~~Confidential~~

Helsinki,26 May 2023

Addressees
Registrant(s) of JS_Tetrabromophthalic_anh as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
09 July 2018

Registered substance subject to this decision ("the Substance")
Substance name: Tetrabromophthalic anhydride
EC number: 211-185-4

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 the deadline of ***02 June 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);

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

2. If negative results are obtained in the test 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);

3. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below;

4. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats.

The reasons for the decision(s) 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 decision
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 decision

Contents

0. Reasons common to several requests

0.1. Assessment of the read-across approach

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.);
- Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.).

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.

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.

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).

Predictions for toxicological properties

You predict the properties of the Substance from information obtained from the source substance tetrachlorophthalic anhydride (TCPA), EC No. 204-171-4.

We have identified the following issue with the predictions of toxicological properties:

0.1.1. Absence of read-across documentation

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).

You have provided robust study summaries for studies conducted with another substance than the Substance in order to comply with the REACH information requirements. However, you have not provided documentation 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).

In the absence of such documentation, you have not demonstrated that the properties of the Substance cannot be reliably predicted from the data on the source substance.

0.1.2. Adequacy and reliability of source studies

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

(1) have adequate and reliable coverage of the key parameters addressed in the

corresponding study that shall normally be performed for a particular information requirement.

Specific reasons why the studies on the source substance do not meet these criteria are explained further below under the applicable information requirement section 1. Therefore, no reliable predictions can be made for these information requirements.

0.1.3. Conclusion on the read-across approach

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 approaches under Annex XI, Section 1.5. are rejected.

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

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

1.1. Information provided

You have adapted this information requirement by using a Grouping of substances and read-across approach based on the following experimental data:

(i) *in vitro* gene mutation study in bacteria according (1993) with the source substance TCPA, EC 204-171-4, flagged as key study.

You have also provided the following study:

(ii) *in vitro* gene mutation study in bacteria, OECD TG 471 (1979), with the Substance, flagged as supporting study.

1.2. Assessment of the information provided

We have assessed this information and identified the following issue(s):

1.2.1. Read-across adaptation rejected

1.2.1.1. Absence of read-across documentation

Study (i) is performed with the source substance TCPA. As explained in Section 0.1, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected.

1.2.1.2. Adequacy of the source study (i)

According to Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case EU B.13/14/OECD TG 471.

Therefore, the following specification must be met: 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).

The study (i) is described as an *in vitro* gene mutation study on bacteria.

However, the following specification is not according to the requirements of the EU B.13/14/OECD TG 471: the test was performed with the strains *S. typhimurium* TA 1535, TA 1537, TA 98 and TA 100 (i.e., the strain *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is missing).

Therefore, the study (i) submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameters of the corresponding OECD TG.

1.2.1.3. Conclusion on the read-across approach

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

1.2.2. The provided study (ii) does not meet the information requirement

To fulfil the information requirement, a study must comply with EU B.13/14/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);
b) the maximum dose tested induces a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance. If no precipitate or limiting cytotoxicity is observed, the highest test dose corresponds to 5 mg/plate or 5 µl/plate;

The study (i) is described as an *in vitro* gene mutation study in bacteria.

However, the following specifications of study (ii) are not according to the requirements of the EU B.13/14/OECD TG 471:

a) the test was performed with the strains S. typhimurium TA 1535, TA 1537, TA1538, TA 98 and TA 100 (i.e., the strain *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is missing);
b) the maximum dose tested (1000 ug/plate) did not induced a reduction in the number of revertant colonies per plate compared to the negative control, or the precipitation of the tested substance and it was less than 5 mg/plate or 5 ml/plate;

The information provided from study (ii) does not cover the key parameter(s) required by the EU B.13/14/OECD TG 471.

For all the reasons above, the information requirement is not fulfilled.

1.3. Specification of the study design

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

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

Reasons related to the information under Annex VIII of REACH

2. In vitro gene mutation study in mammalian cells

Your dossier and your comments on the draft decision contain (I) a negative result for *in vitro* cytogenicity study in mammalian cells, and (II) no data or inadequate data for the other study (*in vitro* gene mutation study in bacteria).

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

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.

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

2.1. Information provided

ECHA understands that you have also adapted this information requirement by using Annex VIII, Section 8.4.3., Column 2. To support the adaptation, you have provided the following information on the source substance TCPA, EC 204-171-4:

(i) somatic mutation and recombination test in Drosophila, gene mutation test (1993)

2.2. Assessment of the information provided

We have assessed this information and identified the following issue(s):

2.2.1. The provided adaptation does not meet the criteria of Annex VIII, Section 8.4.3., Column 2

Under Annex VIII, Section 8.4.3., Column 2, the study may be omitted if adequate data from a reliable *in vivo* mammalian gene mutation test are available. The Guidance on IRs and CSA, Section R.7.7.6.3. clarifies that the *in vivo* study must be a Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay (TGR), performed according to the OECD TG 488. This test investigates gene mutations using reporter genes.

The study (i) is described as a somatic mutation and recombination test in Drosophila. This test detects the occurrence of mutations, both point mutations and small deletions, in the germ line of an insect. However, since this study was conducted in insects it does not investigate gene mutation in mammalian cells as the TGR.

Therefore, the requirements of Annex VIII, Section 8.4.3., Column 2 are not met and your adaptation is rejected already for this reason.

2.2.2. Read-across adaptation rejected

Furthermore, the study (i) is performed with the source substance TCPA. As explained in Section 0.1, your grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected. Therefore this study cannot be used to adapt the information requirement according to Annex VIII, Section 8.4.2., Column 2. Specification of the study design

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.

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

3. Short-term repeated dose toxicity (28 days)

A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1.

Under Annex VIII, Section 8.6.1., Column 2, Paragraph 1, Indent 1, the study may be omitted if a reliable sub-chronic (90 days) or chronic toxicity study is available or proposed by the registrant, provided that appropriate species, dosage, solvent and route of administration are used.

Annex VIII, 8.6.1 column 2 sets the conditions whereby testing by the dermal route or by the inhalation route are more appropriate than testing by the default oral route of administration.

More specifically, testing by the dermal route is appropriate if:
(1) Inhalation of the substance is unlikely; and
(2) skin contact in production and/or use is likely; and
(3) the physicochemical properties suggest a significant rate of absorption through the skin.

Testing by the inhalation route is appropriate if exposure of humans via inhalation is likely taking into account the vapour pressure of the substance and/or the possibility of exposure to aerosols, particles or droplets of an inhalable size.

According to the information provided in the dossier, testing by the dermal route is not appropriate, among others, because:

- skin contact is unlikely during production/use;
- there is no data from *in vitro* tests indicating significant dermal absorption or data on structurally-related substances indicating significant dermal toxicity or dermal penetration.

Furthermore, testing by the inhalation route is not considered appropriate because the Substance has a vapour pressure of 2.7E-6 Pa. According to the information provided in the dossier, the Substance is a solid with a D90 of 100 µm and a D50 of 23 µm. As there is no spraying application under the conditions of use, the potential for exposure to aerosols or particles of an inhalable size is not likely.

Based on this information, ECHA considers that the oral route is the most appropriate route of administration, and data in the registration dossier generated via the dermal and inhalation routes is not considered adequate to meet the information requirement. Therefore, only the data generated via the oral route and included in the dossier is addressed in the following.

3.1. Information provided

Regarding data generated in studies with oral administration, you have provided the following experimental data on the source substance TCPA, EC 204-171-4:

(i) 90-Day Oral Toxicity in Rodents (rat) (1993);

(ii) 90-Day Oral Toxicity in Rodents (mouse) (1993).

3.2. Assessment of the information provided

We have assessed this information and identified the following issue.

As indicated above, information on a 28 days study may be omitted if a reliable sub-chronic (90 days) or chronic toxicity study is available, provided that appropriate species, dosage, solvent and route of administration are used.

Studies (i) and (ii) are 90 days sub-chronic studies performed with the source substance TCPA and oral route of administration. However, as explained in Section 0.1, your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5 is rejected due to absence of read-across documentation. Therefore the studies (i) and (ii) on the source substance TCPA cannot be used to omit a short-term repeated dose toxicity study (28 days) on the substance.

On this basis, your adaptation according to Annex VIII, Section 8.6.1., Column 2, Paragraph 1, first indent is rejected and the information requirement is not fulfilled.

3.3. Study design

When there is no information available neither for the 28-day repeated dose toxicity (EU B.7, OECD TG 407) nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided. (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

The study design is further addressed in section 4.3 below.

4. Screening for reproductive/developmental toxicity

A screening for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1., if there is no evidence from analogue substances, QSAR or in vitro methods that the substance may be a developmental toxicant.

4.1. Information provided

You have not submitted any information for this requirement.

4.2. Assessment of the information provided

4.2.1. No information provided

You have not provided any information for this information requirement.

On this basis, the information requirement is not fulfilled.

4.3. Specification of the study design

When there is no information available neither for the 28-day repeated dose toxicity study (EU B.7, OECD TG 407) nor for the screening study for reproductive/developmental toxicity (OECD TG 421 or TG 422), the conduct of a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) is preferred to ensure that unnecessary animal testing is avoided (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

The information requirement for the 28-day repeated dose toxicity study is not fulfilled for the reasons explained under request 3.

Therefore, a study according to the test method EU B.64/OECD TG 422 must be performed in rats.

As the Substance is a solid, the study must be conducted with oral administration of the Substance (Annex VIII, Section 8.7.1., Column 1).

In the comments to the draft decision, you agree to generate the requested information, and specified you will conduct a study according to OECD TG 422.

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).

All Guidance on REACH is 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 16 June 2021.

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

ECHA took into account your comments and your tonnage downgrade and amended the request(s).

You have provided comments during the decision-making phase which were found to address an incompliance identified in the draft decision. You included this information in an update of your registration dossier (submission number [redacted]). Therefore the original request for an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study was removed.

You have also provided comments during the decision-making phase indicating a tonnage band downgrade. You included this information in an update of your registration dossier (submission number [redacted]). As a result of this change of registration tonnage band, the requests for a sub-chronic study, a pre-natal developmental toxicity study, simulation testing on ultimate degradation in surface water and identification of degradation products were removed from the decision.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments and referred the modified 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-82 written procedure and ECHA took the decision according to Article 51(6) of the REACH Regulation.

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]

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

(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 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.

This information is needed to assess whether the Test Material is relevant for the Substance.

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