EUROPEAN CHEMICALS AGENCY

Helsinki, 21 March 2017

Addressee: [redacted]

Decision number: CCH-D-2114355673-44-01/F
Substance name: N,N,N',N',N'',N''-HEXAMETHYL-1,3,5-TRIAZINE-1,3,5(2H,4H,6H)-TRIPROPANAMINE
EC number: 240-004-1
CAS number: 15875-13-5
Registration number: [redacted]
Submission number: [redacted]
Submission date: 07.01.2016
Registered tonnage band: 100-1000T

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 (Annex VI, Section 2.3.) of the registered substance;**
   - **Percentage of (significant) main impurities**

2. ***In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1; test method: Bacterial reverse mutation test, EU B.13/14. / OECD TG 471) with the registered substance;**

3. **Robust study summary for *In Vitro* Mammalian Cell Micronucleus Test (Annex VIII, Section 8.4.2. in conjunction with Annex I, Section 1.1.4.);**

4. **Robust study summary for *In Vitro* Mammalian Cell Gene Mutation Test (Annex VIII, Section 8.4.3. in conjunction with Annex I, Section 1.1.4.);**

5. **Robust study summaries for Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (Annex VIII, Section 8.7.1. in conjunction with Annex I, Section 1.1.4.);**

6. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats with the registered substance; and**

7. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first 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 of the REACH Regulation. In order 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 an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **28 March 2019**. You shall also 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. 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, shall 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 Ofelia Bercaru, Head of Unit, Evaluation E3

[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. Percentage of (significant) main impurities (Annex VI, Section 2.3.3.)

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

Annex VI, section 2.3. of the REACH Regulation requires that each registration dossier contain 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: 1.3, February 2014) – referred to as "the Guidance" thereinafter, the Registrant shall note that, for well-defined substances, the following applies:

- Each main constituent (i.e. the constituent present at ≥80% for mono-constituent substance or each constituent present at ≥10% and 80% for multi-constituent substance) shall be identified and reported individually; and

- Each impurity present at ≥1% or relevant for the classification and/or PBT assessment of the registered substance shall be identified and reported individually.

- For each constituent, the typical, minimum and maximum concentration levels shall be specified regardless of the substance type.

In the present dossier, you identified the registered substance as the well-defined mono-constituent substance N,N,N',N',N'',N''-hexamethyl-1,3,5-triazine-1,3,5(2H,4H,6H)-tripropanamine and specified the typical, minimum and maximum concentration levels.

However, for the three reported impurities you reported only their typical concentrations. The minimum and maximum concentration values for the three impurities are missing from your dossier.

ECHA therefore concludes that the compositional information has not been provided to the required level of detail for establishing the composition of the registered substance and therefore its identity.

You are accordingly requested to correct the information provided on the composition of the registered substance. More specifically, you are requested to provide concentration ranges (minimum and maximum values) for each reported impurity.

Regarding how to report the composition of the registered substance in IUCLID, the following applies: you shall report individually any impurity required to be identified and specify at least one of the following identifiers: chemical name, CAS number, EC number and/or molecular formula, as well as the minimum, maximum and typical concentration, in the appropriate fields in Section 1.2 of the IUCLID dossier.

Further technical details on how to report the composition of well-defined substances in IUCLID are available in the Manual "How to prepare registration and PPORD dossiers" on the ECHA website.

You shall ensure that the composition is verifiable and therefore supported by a description of the analytical methods for the identification and quantification of the constituents required to be reported, as required under Annex VI, 2.3.7. of the REACH Regulation.

2. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

An "*In vitro* gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. 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.

According to Article 13(3) of the REACH Regulation, tests required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA.

Other tests may be used if the conditions of Annex XI are met. More specifically, Section 1.1.2 of Annex XI provides that existing data on human health properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3) may be used if the following conditions are met:

(1) Adequacy for the purpose of classification and labelling and/or risk assessment;
(2) Adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3);
(3) Exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3) if exposure duration is a relevant parameter; and
(4) Adequate and reliable documentation of the study is provided.

You have provided the following information:

(i) Experimental results on the registered substance; Reliability 2 (reliable with restrictions); 1981; non-GLP; non-Guideline (Principle of the test: "*Agar overlay plate method; nonactivated and Aroclor 1254 induced rat liver microsome S-9 activated tests*"); Strains: S. *typhimurium* TA 1535, TA 1537, TA 98 and TA 100;

(ii) Experimental results on the registered substance; Reliability 2 (reliable with restrictions); 1999; non-GLP; non-Guideline (Principle of the test: "*Ames II Assay (Liquid fluctuation test - microtiter version) according to Gee.P et al.: Mut. Res. 412, 115-130, 1998*"); Strains: *S. typhimurium* 98 and TA Mix (mixed strains TA 7001 - TA 7006).

ECHA notes that none of the studies provided were conducted according to the current OECD TG 471(adopted 1997); and none of the studies were conducted according to GLP.

With regard to the study (i) above ECHA notes the following reporting deficiencies/deviations from the current OECD TG 471:

a. According to paragraph 13 of the current OECD TG 471 test guideline (updated 1997) at least five strains of bacteria should be used: *S. typhimurium* TA1535; TA1537 or TA97a or TA97; TA98; TA100; *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101). This includes four strains of *S. typhimurium* (TA1535; TA1537 or TA97a or TA97; TA98; and TA100) that have been shown to be reliable and reproducibly responsive between laboratories. These four *S. typhimurium* strains have GC base pairs at the primary reversion site and it is known that they may not detect certain oxidising mutagens, cross-linking agents and hydrazines. Such substances may be detected by *E.coli* WP2 strains or *S. typhimurium* TA102 which have an AT base pair at the primary reversion site.

   ECHA notes that you have provided a test that used four different strains of *S. typhimurium* TA 1535, TA 1537, TA 98 and TA 100 and it did not include tests with strains *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101). ECHA concludes that a test using *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 has not been submitted and that the test using one of these is required to conclude on *in vitro* gene mutation in bacteria.

b. According to paragraph 20 of the current OECD TG 471 *"At least five different analysable concentrations of the test substance should be used with approximately half log (i.e. √10) intervals between test points for an initial experiment."* ECHA notes that your experiment achieved too few analysable concentrations as only three doses could be analysed for mutagenicity due to excess toxicity. Furthermore, ECHA notes that the interval between the test concentrations is different form that normally used in an OECD TG 471 test. No justification for this deviation has been provided. In addition, there is no information about the purity of the tested substance.

c. According to paragraph 29 of the current OECD TG 471 *"For an adequate estimate of variation, triplicate plating should be used at each dose level."* ECHA notes that no information has been provided on how many plates were used on each dose level.

With regard to the study (ii) above ECHA notes the following reporting deficiencies/deviations from the current OECD TG 471:

a. This study used a different method for the detection of the mutations than that which is stipulated in OECD 471 TG. ECHA notes that no information is provided with regard to the validation of this method of detection and on how this method compares to the one recommended in the current OECD TG 471, thus ECHA is unable to assess the validity of the information.

b. According to paragraph 13 of the current OECD TG 471 test guideline (updated 1997) at least five strains of bacteria should be used: *S. typhimurium* TA1535; TA1537 or TA97a or TA97; TA98; TA100; *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101). This includes four strains of *S. typhimurium* (TA1535; TA1537 or TA97a or TA97; TA98; and TA100) that have been shown to be reliable and reproducibly responsive between laboratories. These four *S. typhimurium* strains have GC base pairs at the primary reversion site and it is known that they may not detect certain oxidising mutagens, cross-linking agents and hydrazines. Such substances may be detected by *E.coli* WP2 strains or *S. typhimurium* TA102 which have an AT base pair at the primary reversion site.

   ECHA notes that you have provided a test that used *S. typhimurium* 98 and TA Mix (mixed strains TA 7001 - TA 7006). ECHA concludes that this test provided information on one of the required strains as outlined above.

Therefore, the provided studies do not meet the current guidelines, nor can they be considered as providing equivalent data according to the criteria in Annex XI, 1.1.2. of the REACH Regulation. This is because they do not cover the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3); and no adequate and reliable documentation of the studies has been provided.

ECHA concludes that none of the studies provided either by themselves or when combined provide equivalent information to cover that of the current OECD TG 471.

In addition to the deficiencies highlighted above, ECHA notes that there is conflicting results in *S. typhimurium* TA98 with metabolic activation between the two tests: In study (i) the registered substance does not induce gene mutations. In contrast, in study (ii) the registered substance induces gene mutations. ECHA considers that the conflicting results merit further investigations.

Therefore, 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.

ECHA considers that the bacterial reverse mutation test (test method EU B.13/14. / OECD TG 471) is appropriate to address the standard information requirement of Annex VII, Section 8.4.1. of the REACH Regulation.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit following information derived with the registered substance subject to the present decision: Bacterial reverse mutation test (test method: EU B.13/14. / OECD TG 471).

3. Robust study summary for *In Vitro* Mammalian Cell Micronucleus Test (Annex VIII, Section 8.4.2. in conjunction with Annex I, Section 1.1.4.);

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Pursuant to Article 10(a)(vii) of the REACH Regulation, the information set out in Annex VII to XI must be provided in the form of a robust study summary. Article 3(28) defines a robust study summary as a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report. Guidance on the preparation of the robust study summaries is provided in the Practical Guide 3[2]: 'How to report robust study summaries' (version 2.0, February 2012).

An *In Vitro* Mammalian Cell Micronucleus Test (OECD 487) is a standard information requirement as laid down in Annex IX, Section 8.4.2. 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. Furthermore, pursuant to Article 10 (a)(vii) and Annex I, Section 1.1.4. if there are several studies addressing the same effect, then, having taken into account possible variables (e.g. conduct, adequacy, relevance of test species, quality of results, etc.), normally the study or studies giving rise to the highest concern shall be used to establish the DNELs and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment.

You have provided a study record for an *In Vitro* Mammalian Cell Micronucleus Test (2013; OECD TG 487) to meet the standard information requirement of Annex IX, Section 8.4.2.

However, ECHA notes that, contrary to Article 3(28) of the REACH Regulation, the documentation of this study is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment. In particular, the following elements are missing: details on materials and methods; tabulated results; justification should be given for choice of tested dose levels; cytotoxic concentrations with and without metabolic activation; genotoxic effects, and statistical results (for details see the aforementioned Practical Guide 3, section 5.4.1). Therefore, you need to provide a complete robust study summary with the above missing elements for this study.

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.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information: Robust study summary for the *In Vitro* Mammalian Cell Micronucleus Test (2013; OECD TG 487).

2 https://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf/1e8302c3-98b7-4a50-aa22-f6f02ca54352

ECHA
EUROPEAN CHEMICALS AGENCY

4. Robust study summary for *In Vitro* Mammalian Cell Gene Mutation Test (Annex VIII, Section 8.4.3. in conjunction with Annex I, Section 1.1.4.);

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Pursuant to Article 10(a)(vii) of the REACH Regulation, the information set out in Annex VII to XI must be provided in the form of a robust study summary. Article 3(28) defines a robust study summary as a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report. Guidance on the preparation of the robust study summaries is provided in the Practical Guide 3[3]: 'How to report robust study summaries' (version 2.0, February 2012).

A *In Vitro* Mammalian Cell Gene Mutation Test (OECD TG 476) is a standard information requirement as laid down in Annex IX, Section 8.4.3. 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. Furthermore, pursuant to Article 10 (a)(vii) and Annex I, Section 1.1.4. if there are several studies addressing the same effect, then, having taken into account possible variables (e.g. conduct, adequacy, relevance of test species, quality of results, etc.), normally the study or studies giving rise to the highest concern shall be used to establish the DNELs and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment.

You have provided a study record for an *In Vitro* Mammalian Cell Gene Mutation Test (Flügge 2013; OECD TG 476) to meet the standard information requirement of Annex VIII, Section 8.4.3.

However, ECHA notes that, contrary to Article 3(28) of the REACH Regulation, the documentation of this study is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment. In particular, the following elements are missing: details on materials and methods; tabulated results; justification should be given for choice of tested dose levels; cytotoxic concentrations with and without metabolic activation; genotoxic effects, and statistical results (for details see the aforementioned Practical Guide 3, section 5.4.1)Therefore, you need to provide a complete robust study summary with the above missing elements for this study.

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.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information: Robust study summary for the *In Vitro* Mammalian Cell Gene Mutation Test (Flügge 2013; OECD TG 476).

5. Robust study summary for Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (Annex VIII, Section 8.7.1. in conjunction with Annex I, Section 1.1.4.);

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Pursuant to Article 10(a)(vii) of the REACH Regulation, the information set out in Annex VII to XI must be provided in the form of a robust study summary. Article 3(28) defines a robust study summary as a detailed summary of the objectives, methods, results and conclusions of a full study report providing sufficient information to make an independent assessment of the study minimising the need to consult the full study report. Guidance on the preparation of the robust study summaries is provided in the Practical Guide 3[3]: 'How to report robust study summaries' (version 2.0, February 2012).

A Reproduction/Developmental Toxicity Screening Test is a standard information requirement as laid down in Annex IX, Section 8.7.1. 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. Furthermore, pursuant to Article 10 (a)(vii) and Annex I, Section 1.1.4. if there are several studies addressing the same effect, then, having taken into account possible variables (e.g. conduct, adequacy, relevance of test species, quality of results, etc.), normally the study or studies giving rise to the highest concern shall be used to establish the DNELs and a robust study summary shall be prepared for that study or studies and included as part of the technical dossier. Robust summaries will be required of all key data used in the hazard assessment.

You have provided a study record for a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (Rösslerova, Z, 2013) to meet the standard information requirement of Annex VIII, Section 8.7.1.

However, ECHA notes that, contrary to Article 3(28) of the REACH Regulation, the documentation of this study is insufficient and does not allow an independent assessment of the adequacy of this study, its results and its use for hazard assessment. In particular, the following elements are missing: details on materials and methods and tabular summary report of effects on reproduction/development (as specified in Annex 3 of the current OECD TG 422). In addition, study conclusions should be revised to reflect the findings in the summary table. Furthermore, since the study investigates both general toxicity and reproduction/developmental toxicity endpoints, the presentation of the results of the study shall allow for the discrimination between reproduction/developmental effects occurring in the absence of general toxicity and those which are only expressed at levels that are also toxic to parent animals (for details see the aforementioned Practical Guide 3, sections 5.3, 5.5 and 5.6). Therefore, you need to provide a complete robust study summary with the above missing elements for this study.

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.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information: Robust study summary for the Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test ([redacted]., 2013).

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

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.

In the technical dossier you have provided a study record for a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422). However, this study does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days.

For these reasons, 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 4.1, October 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, potential inhalation-specific effects are already addressed by the performance of a qualitative assessment for inhalation, local effects. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

According to the test method EU B.26./OECD TG 408 the 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: EU B.26./OECD TG 408) in rats.

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./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 sought to adapt this information requirement. You provided the following justification for the adaptation "*The substance was investigated in a sub acute toxicity investigation that included a screening phase for reproductive and developmental toxicity. The use of preliminary tests and the proposed move to use combined reproductive/development assays to screen for toxicologically significant effects, in preference to conducting a multi-generation study or even a single generation reproduction/fertility assessment can be justified on scientific grounds and in terms of animal welfare and ethical moves to reduce, refine or replace the use of vertebrates in toxicity tests. The information available from the screening test for developmental effects indicates the absence of systemic effects at dose levels of up to 720 mg/kg/b. w., the highest dose tested. None of the developmental parameters evaluated (number of dead and living pups at first litter check, sex ratio, postnatal loss, viability, and early postnatal pup development (mortality, clinica signs and external macroscopy)) gave any evidence of a treatment- related or dose-related effect. In the absence of any indications of the substance affecting rat development in this study, there is no reason to suggest that any effects on development are likely and use of vertebrate tests to confirm the preliminary screening results is not scientifically justifiable.*"

In the technical dossier you have provided a study record for a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422).

However, ECHA notes that a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (test method: OECD TG 422) 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. In addition, a study conducted according to OECD TG 422 does not have a similar statistical power to that of a study conducted according to OECD TG 414.

For the reasons 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 EU B.31./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 4.1, October 2015) R.7a, chapter 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: EU B.31./OECD TG 414) in a first species (rat or rabbit) by the oral route.

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 10 August 2016.

The decision making follows the procedure of Articles 50 and 51 of the REACH Regulation.

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

ECHA did not receive any comments by the end of the commenting period.

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) 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 request(s) in this decision, or to fulfil otherwise the information requirement(s) 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 test(s) 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 test(s) 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 test(s) must be suitable to assess these grades. Finally, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.