EUROPEAN CHEMICALS AGENCY

Helsinki, 11 April 2019

Addressee: [redacted]

Decision number: CCH-D-2114465803-44-01/F
Substance name: Dimethyl carbonate
EC number: 210-478-4
CAS number: 616-38-6
Registration number: [redacted]
Submission number: [redacted]
Submission date: 17/02/2017
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.**

2. ***In vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or OECD TG 490) with the registered substance provided that the study requested under 1. has a negative result;**

You have to submit the requested information in an updated registration dossier by **20 April 2020**. You shall also update the chemical safety report, where relevant. The deadline has been set to allow for sequential testing.

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 Ofelia Bercaru, Head of Unit, Hazard Assessment C4

[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.

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Appendix 1: Reasons

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.

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

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.

You have not provided any study record of an in vitro cytogenicity study in mammalian cells or in vitro micronucleus study in the dossier that would meet the information requirement of Annex VIII, Section 8.4.2.

The technical dossier contains the following three in vitro and one in vivo studies:

1. Experimental study ([redacted]1984). Key study rated KL2. OECD TG 471, Ames test, with S. *typhimurium* TA 1535, TA 1537, TA 1538, TA 98 and TA 100, negative with and without S9

2. Published study by Song et al., (2004). Supporting study rated KL2, OECD TG 471, Ames test with S. *typhimurium* TA 98 and TA 100, negative

3. Published study by Song et al., (2002). Key study rated KL2. In a Comet assay with L 929 mice fibroblasts, dimethyl carbonate gave no indications for a DNA damage at concentrations of up to 150 mg/mL.

4. Published study Song et al., (2004). Key study rated KL2. OECD TG 483, results showed, no increase in chromosome aberrations.

Studies 1 and 2 address in vitro gene mutation in bacteria, and do not provide information on in vitro cytogenicity in mammalian cells. Study 3 is non-GLP and non-guideline, and hence the manifest failure to provide a robust study summary constitutes a failure to provide adequate and reliable documentation (cf. Annex XI, 1.1.2). Further the study does not measure in vitro cytogenicity, but is rather a comet assay, and so there is also a failure to have adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3). Study 4 is of unspecified GLP compliance, and is an in vivo Mammalian Spermatogonial Chromosome Aberration Test. This test does not measure cytogenicity in somatic cells, but rather in germ cells, and so fails to provide adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3) for the endpoint of an in vivo somatic cell cytogenicity test (as per Annex XI, 1.1.2). Consequently, this is not an adequate in vivo cytogenicity test.

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 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 indicated that you will purchase a letter of access from the lead registrant to address the request in the decision.

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).

Notes for your consideration

ECHA informs you that the Lead registrant of your joint submission is in possession of the data requested from you in this decision. Therefore, ECHA recommends that you and the lead registrant try to reach an agreement in sharing the already existing data, according to REACH Articles 11 and 27, to avoid duplication of testing.

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

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.

You have provided four study records for mutagenicity, which are listed in Appendix 1, under section "1. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)". ECHA notes that none of the four study records provide relevant information on (in vitro) gene mutation in mammalian cells and so there is a failure to provide adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3) for this endpoint.

Adequate information on in vitro gene mutation in mammalian cells will however need to be present in the technical dossier for the registered substance to meet this information requirement provided that the study requested under issue 1 has a negative result. ECHA set the deadline for provision of the information to allow for sequential testing.

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 theHprt 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.

In your comments to the draft decision, you indicated that you will purchase a letter of access from the lead registrant to address the request in the decision.

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) provided that the study requested under 1.has a negative result.

Notes for your consideration

ECHA informs you that the Lead registrant of your joint submission is in possession of the data requested from you in this decision. Therefore, ECHA recommends that you and the lead registrant try to reach an agreement in sharing the already existing data, according to REACH Articles 11 and 27, to avoid duplication of testing.

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 20/07/2018.

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 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 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.