Helsinki, 27 May 2019

Addressee: [redacted]

Decision number: CCH-D-2114472917-34-01/F
Substance name: Benzoic acid, 2,3,4,5-tetrachloro-6-cyano-, methyl ester, reaction products with p-phenylenediamine and sodium methoxide
EC number: 600-736-8
CAS number: 106276-80-6
Registration number: [redacted]
Submission number: [redacted]
Submission date: 18/06/2015
Registered tonnage band: 100-1000

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. **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;**

2. **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, provided that the study requested under 1. has negative results;**

3. **Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: OECD 421/422) in rats, oral route with the registered substance;**

4. **Sub-chronic toxicity study (90-day), inhalation route (Annex IX, Section 8.6.2.; test method: OECD TG 413) in rats with the registered substance. The study must include measurements of lung burden and bronchoalveolar lavage fluid (BALF) analysis as described in the current version (25 June 2018) of the test guideline;**

5. **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;**

You are required to submit the requested information in an updated registration dossier by **3 December 2021.** 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 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 Wim De Coen, Head of Unit, Hazard Assessment.

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons

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.

Your registration dossier contains for multiple endpoints adaptation arguments in form of a grouping and read-across approach under Annex XI, Section 1.5. of the REACH Regulation. ECHA has considered first the scientific and regulatory validity of your read-across approach in general before assessing the individual properties sections.

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:

- a sub-chronic toxicity (90-day) study (Annex IX, Section 8.6.2.)
- a screening study for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- a pre-natal developmental toxicity study (Annex IX, Section 8.7.2.).

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. Secondly, it is required that the relevant properties of a substance may be predicted from data for the reference substance(s) (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.

The ECHA Read-across assessment framework foresees that there are two options which 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

[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.
[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).

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 using data of the structurally similar substance 3,4,5,6-tetrachloro-N-[2-(4,5,6,7-tetrachloro-2,3-dihydro-1,3-dioxo-1H-inden-2-yl)-8-quinolyl]phthalimide (EC No 250-063-5) (hereafter the 'source substance').

You have provided a read-across documentation in the endpoint summaries.

For the toxicological endpoints you use the following arguments to support the prediction of properties of the registered substance from data for the source substance: "*Toxicity after repeated dose administration of the test item was not evaluated; reliable, experimental data of an analogue are available. The substances share high similaritiy in structure and have comparable physico-chemical properties. Both substances are solids of poor water solubility and insoluble in most of the common organic solvents. The molecular weight of both compounds is higher than 600 g/mol. The molecules includes phthalimid-like structures, whereas only the analogue compound bears the potential to release chlorinated phthalimid after enzymatic or bacterial cleavage. Therefore, the analogue substance was choosen to examine toxicity after repeated dose administration and toxicity to reproduction and development*".

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

In your comments to the initial draft decision, you provided an updated read-across justification document with an additional source substance ([redacted]) and a hypothesis based (only) on structural similarity.

ECHA's evaluation and conclusion

Your proposed adaptation argument is that the similarity in chemical structure and in some of the physico-chemical properties between the source and registered substance is a sufficient basis for predicting the properties of the registered substance for other endpoints. Structural similarity is a prerequisite for applying the grouping and read-across approach. However similarity in chemical structure, molecular weight and similarity of some of the physico-chemical properties, including solid form and poor water solubility, does not necessarily lead to predictable or similar human health properties in other endpoints. Your justification based on structural similarity and similar physico-chemical properties has not established why the prediction is reliable for the human health endpoints for which the read across is claimed.

More specifically, ECHA observes several deficiencies of the read-across adaptation as listed below, and thus there is no basis to predict properties of the target substance from the source substance:

A. There are marked differences in the molecular structures of the source and target substances (differences in bond-reactivity, e.g. imido-bond versus direct link from

the phthalimide to the aromatic core structure; (heterocyclic) differences in aromatic core structure). The impact of these differences on physico-chemical or toxicological properties is not discussed in the dossier.

B. You have not provided endpoint-specific comparative toxicological data to demonstrate that different compounds have qualitatively and quantitatively similar properties.

The updated read-across justification provided as part of your comments to the initial draft decision incorrectly assigns a newly provided gene mutation study in mammalian cells (mouse lymphoma assay, OECD TG 476) as having been conducted with the registered substance. ECHA notes that it has been conducted with the source substance [redacted] (EC 226-999-5), which is a main constituent of the registered substance. However, you have not provided any justification and supporting evidence how the properties of the registered substance can be predicted in the absence of effects from the other constituents.

Additionally, ECHA has taken into account all of your arguments together. ECHA firstly notes that you have not provided a reasoning as to why these arguments add to one another to provide sufficient basis for read-across. Secondly, the defects of each individual argument are not mitigated by the other arguments you have provided, and so ECHA considers that the arguments when taken all together do not provide a reliable basis for predicting the properties of the registered substance.

Therefore, ECHA considers that this grouping and read-across approach does not provide a reliable basis whereby the human health effects of the registered substance may be predicted from data for reference substance(s) within the group. Hence, this approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation.

As described above, further elements are needed to establish a reliable prediction for a toxicological or ecotoxicological property, based on recognition of the structural similarities and differences between the source and registered substances. This could be achieved (if it is possible) by a well-founded hypothesis of (bio)transformation to a common compound(s), or that the registered and source substance(s) have the same type of effect(s), together with sufficient supporting information to allow a prediction of human health properties.

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

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.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex VIII, Section 8.4.2., column 2 (adequate data from an in vivo cytogenicity test). In the technical dossier you have provided a study record for an *in vivo* Mammalian erythrocyte micronucleus test (study similar or equivalent to OECD TG 474) performed in mice with oral administration of the registered substance in doses up to 2000 mg/kg bw/d. The results of the test indicate that the substance does not cause genotoxicity. The acceptability criteria for the test guideline (OECD TG 474) state that target tissue (bone marrow) exposure must be demonstrated. However, in the endpoint study record there is no data showing exposure

of the target tissue (bone marrow) to the test substance. Hence, in the absence of such evidence, the provided test is not adequate and your adaptation must be rejected because this study does not meet one of the acceptability criteria for this test.

In your comments to the initial draft decision, you explain that the substance is not systemically available after oral or inhalation exposure and therefore cannot be detected in blood plasma samples. As the exposure of the target tissue has not been demonstrated, ECHA considers that the provided test is not adequate.

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 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).

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

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.

You have sought to adapt this information requirement according to Annex VIII, Section 8.4.3., column 2. You provided the following justification for the adaptation: *"According REACH Regulation AnnexVIII, 8.4.3 : "The study does not need to be conducted if adequate data from a in vivo mammalian gene mutation test are available." Data froma micronucleus assay in mouse as well as data from an UDS in rats are available".* In the technical dossier you have provided a study record for an Unscheduled DNA Synthesis (UDS) test in rats with mammalian liver cells *in vivo* (OECD TG 486) performed with the registered substance in doses up to 2000 mg/kg bw/d. However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex VIII, Section 8.4.3., column 2, because the UDS test is an indicator test detecting putative DNA lesions which should be used only when it can be reasonably assumed that the liver is a target organ. For further information, see ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7a, Section R.7.7.6.3. However, you did not demonstrate that the liver is a target organ. Hence, in the absence of such evidence, the provided test cannot be considered as adequate data from a reliable *in vivo* mammalian gene mutation test or as valid to identify a mutagenic property of the registered substance. Therefore, your adaptation of the information requirement is rejected.

In your comments to the initial draft decision, you explained that you already have test information from a study performed according to OECD TG 490 with the registered substance. Such information is however not included in the updated CSR or IUCLID file attached to to your comments. Instead, your CSR and IUCLID file describe a study,

performed according to OECD TG 476 with a read-across substance (EC 226-999-5), which was not included in the dossier evaluated for this decision. In addition, that substance is not included as a source substance in your read-across justification document and you have not addressed the differences in chemical structures between the two substances. Hence, ECHA cannot verify that the properties of the registered substance can be predicted from the data on the source substance. On the contrary, different effects are observed in an Ames test conducted with the registered substance ([redacted] 2010, OECD TG 471).

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 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 the study requested under 1. has negative results.

3. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

"Screening for reproductive/developmental toxicity" (test method OECD TG 421 or 422) is a standard information requirement as laid down in Annex VIII, Section 8.7.1. of the REACH Regulation if there is no evidence from available information on structurally related substances, from (Q)SAR estimates or from in vitro methods that the substance may be a developmental toxicant. Therefore, 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 screening for reproductive/developmental toxicity in the dossier that would meet the information requirement of Annex VIII, Section 8.7.1.

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" (OECD TG 422) with the analogue substance 3,4,5,6-tetrachloro-N-[2-(4,5,6,7-tetrachloro-2,3-dihydro-1,3-dioxo-1H-inden-2-yl)-8-quinolyl]phthalimide (EC no 250-063-5). However, as explained above in Appendix 1, section "Grouping of substances and read-across approach" of this decision, your adaptation of the information requirement is rejected. Consequently there is an information gap and it is necessary to provide information for this endpoint.

In your comments to the initial draft decision, you agreed to perform the requested study (test method OECD TG 422) with the registered substance.

According to the test methods OECD TG 421/422, the test is designed for use with rats. On the basis of this default assumption ECHA considers testing should be performed with rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a 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: Reproductive/developmental toxicity screening test (test method: OECD TG 421) or Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (test method: OECD TG 422) in rats by the oral route.

4. Sub-chronic toxicity study (90-day), inhalation 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 not provided any study record of a sub-chronic toxicity study (90 day) in the dossier that would meet the information requirement of Annex IX, Section 8.6.2.

You have sought to adapt this information requirement according to Annex IX, Section 8.6.2., column 2, fourth indent. You provided the following justification for the adaptation *"In the course of an OECD 422 study it was clearly shown that the material does not cause any effect; the NOAEL is considered to be 1000 mg/kg bw. Furthermore, yellowish disoloration of the feces indicates that the substance will be excreted unchanged. Furthermore, the solubility of the test item is below 0.05 mg/l water. In conclusion, there is no need for a 90 day study".*

However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 8.6.2., column 2, fourth indent, for the following reasons:

- You did not provide evidence to show that the substance is unreactive.
- The registration dossier indicates that the registered substance is inhalable. Indeed, according to the particle size distribution data the registered substance itself is a powder consisting of particles with significant proportion (>1% on weight basis) in the inhalable size range (MMAD < 50 µm).
- You did not provide sufficient information demonstrating that there is no evidence of absorption. Although the substance has low solubility in water, a demonstration of lack of absorption or dissolution of the substance in the lung environment following inhalation exposure or the gastrointestinal tract following oral exposure on that basis is speculative and unsubstantiated. A discoloration of the feces or an OECD 422 study does not provide sufficient evidence (e.g. toxicokinetic data) to show that the substance is excreted unchanged or to show no evidence of absorption.

Further, you provided a 1 week and a 4 week toxicity study with the registered substance, by the dermal route with a NOAEL of 150 mg/kg bw/d (highest dose tested). However, these studies do 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). Furthermore, the highest dose did not elicit toxic effects and the limit dose of 1000 mg/kg bw/d (as specified in OECD TG 410 and TG 411) was not reached. Hence, these studies cannot be considered as acceptable. In addition, these studies cannot be considered appropriate to fulfill the standard information requirement for a sub-acute toxicity study, because the criteria of REACH Annex VIII, Section 8.6.1, column 2 with respect to the appropriateness of testing by the dermal route are not met. More specifically, you did not demonstrate that the physicochemical and toxicological properties of the registered substance suggest potential for a significant rate of absorption through the skin. Finally, the 4 week toxicity study do not fulfil the conditions to adapt the information requirement according to Annex IX, Section 8.6.2, column 2, in the absence of severe toxicity effects according to the criteria for classifying the substance as R48, nor the conditions to adapt the information requirement according to Annex XI, section 1.2, because for the same reasons as those developed above. Hence, this adaptation of the information requirement is rejected.

In addition, you have sought to adapt this information requirement according to Annex XI, Section 1.5. of the REACH Regulation by providing a study record for a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (OECD TG 422) with the analogue substance 3,4,5,6-tetrachloro-N-[2-(4,5,6,7-tetrachloro-2,3-dihydro-1,3-dioxo-1H-inden-2-yl)-8-quinolyl]phthalimide (EC no 250-063-5). However, as explained above in Appendix 1, section "Grouping of substances and read-across approach" of this decision, your adaptation of the information requirement is rejected.

Therefore, ECHA considers that this read-across approach does not provide a reliable basis whereby the human health effects of the registered substance may be predicted from data for the analogue substance. Hence, this approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation and your adaptation of the information requirement is rejected.

In your comments to the initial draft decision, you explained that you consider that the specific rules for adaptation according to Annex IX, Section 8.6.2., column 2, fourth indent are fulfilled. You described that biosolubility and biopersistence tests have been performed, indicating that the test item is not dissolved or degraded after cellular uptake. However, you did not provide the results of those tests. In the attachments you included, it is said that such studies are planned/ongoing.

In the CSR/IUCLID file attached to your comments you present physicochemical properties and exposure scenarios (ES). For the granulometry you describe that the MMD is [redacted] and D90 is [redacted] for the registered substance. Many of the provided ESs have conditions of use that create dust or aerosol e.g. spraying (PROC 11), rolling application and brushing (PROC 10) and low or high energy manipulation of substances bound in/on materials or articles (PROC 21 and 24). You also predict notable exposures via inhalation in many mixing and transferring tasks ([redacted] for PROCs 5, 8a and 8b). The highest exposure estimates are [redacted] (PROC 11) and [redacted] (PROC 10) in ES 10 and 16. You compare your estimated exposure levels to a general dust limit value for inhalable dust (10 mg/m^3). According to ECHA Guidance R.5 (version 1.2 December 2011), the negligible exposure assessment should be based on robust information and the formation of dust or aerosol should not be significant due to the specific operational conditions. Due to the granulometry, the registered substance is inhalable and the predicted exposure levels do not describe "limited human exposure". Hence, ECHA considers that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 8.6.2., column 2, fourth indent.

In your comments to the initial draft decision, you also refer to a screening study performed according to OECD TG 422. As explained above, based on that study, there is not sufficient information demonstrating that there is no evidence of absorption.

Your adaptation of the information requirement is rejected. 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. The information provided in the technical dossier and the chemical safety report on properties of the registered substance and its uses (including for example transfer of substance or mixture at non-dedicated facilities, non-industrial spraying, and abrasion by professionals and consumers) indicate that human exposure to the registered substance by the inhalation route is likely. More specifically, the substance is reported to occur as a dust with a significant proportion (>1% on weight basis) of particles of inhalable size (MMAD < 50 µm). Furthermore, the substance is respirable, of low water solubility and consequently there is a potential for accumulation of the substance in the lungs. Hence, the test shall be performed by the inhalation route using the test method OECD TG 413.

There is evidence that the lower respiratory tract is a site of deposition and retention of the registered substance because the substance is poorly soluble in water and respirable. Therefore, you are requested to perform measurements of lung burden and bronchoalveolar lavage fluid (BALF) which are specifically designed to address such situation. The latest guidance on how to perform such measurements are described in the revised version of the OECD 413 test guideline adopted on 25 June 2018. The measurements shall therefore be conducted as described in the guideline version adopted on 25 June 2018.

According to the test method OECD TG 413 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 carry out the study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats inhalation route (test method: OECD TG 413). The study must include measurements of lung burden and bronchoalveolar lavage fluid (BALF) analysis as described in the current version (25 June 2018) of the test guideline.

5. 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" (OECD TG 422) with the analogue substance 3,4,5,6-tetrachloro-N-[2-(4,5,6,7-tetrachloro-2,3-dihydro-1,3-dioxo-

1H-inden-2-yl)-8-quinolyl]phthalimide (EC no 250-063-5). However, as explained above in Appendix 1, section "Grouping of substances and read-across approach" of this decision, your adaptation of the information requirement is rejected.

Therefore, ECHA considers that this read-across approach does not provide a reliable basis whereby the human health effects of the registered substance may be predicted from data for the analogue substance. Hence, this approach does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. of the REACH Regulation and your adaptation of the information requirement is rejected.

In addition, ECHA notes that the "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" 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 your comments to the initial draft decision, you agreed to perform the requested study with the registered substance.

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 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: 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 24 July 2018.

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.

As no amendments were proposed, ECHA adopted the decision under 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 requests in this decision will result in a notification to the enforcement authorities of your Member State.

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

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

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