~~Confidential~~

Helsinki, 20 June 2023

Addressees
Registrants of JS_TMAHP as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
08/05/2015

Registered substance subject to this decision ("the Substance")
Substance name: Tetramethylammonium hydrogen phthalate
EC/List number: 416-900-5

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***25 September 2025***.

Requested information must be generated using the Substance unless otherwise specified.

Information required from all the Registrants subject to Annex VII of REACH

1. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: OECD TG 471, 2020)

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)

3. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: EU C.4. A/B/C/D/E/F/OECD TG 301A/B/C/D/E/F or EU C.29./OECD TG 310)

Information required from all the Registrants subject to Annex VIII of REACH

4. If negative results are obtained in tests performed for the information requirement of Annex VII, Section 8.4.1. then: In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

The reasons for the requests are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You

must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 for the request(s)

Contents

0. Reasons common to several requests

0.1. Assessment of the read-across approach

1 You have adapted the following standard information requirements by using grouping and read-across approach under Annex XI, Section 1.5:

- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)

2 ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following sections.

3 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, 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.

4 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

0.1.1. Predictions for toxicological properties

5 You have not provided a read-across justification document in either your IUCLID dossier or your CSR.

6 You predict the properties of the Substance from information obtained from the following source substances:

TMAC	tetramethylammonium chloride, EC No. 200-880-8
TMAH	tetramethylammonium hydroxide, EC No. 200-882-9
PA	phthalic acid, EC No. 201-873-2
PA	phthalic anhydride, EC No. 201-607-5
[redacted]	no EC No

7 We have identified the following issue with the predictions of in vitro gene mutation:

0.1.1.1. Absence of read-across documentation in your dossier

8 Annex XI, Section 1.5. requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include an explanation why the properties of the Substance may be predicted from information on the source substance(s).

9 You have provided robust study summaries for studies conducted with other substances than the Substance in order to comply with the REACH information requirements. However, you have not provided documentation in your dossier as to why this information is relevant for the Substance and thus why the properties of the Substance may be predicted from information on the source substance(s).

10 In the absence of such documentation in your dossier, the properties of the Substance cannot be reliably predicted from the data on the source substance(s).

11 In the comments to the draft decision you provided a read-across justification document and you indicated your intention to update the registration dossier accordingly.

12 ECHA did not identify concerns regarding the read-across hypothesis provided in the justification document submitted with your comments.

13 However, the justification document is currently not available in your registration dossier. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

0.1.2. Conclusion on the read-across approach

14 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

15 An in vitro gene mutation study in bacteria is an information requirement under Annex VII, Section 8.4.1.

1.1. Information provided

16 In your dossier, you have adapted the following standard information requirements by applying weight of evidence (WoE) adaptation in accordance with Annex XI, Section 1.2.:

(i) OECD TG 471 in vitro gene mutation in bacteria with the Substance
(ii) OECD TG 471 in vitro gene mutation in bacteria, with the source substance N,N,N-trimethylmethanaminium chloride, EC No. 200-880-8
(iii) OECD TG 471 in vitro gene mutation in bacteria, with the source substance, tetramethylammonium hydroxide, EC No. 200-882-9
(iv) Equivalent/similar OECD TG 471 in vitro gene mutation in bacteria, with the source substance phthalic acid, EC No. 201-873-2

17 In the comments to the draft decision, you provided a justification document on the read-across approach.

18 Based on your comments, we understand that you intend to update your dossier with a read-across adaptation.

1.2. Assessment of the information provided

1.2.1. Read-across adaptation rejected (studies ii, iii, iv)

19 For the reasons already explained under Section 0.1., the adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. currently in your dossier is rejected. In addition, ECHA identified the endpoint-specific issue addressed below.

1.2.2. The studies (i-iv) in your dossier do not meet the specifications of the test guideline(s)

20 To fulfil the information requirement, a study must comply with OECD TG 471 (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the test is performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

   However, in study (i) the test was performed with the strains TA1535, TA100, TA1537, TA1538, and TA98 (i.e., the strain S. typhimurium TA102 or E. coli WP2 uvrA or E. coli WP2 uvrA (pKM101) is missing).

b) the mean number of revertant colonies per plate is reported for the treated doses and the controls.

However, in studies (i-iv) , as currently reported in your dossier, the mean number of revertant colonies per plate for the treated doses and the controls was not reported.

21 The information provided currently in your dossier does not cover the specification(s) required by the OECD TG 471 and the information requirement is not fulfiled.

22 Therefore, the read-across adaptation currently in your dossier is rejected and the information requirement is currently not fulfilled.

23 In the comments to the draft decision, you provide data on the number of revertant colonies for studies (i-iv). The information you have provided in your comments addresses the incompliance (see point b) above). ECHA also takes note that you provided a read-across justification document in your comments on the draft decision and that you indicated your intention to update the registration dossier accordingly. As explained in Section 0.1, ECHA did not identify concerns regarding the read-across hypothesis provided in the justification document submitted with your comments.

24 However, as the additonal information is currently not available in your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

1.3. Specification of the study design

25 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) is considered suitable.

2. Growth inhibition study aquatic plants

26 Growth inhibition study on aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

2.1. Information provided

27 You have provided a growth inhibition study on algae according to OECD TG 201 (1994) with the Substance.

2.2. Assessment of the information provided

2.2.1. The provided study does not meet the specifications of the test guideline

28 To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH). Therefore, the following specifications must be met:

29 Reporting of the methodology and results

a) the test conditions are reported (*e.g.*, composition of the test medium);
b) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form.

30 In the provided study described as growth inhibition study on aquatic plants/algae:

31 Reporting of the methodology and results

a) on the test conditions, you have not specified the composition of the test medium.
b) tabulated data on the algal biomass determined daily for each treatment group and control are not reported.

32 The information provided currently in your dossier does not cover the specification(s) required by the OECD TG 201 and the information requirement is not fulfiled.

33 In the comments to the draft decision, you provided the missing information listed under points a) and b) above. The information you have provided in your comments addresses the incompliance.

34 However, as the information is currently not available in your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

3. Ready biodegradability

35 Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

3.1. Information provided

36 You have provided a ready biodegradability study according to OECD TG 301D (1993) with the Substance.

3.2. Assessment of information provided

3.2.1. The provided study does not meet the specifications of the test guideline

37 To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301D, the following requirements must be met:

38 Reporting of the methodology and results

a) insufficient information is provided on the dilution water to verify that it contained less than 10% of the organic carbon content introduced by the test material as required by the test guideline;
b) the results of measurements at each sampling point in each replicate is reported in a tabular form.

39 In provided study described as a study on ready biodegradability according to OECD TG 301D:

40 Reporting of the methodology and results

a) the organic carbon content of the dilution water is not reported.
b) the results of measurements at each sampling point in each replicate is not reported.

41 Based on the above and the information provided in your comments, the reporting of the study in the current dossier is not sufficient to conduct an independent assessment of its reliability. More specifically:

- the results of measurements are not provided. Therefore, ECHA cannot verify whether the general and specific validity criteria applicable to the OECD 301D are met;
- in the absence of adequate information on the dilution water, it cannot be verified whether its organic carbon content was low enough to ensure that it did not bias the measurement of degradation of the test material.

42 Therefore, the requirements of OECD TG 301 D are currently not met and the information requirement is not fulfilled.

43 In your comments, you submitted information on how the standard medium was prepared as well as the oxygen consumption of the water as a justification for not having measured the organic carbon content. You also provided the results of measurements at each sampling point in each replicate. The information you have provided in your comments addresses the incompliances identified in this decision for this information requirement. However, as the information is currently not available in your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

Reasons related to the information under Annex VIII of REACH

4. In vitro gene mutation study in mammalian cells

44 An in vitro gene mutation study in mammalian cells is an information requirement under Annex VIII, Section 8.4.3., in case of a negative result in the in vitro gene mutation test in bacteria and the in vitro cytogenicity test.

4.1. Triggering of the information requirement

45 Your dossier contains (I) a negative result for in vitro micronucleus study, and (II) inadequate data for the in vitro gene mutation study in bacteria.

46 The in vitro gene mutation study in bacteria provided in the dossier is rejected for the reasons provided in request 1.

47 The result of the request 1 will determine whether the present requirement for an in vitro mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

48 Consequently, you are required to provide information for this information requirement, if the in vitro gene mutation study in bacteria provides a negative result.

4.2. Information provided

49 You have adapted this information requirement by using Annex XI, Section 1.5. (Grouping of substances and read-across approach) based on experimental data from the following substances:

(i) *in vitro* gene mutation study in mammalian cells (2010) with the source substance phthalic anhydride, EC No. 201-607-5
(ii) *in vitro* gene mutation study in mammalian cells (2013) with the source substance [redacted], no EC No.

4.3. Assessment of the information provided

4.3.1. Read-across adaptation rejected

50 As explained in Section 0.1., the adaptation currently in your dossier based on grouping of substances and read-across approach under Annex XI, Section 1.5 is currently rejected.

51 Therefore, the information requirement is currently not fulfilled.

52 ECHA takes note that you provided a read-across justification document in your comments on the draft decision and that you indicated your intention to update the registration dossier accordingly.

53 As explained in Section 0.1, ECHA did not identify concerns regarding the read-across hypothesis provided in the justification document submitted with your comments. However, the justification document is currently not available in your registration dossier. You should therefore submit this information in an updated registration dossier by the deadline set out in the decision.

4.4. Specification of the study design

54 To fulfil the information requirement for the Substance, either the in vitro mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2012).
Guidance on intermediates; ECHA (2010).
All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017).
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs; ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

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

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 07 December 2021.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and did not amend the requests or 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 adopted the decision under Article 51(3) of REACH.

Appendix 3: Addressees of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. Test methods, GLP requirements and reporting

(1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

(2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)
The Test Material used to generate the new data must be selected taking into account the following:
- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

(2) Information on the Test Material needed in the updated dossier
- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[3].

[2] https://echa.europa.eu/practical-guides
[3] https://echa.europa.eu/manuals