~~Confidential~~

Helsinki, 05 May 2023

Addressee
Registrant listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
29/08/2011

Registered substance subject to this decision ("the Substance")
Substance name: Butyl (dialkyloxy(dibutoxyphosphoryloxy))titanium(trialkyloxy)titanium phosphate
EC/List number: 401-100-0

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

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

2. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) by oral route, in rats

A screening for reproductive / developmental toxicity (2016), is available in the jointly submitted registration for the Substance (Registration No. [redacted]). Under Article 26(3) of REACH, you must not repeat a study involving vertebrate animals conducted on the Substance.

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

3. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats

4. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

5. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

6. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210)

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

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0. Reasons common to several requests

0.1. Assessment of exposure-based adaptation

1 ECHA understands that you have adapted the following standard information requirement(s) under Annex XI, Section 3.2 (a) and (b) substance-tailored exposure-driven testing

- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

2 ECHA assessed this information and identified the following issues:

3 A substance-tailored exposure-driven testing adaptation must fulfil the cumulative conditions set out under Annex XI, Sections 3(1) as well as 3(2)(a), (b) or (c).

4 Under Annex XI, Section 3(2)(a)(i), the results of the exposure assessment covering all relevant exposure throughout the life cycle of the substance must demonstrate absence of or no significant exposure in all scenarios of the manufacture and all identified uses.

5 As an example, in worker exposure scenario [redacted] workplace measurements of [redacted] are recorded. The measurements are for another ingredient of the mixture. Nevertheless this demonstrates significant exposure. When the exposure is compared with the DNEL, the resulting RCRs are [redacted]. Based on this information, you have not demonstrated absence of or no significant exposure in all scenarios of the manufacture and all identified uses.

6 Under Annex XI, Section 3(2)(b)), it must be demonstrated and documented for all relevant scenarios that throughout the life cycle strictly controlled conditions as set out in Article 18(4)(a) to (f) apply (see further Guidance on Intermediates and Practical Guide 16).

7 You have provided a claim of strictly controlled conditions without any documentation.

8 The Substance is not handled under strictly controlled conditions as demonstrated by your exposure estimates discussed in the previous paragraph. In particular, condition (a) as set out in Article 18(4) does not appear to be fulfilled because it has not been demonstrated that the substance is rigorously contained by technical means during its whole lifecycle.

9 Therefore, the use of the Substance under strictly controlled conditions is not demonstrated.

0.1.1. Conclusion

10 Based on the above, your adaptations are rejected.

Reasons related to the information under Annex VII of REACH

1. In vitro gene mutation study in bacteria

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

1.1. Information provided

12 You have provided:

i. In vitro gene mutation study in bacteria (1986).

1.2. Assessment of the information provided

13 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).

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

15 However, the following specifications are not according to the requirements of the OECD TG 471:

a) the test was performed with the strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 (i.e., the strain TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101) is missing).

16 The information provided does not cover the key parameter(s) required by the OECD TG 471.

17 Therefore, the information requirement is not fulfilled.

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

1.3. Specification of the study design

19 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.

Reasons related to the information under Annex VIII of REACH

2. Screening for reproductive/developmental toxicity

20 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.

2.1. Information provided

21 You have adapted this information requirement by using substance-tailored exposure-driven testing as presented in section 0.1.

2.2. Assessment of the information provided

22 The Screening study for reproductive/developmental toxicity does not need to be conducted if relevant human exposure can be excluded in accordance with Annex XI, Section 3.

23 As explained in Section 0.1., your adaptation based on substance-tailored exposure-driven testing under Annex XI, Section 3. is rejected.

2.3. Specification of the study design

24 A study according to the test method EU B.63/OECD TG 421 or EU B.64/OECD TG 422 must be performed in rats.

25 The study must be conducted with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

26 Therefore, the study must be conducted in rats with oral administration of the Substance.

2.4. Information regarding data sharing obligations

27 The jointly submitted registration for the Substance contains a study according to OECD TG 421 (2016) which is adequate for this information requirement. In accordance with Title III of the REACH Regulation, you must request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

28 In the comments to the draft decision, you indicate that you will make every effort to reach an agreement on the sharing of data and costs for the available study (OECD TG 421, 2016).

Reasons related to the information under Annex IX of REACH

3. Sub-chronic toxicity study (90-day)

29 A sub-chronic toxicity study (90 day) is an information requirement under Annex IX, Section 8.6.2.

3.1. Information provided

30 You have provided:

(i) a repeated dose toxicity study (1986) with the Substance

31 You have also adapted this information requirement claiming that testing is not technically possible. To support the adaptation, you have provided the following justification:

> *"In the presence of most vehicles, the substance is subjected to solvolysis, and, in the presence of water polymeric complexes are formed. The substance was therefore administered rapidly using microsyringes. The difficulties attendant with this method of administration (partial or complete syringe blockage, mechanical trauma to stomach /oesophagus) are considerd to be the likely cause for the large number of unexplained deaths in this study, and for the noisy respiration, pallor and piloerection noted in all groups.*
>
> *At level 1 (100 tpa) histopathological examination was extended (using the stored tissues and organs from the 28 day study) to cover the full range of tissues investigated in an Annex V 90 -day study. No substance-related effects were observed in any tissue."*

3.2. Assessment of the information provided

3.2.1. Assessment of the study

32 To fulfil the information requirement, the sub-chronic toxicity study (90 day) has to meet the requirements of the OECD TG 408. Therefore, the following specifications must be met:

a) dosing of the Substance is performed daily for a minimum of 90 days.

33 In study (i) described as repeated dose toxicity study:

a) the exposure duration was limited to 28 days.

34 The information provided does not cover the specification(s) required by the OECD TG 408.

35 Therefore, the information requirement is not fulfilled.

3.2.2. Assessment of the adaptation

36 According to Annex XI Section 2, testing for a specific endpoint may be omitted, if it is technically not possible to conduct the study as a consequence of the properties of the substance.

37 You indicate that the Substance is subject to solvolysis, and in the presence of water form polymeric complexes. ECHA notes that there is a screening study for reproduction/developmental toxicity according to OECD TG 421 (2016) for your Substance,

where testing was performed via gavage up to limit dose. Therefore it seems possible to perform studies with the Substance and your adaptation is rejected.

38 On this basis, the information requirement is not fulfilled.

39 In the comments to the draft decision you agree with ECHA's assessment, and you indicate your intention to downgrade the tonnage band of your registration but no related dossier update was submitted by the time of the final adoption of this decision. Therefore, you must comply with all the requests in this decision that are relevant for the registered tonnage band indicated in your registration dosser at the time of adoption of this decision.

3.3. Specification of the study design

40 Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance; Guidance on IRs and CSA, Section R.7.5.6.3.2.

41 According to the OECD TG 408, the rat is the preferred species.

42 Therefore, the study must be performed in rats according to the OECD TG 408 with oral administration of the Substance.

4. Pre-natal developmental toxicity study in one species

43 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX, Section 8.7.2.

4.1. Information provided

44 You have adapted this information requirement by using substance-tailored exposure-driven testing as presented in section 0.1.

4.2. Assessment of the information provided

45 The PNDT study does not need to be conducted if relevant human exposure can be excluded in accordance with Annex XI, Section 3.

46 As explained in Section 0.1., your adaptation based on substance-tailored exposure-driven testing under Annex XI, Section 3. is rejected.

47 Therefore, the information requirement is not fulfilled.

48 In the comments to the draft decision you agree with ECHA's assessment, and you indicate your intention to downgrade the tonnage band of your registration but no related dossier update was submitted by the time of the final adoption of this decision. Therefore, you must comply with all the requests in this decision that are relevant for the registered tonnage band indicated in your registration dosser at the time of adoption of this decision.

4.3. Specification of the study design

49 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species.

50 The study must be performed with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

51 Therefore, the study must be conducted in rats or rabbits with oral administration of the Substance.

5. Long-term toxicity testing on aquatic invertebrates

52 Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

5.1. Information provided

53 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following information:

> *(i) "The chemical safety assessment does not indicate any likely exposure of the substance to the aquatic compartment. This test is unnecessary as the substancet is unstable (rapidly hydrolyses) and hydrolysis products are unlikely to adsorb to soil as they a solid (TiO2) and volatile liquids (IPA, ethanol and butyl phosphate).*

5.2. Assessment of the information provided

54 Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. It must be understood as a trigger for providing further information on aquatic invertebrates if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018). Your adaptation is therefore rejected.

55 Therefore, the information requirement is not fulfilled.

56 In the comments to the draft decision you agree with ECHA's assessment, and you indicate your intention to downgrade the tonnage band of your registration but no related dossier update was submitted by the time of the final adoption of this decision. Therefore, you must comply with all the requests in this decision that are relevant for the registered tonnage band indicated in your registration dosser at the time of adoption of this decision.

5.3. Study design and test specifications

57 The Substance is difficult to test due to the rapid hydrolysis (DT50 < 10 s). OECD TG 211 specifies 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 211. 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.

5.4. Information regarding data sharing

58 The jointly submitted registration for the Substance contains a study: VERTEC(TM) IA10: Daphnia Magna reproduction test (2008) which is adequate for this information

requirement. In accordance with Title III of the REACH Regulation, you may request it from the other registrants and then make every effort to reach an agreement on the sharing of data and costs (Guidance on data-sharing).

6. Long-term toxicity testing on fish

59 Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

6.1. Information provided

60 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided in section 6.1.2 of the IUCLID file the following information:

(i) REACH Annex IX 9.1: Study not needed as substance is readily biodegradable. The chemical safety assessment does not indicate a need for this test to be carried out as all identified uses are under strictly controlled conditions in dedicated facilities.
(ii) Chemical safety assessment does not indicate a need for long-term testing as the substance is hydrolytically unstable.

6.2. Assessment of the information provided

61 Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

62 Your adaptation is therefore rejected.

63 Therefore, the information requirement is not fulfilled.

64 In the comments to the draft decision you agree with ECHA's assessment, and you indicate your intention to downgrade the tonnage band of your registration but no related dossier update was submitted by the time of the final adoption of this decision. Therefore, you must comply with all the requests in this decision that are relevant for the registered tonnage band indicated in your registration dosser at the time of adoption of this decision.

6.3. Study design and test specifications

65 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.).

66 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 and test specifications' under Request 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).

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 31 August 2021.

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

ECHA took into account your comments and did not amend the request(s).

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 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;

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

Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

a) the boundary composition(s) of the Substance,
b) 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.

Information on the Test Material needed in the updated dossier

a) 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.
b) The reported composition must include the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

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

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

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

2. General recommendations for conducting and reporting new tests

2.1. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in Guidance on IRs & CSA, Section R.11.4.2.2, you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

References to Guidance on REACH and other supporting documents can be found in Appendix 1.

[3] https://echa.europa.eu/manuals