ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 9 June 2016

Addressee: [redacted]

Decision number: CCH-D-2114330385-54-01/F
Substance name: N,N'-ethylenebis(3,4,5,6-tetrabromophthalimide)
EC number: 251-118-6
CAS number: 32588-76-4
Registration number: [redacted]
Submission number: [redacted]
Submission date: 02.04.2013

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. **Spectral data (Annex VI, Section 2.3.5);**

2. **Description of the analytical methods (Annex VI, Section 2.3.7);**

3. **In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3; test method: OECD TG 476 or OECD TG 490)[1] 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 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 and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **16 June 2017. You shall also 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. 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, 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/web/guest/regulations/appeals.]

Authorised[2] by Ofelia Bercaru, Head of Unit, Evaluation E3

[1] Only the OECD TG is mentioned since it has recently been updated while the corresponding EU test method has not yet been updated.

[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

1. **Spectral data (ultra-violet, infra-red, nuclear magnetic resonance or mass spectrum) (Annex VI, Section 2.3.5.);**

Pursuant to Article 10(a)(ii) of the REACH Regulation, the technical dossier shall contain information on the identity of the substance as specified in Annex VI, Section 2 of the REACH Regulation. In accordance with Annex VI, Section 2 the information provided shall be sufficient to enable the identification of the registered substance.

Spectral data are a formal information requirement of Annex VI Section 2.3.5.

ECHA notes that the registration contains an Infra-red (IR) spectrum but it does not contain any nuclear magnetic resonance (NMR) spectrum or Mass spectrum (MS). ECHA also notes that you provided a waiving justification ("[redacted]").

ECHA points out that the identity of the substance cannot be confirmed based exclusively on the IR spectrum. The NMR spectrum or MS spectrum are required to support the identity of the registered substance. ECHA regards NMR as scientifically necessary for the identification of the registered substance as NMR spectroscopic analyses such as a ^{1}H-NMR or a ^{13}C-NMR or a bromide NMR are powerful tools for structure characterisation and elucidation due to characteristic chemical shifts and spin-spin coupling which also reflects the relative abundance of individual atoms.

Additionally, the waiving justification that you provided is not acceptable as the substance can be analysed by spectroscopic techniques (i.e. dry Mass spectroscopy or solid state NMR) that do not require the use of solvents.

Accordingly, you are requested to provide the missing NMR spectrum, such as a ^{1}H-NMR or a ^{13}C-NMR or a bromide NMR. As an alternative to an NMR spectrum, mass spectra (MS) generated as part of mass spectroscopic analysis for the elucidation of the structure of the constituents in the substance can be provided.

ECHA acknowledges that in your comments on the draft decision you outlined how you intend to address the information requirement by stating that "*The registrant will update the dossier with solid state NMR data, a method that has newly become available to the internal analytical laboratory*".

As for the reporting of the spectral data in the registration dossier, the information shall be included in IUCLID section 1.4.

2. **Description of the analytical methods (Annex VI, Section 2.3.7.);**

Pursuant to Article 10(a)(ii) of the REACH Regulation, the technical dossier shall contain information on the identity of the substance as specified in Annex VI, Section 2 of the REACH Regulation. In accordance with Annex VI, Section 2 the information provided shall be sufficient to enable the identification of the registered substance.

Annex VI, section 2.3.7 of the REACH Regulation requires that each registration dossier contains a sufficiently detailed description of the analytical method used for establishing the composition of the registered substance and therefore its identity. This information shall be sufficient to allow the method to be reproduced.

ECHA observes that you have used elemental analysis to quantify the substance and provided the following statement [redacted]

ECHA points out that it is not accurate to quantify the substance based exclusively on the elemental analysis as it is not a specific quantification method. Other analytical methods (e.g dry mass spectroscopy) need to be combined with elemental analysis to provide a resonably accurate quantification of the substance.

Consequently, you shall provide additional analytical method(s), to identify and quantify the registered substance as precise as possible.

The information shall be sufficient for the method to be reproduced and shall therefore include details of the experimental protocol followed, the calculation used and the result obtained. You shall ensure that the composition reported in the dossier is consistent with the analytical results obtained.

As for the reporting of the above data in the registration dossier, the information shall be attached in IUCLID section 1.4.

3. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(d) and 13(4) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to IX of the REACH Regulation.

An "*In vitro* gene mutation study in mammalian cells" is an information requirement as laid down in Annex VIII, Section 8.4.3. of the REACH Regulation, "if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2." is obtained. ECHA notes that the registration dossier contains negative results for both these information requirements. Therefore, adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have not provided any study record of an *in vitro* gene mutation study in mammalian cells in the dossier that would meet the information requirement of Annex VIII, Section 8.4.3.

The technical dossier does not contain an adaptation in accordance with column 2 of Annex VIII, Section 8.4.3. or with the general rules of Annex XI for this standard information requirement.

As explained above, 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.

In the comments on the draft decision, you stated that "*The registrant admits the oversight of providing a justification for the adaptation of the testing for gene mutation in mammalian cells in the registration dossier. However, the conduct of a meaningful test is technically hampered by the low solubility of the test substance in the test medium and also in organic solvents. Furthermore QSAR methods contained in the OECD toolbox did not indicate a concern for direct DNA reactivity or genotoxicity endpoints. The registrant would therefore appreciate a re-consideration of this testing requirement*".

However, ECHA considers that a low solubility is not a valid column 2 or Annex XI adaptation. ECHA also notes that QSARs are a valid adaptation option according to Annex XI, 1.3, provided that the conditions of Annex XI, 1.3 are satisfied.

You state that the conduct of a meaningful test, specifically an *in vitro* gene mutation study in mammalian cells, is hampered by the low solubility of the test substance in the test medium and twelve other organic solvents. Nevertheless, in the registration dossier Section 7.6.1., two *in vitro* genotoxicity studies ([redacted]) are presented. According to the registration dossier, the vehicles used were DMSO and ethanol, respectively. In these studies, with both vehicles, sufficiently high concentrations (e.g. [redacted] with DMSO and [redacted] in ethanol) were achieved. The OECD test guidelines 476 and 490 (2015) give instructions on suitable solvents (paragraphs 16 and 21, respectively) and on how to test poorly soluble substances (paragraphs 21 and 29, respectively). Therefore, a conduction of the requested in vitro gene mutation study in mammalian cells seems to be possible with either DMSO or ethanol as solvent.

ECHA considers that the *in vitro* mammalian cell gene mutation tests using the *Hprt* and *xprt* test genes (OECD TG 476) and the *in vitro* mammalian cell gene mutation tests using the thymidine kinase gene (OECD TG 490) are appropriate to address the standard information requirement of Annex VIII, Section 8.4.3.

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 cell gene mutation test (test method: OECD TG 476 or OECD TG 490).

Ona final note, ECHA reminds that this decision does not take into account any updates submitted after 29 September 2015. All the 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.

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 9 September 2015.

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(s).

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment(s).

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s).

In 2015, the OECD TG 476 was updated and split into two separate TGs (476 and 490) and the draft decision was modified accordingly.

ECHA referred the draft decision to the Member State Committee.

You did not provide any comments on the proposed amendment(s).

The Member State Committee reached a unanimous agreement on the draft decision in its MSC-47 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

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Appendix 3: Further information, observations and technical guidance

1. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for start of substance evaluation in 2017.

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

3. 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 your Member State.

4. In carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new test(s) must be suitable to assess these. Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.