~~Confidential~~

Helsinki, 18 January 2024

Addressees
Registrants of JS_FR-370_19186-97-1 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
21 February 2018

Registered substance subject to this decision ("the Substance")
Substance name: tris[3-bromo-2,2-bis(bromomethyl)propyl] phosphate
EC/List number: 413-060-1

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 ***27 April 2026***.

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: Bacterial reverse mutation test OECD TG 471 (2020)) using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102.

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

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

3. *In vitro* micronucleus study (Annex VIII, Section 8.4.2., test method: OECD TG 487). The aneugenic potential of the Substance must be assessed with an additional control group for aneugenicity on top of the control group for clastogenicity, if the Substance induces an increase in the frequency of micronuclei.

4. Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, *in vitro* gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: EU B.17./OECD TG 476 or EU B.67./OECD TG 490).

5. Long-term toxicity testing on fish (triggered by Annex VIII, Section 9.1.3., column 2; test method: EU C.47./OECD TG 210)

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.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

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

Reasons related to the information under Annex VII of REACH

1. *In vitro* gene mutation study in bacteria

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

1.1. Information provided

2 You have provided an *in vitro* gene mutation study in bacteria (1990) with the Substance.

1.2. Assessment of the information provided

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

3 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);

4 In the provided study:

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

5 The information provided does not cover the specification(s) required by the OECD TG 471.

6 Therefore, the information requirement is not fulfilled.

7 In your comments to the draft decision, you agree to perform the requested study.

1.3. Study design

8 To fulfil the information requirement for the Substance, the in vitro gene mutation study in bacteria (OECD TG 471, 2020) should be performed using one of the following strains: E. coli WP2 uvrA, or E. coli WP2 uvrA (pKM101), or S. typhimurium TA102.

2. Growth inhibition study aquatic plants

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

2.1. Information provided

10 You have provided a Growth inhibition study on aquatic plants/algae (1993) 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

11 To fulfil the information requirement, a study must comply with OECD TG 201 and the specifications of OECD GD 23 if the substance is difficult to test (Article 13(3) of REACH). The Substance is difficult to test as it has low water solubility (0.0156 mg/L) and high adsorptive properties (Log K_{ow} = 4.87 and Log K_{oc} >5.6). Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

a) the pH of the control medium does not increase by > 1.5 units;

Reporting of the methodology and results

b) the test conditions are reported (*e.g.*, composition of the test medium, vehicle);

c) adequate information on the analytical method (including performance parameters of the method) and on the results of the analytical determination of exposure concentrations is provided;

d) as explained above the Substance is difficult to test. Therefore, the following additional information must be provided:

- the results of a preliminary solubility and stability study,
- a description of the methods used to prepare stock and test solutions,
- if the test material is tested at the saturation concentration, evidence that all reasonable efforts have been taken to achieve a saturation concentration.

12 In the provided study:

Technical specifications impacting the sensitivity/reliability of the test

a) the pH increase in the controls was 2 units, i.e. from pH 8.2 to 10.2;

Reporting of the methodology and results

b) on the test conditions, you have not specified composition of the test medium and identity and concentration of the carrier solvent;

c) on the analytical method adequate information, i.e. performance parameters of the method such as accuracy, application range, recovery rate, limit of detection/quantification and selectivity are not reported. In addition, the results of the analytically determined exposure concentrations are not provided;

d) as explained above the Substance is difficult to test. Therefore, the following additional information must be provided:

- the results of a preliminary solubility and stability study,
- a description of the methods used to prepare stock and test solutions,
- if the test material is tested at the saturation concentration, evidence that all reasonable efforts have been taken to achieve a saturation concentration.

13 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More specifically, the pH of the test solutions increased more than the TG 201 allows and therefore, the reliability of the test results is questionable.
- the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, the composition of the test medium is not provided and it is not known that the used medium contained all necessary components to guarantee healthy and normal growth of algae. Also, the identity and concentration of the carrier solvent are not provided and since the solvent may influence the growth of algae, the identity and concentration must be reported that their acceptability of the solvent use can be assessed. Finally, in the absence of the information listed under points c) and d) above, you have not demonstrated that test organisms were satisfactorily exposed to the test material during the exposure phase.

14 On this basis, the specifications of OECD TG 201 are not met.

15 Therefore, the information requirement is not fulfilled.

16 From your comments to the draft decision, ECHA understands that you agree to perform the requested study.

2.3. Study design

17 The Substance is difficult to test due to the low water solubility (0.0156 mg/L) and adsorptive properties (Log K_{ow} = 4.87 and Log K_{oc} >5.6). OECD TG 201 that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 201. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

18 In your comments to the draft decision, you state that you intend to conduct a limit test at the limit of solubility of the Substance.

19 ECHA takes note of your comments and emphasizes that a limit test at the limit of solubility of the Substance is considered adequate to meet the information requirement only if no effects are observed at the limit of solubility. If relevant effects are observed at the limit dose, a full test may be required to obtained quantitative figures for the purpose of classification and labelling and risk assessment (ECHA Guidance on IRs and CSA, Section 7.8.5.).

Reasons related to the information under Annex VIII of REACH

3. *In vitro* micronucleus study

20 An in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study is an information requirement under Annex VIII, Section 8.4.2.

3.1. Information provided

21 You have provided an *in vitro* cytogenicity study in mammalian cells (1993) with the Substance.

3.2. Assessment of the information provided

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

22 To fulfil the information requirement, the study has to be an in vitro chromosomal aberration test or an in vitro micronucleus test conducted in mammalian cells. The study must comply with the OECD TG 473 or the OECD TG 487, respectively (Article 13(3) of REACH). Therefore, the following specifications must be met:

e) data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures is reported;

f) to conclude on a negative outcome, a negative response is obtained in all three experimental conditions described in paragraph 28 of OECD TG 473, using a short-term treatment with and without metabolic activation and long-term treatment without metabolic activation.

23 In the provided study:

a) data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures were not reported;

b) two experimental conditions described in paragraph 28 of OECD TG 473 (i.e. a short-term treatment without metabolic activation and a long-term treatment with metabolic activation) are missing to conclude on a negative outcome.

24 The information provided does not cover the specifications(s) required by the OECD TG 473.

25 Therefore, the information requirement is not fulfilled.

26 In your comments to the draft decision, you agree to perform the requested study.

3.3. Study design

27 According to the Guidance on IR & CSA, Section R.7.7.6.3., either the in vitro mammalian chromosomal aberration ("CA") test (test method OECD TG 473) or the in vitro mammalian cell micronucleus ("MN") test (test method OECD TG 487) can be used to investigate chromosomal aberrations in vitro. However, while the MN test detects both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the CA test detects only clastogenicity, as OECD TG 473 is not designed to measure aneuploidy (see OECD TG 473, paragraph 2).Therefore, you must perform the MN test (test method OECD TG 487), as it enables a more comprehensive investigation of the chromosome damaging potential in Vitro. Moreover, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen [1] (OECD TG 487, paragraphs 33 to 35).

3.3.1. Assessment of aneugenicity potential

28 If the result of the MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance.

29 In line with the OECD TG 487 (paragraph 4), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

[1] According to the TG 487 (2016) "At the present time, no aneugens are known that require metabolic activation for their genotoxic activity" (paragraph 34).

4. *In vitro* gene mutation study in mammalian cells

30 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

31 Your dossier contains data for an in vitro gene mutation study in bacteria, and data for an in vitro cytogenicity study in mammalian cells or in vitro micronucleus study.

32 The information for the in vitro gene mutation study in bacteria and for the in vitro cytogenicity study in mammalian cells or in vitro micronucleus study provided in the dossier are rejected for the reasons provided in requests 2 and 4.

33 The result of the requests for an in vitro gene mutation study in bacteria and for an in vitro cytogenicity study in mammalian cells 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.

34 Consequently, you are required to provide information for this information requirement, if the in vitro gene mutation study in bacteria (the missing fifth strain) and the in vitro micronucleus study provides a negative result.

4.2. Information provided

35 You have provided an *in vitro* gene mutation study in mammalian cells (1995) with the Substance.

4.3. Assessment of the information provided

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

36 To fulfil the information requirement, a study must comply with the OECD TG 476 or the OECD TG 490 (Guidance on IRs and CSA, Table.7.7-2) (Article 13(3) of REACH). Therefore, the following specifications must be met:

a) the maximum concentration tested induces 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test concentration corresponds to 10 mM, 2 mg/mL or 2 µL/mL, whichever is the lowest;

b) the concurrent positive controls induce responses that are compatible with those generated in the historical positive control database and does not induce more than 90% of cytotoxicity compared to the negative control

c) the concurrent positive controls produce a statistically significant increase compared with the concurrent negative control.

d) the negative control data is ideally within the 95% control limits of the distribution of the laboratory's historical negative control.

e) data on the cytotoxicity and the mutation frequency for the treated and control cultures are reported.

37 In the provided study:

a) the maximum tested concentration did not induce 80-90% of cytotoxicity compared to the negative control, or the precipitation of the tested substance, and it was less than 10 mM, 2 mg/mL or 2 µL/mL; In the comments to the draft decision you provide the information on the top dose (i.e. 5000 µL/mL).

b) the positive control did not induce responses that are compatible with those generated in the historical positive control database and/or induces more than 90% of cytotoxicity compared to the negative control; In the comments to the draft decision you provide information on the historical control data.

c) the positive control did not produce a statistically significant increase in the induced response when compared with the concurrent negative control. In the comments to the draft decision you provide data on the response of the positive and negative controls.

d) the response of the negative control was not inside the historical control range of the laboratory. In the comments to the draft decision you provide the historical control range data for the negative controls.

e) data on the cytotoxicity and the mutation frequency for the treated and control cultures were not reported. In the comments to the draft decision you provide the experimental data of the four trials.

38 In your comments to the draft decision, you address the study deficiencies identified above. However, as the information is currently not available in your registration dossier, the data gap remains. You should therefore submit this information in an updated registration dossier by the deadline set in the decision.

39 Therefore, the information requirement is currently not fulfilled.

4.4. Study design

40 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.

5. Long-term toxicity testing on fish

41 Short-term toxicity testing on fish is an information requirement under Annex VIII, Column 1, Section 9.1.3. However, long-term toxicity testing on fish may be required by the Agency (Section 9.1.3., Column 2) if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

5.1. Triggering of the information requirement

42 As already explained in Request 3, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

43 Therefore, the Substance is poorly water soluble and information on long-term toxicity on fish must be provided.

5.2. Information provided

44 You have provided the following statement: "*The acute toxicity studies for aquatic organisms show no toxicity to fish, daphnia and algae at test concentrations higher than water solubility of the substance. A long term toxicity study was performed on daphnia. No toxic effects were found for adults and no effects on reproduction were observed at concentrations higher than water solubility of the substance. In addition, the Bioconcentration factor (BCF) is 200 indicating that the substance is unlikely to bioaccumulate in aquatic organisms. Therefore, additional long term study to aquatic organism is not necessary.*"

5.3. Assessment of information provided

5.3.1. Your justification to omit the study has no legal basis

45 A registrant may only adapt this information requirement based on the general rules set out in Annex XI or column 2 of the relevant information requirement.

46 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH or column 2 of the relevant information requirement and the legal basis you would be relying on for your intended adaptation is not apparent to ECHA.

47 Therefore, you have not demonstrated that this information can be omitted.

48 Minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI or Annex IX, Section 9.1., Column 2.

49 Therefore, the information requirement is not fulfilled.

5.4. Study design

50 To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (Guidance on IRs and CSA, Section R.7.8.2.).

51 OECD TG 210 specifies that, for difficult to test substances, OECD GD 23 must be followed. As already explained above, the Substance is difficult to test. Therefore, you must fulfil the requirements described in "Study design" under Request 2.

52 In your comments to the draft decision, you state that you intend to conduct a limit test at the limit of solubility of the Substance.

53 ECHA takes note of your comments and emphasizes that a limit test at the limit of solubility of the Substance is considered adequate to meet the information requirement only if no effects are observed at the limit of solubility. If relevant effects are observed at the limit dose, a full test may be required to obtained quantitative figures for the purpose of classification and labelling and risk assessment (ECHA Guidance on IRs and CSA, Section 7.8.5.).

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 24 August 2022.

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 amended the request. More specifically, you have provided comments during the decision-making phase which were found to address the incompliance identified in the draft decision. Therefore the original request for Skin sensitisation (Annex VII, Section 8.3.) was removed.

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: Addressee(s) 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]
[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 (https://echa.europa.eu/practical-guides).

(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.

With that detailed information, ECHA can confirm 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 (https://echa.europa.eu/manuals).