EUROPEAN CHEMICALS AGENCY

Helsinki, 14 December 2016

Addressee: [redacted]

Decision number: CCH-D-2114350549-42-01/F
Substance name: methyl vinyl ether
EC number: 203-475-4
CAS number: 107-25-5
Registration number: [redacted]
Submission number: [redacted]
Submission date: 30.05.2016
Registered tonnage band: [redacted]

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 gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490) 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 **21 December 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/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

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

Pursuant to Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at [redacted] per year shall contain as a minimum the information specified in Annexes VII to X of 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* 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 in vitro* gene mutation in mammalian cells needs to be present in the technical dossier for the registered substance to meet this information requirement.

You have sought to adapt this information requirement according to Annex XI, Section 1.2., weight of evidence. Hence, ECHA has evaluated your adaptation with respect to this provision.

You have provided the following sources of individual information:

- Weight of evidence study: in vitro gene mutation study in mammalian cells, (OECD TG 476; GLP) with the analogue substance ethyl vinyl ether EC No 203-714-4, [redacted], 1998, rel. 1,
- Weight of evidence study: in vitro gene mutation study in mammalian cells, (OECD TG 476; GLP), with the analogue substance isobutyl vinyl ether EC No 203-678-8, [redacted] 1993, rel. 1
- Weight of evidence study: in vitro gene mutation study in mammalian cells, (OECD TG 476; GLP) with the analogue substance hydroxybutyl vinyl ether, EC No 241-793-5, [redacted] 2010
- Weight of evidence study: in vitro gene mutation study in mammalian cells, (OECD TG 476; GLP) with the analogue substance cyclohexane dimethanol divinyl ether, CAS No. 17351-75-6, [redacted] 1995

ECHA notes that you have not provided a conclusion for the weight of evidence adaptation. ECHA understands that you conclude that the registered substance does not have a dangerous (hazardous) property with respect to in vitro gene mutation in mammalian cells.

ECHA has evaluated your weight of evidence information according to REACH Annex XI, Section 1.2., and has assessed whether you have provided "*sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that the substance has or has not a particular dangerous property*" with respect to the information requirement of Annex VIII, Section 8.4.3 for an in vitro gene mutation study in mammalian cells.

ECHA has further evaluated the information according to ECHA Guidance R.4.4. by considering whether the criteria given in that guidance i.e. relevance, reliability and adequacy for the purpose apply to the information you have provided. In its assessment, ECHA has considered the number of animals used in the studies provided and the consistency in the effects presented across the lines of information. ECHA came to a view on whether the set of information presented addresses the properties of the substance by covering, as a minimum, the most relevant elements investigated in an in vitro gene mutation study in mammalian cells.

ECHA observes that while each of these studies covers the most relevant elements investigated for this endpoint, all of the studies were performed on analogue substances.

ECHA notes, however, that all four studies in question provided in your weight of evidence adaptation were performed on analogue substances, rather than on the registered substance. Therefore, it is necessary to examine whether this information on analogue substances can be used in a weight of evidence approach. Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated from structurally related substances (grouping of substances and read-across), "provided that the conditions set out in Annex XI are met". According to Annex XI, Section 1.5 there needs to be structural similarity among the substances within a group or category and furthermore, 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 by interpolation to other substances in the group (read-across approach). Furthermore, Annex XI, Section 1.5 lists several additional requirements, including that adequate and reliable documentation of the applied method have to be provided.

You have provided an endpoint study record on the structurally similar substances described above (hereafter the 'source substances') as part of a weight of evidence approach. However, there is no documentation for the read-across so that your dossier is lacking a basis for predicting relevant human health properties of the registered substance from data for the source substances. Therefore, ECHA considers that you have failed to provide an adequate and reliable documentation of the applied method as required by Annex XI, Section 1.5 of the REACH Regulation.

In the absence of this information, ECHA cannot consider your justification for whether the properties of the registered substance can be predicted from the data on the source substances above, and ECHA therefore concludes that you have not established that relevant properties of the registered substance can be predicted from data on the analogue substance as required by the provisions of Annex XI, Section 1.5 of the REACH Regulation. Since the adaptation does not comply with the general rules of adaptation as set out in Annex XI, section 1.5, it is rejected.

ECHA notes that you have not provided any documentation for the weight of evidence approach in accordance with the principles set out in Annex XI, Section 1.2, as you have not explained how the information from analogue substances can be used in a weight of evidence approach to show that the substance does not have a dangerous property with respect to this endpoint.

Therefore, your adaptation of the information requirement based on a weight of evidence approach is rejected.
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.

ECHA considers that the *in vitro* mammalian cell gene mutation tests using the *Hprt* and *xprt* 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)

Since the test substance is a gas the test needs to be performed in sealed vessels according to instructions in OECD TG 476 or TG 490 ('Gaseous or volatile test chemicals should be tested by appropriate modifications to the standard protocols, such as treatment in sealed culture vessels').

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 17 August 2016.

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 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. 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 relation to the information required by the present decision, the sample of the substance used for the new test(s) 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 test(s) 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 test(s) must be suitable to assess these grades. Finally 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.