EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-2114315856-44-01/F Helsinki, 18 February 2016

DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006

For triethyl phosphate, EC No 201-114-5 (CAS No 78-40-0), registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration for triethyl phosphate, CAS No 78-40-0 (EC No 201-114-5), submitted by [redacted] (Registrant).

The scope of this compliance check is limited to the standard information requirement of Annexes VII to X, of the REACH Regulation, excluding the information requirement of Annex IX/ X, Section 8.7.3.

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more per year. This decision does not take into account any updates after the deadline for updating (14 May 2015) communicated to the Registrant by ECHA on 7 April 2015.

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

The compliance check was initiated on 29 November 2013.

On 28 November 2014 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision. That draft decision was based on submission number [redacted].

On 19 January 2015 ECHA received comments from the Registrant on the draft decision and an updated registration dossier with the submission number [redacted].

The ECHA Secretariat considered the Registrant's comments and update.
On basis of this information, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

On 3 September 2015 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals for amendment of the draft decision within 30 days of the receipt of the notification.

Subsequently, a proposal for amendment to the draft decision were submitted.

On 9 October 2015 ECHA notified the Registrant of the proposal for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposal for amendment within 30 days of the receipt of the notification.

The ECHA Secretariat reviewed the proposal for amendment received and did not amend the draft decision.

On 19 October 2015, ECHA referred the draft decision to the Member State Committee.

By 9 November 2015, in accordance to Article 51(5), the Registrant provided comments on the proposal for amendment. In addition, the Registrant provided comments on the draft decision. The Member State Committee took the comments on the proposal for amendment of the Registrant into account. The Member State Committee did not take into account the Registrant's comments on the draft decision as they were not related to the proposal for amendment made and are therefore considered outside the scope of Article 51(5).

After discussion in the Member State Committee meeting on 7-11 December 2015, a unanimous agreement of the Member State Committee on the draft decision was reached on 10 December 2015.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

A. Information in the technical dossier derived from the application of Annexes VII to XI

Pursuant to Articles 41(1), 41(3), 10(a)(vi) and/or (vii), 12(1)(e), 13 and Annexes VIII, IX, X of the REACH Regulation the Registrant shall submit the following information using the indicated test methods and the registered substance subject to the present decision:

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD 408) in rats;
2. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: EU B.31./OECD 414) in rabbits, oral route.

Note for consideration by the Registrant:

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

Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

B. Deadline for submitting the required information

Pursuant to Articles 41(4) and 22(2) of the REACH Regulation the Registrant shall submit to ECHA by **26 February 2018** an update of the registration dossier containing the information required by this decision. The timeline has been set to allow for sequential testing as appropriate.

III. Statement of reasons

Pursuant to Article 41(3) of the REACH Regulation, ECHA may require the Registrant to submit any information needed to bring the registration into compliance with the relevant information requirements.

A. Information in the technical dossier derived from the application of Annexes VII to XI

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) of the REACH Regulation, a technical dossier for a substance manufactured or imported by the Registrant in quantities of 1000 tonnes or more per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

1. Sub-chronic toxicity study (90-day), oral 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.

In the technical dossier the Registrant has provided a study record for a 28-day study (test method: OECD 407, 1992) in rats, with reliability 1, and a weight of evidence consisting of 3 studies not carried out according to GLP or test guidelines, with reliability 4.

The 28-day key study does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days and the number of animals per dose group is significantly lower (10 vs. 20).

In relation to a weight of evidence approach, ECHA emphasises that if such an approach is applied, the Registrant should address all the parameters of the endpoint concerned that may give rise to a conclusion that a substance has or has not a particular dangerous property. In this specific case, the documentation and justification should therefore address all the relevant parameters of the endpoint "sub-chronic toxicity". ECHA notes however that the presented documentation and justification, based on 3 studies with reliability 4, does not adequately and reliably cover all the key parameters of this endpoint. In particular, 2 out of 3 studies were performed using only one or 2 doses (compared to 3 doses required in a 90-day study) and two studies have an exposure duration of less than 90 days and only the third study is a a long term, 5-month – however it is non GLP, non-guideline study by [redacted]. Moreover the studies are poorly reported and no specific guideline was reported in 2 out of 3 studies. The Registrant himself considered them as not assignable to any reliability class.

Following the receipt of the draft decision the Registrant has submitted his comments together with an update of his IUCLID dossier on 19 January 2015 (submission number [redacted]). In his comments and the update the Registrant has changed his approach for the [redacted] study from a Weight of evidence approach to a key study with reliability 2. In particular he has provided more information to demonstrate that the study would fulfill the endpoint requirements for a sub-chronic toxicity study. In particular, he has derived a NOAEL (335 mg/kg bw/day) from the [redacted] study, which is more conservative than the NOAEL in OECD SIDS report (670 mg/kg bw/day) and the NOAEL derived from the 28 day study in the technical dossier (1000 mg/kg bw/day). Additionally, he provided more detailed information on methods and parameters assessed in this study in the robust study summary.

However, ECHA notes the following deficiencies of [redacted] study which render this study insufficient as to fulfil the requirements of Annex IX, 8.6.2. of the REACH Regulation. Specifically, the study, being a non-guideline and no GLP study, does not have an adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3), as stipulated in Annex XI, section 1.1.2. of the REACH Regulation: (i) has too few number of animals; 10 (5 males + 5 females) instead of 20 (10 + 10),(ii) does not provide data on clinical observations, opthalmological examination, sensory and functional observations, (iii) does not provide organ weights provided for uterus, ovaries, epididymes and thymus.

There is therefore a failure to prove that this study is meeting the test criteria required for the sub-chronic toxicity study by oral route or TG OECD 408. .

As explained above, the information available 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 light of the physico-chemical properties of the substance, as a liquid with low vapour pressure and water soluble, the oral route is appropriate. It is however noted, that the exposure via inhalation is likely due to spray applications in the view of the information provided on uses and human exposure. The concentration of the substance in the few spray applications identified by the Registrant varies from [redacted] %. Nevertheless, due to the low vapour pressure, it is estimated that, in worst case, workers will be exposed to [redacted] % of the substance. Moreover, the available information (12 day inhalation study) does not indicate a relevant concern for respiratory tract irritation. Furthermore in the available toxicological studies available, some systemic absorption of the substance occurred and the liver appeared as the most sensitive target organ.

Therefore, ECHA considers that testing by the oral route is most appropriate.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, the Registrant is requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD 408) in rats.

2. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.)

Pre-natal developmental toxicity studies 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).

The technical dossier contains information on a pre-natal developmental toxicity study in rats by the oral route (OECD 414, [redacted]) using the registered substance as test material.

However, there is no information available for a pre-natal developmental toxicity study in a second species.

Furthermore, the technical dossier does not contain an adaptation in accordance with column 2 of Annex X, Section 8.7. or with the general rules of Annex XI for this standard information requirement.

Consequently there is an information gap for Annex X, Section 8.7.2. and it is necessary to provide information for this endpoint.

As explained above, the information available 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 his comments and the updated dossier the registrant claims that "Based on a guideline study in rats TEP is not a developmental toxicant and this study does not trigger further testing in another species. Consequently, further testing is of low priority and has to be weighed taking into account also animal welfare considerations."
However, ECHA notes that the study on a second species is a standard information requirement at Annex X level and no valid Annex XI or Column 2 adaptation to omit this study was provided.

The test in the first species was carried out by testing a rodent species and ECHA therefore considers that the test in a second species should be carried out in a non-rodent species. According to the test method EU B.31/OECD 414, the rabbit is the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rabbit as a second species to be used.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation,the Registrant is 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 414) in rabbits by the oral route.

IV. Adequate identification of the composition of the tested material

In relation to the information required by the present decision, the sample of substance used for the new studies must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given 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 substance tested in the new studies 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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies must be suitable to assess these grades.

Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the studies to be assessed.

V. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on ECHA's internet page at http://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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.