EUROPEAN CHEMICALS AGENCY

Helsinki, 8 October 2020

Addressees
Registrants of JS_methylphosphonic-acid listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of a decision
11 February 2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Methylphosphonic acid
EC number: 213-607-2
CAS number: 993-13-5

Decision number: [Please refer to the REACH-IT message which delivered this communication (in format TPE-D-XXXXXXXXXX-XX-XX/F)]

DECISION ON TESTING PROPOSALS

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***19 April 2022***.

A. Requirements applicable to all the Registrants subject to Annex IX of REACH

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method OECD TG 408) in rats using the analogue substance methylphosphonic acid, compound with amidinourea (1:1), EC 282-758-4;

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat), oral route using the analogue substance methylphosphonic acid, compound with amidinourea (1:1), EC 282-758-4.

Conditions to comply with the requests

You are bound by the requests for information corresponding to the REACH Annexes applicable to your own registered tonnage of the Substance at the time of evaluation. Therefore you have to comply with the requirements of Annexes VII to IX of REACH, if you have registered a substance at 100-1000 tpa.

Registrants are only required to share the costs of information they are required to submit to fulfil the information requirements for their registration.

The Appendix on general considerations addresses issues relevant for several requests while the other Appendices state the reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

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] under the authority of Christel Schilliger-Musset, Director of 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 on general considerations

Assessment of the Grouping of substances and read-across approach, in light of the requirements of Annex XI, Section 1.5.

You seek to adapt the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

You proposed to conduct these studies with the analogue substance methylphosphonic acid, compound with amidinourea (1:1), EC 282-758-4. ECHA has considered the scientific and regulatory validity of your read-across approach in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

Legal background on ECHA's assessment of the grouping of substances and read-across hypothesis

The evaluation by ECHA of testing proposals submitted by registrants aims at ensuring that generation of information is tailored to real information needs. To this end, it is necessary to consider whether testing proposed by you may be appropriate to fulfil the relevant information requirements and to guarantee the identification of health and environmental hazards of substances. In that respect, the REACH Regulation aims at promoting wherever possible the use of alternative means, where equivalent results to the prescribed test are provided on health and environmental hazards.

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated whenever possible by means other than vertebrate animal tests, including information from structurally related substances (grouping of substances and read-across), "provided that the conditions set out in Annex XI are met".

The first Recital and the first Article of the REACH Regulation establish the "promotion of alternative methods for assessment of hazards of substances" as an objective pursued by the Regulation. In accordance with that objective, ECHA considers whether a prediction of the relevant properties of the substance subject to the present decision by using the results of the proposed tests is plausible based on the information currently available.

General considerations

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group (addressed under 'Predictions for toxicological properties').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance and related documents.

A. Predictions for toxicological properties

You have provided a read-across justification document in IUCLID Section 13.

You propose to read-across between the structurally similar substances, methylphosphonic acid, compound with amidinourea (1:1) (MPAAU), EC No. 282-758-4 (CAS No. 84402-58-4) as source substance and the Substance (MPA).

You have provided the following reasoning for the prediction of toxicological properties: *"Both chemicals are phosphonate derivatives. The chemical stability of the two chemical structures is very similar in the application on fabric. The molecular weight is quite close, and the size of both molecules indicates a very low bioavailability. Both chemicals contain phosphonate reactive groups, and are therefore highly soluble in water, which helps to attain application properties on fabric. Based on their chemical similarity, comparable properties are expected for MPA and MPAAU in both human and the environment."*

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which is based on the dissociation of the source substance into the Substance and a non-common compound. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

In your comments, you additionally state that *"Methyl phosphonic acid has been reported to have a water solubility >20 g/L and publication of dissociation constants of 2.2 and 7.7 demonstrate that the acid easily dissociates in aqueous solutions. Methyl phosphonic acid, compound with amidinourea (1:1) has a reported water solubility of > 470 g/L and a dissociation constant of 2.1 and 7.3 which is totally paralleled to the pure methyl phosphonic acid. So, both substances can be expected to readily dissolve in aqueous solutions. That means upon gastric intubation methyl phosphonic acid and its amidinourea salt form will both be present in ionic form upon dissolution in gastric fluid. Therefore, in case of test substance application of both chemicals methyl phosphonate will be present in equilibrium with its acid form to be taken up in the intestine and be further metabolized. Therefore, in both settings the animals are exposed to the identical molecules with the difference that in case of MPAAU the amidinourea is additionally present that might exhibit additional toxic effects. Therefore, the registrant considers MPAAU as the worst-case chemical compared to MPA and regards the read-across as justified based on physical chemical data relevant for toxicokinetics."*

A reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. Therefore you have provided sufficient supporting information to strengthen the rationale for the read-across.

B. Conclusions on the read-across approach

As explained above, you have established that relevant properties of the Substance can be predicted from data on the analogue substance. ECHA agrees with your read-across hypothesis. However, we emphasise that any final determination on the validity of your read-across adaptations will only be possible when the information on the requested studies will be available in the dossier.

Appendix A: Reasons for the requirements applicable to all the Registrants subject to Annex IX of REACH

This decision is based on the examination of the testing proposals you submitted.

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

Under Article 40(3)(a) of the REACH Regulation, ECHA may request the registrant to carry out the proposed test.

A sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX, Section 8.6.2. to REACH.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to OECD TG 408 with methylphosphonic acid, compound with amidinourea (1:1), EC No. 282-758-4 (CAS No. 84402-58-4) as source substance. You propose, as an alternative method to testing the Substance, read-across from the information obtained with the source substance to fulfil the respective information requirement for the Substance.

You proposed testing by the oral route, in rats. ECHA agrees with your proposal regarding the route and the species. Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity. The sub-chronic toxicity study must be performed according to the OECD TG 408 in rats.

You propose to adapt the standard information requirement in accordance with Annex XI, section 1.5. to REACH by providing the justification discussed in the Appendix on general considerations above.

As explained in the Appendix on general considerations, ECHA agrees that the provided information supports your hypothesis for predicting the properties of the Substance based on data of the source substance.

Therefore, under Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the analogue substance methylphosphonic acid, compound with amidinourea (1:1), EC No. 282-758-4.

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

Under Article 40(3)(a) of the REACH Regulation, ECHA may request the registrant to carry out the proposed test.

A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX, Section 8.7.2. to REACH.

You have submitted a testing proposal for a PNDT study according to OECD TG 414 in rats by the oral route with the analogue substance methylphosphonic acid, compound with amidinourea (1:1), EC No. 282-758-4, (CAS No. 84402-58-4).

You propose, as an alternative method to testing the Substance, read-across from the information obtained with the source substance to fulfil the respective information requirement for the Substance.

As explained in the Appendix on general considerations, ECHA agrees that the provided information generally supports your hypothesis for predicting the properties of the Substance based on data of the source substance. .

You proposed testing with the rat as a first species and by the oral route. ECHA agrees with your proposal regarding the route and the species. You may select between the rat or the rabbit because both are preferred species under the OECD TG 414[2]. The oral route is the most appropriate route of administration to investigate reproductive toxicity[2].

Therefore, under Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the analogue substance methylphosphonic acid, compound with amidinourea (1:1), EC No. 282-758-4.

[2] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix B: Procedural history

ECHA received your registration containing the testing proposals for examination on 22 February 2019.

ECHA held a third party consultation for the testing proposals from 27 May 2019 until 11 July 2019. ECHA did not receive information from third parties.

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of REACH.

The decision making followed the procedure of Articles 50 and 51 of REACH, as described below:

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

ECHA took into account your comments and amended 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 REACH.

Appendix C: Observations and technical guidance

1. This testing proposal examination decision does not prevent ECHA from initiating compliance checks at a later stage on the registrations present.

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(s).

3. Test guidelines, GLP requirements and reporting

   Under Article 13(3) of REACH, all new data generated as a result of this decision needs to be conducted according to the test methods laid down in a European Commission Regulation or according to international test methods recognised by the Commission or ECHA as being appropriate.

   Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

   Under Article 10 (a) (vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide: 'How to report robust study summaries'[3].

4. Test material

   Selection of the test material(s)

   The registrants of the Substance are responsible for agreeing on the composition of the test material to be selected for carrying out the tests required by the present decision. The test material selected must be relevant for all the registrants of the Substance, i.e. it takes into account the variation in compositions reported by all members of the joint submission. The composition of the test material(s) must fall within the boundary composition(s) of the Substance.

   While selecting the test material you must take into account the impact of each constituent/impurity is known to have or could have on the test results for the endpoint to be assessed. For example, if a constituent/impurity of the Substance is known to have an impact on (eco)toxicity, the selected test material must contain that constituent/impurity.

   Technical reporting of the test material

   The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

   Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"[4].

[3] https://echa.europa.eu/practical-guides
[4] https://echa.europa.eu/manuals

5. List of references of the ECHA Guidance and other guidance/ reference documents[5]

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)[6]

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

OECD Guidance documents
Guidance Document on aqueous –phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.

[5] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[6] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

Appendix D: List of the registrants to which the decision is addressed and the corresponding information requirements applicable to them

Registrant Name	Registration number	(Highest) Data requirements to be fulfilled
[redacted]	[redacted]	[redacted]