethyl-1,3-dioxane-5-methanol). These testing proposals are not present in the dossier of the registered substances. Thus, such testing proposals cannot contribute to meeting this information requirement.

In your comments to the draft decision, you indicate "*After reviewed the reasons of above testing requests, we have gathered relevant information to justify that the data gaps of above endpoints can be fulfilled by the data from the 3 constituents presented in the registered substance. Please find the detail justification information in the attached document*".

In addition, in your comments to the draft decision, you indicate "*Given the availability of reliable animal studies on two of the constituents/source substances, and the submitted testing proposals in the third constituent/source substance dossier, in our opinion, its not scientifically justified to undertake additional toxicity studies on the registered multi-constituent substance again. To avoid unnecessary use of animals in testing, we kindly ask ECHA to withdraw the 3 testing requests for the registered substance*".

ECHA has addressed your revised read-across justification information in Section 0 of this decision above. Moreover, ECHA notes for this endpoint, your read-across justification is still rejected by ECHA as outlined in Section 0 of this decision.

It is your responsibility to adapt the standard information and thus avoid the proposed testing to provide the required information. For any such adaptation to comply with the respective information requirement, it needs to be scientifically justified, referring and conforming to the appropriate rules in the respective annex, and adequate and reliable documentation must be provided in the registration dossier.

ECHA notes that as you currently hold a registration for the tonnage band of above 1000 tpa, you are responsible to comply with the standard information requirements of Annex X, which includes this endpoint request.

Therefore, this adaptations 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.
ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 5.0, December 2016) 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. Uses with industrial spray application are reported in the chemical safety report. However, the reported concentrations are low. Hence, the test shall be performed by the oral route using the test method OECD TG 408.

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

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: Repeated dose 90-day oral toxicity study (test method: OECD TG 408) in rats.

Notes for your consideration

The Extended one-generation reproductive toxicity study (EOGRTS) according to Annex X, Section 8.7.3. is not part of this decision because the results of the Sub-chronic toxicity study (90-day) are considered crucial to inform on the study design of the EOGRTS. Therefore, the results of the Sub-chronic toxicity study (90-day) should be used, among other relevant information, to decide on the study design of the EOGRTS.

ECHA may therefore launch a separate compliance check at a later stage addressing the EOGRTS information requirement.

Alternatively, you may also consider submitting a testing proposal for an Extended one-generation reproductive toxicity study together with the results of the requested Sub-chronic toxicity study (90-day). The testing proposal should include a justification for its study design 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

A "pre-natal developmental toxicity study" (test method OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. 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.

You have not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex IX, Section 8.7.2.
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 "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422) using the analogue substance TMP (propylidynetrimethanol). However, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement is rejected.

Furthermore, this provided study does not provide the information required by Annex IX, Section 8.7.2. because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations. Therefore, your adaptation of the information requirement is rejected.

ECHA has addressed your comments to the draft decision in Section 0 and Section 1 of this decision above.

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 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 assumption ECHA considers testing should be performed with rats or rabbits as a first 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.

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).

The technical dossier does not contain information on a pre-natal developmental toxicity study with the registered substance.

As explained above under "Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species", the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Additionally, you have not provided information on pre-natal developmental toxicity in a second species. Consequently there is an information gap and it is necessary to provide information for this endpoint.

After a proposal for amendment (PfA), to introduce a request for a pre-natal developmental toxicity study in a second species, submitted by one of the Member State Competent Authorities (MSCAs), you argued that this PfA was out of scope of this decision. However, PfAs are foreseen by the legal text, and introduce the request into the scope of this decision. You also argue that the pre-natal developmental toxicity study shall initially be done in one species, so that the decision to conduct the second species shall take into account the results of the first species study, and any applicable column 2 adaptations. ECHA considers that the deadline gives sufficient time to perform the two pre-natal developmental toxicity studies sequentially, and hence take into account the results of the first-species study, as indicated hereunder under the notes for your condsideration. In addition, as explained above, at Annex X, a pre-natal developmental toxicity study in a second species is a standard information requirement.

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 rabbits or rats as a second species, depending on the species tested in the first pre-natal developmental toxicity study.

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.

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 or rat) by the oral route.

Notes for your consideration

You are reminded that before performing a pre-natal developmental toxicity study in a second species you must consider the specific adaptation possibilities of Annex X, Section 8.7., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species with other available information enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

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 08 May 2018.

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

The draft decision was sent to the registrant on 18 June 2018.

The registrant provided comments on the draft decision.

ECHA did not amend the draft decision based on the comments received.

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

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments.

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.

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-63 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

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 carrying out the tests required by the present decision, it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new tests must be suitable to assess these.

   Furthermore, 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.