ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 21 March 2018

Addressee: [redacted]

Decision number: CCH-D-2114397993-26-01/F
Substance name: Triclocarban
EC number: 202-924-1
CAS number: 101-20-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 11.03.2016
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. ***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) [using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102] with the registered substance;**

2. **In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method: OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2, test method: OECD TG 487) with the registered substance;**

3. **If the above two tests are negative, then In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490) with the registered substance; the registered substance;**

4. **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 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.

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 30 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also requested another study (extended one-generation reproductive toxicity study, Annex X, Section 8.7.3). As this study is not addressed in the present decision, the decision was therefore modified accordingly. You have 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 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, Evaluation **E2**

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 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.

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.

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.

You have provided a tests and predictions from the years Zeiger (1987), NTP (2012), QSAR Toolbox predictions (2011) according to OECD TG 471 and GLP with an assigned reliability score of 2. The tests 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). Since the test was conducted, significant changes have been made to OECD TG 471 so that additionally testing with *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is now required.

Therefore, the provided study does not meet the current guidelines, nor can it be considered as providing equivalent data according to the criteria in Annex XI, Section 1.1.2. of the REACH Regulation.

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.

In your comments to the draft decision, you commented in general that you do not see the need for fresh studies, but as already recommended in the draft decision you may use applicable adaptation within annex VII and IX and update the dossiers for these endpoints to be able to fulfil ECHA's concerns with the existing and other available data / studies. ECHA will evaluate the information provided at follow-up of the decision. If the information provided is not acceptable, ECHA may issue a communication to the national enforcement authorities, informing them about the non-compliance, or undertake decision-making according to Article 42(1).

In your comment to the draft decision, for this endpoint, you commented with information on an Ames test on triclocarban, on *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA 1537. ECHA considers that you have not provided information that addresses the data gap identified by ECHA's decision, i.e. studies on *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 which are required by the test guideline. Therefore the data gap remains.

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 the 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) using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102.

2. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 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.

An "*In vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study" is a standard information requirement as laid down in Annex VIII, 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.

You have not provided any study record of an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study in the dossier that would meet the information requirement of Annex VIII, Section 8.4.2.

You have sought to adapt this information requirement Annex XI, Section 1.2. You have not provided a justification for the adaptation.

However, ECHA notes that your adaptation does not meet the general rule for adaptation of Annex XI; Section 1.2. because gene mutation results in a bacterial system do not give information on the clastogenic properties of the substance.

Therefore, your adaptation of the information requirement is rejected.

In your comment to the draft decision, you provided information on a chromosome aberration study performed with triclocarban in CHO cells. You have referred to a robust study summary which is present in the dossier ("*OECD / Genetic toxicity in vitro / 101-20-2 - WoE - 3 / 101-20-2-Updated - 10.03.2016*"). In your dossier, you consider this study to be of unassignable reliability (Klimisch score 4) and not performed according to GLP. Additionally, you state that (1) Negative controls, true negative controls and solvent controls are "not specified" (2) for test systems and conditions, evaluation criteria and statistics, there is "no data" (3) you have not provided tabulated data of results on experimental findings.

However, according to Annex XI, Section 1.1.2, you must provide adequate and reliable documentation. ECHA notes that a robust study summary is required under Article 10(a)(vii), and ECHA considers that the information provided in the endpoint study record does not meet the requirements of a robust study summary, as defined in Article 3(28). Specifically, the endpoint study record does not provide information on the negative controls, the test systems and conditions, evaluation criteria and statistics, or tabulated data of results on experimental findings.
ECHA has provided a practical guide for "How to report robust study summaries", available at:
http://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf.

ECHA considers there is not sufficient information to make an independent assessment of the study minimising the need to consult the full study report, and accordingly considers that for this study, you have failed to meet the requirement of Annex XI, Section 1.1.2. This information is not provided in your comment, and so ECHA maintains that there is a data gap for this endpoint.

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.

In conclusion, ECHA considers that the *in vitro* mammalian chromosome aberration test (test method OECD TG 473) and the *in vitro* mammalian cell micronucleus test (OECD TG 487) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.2. of the REACH Regulation.

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: *In vitro* mammalian chromosome aberration test (test method: OECD TG 473) or *in vitro* mammalian cell micronucleus study (test method: OECD TG 487).

3. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 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.

An "*In vitro* gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained.

ECHA notes that the registration dossier does not contain study records for the information requirement of "*In vitro* gene mutation study in mammalian cells" that would meet the information requirement of Annex VIII, Section 8.4.3. Therefore, adequate information *on in vitro* gene mutation in mammalian cells needs to be present in the technical dossier for the registered substance to meet this information requirement provided that both studies requested under 2 and 3 have negative results.

You have flagged your endpoint study summaries as "WoE", that is, you have sought to adapt this information requirement Annex XI, Section 1.2. You have not provided a justification for the adaptation. You have provided five endpoints study records concerning *in vitro* gene muation in bacteria, and one endpoint study record concerning *in vitro* cytogenicity / chromosome aberration study in mammalian cells (of Klimisch reliability 4). In the dossier section 7.6 summary you state: "*In the AMES test conducted with Triclocarban did not exhibit genotoxicity in S. typhimurium TA 1535, TA 1537, TA 98 and TA 100.with and without S9 metabolic activation. Hence it was estimated that Triclocarban does not exhibit positive gene mutation effect.*"

However, ECHA notes that your adaptation does not meet the general rule for adaptation of Annex XI; Section 1.2. Firstly because you have not provided a justification for the adaptation, i.e. why all the individual studies add together to provide sufficient weight of evidence. Secondly, all the individual gene mutation studies in a bacterial system do not give information on the mutagenic properties of the substance in mammalian cells, and for this reason they fail to cover key parameters of the endpoint of Annex VIII, 8.4.3. The *in vitro* cytogenicity study is of Klimisch reliability score 4, and there is insufficient information for ECHA to consider that it is reliable information. Moreover, an *in vitro* mammalian chromosome aberration test is not an appropriate assay to cover for the information requirement of an *in vitro* gene mutation study in mammalian cells. In view of the defects of the individual studies for this endpoint, ECHA considers that there is no reliable basis under Weight of Evidence to consider that all the studies together provide a sufficient Weight of Evidence to meet the information requirement of Annex VIII, 8.4.3.

Therefore, your adaptation of the information requirement is rejected.

In your comment to the draft decision, you have provided information about a two-year study in rats. However, this study does not provide information about mutagenicity, and so does not satisfy the information requirement.

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 *in vitro* mammalian cell gene mutation tests using the *Hprt* and *xprt* genes (OECD TG 476) and the *in vitro* mammalian cell gene mutation tests using the thymidine kinase gene (OECD TG 490) are appropriate tests to address the standard information requirement of Annex VIII, Section 8.4.3.

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: *In vitro* mammalian cell gene mutation test (test method: OECD TG 476 *or* OECD TG 490) provided that both studies requested under 2 and 3 have negative results.

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

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 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.

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.

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests. Such other means include the use of information from structurally related substances (grouping of substances and read-across), "provided that the conditions set out in Annex XI are met".

You have provided the following studies:
1. Three-generation reproductive and teratogenicity study in rats (Nolen and Dierkman, 1979),
2. Two-generation reproductive and teratogenicity study in rabbits (Nolen and Dierkman, 1979),
3. One-generation reproductive and teratogenicity study in rats (Nolen and Dierkman, 1979).

These three studies ("Reproduction and Teratogenic Studies of a 2:1 Mixture of 3,4,4'-Trichlorocarbanilide and 3-Trifluoromethyl-4,4'-dichlorocarbanilide in Rats and Rabbits" from Nolen and Dierkman, 1979) were conducted with the analogue substance, 2:1 Mixture of 3,4,4'-Trichlorocarbanilide and 3-Trifluoromethyl-4,4'-dichlorocarbanilide. For these studies you have assigned a reliability score of 2, and indicated no guideline.

4. QSAR Toolbox prediction based on read-across Prediction of LOEL for [redacted],
5. A one-generation study in mice on isopropyl (3-chlorophenyl)carbamate / 101-21-3 / 202-925-7 (chlorpropham).

All of these studies are marked as a Weight of Evidence.

(i) Read-across adaptation

Studies 1-3

In the registration, you have adapted the standard information requirements for Annex IX, section 8.7.2., Prenatal developmental toxicity study, by applying a read-across adaptation following REACH Annex XI, Section 1.5 from data on an analogue substance, 2:1 Mixture of 3,4,4'-Trichlorocarbanilide and 3-Trifluoromethyl-4,4'-dichlorocarbanilide.

You have sought to adapt the information requirements for a prenatal developmental toxicity study (Annex IX, Section 8.7.2.) by applying a read-across approach in accordance with Annex XI, Section 1.5. According to Annex XI, Section 1.5. there needs to be structural

similarity among the substances within a group or category and furthermore, 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). Furthermore, Annex XI, Section 1.5. lists several additional requirements, including that adequate and reliable documentation of the applied method have to be provided. You consider to achieve compliance with the REACH information requirements for the registered substance triclocarban (3,4,4'-Trichlorocarbanilide) using data of structurally similar substances 2:l Mixture of 3,4,4'-Trichlorocarbanilide and 3-Trifluoromethyl-4,4'-dichlorocarbanilide (hereafter the 'source substance').

However, apart from the studies submitted on the anlogue substance, you did not provide and no documentation for the read-across. Therefore, your dossier is lacking a basis for predicting relevant human health properties of the registered substance from data for the source substances.

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.

Additionally, according to the study protocol in rat (Nolen and Dierkman, 1979), *"A third breeding of the original (F0) stock provided material for teratogenic studies. When the dams became pregnant for the third time half of them were sacrificed by ether inhalation on Day 13, and the remainder on Day 21. The numbers of corpora lutea of pregnancy, implantations, and resorptions were recorded for all the dams. For those sacrificed at Day 21, the numbers of live and dead fetuses and their positions in the uterine horns were recorded."*

From this it is not clear that skeletal or soft tissue alterations examinations were performed to the offspring (as required in TG OECD 414 paragraphs 28 – 31), and so ECHA considers that key parameters of the Test Guideline have not been fulfilled.

ECHA notes that even less details were given for the two rabbit studies (Nolen and Dierkman, 1979) design or results, and observes that at least the following parameters were not reported or results were not given in sufficient detail: For example the study summary reports: *"One-third of the fetuses were cleared and stained with alizarin red stain and examined for skeletal defects and variations."* Also, offspring viability indices were not reported. ECHA notes that a robust study summary is required under Article 10(a)(vii), and ECHA considers that the information provided in the endpoint study record does not meet the requirements of a robust study summary, as defined in Article 3(28). Specifically, the endpoint study record does not provide information on embryotoxic or teratogenic effects, such as, external, soft tissue, and skeletal malformations or other relevant alterations. ECHA has provided a practical guide for "How to report robust study summaries", available at:
http://echa.europa.eu/documents/10162/13643/pg_report_robust_study_summaries_en.pdf.

ECHA considers there is not sufficient information to make an independent assessment of the study minimising the need to consult the full study report, and accordingly considers that for this study, you have failed to meet the requirement of Annex XI, Section 1.5 that adequate and reliable documentation of the applied method shall be provided.

Study 4

You have attached a QSAR Toolbox prediction report to the endpoint study record. This report provides information on the method used for identifying the analogue substances used for the prediction and reports a dose descriptor of 101 mg/ kg/ day for the registered substance (LOEL).

The report claims to provide information about the target substance, chemical characteristics used for the grouping, the resulting boundaries of the group of chemicals (applicability domain), the type of data gap filling approach that was applied (read-across, trend analysis or QSAR models), the predicted result(s) and in the Annex information about the category members or training set and test set chemicals.

However, ECHA observes that you did not clearly establish, as part of an endpoint-specific read-across hypothesis, how the presence of different structural elements among the category members can be linked with the possibility for predicting the properties of the registered substance from data on the category members. According to information provided in the appendix 1 of the report, significant structural and mechanistic differences exist among the analogue substances. The impact of these considerable differences in the chemical structures of the category members on the possibility to predict properties of the registered substance has not been accounted for in the read-across hypothesis.

You have provided information on category members obtained from the OECD QSAR Toolbox. ECHA considers that you have not established how data generated with category members can be used to predict the properties of the registered substance. The endpoint is called "Developmental toxicity/teratogenicity". From the information provided, it is not clear what duration and route of exposure are involved. Documentation on the experimental values for the source substances is not provided. You have provided a prediction from category members, which is taking an average from the nearest 2 members as stated, although it remains unclear which data points are used for calculation. We note the structural differences between the target ad the "source" substances.
This cannot be considered a valid approach for deriving a prediction when the observed toxicity varies in a wide range of values.

In the light of these deficiencies, ECHA considers that the information is not sufficient to conclude that the registered substance has or has not a particular dangerous property in relation to the endpoint under consideration. Therefore, the general rule for adaptation of Annex XI, Section 1.5 are not met and the adaptation of the information requirement cannot be accepted.

Study 5

You have provided a toxicity study in which "Maternal and developmental effect of chlorpropham in CD-1 mice were assessed in a one-generation study (Toyohito *et al.*, 2007). No standard guideline or adherence to GLP was indicated. The test substance administered 15 females at 3000 mg/kg body weight/day by gavage on Days 8, 9, 10, 11, 8.3 and 9.3 of gestation or to 20 females at 0, 750, 1500 or 3000 mg/kg on GD 8.3.

Also in this case, ECHA considers that the registered substance and analogue substance display significant structural differences: the registered substance is a trichlorinated carbanilide with two mono or dichlorinated aromatic rings whereas chloropropham used as the source substance is a monochlorinated carbanilide with an isopropyl group instead of the aromatic ring. You have not provided any information on how these structural differences may impact the toxicity of the substances and thus affect the possibility to predict the properties of the registered substance from the data of the analogue substance.

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 in order to establish a scientific credible link between the structural similarity and the prediction. ECHA considers that there is not a reliable basis for predicting the properties of the registered substance.

In addition, ECHA observes the following aspects of the study design by Toyohito *et al.* (2007):

- the test 1 used several gestation days of exposure but only one dose group (3000 mg/kg) whereas the OECD TG 414 requires three dose groups. Test 2 used several dose groups.
- Both tests had only 12-15 pregnant females when no less than 16 is recommended in the OECD TG 414.
- Also, the animals were exposed only on GD 8, 9, 10, 11, 8.3 and 9.3 (test 1) or GD 8.3 (test 2), whereas the OECD TG 414requires exposure of the animal from gestation day 6 through to the day before birth. Thus both studies fail to address key parameters of the corresponding Guideline.

Conclusion

As explained above, ECHA considers that your adaptation does not meet the general rules for adaptation of Annex XI, Section 1.5. Therefore, your adaptation on the basis of read-across is rejected.

(ii) Weight of Evidence

You have indicated that all five studies assessed above should also be considered as part of a weight of evidence, but you have not provided any justification for the Weight of Evidence.

ECHA has set out above why each of the individual studies fails to meet the information requirement by itself. You have not provided any justification to explain why there is sufficient weight of evidence from all five studies together, and on this basis alone, ECHA considers that you have not met the requirement of Annex XI, Section 1.2. ECHA additionally considers that the defects in each individual study are such that they do not complement the defects in the other studies, and that consequently, there is not sufficient weight of evidence from all five studies to meet the requirements of Annex XI, Section 1.2. Therefore, your adaptation of the information requirement is rejected.

In your comment to the draft decision, you suggested that a 'three-generation' reproduction toxicity study on the registered substance provides information that satisfies the information requirement. ECHA notes that (i) it is presumably a non-guideline and/ or non-GLP study and this information fails to meet the requirement of Annex XI for adequate and reliable documentation of the study, Section 1.1.2, for the same reasons as set out above under your comment on Extended one-generation reproductive toxicity study (section 4), *mutatis mutandis* for the endpoints study requirements for developmental toxicity, and (ii) the study does not have adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3), specifically, examinations of foetuses for skeletal and visceral alterations. For these reasons, this information provided in your comment would not meet the information requirement, and a data gap remains.

Consequently, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement and there is an information gap and it is necessary to provide information for this endpoint. Thus, a prenatal developmental toxicity study according to Annex IX, Section 8.7.2. is required. The following refers to the specifications of this required study.

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*, chapter R.7a (version 6.0, July 2017), section R.7.6.2.3.2. Since the substance to be tested is a solid, 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 14 March 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 request(s).

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

ECHA received proposal(s) 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 amendments 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 request for an extended one-generation reproductive toxicity study (Annex IX, Section 8.7.3) has been removed from the draft decision. This study can to a certain extent clarify the endocrine disrupter concern identified under CoRAP (Community Rolling Action Plan) for this substance. Therefore, the Member State Committee agreed that the need for and design of this study would be better addressed under Substance evaluation which would allow, if necessary, investigation of additional parameters which may go beyond the standard information requirements, while avoiding unnecessary animal testing. ECHA reserves the right to address this endpoint in a subsequent compliance check in case it is not addressed under substance evaluation.

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-58 meeting and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for the start of substance evaluation in 2020.

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

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

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

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

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