EUROPEAN CHEMICALS AGENCY

Helsinki, 8 December 2017

Addressee: [redacted]

Decision number: CCH-D-2114381488-35-01/F
Substance name: TRIBUTYL O-ACETYLCITRATE
EC number: 201-067-0
CAS number: 77-90-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 25/09/2013
Registered tonnage band: Over 1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **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;**

2. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a second species (rat or rabbit), oral route with the registered substance;**

ECHA reminds you of the obligation to registrants of the same substance to form substance information exchange fora and register through a joint registration. ECHA notes that a parallel registration for this substance exists.

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 have to submit the requested information in an updated registration dossier by **17 June 2019**. You also have to 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 Kevin Pollard, Head of Unit, Evaluation E1

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

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

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier you have provided a study record for a 12-month toxicity study with pairing of animals in the 9th month and subsequent examination of reproductive parameters and offspring (Larionov & Cherkasova 1977) in both rats and mice (rodent species), by the oral route with the registered substance. However, this study does not provide the information required by Annex IX, Section 8.7.2.

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 XI, Section 1.1.2. However, ECHA notes that your adaptation does not meet the general rule for adaptation of Annex XI, Section 1.1.2. Pursuant to that provision data on human health and environmental properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3) of the REACH Regulation shall be considered to be equivalent to data generated by the corresponding test methods referred to in Article 13(3) 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.

The study does not adequately and reliably cover the key parameters foreseen to be investigated in a pre-natal developmental toxicity study according to OECD TG 414. A study according to OECD TG 414 requires – *inter alia* - caesarean section and skeletal and visceral staining of the foetuses. Therefore the second condition in section 1.1.2 of Annex XI has not been met. However, in the provided study, post-natal effects on the offspring after natural delivery were investigated. Hence, the study does not allow investigation of pre-natal effects, and is neither adequate for the purpose of classification and labelling and/or risk assessment. Therefore the first condition of section 1.1.2 of Annex XI has not been met. In addition, no adequate and reliable documentation of the study in the form of a robust study summary describing a non-guideline study in sufficient detail was provided in the technical dossier to meet the requirement of the fourth condition of section 1.1.2 of Annex XI.

ECHA concludes that the provided information is insufficient to meet the information requirements for this endpoint. Therefore, your adaptation of the information requirement is rejected.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

In your comments according to Article 50(1) of the REACH Regulation, you stated that "[redacted] *has the intension to upgrade their individual dossier for the substance tributyl O-Acetylcitrate cas :77-90-7, in order to be part of the same joint submission as* [redacted] *SIEF negotiations are ongoing, with the aim to conduct both pre-natal developmental studies through a joint registration."*

ECHA acknowledges your agreement to both requests for tests on pre-natal developmental toxicity.

According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a first species (rat or rabbit) by the oral route.

Notes for your consideration

ECHA informs you that the lead registrant of the joint submission for this substance has received the same request for a pre-natal developmental toxicity study in a first species. ECHA expects you and the lead registrant to coordinate and agree who shall perform the test on behalf of all registrants for the same substance, according to REACH Article 53, to avoid unnecessary testing on vertebrates.

2. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

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

Pre-natal developmental toxicity studies (test method EU B.31./OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

In the technical dossier you have provided a study record for a 12-month toxicity study with pairing of animals in the 9th month and subsequent examination of reproductive parameters and offspring (Larionov & Cherkasova 1977) in both rats and mice (rodent species), by the oral route with the registered substance. However, this study does not provide the information required by Annex IX, Section 8.7.2. as explained above under section 5.

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.

As indicated above in section (1), ECHA acknowledges your agreement to both requests for tests on pre-natal developmental toxicity.

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 consideration, ECHA considers testing should be performed with rabbits or rats as a second species, depending on the species tested in the first pre-natal developmental toxicity study.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a second species (rabbit or rat) by the oral route.

Notes for your consideration

You are reminded that before performing a pre-natal developmental toxicity study in a second species you must consider the specific adaptation possibilities of Annex X, Section 8.7.2., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

ECHA informs you that the lead registrant of the joint submission for this substance has received the same request for a pre-natal developmental toxicity study in a second species. ECHA expects you and the lead registrant to coordinate and agree who shall perform the test on behalf of all registrants for the same substance, according to REACH Article 53, to avoid unnecessary testing on vertebrates.

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 28 November 2016.

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.

In your comments you agreed to the draft decision. ECHA took your comments into account 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 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. ECHA reminds you to provide missing information beyond the requests made in the section above pointing your attention specifically to the information required by sections 9 of Annexes VII to X of the REACH Regulation (ecotoxicology). This information should be obtained from the joint submission of this substance in accordance with the data sharing provisions set out in Article 30 of the REACH Regulation.

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.