Helsinki, 29 April 2020

Addressee: [redacted]

Decision number: CCH-D-2114507394-52-01/F
Substance name: Barium dodecairon nonadecaoxide (the Substance)
EC number: 234-974-5
CAS number: 12047-11-9
Registration number: [redacted]
Submission number subject to follow-up evaluation: [redacted]
Submission date subject to follow-up evaluation: 11 December 2018

DECISION TAKEN UNDER ARTICLE 42(1) OF THE REACH REGULATION

By decision CCH-D-2114312646-52-01/F of 30 March 2016 ("the original decision") ECHA requested you to submit information by 6 April 2018 in an update of your registration dossier.

Based on Article 42(1) of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA examined the information you submitted with the registration update specified in the header above, and concludes that

Your registration still does not comply with the following information requirement:

In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) in rats, inhalation route or using tracheal installation as justified, target tissue lung.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Advice and further observations are provided in Appendix 3.

The respective Member State competent authority (MSCA) and National enforcement authority (NEA) will be informed of this decision. They may consider enforcement actions to secure the implementation of the original decision and exercise the powers reserved to them under Article 126 of Regulation No 1907/2006 (penalties for non-compliance) for the period during which the registration dossier was not compliant[1].

[1] See paragraphs 61 and 114 of the judgment of 8 May of the General Court of the European Court of Justice in Case T-283/15 Esso Raffinage v. ECHA

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, shall 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[2] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[2] 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

This decision is necessary according to Article 42(1) of the REACH Regulation because in your updated registration as a response to the original decision you have provided information that ECHA has assessed for compliance with the information requirements of the REACH Regulation and the outcome is that your registration still does not comply with the information requirements addressed in the compliance check decision.

In vivo mammalian alkaline comet assay (Annex IX, Section 8.4, column 2)

In the original decision you were requested to submit information derived with the registered substance ('the Substance') for an "*In vivo* mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD 489), in rats, inhalation route or using tracheal instillation as justified, target tissue lung".

In the updated dossier, you did not provide data from a study according to OECD TG 489. Instead, you provided a justification on technical unfeasibility to perform the study via inhalation route, both via intra-tracheal installation or inhalation exposure (nose only). More specifically you have provided the following statements:

- Regarding the intra-tracheal installation: it was not possible to identify suitable formulations/mixtures for intra-tracheal dosing for this high-density compound (the Substance could not be instilled as such).

- Concerning the inhalation exposure: it was not possible to generate stable concentration of the Substance that would reflect the characteristics of the Substance.

- Therefore, in spite of the efforts made, you consider the comet assay technically unfeasible.

We have assessed this information and identified the following issues:

(1) Inhalation study not provided

Firstly, ECHA considers whether you have complied with the request for an inhalation study.

Your justification is that "*The results provided by the laboratory were obtained with a powder with a granulometry that does not reflect at all the characteristics of the substance under registration...*". ECHA notes that this argument does not demonstrate that the study (as required by the Test Guideline) is not technically feasible. The Test Guidelines for inhalation testing (OECD 412/413) specify a size range (the mass median aerodynamic diameter) for aerosols for inhalation studies, and it is foreseen that substances must be processed so that they meet this size specification (to the extent technically possible). Therefore your justification for not providing the requested study on the grounds that testing is not technically possible (Annex XI, 2) cannot be accepted.

The relevant OECD Test Guideline is OECD TG 489. The version in force at the time of the decision (i.e. adopted on 26 September 2014) deals with the preparation of doses for inhalation exposures in para. 26; it states that "*test chemicals can be administered as gas, vapour, or a solid/liquid aerosol, depending on their physicochemical properties (50) (51).*"[3]

[3] This text is identical in the OECD TG 489 of 29 July 2016

The references (50) and (51) are for the OECD TG 412 and 413, respectively, which set out how solid aerosols must be prepared for inhalation exposure. The version of OECD 412 in force at the time of the decision (i.e. adopted on 7 September 2009) specifies that "*aerosols with mass median aerodynamic diameters (MMAD) ranging from 1 to 3 µm with a geometric standard deviation (σg) in the range of 1.5 to 3.0 are recommended (4). Although a reasonable effort should be made to meet this standard, expert judgement should be provided if it cannot be achieved.*" (Para. 19).[4] The OECD TG for 413 was adopted on the same date as the relevant 412 TG, and provide the same specifications for particle size as the contemporary OECD TG 412.

In your justification, you wrote "*Concentration measurements showed that the highest test item concentration that could be maintained stable for four hours was 2.5 mg/L. Particle size measurements showed a MMAD between 4 and 4.5 µm*". The relevant TGs require a particle size of MMAD ranging from 1 to 3 µm with a geometric standard deviation (σg) in the range of 1.5 to 3.0. You claim that particles with an MMAD of 4-4.5 µm are not in the range specified by the TG.

You have neither justified that the production of a particle of appropriate size is not possible, nor that such an atmosphere is not feasible. Therefore, a study provided with particles of this size would be incompliant with the TG unless there is a valid justification.

According to paragraph 19 of the OECD TG 412 (version from 2009) "*Although a reasonable effort should be made to meet this standard, expert judgement should be provided if it cannot be achieved.*" This means, for example, that if it is not possible to make a particle with an MMAD of 1-3 µm then you can use larger particles provided that you still have sufficient exposure of all relevant regions of the respiratory tract (especially the lower respiratory tract).

Based on this, if you were able to adequately justify that it is not technically feasible to generate particles of with an MMAD of 1 to 3 µm, then your evidence of a stable atmosphere of 4-4.5 µm particles at 2.5 mg/L would constitute evidence that the inhalation exposure is technically feasible (i.e. under these circumstances such a study would be acceptable).

In your comments to the Proposal for Amendment (PfA) submitted by one of the Member States Competent Authorities (MSCAs), you still claim that the inhalation route is not feasible. You argue that:
(a) the Substance has a granulometry such that the MMAD is incompatible with the requirements of the Test Guideline, that the Decision requested testing of the Substance, with the consequence that it is required to test the Substance at an MMAD outside the requirements of the Test Guideline;
(b) the Substance has an inherent magnetisation that causes prompt aggregation of particles; and
(c) the requirements of the OECD Test Guideline 412/413 were not met for the concentration in air, the period of stable concentration and the MMAD.

With reference to your arguments (a) to (c) we note the following:

[4] The OECD TG 412 adopted on 9 October 2017 specifies that you have to generate particles of Mass Median Aerodynamic Diameter (MMAD) of ≤2 µm with a σg of 1-3 (para. 39). Studies performed according to this OECD TG would also be acceptable.

(a) As explained above, the Test Guideline foresees that you must generate particles of an appropriate MMAD, i.e. substances must be processed so that they meet this size specification.

(b) ECHA notes your argument, but as indicated above you have not justified that the production of a particle of appropriate size is not possible. Additionally, we note that in the dossier you state that "*Concentration measurements showed that the highest test item concentration that could be maintained stable for four hours was 2.5 mg/L. Particle size measurements showed a MMAD between 4 and 4.5 µm*". This shows that there is no prompt aggregation under those circumstances.

(c) You assert that the requirements of the Test Guideline cannot be met, but provide no detailed justification. Without detailed justification ECHA cannot accept this argument. In addition, ECHA notes that for aerosols, according to OECD TG 412/413[5] the 5mg/L is only a limit dose, not a recommended concentration. Therefore, performing the test with lower concentration would still be according to the test guideline. Moreover, as regards the period of stable concentration, according to paragraph 18 of OECD TG 412/413 "*A rationale should be provided when using exposure duration less than 6 hours/day, [...].*" Based on this, shorter exposure duration might be acceptable if it is scientifically justified.

As indicated above, ECHA has set out that you must make reasonable efforts to meet the MMAD requirement to comply with the Test Guideline, but that expert judgement must be used when there are physico-chemical limitations.

(2) Feasibility of tracheal instillation

Secondly, ECHA considers that you have not justified that tracheal instillation is an appropriate route. Indeed, in the dossier and in your comments to the PfA you have concluded that this route is technically not possible, and hence it is not an appropriate route.

(3) Outcome

Thus, based on the information provided in the updated dossier, ECHA considers that you have not demonstrated that the *in vivo* mammalian alkaline comet assay via the inhalation route is not technically feasible, nor that tracheal instillation is justified.

As detailed above, the request in the original decision was not met, and you are still required to provide information on *In vivo* mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) in rats, inhalation route or using tracheal installation as justified, target tissue lung. The test should be performed according to the most recent OECD Test Guideline.

ECHA notes that in your comments to the PfA you fully agreed with the Draft Decision in its revised version of 9 January 2020.

[5] According to paragraph 10 of OECD TG 412 and paragraph 13 of OECD TG 413.

Appendix 2: Procedural history

In accordance with Article 42(1) of the REACH Regulation, the Agency examined the information submitted by you in consequence of the original decision. The Agency considered that this information did not meet one or more of the requests contained in that decision. Therefore, a new decision-making process was initiated under Article 41 of the REACH Regulation.

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 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 amended the request.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments and referred the modified draft decision to the Member State Committee.

Your comments on the proposed amendment were taken into account by the Member State Committee.

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-69 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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