EUROPEAN CHEMICALS AGENCY

Helsinki, 21 August 2018

Addressee: [redacted]

Decision number: CCH-D-2114440673-50-01/F
Substance name: HEXABORON DIZINC UNDECAOXIDE
EC number: 235-804-2
CAS number: 12767-90-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 08/03/2017
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. **In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method: OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2, test method: OECD TG 487) with the registered substance;**

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 ***28 August 2019***. You also have to update the chemical safety report, where relevant.

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. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)

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

An "*In vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study" is a standard information requirement as laid down in Annex VIII, Section 8.4.2. 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 mammalian chromosome aberration test ([redacted] 1996) according to EU Method B.10 with the substance 'Firebrake 415' ([redacted]). In IUCLID, you are interpreting the result as "*positive with metabolic activation*": "*The test material induced statistically significant increases in the frequency of cells with aberrations in the presence of metabolic activation. The response seen in Experiment 1 was confirmed in Experiment 2 at two time points. The test material was shown to be toxic to CHL cells in vitro in all six treatment cases, with a very steep dose response curve. The test material, Firebrake 415, was shown to be clastogenic to CHL cells in vitro. Read-across is justified on the basis detailed in the rationale for reliability above. This study is therefore considered to be of sufficient adequacy and reliability to be used as a supporting study.*"

However, in the overall conclusion, you disregard this conclusion without providing further explanation: "*In vitro gene mutation studies in bacteria ([redacted] 1981; [redacted] 1995 and [redacted] 1993) in vitro gene mutation studies in mammalian cells ([redacted] 2010) and in vitro mammalian chromosome aberration studies ([redacted] (1996) concluded that zinc borate is not genotoxic under the conditions of the studies.*"

ECHA notes your conflicting conclusions. ECHA also notes that the study [redacted] (1996) has relevant shortcomings compared to the requirements of EU method B.10:

- The first experiment with metabolic activation, 12 h harvest time, was negative [redacted]
- The second experiment with metabolic activation, 12 h harvest time, was considered positive [redacted] However, the positive control of this experiment was negative and according to the validity criteria of the test method, this experiment is considered as invalid. The study performer should therefore have repeated this experiment.
- The second experiment with metabolic activation, 24 h harvest time, was also considered positive [redacted] However, the positive result is limited to the highest concentration and no concentration-response relationship could be observed at the lower concentrations. Therefore, ECHA considered the results of this study being

equivocal. Under such circumstances, the EU method B.10 prescribes that "*Equivocal results should be clarified by further testing preferably using modification of experimental conditions.*" Hence, the study performer should have performed another experiment using an additional concentration between 16 and 32 µg/ml to clarify the concern stemming from this experiment.

Due to those shortcomings, for which no scientific justification has been provided, ECHA considers that this study does not provide the information required by Annex VIII, Section 8.4.2., because this study does not allow to conclude on the hazardous properties of the registered substance with respect to cytogenicity *in vitro* in mammalian cells. Consequently, this study is not adequate for the purpose of classification and labelling as required by Article 13(3) in conjunction with Annex XI, Sections 1.1.2. (1) and 1.5 of the REACH Regulation. Therefore, 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.

ECHA considers that the *in vitro* mammalian chromosome aberration test (test method OECD TG 473) and the *in vitro* mammalian cell micronucleus test (OECD TG 487) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.2. of the REACH Regulation.

In your comments to the draft decision, you agree that the mammalian chromosome aberration test for "firebrake 415" ([redacted] 1996) might not be adequate to provide the information required by Annex VIII, Section 8.4.2. You indicate this information for the dossier must fulfil the criteria in Article 13(1) of the REACH regulation. You indicate your intentions to provide information to fulfil this request by adapting the information requirement according to the general rules for adaptation (grouping and read-across) set out in Annex XI, Section 1.5. ECHA observes that your attempt to adapt the information requirement fails to fulfil the general rules for adaptation set out in this provision. More specifically, you did *inter alia* not provide experimental proof, e.g. of the claimed rates of hydrolysis and the rates of solvation for the registered substance. Instead, data is provided for [redacted] without quantification of rates of hydrolysis. The registration dossier contains a waiver instead of hydrolysis data. Also, there is no consideration documented whether other analogous substances would be more appropriate (e.g. other borate salts, zinc hydroxide/oxide, or other zinc salts) to predict the properties of the registered substance. ECHA notes that failure to choose, from several analogous substances, the most adequate analogous substance would constitute a bias. The most adequate choice shall be justified and supported with experimental data. In addition, ECHA observes that you provided (only) one available study for each of the proposed source substances and did not justify the exclusion of other potentially available studies. Furthermore, there is no comparison of toxicity profiles between the target and the source substances. Experimental data relating to endpoints other than genotoxicity are provided only for the target substance. There is no endpoint-specific consideration of read-across in relation to genotoxicity available, specifically chromosomal aberration.

You are reminded that this decision does not take into account any updates submitted after the notification of the draft decision to you. All new information in the later update(s) of the registration dossier will however be assessed for compliance with the REACH requirements in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

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: *In vitro* mammalian chromosome aberration test (test method: OECD TG 473) or *in vitro* mammalian cell micronucleus study (test method: OECD TG 487).

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 1 March 2017.

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 did not amend the request and the deadline.

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.

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.