~~Confidential~~

Helsinki, 06 June 2024

Addressees
Registrants of JS_Full_1530-48-9 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
22 August 2019

Registered substance subject to this decision ("the Substance")
Substance name: allyltributylphosphonium chloride
EC/List number: 216-231-7

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 ***11 September 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. Skin sensitisation (Annex VII, Section 8.3.)
   a) *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.); and
   b) only if the *in vitro/in chemico* test methods specified under point a) above are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429).

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

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

The reasons for the request(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 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)

Reasons common to several requests

0.1. QSAR adaptation rejected

1 You seek to adapt the following standard information requirements by applying (Q)SAR approaches in accordance with Annex XI, Section 1.3.:

- Skin sensitisation (Annex VII, Section 8.3.)
- *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)

2 ECHA has considered the scientific and regulatory validity of your (Q)SAR adaptations in general before assessing the specific standard information requirements in the following appendices.

3 Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

(2) the prediction needs to be derived from a scientifically valid model,

(3) the substance must fall within the applicability domain of the model,

(4) results need to be adequate for the purpose of risk assessment or classification and labelling, and

(5) adequate and reliable documentation of the method must be provided.

0.1.1. (Q)SAR for toxicological properties

0.1.1.1. The QSAR result is not equivalent to results obtained from the required experimental test

4 Results from (Q)SAR models are adequate for risk assessment or classification and labelling when they are equivalent to results obtained from the required experimental test.

5 For the in vitro gene mutation study in bacteria, the corresponding study that must normally be performed in bacteria is OECD TG 471. The OECD TG 471 require that two separate test conditions are assessed: in absence of metabolic activation and in presence of metabolic activation.

6 For the skin sensitisation, the *in vitro/in chemico* studies (OECD TG 442C, 442D and 442E) or the in vivo OECD TG 429 test are considered suitable. To conclude based on in silico/(Q)SAR predictions on whether the substance is a skin sensitiser, a potential for substances requiring metabolic activation before becoming sensitisers must be considered. Metabolic activation must be taken into account in the *in vitro/in chemico* testing strategies and in the *in vivo* studies that are considered suitable under REACH.

7 You have provided:

- predictions for an impurity as non-mutagenic by the SciQSAR, LeadScope and Case Ultra models in the Danish QSAR Database without metabolic activation;
- predictions for a main constituent as a non-sensitiser and as inactive for in vitro mutagenicity in E.coli and in S. typhimurium based on Derek Nexus without consideration for metabolic activation.

8 The model predicts in vitro gene mutation in bacteria and skin sensitisation but do not consider potential (a)biotic metabolism of the Substance. Therefore, the prediction is not adequate to meet the information requirement for in vitro gene mutation in bacteria and skin sensitisation for the purpose of classification and labelling and/or risk assessment.

0.1.1.2. Inappropriate measures of robustness of the model

9 The Guidance on IRs and CSA R.6.1.3. states that for (Q)SAR models, to be scientifically valid, i.e. condition (1), they must fulfil the principles listed in the OECD Principles for (Q)SAR validation (ENV/JM/MONO(2007)2). The fourth of these principles requires that a model has appropriate measures of the internal performance (i.e. goodness-of-fit and robustness) and predictivity.

10 For the main constituent and the impurities of the Substance, you use a Toolbox profiler to make a prediction for the endpoints skin sensitisation and genetic toxicity without measures of internal performance and predictivity of the profiler for the prediction of this endpoint.

11 Toolbox profilers are models developed for the purpose of identifying analogues and not to make predictions (as indicated on the official QSAR Toolbox website https://qsartoolbox.org/features/profiling/). In absence of measures of internal performance and predictivity, a profiler is not considered a scientifically valid approach to meet this information requirement.

0.1.1.3. Inadequate documentation of the prediction (QPRF)

12 ECHA Guidance R.6.1.6.3. states that the information specified in or equivalent to the (Q)SAR Prediction Reporting Format document (QPRF) must be provided to have adequate and reliable documentation of the applied method. For a QPRF this includes, among others:

- the relationship between the modelled substance and the defined applicability domain;
- the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

13 You provided the following information about the prediction:

- predictions for an impurity as non-mutagenic by the SciQSAR, LeadScope and Case Ultra models in the Danish QSAR Database;
- predictions for a main constituent as a non-sensitiser and as inactive for in vitro mutagenicity in E.coli and in S. typhimurium based on Derek Nexus.

14 The information you provided about the prediction lacks the following elements:

- information to independently verify that the substance falls within the applicability domain as described in the QMRF of the models, and
- information on analogues and how their predicted and experimental data supports the prediction.

15 In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

0.1.2. Conclusion

16 Based on the above, your (Q)SAR adaptation under Annex XI, Section 1.3. is rejected.

Reasons related to the information under Annex VII of REACH

1. Skin sensitisation

17 Skin sensitisation is an information requirement under Annex VII, Section 8.3. Under Section 8.3., Column 1, the registrants must submit information allowing (1) a conclusion whether the substance is a skin sensitiser and (2) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

1.1. Information provided

18 You have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs). To support the adaptation, you have provided the following information:

(i) a prediction from QSAR Nexus DEREK v 6.0.1 (2018);

(ii) a prediction from OECD QSAR Toolbox v4.2 (2018).

1.2. Assessment of the information provided

1.2.1. Assessment whether the Substance causes skin sensitisation

1.2.1.1. (Q)SAR adaptation rejected

19 As explained in Section 0.1., your adaptation based on Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs) under Annex XI, Section 1.3. is rejected.

1.2.2. No assessment of potency

20 To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

21 As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section 1.2.1. above), this condition cannot be assessed.

22 Therefore, the information requirement is not fulfilled.

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

1.3. Study design

24 To fulfil the information requirement for the Substance, information on molecular interaction with skin proteins and inflammatory response in keratinocytes and activation of dendritic cells (OECD TG 442C and OECD TG 442D and OECD TG 442E) must be provided. Furthermore an appropriate risk assessment is required if a classification of the Substance as a skin sensitiser (Cat 1A or 1B) is warranted.

25 In case no conclusion on the skin sensitisation potency can be made for the Substance based on the existing data or newly generated *in vitro/in chemico* data, in vivo skin sensitisation study must be performed and the murine local lymph node assay (EU Method B.42/OECD TG 429) is considered as the appropriate study for the potency estimation.

2. *In vitro* gene mutation study in bacteria

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

2.1. Information provided

27 You have adapted this information requirement by using Annex XI, Section 1.3. (Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs). To support the adaptation, you have provided the following information:

(i) a prediction from QSAR Nexus DEREK v 6.0.1(2018);

(ii) a prediction from OECD QSAR Toolbox v4.2 (2018);

(iii) a prediction from Danish QSAR Database (2018).

2.2. Assessment of the information provided

2.2.1. (Q)SAR adaptation rejected

28 As explained in Section 0.1., your adaptation based on Qualitative or Quantitative Structure-Activity Relationships ((Q)SARs) under Annex XI, Section 1.3. is rejected.

29 In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

30 Therefore, the information requirement is not fulfilled.

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

3. Growth inhibition study aquatic plants

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

3.1. Information provided

33 You have provided:

(i) Growth inhibition study on aquatic plants/algae (2019) 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(s)

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

Reporting of the methodology and results

a) the test design is reported (*e.g.*, number of replicates)

b) the test conditions are reported (e.g., biomass density at the beginning of the test);

c) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

35 In study (i):

Reporting of the methodology and results

a) on the test design, you have not specified the number of replicates;

b) on the test conditions, you have not specified biomass density at the beginning of the test;

c) tabulated data on the algal biomass determined daily for each treatment group and control are not reported;

36 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically, as you have not provided information on the number of replicates and on the algae biomass at the beginning of the test, ECHA cannot verify that the test has been conducted under condition that are consistent with the OECD TG 201 requirements. Furthermore, in the absence of raw biomass data, ECHA cannot conduct an independent assessment as to whether the validity criteria of the test quideline have ben met..

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

38 In your comments to the draft decision, you provide information on the missing technical specifications and results of the study listed above. You have also attached a copy of a Robust Study Summary (RSS) that includes the information listed above as missing in the dossier. 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 In the meantime, the information requirement is not fulfilled.

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 (2023).
***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 22 February 2023.

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.

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]

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.

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).