[If applicable: MSC identifiers]

Helsinki, 30 November 2018

Addressee: [redacted]

Decision number: TPE-D-2114453183-54-01/F
Substance name: inorganic phosphorus salt
EC number: 428-310-5
CAS number: NS
Registration number: [redacted]
Submission number: [redacted]
Submission date: 05/03/2018
Registered tonnage band: Over 1000 tonnes per year

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation ((EC) No 1907/2006) (the REACH Regulation), ECHA examined your testing proposal and decided as follows.

Your testing proposal is accepted and you are requested to carry out:

Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route with the registered substance specified as follows:

- **Ten weeks premating exposure duration for the parental (P0) generation;**
- **Dose level setting shall aim to induce systemic toxicity at the highest dose level;**
- **Cohort 1A (Reproductive toxicity); and**
- **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation**

You have to submit the requested information in an updated registration dossier by ***7 December 2020***. You also have to update the chemical safety report, where relevant.

The reasons for 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 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

The decision of ECHA is based on the examination of the testing proposals you submitted and scientific information submitted by third parties.

Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

a) Examination of the testing proposal

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

The basic test design of an extended one-generation reproductive toxicity study (Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of Section 8.7.3., Annex X of the REACH Regulation, whereas column 2 defines when the study design needs to be expanded.

The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a basic study design of an extended one-generation reproductive toxicity study according to OECD TG 443 by the oral route (gavage with the vehicle PEG 400) in rats with a 10-week premating exposure duration and dose level selection based on the available OECD TG 421 and 414 studies which were performed with the registered substance. You state that (i) Cohorts 2A and 2B are not triggered because the registered substance is an aluminium salt with low water-solubility and bioaccessibility and there is no concern for (developmental) neurotoxicity from the available information; and that (ii) Cohort 3 is not triggered because there is no indication for immunotoxicological effects in the available studies. With respect to extension of Cohort 1B to produce the F2 generation, you state that the need for a second generation will depend on the outcome of cohort 1A.

ECHA agrees to the proposed basic study design.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (extended one-generation reproductive toxicity study). ECHA notes that you provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

Thus, an extended one-generation reproductive toxicity study according to column 1 of Section 8.7.3., Annex X is required. The following refers to the specifications of this required study.

Premating exposure duration and dose-level setting

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance[2], the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and

[2] ECHA Guidance *on information requirements and chemical safety assessment*, Chapter R.7a, Section R.7.6 (version 6.0, July 2017)

folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

You proposed a 10-week premating exposure duration and ECHA agrees with your proposal because there is no substance specific information in the dossier supporting shorter premating exposure duration.

You state that the dose level selection will be based on the available OECD TG 421 and 414 studies which were performed with the registered substance. ECHA agrees with your proposal. You are reminded that the highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

Species and route selection

You proposed testing in rats. ECHA agrees with your proposal as, according to the test method OECD TG 443, the rat is the preferred species.

You proposed testing by the oral route, and more specifically via gavage-dosing with the vehicle PEG 400. ECHA agrees that the oral route is the most appropriate route of administration, since the substance to be tested is a solid. Furthermore, gavage-dosing with PEG 400 seems appropriate based on the OECD TG 414 and 421 studies provided with the registered substance.

Cohorts 2A and 2B

The developmental neurotoxicity Cohorts 2A and 2B need to be conducted in case of a particular concern on (developmental) neurotoxicity as described in column 2 of Section 8.7.3., Annex X. You proposed not to include Cohorts 2A and 2B and provided justifications following the criteria described in column 2 of Section 8.7.3 of Annex X and detailed in ECHA Guidance[2].

ECHA notes that the available 28-day study on the registered substance according to OECD TG 407 study does not raise a concern for (developmental) neurotoxicity. Furthermore, ECHA identified other aluminium salts as substances structurally analogous to the registered substance because the dissociated aluminium cation is considered the toxicophore. In this respect, ECHA notes that a One-Year Developmental and Chronic Neurotoxicity Study in rats according to OECD TG 426 and TG 452 (2010), which was performed with the most water-soluble aluminium salt (i.e. aluminium citrate), is available in the registration dossiers of analogue aluminium salts (e.g. in the registration dossier of aluminium trichloride). Aluminium citrate with its high solubility and bioaccessibility is considered a worst case for the registered substance which in comparison is poorly soluble and bioaccessible.

In the OECD TG 426/452 study on aluminium citrate, effects were mainly limited to renal damage and reduced grip strength which was attributed to lower body weights; cognitive impairment (no evidence of effects on memory or learning) was not observed in the pups and no treatment-related differences in FOB characteristics were observed in the neonatal and juvenile pups. From this information, no particular concern for developmental neurotoxicity could be established for the registered substance. Therefore, ECHA agrees that the developmental neurotoxicity Cohorts 2A and 2B need not to be conducted.

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation.
The third party considered that the registered substance was registered at Annex IX (100-1000 tpa) and that no trigger for EOGRTS was identified. Therefore, conducting the Extended one-generation reproductive toxicity study was not justified.

However, ECHA notes that the registered substance is registered at Annex X (above 1000 tpa) and that the Extended one-generation reproductive toxicity study is therefore an information requirement independent of the specific triggering requirements of Section 8.7.3. which only apply to Annex IX registrations.

ECHA notes that the third party did not provide any scientific data which would fulfil this information requirement.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance, as specified above.

Notes for your consideration

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if new information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the available information, together with the new information, shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA Guidance[2]. You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 5 March 2018.

ECHA held a third party consultation for the testing proposals from 26 March 2018 until 11 May 2018. ECHA received information from third parties (see Appendix 1).

This decision does not take into account any updates after **5 September 2018**, 30 calendar days after the end of the commenting period.

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 did not receive any comments by the end of the commenting period.

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 decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the 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 the Member States.

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.

4. 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.