EUROPEAN CHEMICALS AGENCY

Helsinki, 23 November 2018

Addressee [redacted]

Decision number: CCH-D-2114449796-31-01/F
Substance name: BENZENESULFONIC ACID, 4-C10-13-SEC-ALKYL DERIVS., COMPDS. WITH TRIETHANOLAMINE
EC number: 939-464-2
CAS number: NS
Registration number: [redacted]
Submission number: [redacted]
Submission date: 30/01/2018
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* 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. **Robust study summaries ("RSS") for: "Ito et al., 1978", 28-day repeated dose toxicity study conducted with LAS Na (EC: 270-115-0); "Yoneyama *et al.*, 1978", 6-month repeated dose toxicity study conducted with LAS Na (EC: 274-070-8); "Yoneyama *et al.*, 1976", 9-months repeated dose toxicity study conducted with LAS Na (EC: 274-070-8); "[redacted], *1989*", 91 day repeated dose toxicity study conducted with TEA (EC: 203-049-8), (Annex IX, Section 8.6.2. in conjunction with Annex I, Section 1.1.4.);**

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

You are required to submit the requested information in an updated registration dossier by ***1 June 2020***, except for the information requested under point 2 (the robust study summaries) which shall be submitted in an updated registration dossier by **4 March 2019**.

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.

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Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by 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

TOXICOLOGICAL INFORMATION

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

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.

Information obtained with the registered substance
In order to fulfill this information requirement you have provided study records for an *in vitro* Bacterial reverse mutation test (EU Method B.13/14/OECD TG 471; according to GLP) with the registered substance LAS-TEA (*key study* [redacted] *1992*). According to the information provided in the technical dossier, the study has been conducted with the registered substance LAS-TEA ([redacted]; the applied test material concentrations were calculated on the basis of active substance). You have assigned a Klimish score of 2 to this study, indicating that the "*Study performed according to older guidelines (No strain susceptible to cross-linking mutagens included (e.g. TA 102)*". You reported that there was no evidence of induced mutant colonies over negative control values. ECHA regards the study results as adequate and reliable for the strains tested but notes that the study does not include the test strains *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102.

Information obtained with the dissolution products derived from the registered substance
Based on the information provided in the attachment "[redacted]" in Section 13 in the IUCLID dossier, ECHA understands that your main read-across hypothesis is based on the dissolution of the target substance LAS-TEA to "*its constituent ions" LAS^- and TEA^+*. You have also provided study records for supporting studies, performed with the dissolution products TEA (*Supp- Ames test-Mortelmans et al., 1986*) and LAS ([redacted] *1993).* According to the information provided, they have been performed according to test methods equivalent or similar to OECD TG 471. For both studies you have assigned a Klimish score of 2. ECHA notes that the study with LAS ([redacted] *1993*) has been performed with the following S. *typhimurium* strains*: TA98, TA100, TA1535, TA1537 and TA1538,* and the study with TEA (*Mortelmans et al., 1986*) has been performed, using four S. *typhimurium* strains: TA1535, TA1537 or TA97, TA98, TA100.

However, ECHA underlines that no results are reported for the study conducted with TEA (*Supp- Ames test-Mortelmans et al., 1986)* and that the reporting of the study results obtained with LAS is consisting of one sentence "*LAS is not mutagenic in the Ames test*". This reporting does not allow verification of the results by ECHA.

Outcome
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.

As outlined above, for the registered substance you have provided a test from the year 1992 ([redacted], 1992) according to EU Method B.13/14 and GLP with an assigned reliability score of 2. While the test used five different strains of S. typhimurium TA 1535, TA 1537, TA 1538, TA 98 and TA 100, it did not include tests with strains S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101). However, since the test was conducted, significant changes have been made to OECD TG guideline 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, 1.1.2. of the REACH Regulation.

With reference to the information provided for the dissolution products, ECHA notes that the studies provided are not supported by adequate and realiable documentation, and therefore ECHA cannot establish whether predictions for the registered substance on the basis of information obtained with the dissolution products meet the criteria of Annex XI, Section 1.5. In any case, according to the reported method, E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102 were not tested in the studies on the dissolution product.

ECHA concludes that a test using *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 has not been submitted for the registered substance or the dissolution products 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 agreed to conduct the study according to OECD TG 471 in the fifth strain.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to complete 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. **Robust study summaries ("RSS") for: "Ito et al., 1978", 28-day repeated dose toxicity study conducted with LAS Na (EC: 270-115-0); "Yoneyama et al., 1978", 6-month repeated dose toxicity study conducted with LAS Na (EC: 274-070-8); "Yoneyama et al., 1976", 9-months repeated dose toxicity study conducted with LAS Na (EC: 274-070-8); "[redacted], 1989", 91 day repeated dose toxicity study conducted with TEA (EC: 203-049-8), (Annex IX, Section 8.6.2. 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.

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 did not provide information on the registered substance. Instead you provide information obtained with the dissolution products TEA and LAS (LAS-Na).

Your statement in section 5.6.3. of the Chemical Safety Report indicates that "*No information is available on the repeated dose toxicity of LAS TEA. The endpoint was addressed with data from LAS Na and TEA*".

Based on the information provided in the attachment "[redacted]" in Section 13 in the IUCLID dossier, ECHA understands that you propose to adapt the information requirement pursuant to Annex XI, Section 1.5 of the REACH Regulation. Further, ECHA noted that the studies listed under a) to d) below are also flagged as WoE in the IUCLID dossier. Therefore, ECHA analysed first the proposed adaptation based on Annex XI, Section 1.5 and then analysed additionally the merit of an adaptation based on Annex XI, Section 1.2.

Adaptation according to Annex XI, Section 1.5

Your read-across hypothesis is mainly based on the dissolution of the target substance LAS-TEA to "*its constituent ions" LAS^- and TEA^+*. In summary, you argue that "[redacted]."

ECHA notes that the solubilty of the registered substance in water is high, indicating that the counter ions LAS and TEA are rapidly formed in aqueous solutions. Moreover, ECHA acknowledges that the substance subject to this decision dissolves into TEA and LAS and that its properties subject to this decision may be predicted from information obtained on TEA and LAS. Most of the studies provided for the dissociation product LAS were in fact conducted with LAS-Na (the sodium salt). Since rapid dissolution for the sodium salt is also plausible and sodium is a physiological constituent in biological animal systems, ECHA acknowledges that studies with LAS-Na provide information on LAS. However, ECHA stresses that the predictions relying on the dissolution products LAS and TEA can only be considered as valid if adequate and reliable information on both dissolution products is included in your technical dossier. In particular:

Information provided with the dissolution products

You have provided the following information:

a) Ito *et al.*, 1978: a 28-day repeated dose toxicity study (No guidance provided, pre-GLP) conducted with LAS Na (EC: 270-115-0) in rats by gavage, leading to the identification of a NOAEL of 125 mg/kg/d based on decreased body weight and serum biochemical differences from the controls, observed at 250 mg/kg bw/day (LOAEL).
b) Yoneyama *et al.*, 1978: a 6-month repeated dose toxicity study (No guidance provided, pre-GLP) conducted in rats administered LAS Na (EC: 274-070-8) in their

diet. A NOAEL of 40mg/kg/d was identified based on the observation of "*diarrhea, suppressed growth, increased cecal weight and degeneration of renal tubules*" of various severity in the two intermediate dose groups and in the high dose groups. LOAEL = 115 mg/kg bw/day

c) Yoneyama *et al.*, 1976: a 9-months repeated dose toxicity study (No guidance provided, pre-GLP) conducted in rats administered LAS Na (EC: 274-070-8) via the drinking water. A NOAEL of 85mg/kg/d was established based on decreased GGT, LDH and Na/K-ATPase activity at 145 mkg/day (LOAEL)

d) [redacted] *1989*: 91-day repeated dose toxicity study (equivalent to OECD 408) conducted in rats administered TEA (EC: 203-049-8) in the diet. No treatment related effects were observed in the animals. The NOAEL is 1000 mg/kg bw/day (the HDT)

ECHA observes that the data intended to be used as source data for the proposed prediction does not fulfil the following provision of Annex XI, Section 1.5 of the REACH Regulation:

- adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3); and
- adequate and reliable documentation of the applied method.

Specifically, the level of the information provided in the endpoint study records for each of the three repeated dose toxicity studies conducted with LAS as well as the information from the study conducted with TEA is very limited. Therefore, the reporting of these results does not allow ECHA to independently assess the study results and conclude on the outcome. In line with this observation, you state in the endpoint study summary: "*...the original report was not available for review*". ECHA notes that a robust study summary is required under Article 10(a)(vii) and Annex I, Section 1.1.4., and ECHA considers that the information provided in the endpoint study records does not meet the requirements of a robust study summary, as defined in Article 3(28). Specifically, the endpoint study records do not provide information on the scope of the investigations on haematology, biochemistry, histopathology, and the behavioural test battery conducted in each of these studies.

In this respect, please note that ECHA has provided a practical guide for "How to report robust study summaries" (Practical Guide 3, Version 2.0, November 2012).

ECHA concludes that currently the source studies which investigated the properties to be read-across to the registered substance cannot be assessed in the dossier on the registered substance. It can therefore not be verified in this dossier whether the study design is adequate and reliable for the purpose of the prediction, whether the test material used represents the source substance as described in the justification documents, and whether the results are adequate for the purpose of classification and labelling and/or risk assessment.

Adaptation according to Annex XI, Section 1.2

ECHA notes that the studies listed under a) to d) above are flagged as WoE in the IUCLID dossier. According to the provision of Annex XI, Section 1.2, in a weight of evidence approach there has to be sufficient evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while the information from each single source alone is regarding insufficient to support this notion.
Therefore, an evidence based approach involves an assessment of the relative values/weights of different pieces of the available information that have been retrieved and gathered in previous steps. To this end, a value needs to be assigned to each piece of

information. These weights/values can be assigned either in an objective way by using a formalised procedure or by using expert judgement. The weight given to the available evidence depends on factors such as the quality of the data, consistency of results, nature and severity of effects and relevance of the information for the given regulatory endpoint.

ECHA notes that you did not provide any justification on how the information obtained from the studies would contribute to a weight of evidence approach, intended to determine whether the registered substance has or has not a dangerous property for the endpoint under consideration. ECHA is there not in a position to analyse this further.

In the comments to the draft decision you "*....agree to update the Robust study summaries for studies by Ito et al., 1978, Yoneyama et al., 1978, Yoneyama et al., 1976,* [redacted]*, 1989 to the extent possible based on the available reports.*"
ECHA acknowledges that you intend also to perform "*....a literature review to determine whether additional information (e.g. from carcinogenicity studies, from dermal repeated dose toxicity studies) is available to address the repeated dose toxicity of TEA*".

Further, at this point in time, ECHA removes the conditional request to conduct a 90-day toxicity study with the registered substance. However, if the requested robust study summaries do not meet the information requirement of Annex IX, Section 8.6.2., ECHA will request the 90-day toxicity study with the registered substance, in a new decision, according to Article 42 (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:

A robust study summary that needs to cover the following data as a minimum to allow an independent assessment:

- Scope of the investigations for older studies not conducted according to current guidelines and GLP (which parameters were investigated)
- Toxic response/effects by sex and dose level
- Data preferably in tabular form where applicable
- Additional information that may be needed to adequately assess data for reliability including the following dose-related effects if available: body weight and body weight changes, haematological and clinical biochemistry findings, gross pathology and histopathology.
- Statistical treatment of results, where appropriate
- Historical control values, if needed to interpret the results

for each of the following studies:

a) Ito et al., 1978, 28-day repeated dose toxicity study conducted with LAS Na (EC: 270-115-0)
b) Yoneyama *et al.*, 1978, 6-month repeated dose toxicity study conducted with LAS Na (EC: 274-070-8)
c) Yoneyama *et al.*, 1976, 9-months repeated dose toxicity study conducted with LAS Na (EC: 274-070-8)
d) [redacted] *1989*, 91 day repeated dose toxicity study conducted with TEA (EC: 203-049-8)

3. 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 did not provide information on the registered substance. Instead you provided information obtained with the dissolution products TEA and LAS (LAS-Na) and with monoethanolamine (MEA).

In Section 13 in the IUCLID dossier you have provided a justification document, "[redacted]" in which you state your read-across hypothesis, based on the dissociation of the target substance LAS-TEA to "*its constituent ions" LAS^- and TEA^+. The* "[redacted]" does not specifically adress the individual information requirements, but covers generically "*systemic exposure*". On this basis, ECHA understands that you propose to adapt the information requirement in Annex IX, Section 8.7.2 for pre-natal developmental toxicity in a first species on the basis of the provisions of Annex XI section 1.5 of the REACH Regulation (grouping and read-across), but without providing endpoint specific arguments.

ECHA notes that in section 5.9.3. in the CSR you provide the following justification for the purpose of the information obtained with MEA: "*As no complete developmental toxicity study (OECD guideline 414) is available for TEA, read across with the structural analogue MEA, for which developmental toxicity studies are available, is applied*". You did not provide any other justification. ECHA understands that you intend to predict the pre-natal developmental toxicity of TEA on the basis of study results obtained with MEA.

ECHA acknowledges that the substance subject to this decision dissolutes into TEA and LAS and that its properties subject to this decision may be predicted from information obtained on TEA and LAS, but only when adequate and reliable information on both dissolution products (i.e. TEA and LAS) is included in your technical dossier for each information requirement concerned.

ECHA noted that the studies listed under e) to h) below are flagged as WoE in the IUCLID dossier. Therefore, ECHA analysed first the proposed adaptation based on Annex XI, Section 1.5 and then analysed additionally the merit of an adaptation based on Annex XI, Section 1.2.

<u>Adaptation based on Annex XI, Section 1.5</u>
The following information for the dissolution products TEA and LAS-Na is provided and assessed:

e) Screening for reproductive/developmental toxicity (OECD TG 421) (*WoE-[redacted], 2010*) conducted with triethanolamine (TEA; EC: 203-049-8);

   This study does not provide the information required by Annex IX, Section 8.7.2., because it does not cover key parameters of a pre-natal developmental toxicity study according to OECD TG 414, such as examinations of foetuses for skeletal and visceral alterations. Therefore this study is not adequate as source study to predict the pre-natal developmental toxicity for the registered substance.

f) [redacted] teratogenicity screening test in CD-1 mice (*WoE-[redacted]*) conducted with triethanolamine (TEA; EC: 203-049-8);

No information on the study protocol is available. ECHA notes in general that the [redacted] study does not cover key parameters of a pre-natal developmental toxicity study according to OECD TG 414. Specifically, the study is based on the assumption that most developmental toxicity becomes manifest postnatally as reduced viability and/or impaired growth of the young ([redacted], 1982). According to the TG 414 "females should be killed one day prior to the expected day of delivery", while in the Chernoff-Kavlok study the dams are allowed to give birth and the litters are counted, weighed at birth and on day 4 post-partum and then discarded. The study provides information on "foetal death, pup growth and survival, external malformations and cleft palate". However, the study does not provide information on "skeletal and soft tissue alterations (e.g. variations and malformations or anomalies)", required in the TG 414. Therefore this study is not adequate as source study to predict the pre-natal developmental toxicity for the registered substance.

g) Two non-guideline, not GLP-compliant pre-natal developmental studies in rats ([redacted], 1971) and in mice ([redacted], 1975), performed with the LAS-Na (EC no. 270-115-0).
In the first study rats were treated with the test substance via oral-gavage at 0.2, 2, 300, 600 mg/kg bw/day; test period: 6-15 GD. The NOAEL for both maternal and developmental toxicity was 300 mg/kg bw/day based on decreased weight gain and transient diarrhoea and marginal retardation of sternabral ossification, respectively, observed at 600 mg/kg bw/day (*WoE-[redacted] 1971*).

In the second study mice were treated with the test substance via oral-gavage at 0.2, 2, 300, 600 mg/kg bw/day; test period: 6-15 GD. The NOAEL for maternal toxicity was 2 mg/kg bw/day based on increased mortality, retarded weight gain and adverse signs in the necropsy - tympanites, sometimes associated with gastritis, observed at 300 mg/kg bw and above. The NOAEL for developmental toxicity was 300 mg/kg bw/day based on *"Minor anomilies, including gross or visceral and skeletal anomalies were increased" (WoE-[redacted]., 1975).*

ECHA notes that the developmental effects observed in both rats and mice are secondary to the maternal toxicity. Hence, ECHA considers that the results of the pre-natal developmental studies in rats and mice obtained with LAS-Na as test material did not indicate concern for pre-natal developmental toxicity.

ECHA concludes on the proposed adaptation based on Annex XI, Section 1.5, that for the linear alkylbenzenesulfonic moiety of the registered substance no concern was identified in two species for pre-natal developmental toxicity studies (g). However, for the dissolution product TEA there is no adequate source study available. Therefore, there is no adequate basis to predict the outcome of the pre-natal developmental toxicity study for the registered substance on the basis of the dissolution products. ECHA therefore rejects the proposed adaptation based on Annex XI, Section 1.5.

The following information on MEA to predict properties of TEA is provided and assessed:

h) Oral study in rats (*WoE-[redacted] 1994*) and two dermal pre-natal developmental toxicity studies (OECD TG 414) in rat and rabbit (*WoE-[redacted], 1996*), performed with MEA (EC no 205-483-3).

The results of the OECD TG 414 oral-gavage study in rats with MEA (99.5%) (WoE-[redacted], 1994, GLP status is not specified) did not show pre-natal developmental toxicity. The NOAEL developmental was set at 450 mg/kg bw/day. The results of the OECD TG 414 studies in rats and rabbit with dermal administration of MEA (100%) (WoE-[redacted]., 1996 GLP status not specified) did not show pre-natal developmental effects up to the highest dose tested: The NOAEL developmental was set to 225 mg/kg bw/day fro rats and to 75 mg/kg bw/day for rabbits.

ECHA acknowledges the data you have provided for MEA. However, in the absence of any justification on why and how a prediction from MEA to TEA would meet the provision in Annex XI, Section 1.5, ECHA concludes that there is no adequate basis to predict the outcome of the pre-natal developmental toxicity study for TEA on the basis of proposed analogue substance MEA. ECHA therefore rejects this proposed adaptation.

Adaptation according to Annex XI, Section 1.2

ECHA notes that the studies listed under g) to h) above are flagged as WoE in the IUCLID dossier. According to the provision of Annex XI, Section 1.2, in a weight of evidence approach there has to be sufficient evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while the information from each single source alone is regarding insufficient to support this notion.

Therefore, an evidence based approach involves an assessment of the relative values/weights of different pieces of the available information that have been retrieved and gathered in previous steps. To this end, a value needs to be assigned to each piece of information. These weights/values can be assigned either in an objective way by using a formalised procedure or by using expert judgement. The weight given to the available evidence depends on factors such as the quality of the data, consistency of results, nature and severity of effects and relevance of the information for the given regulatory endpoint.

ECHA notes that you did not provide any justification on how the information obtained from the studies g) to h) would contribute to a weight of evidence approach (in addition to the grouping and read-across approach already assessed above) to determine whether the registered substance has or has not a dangerous property for the information requirement under consideration.

In conclusion, ECHA rejects adaptations based on Annex XI, Section 1.5 or based on Annex XI, Section 1.2

Outcome

ECHA concluded for the information requirements Annex IX, Section 8.7.2 that there is information lacking for the dissolution product TEA. Therefore there is no adequate basis to predict the outcome of a prenatal developmental toxicity study for the registered substance on the basis of results obtained with the dissolution products according to Annex XI, Section 1.5. ECHA considers also there is no basis from a weight of the evidence approach to assume/conclude on whether the registered substance has or has not a dangerous property for the information requirement under consideration according to the provisions of Annex XI, Section 1.2 of the REACH Regulation.

Consequently there is an information gap and it is necessary to provide information for this endpoint with the registered substance.

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.

In your comments to the draft decision you agreed to conduct the study according to OECD TG 414.

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.

Deadline to submit the requested information

Your comments with regard to the deadline for the conduct of the EOGRTS are no longer relevant, since ECHA has removed the request for the EOGRTS from the decision.

ECHA has also removed the request for the sub-chronic (90-day) toxicity study with the registered substance. You are therefore required to submit robust study summaries for the studies described in Appendix 1, point 2 of this decision, only. The deadline for the submission of the robust study summaries is set to three months. With the submission of this information, you should also submit your conclusion on the need to conduct the 90-day subchronic toxicity study with the registered substance. ECHA will review this information and, if necessary, draft an appropriate decision according to Article 42 (1) of the Reach Regulation.

Due to the removal of the request for the sub-chronic (90-day) toxicity study and the EOGRT study, the overall deadline was reduced to 18 months.

ECHA points out that removal of the request for EOGRT study from this draft decision does not imply that the information requirement for this endpoint in accordance with Column 2, Annex IX, Section 8.7.3. is compliant with the REACH requirement. ECHA will address the EOGRTS in a subsequent decision at a later stage, once reliable information for the sub-chronic (90-day) toxicity endpoint is made available.

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

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

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

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