~~Confidential~~

Helsinki, 16 May 2024

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

Date of submission of the dossier subject to this decision
23 June 2020

Registered substance subject to this decision ("the Substance")
Substance name: Phosphorous acid, mixed 2,4-bis(1-methyl-1-phenylethyl)phenyl and isodecyl and 2-(1-methyl-1-phenylethyl)phenyl and 4-(1-methyl-1-phenylethyl)phenyl and phenol triesters)
EC/List number: 852-824-2

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

DECISION ON A COMPLIANCE CHECK

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

Requested information must be generated using the Substance unle 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).

2. Long-term toxicity testing on aquatic invertebrates (triggered by Annex VII, Section 9.1.1., Column 2; test method: EU C.20./OECD TG 211).

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 addressee of the decision and its corresponding information requirements based on registered tonnage band are listed in Appendix 3.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

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

Appeal

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

Failure to comply

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

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

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

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons for the request(s)

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 the following information in Section 7.6. (Genetic toxicity):

(i) *in vitro* gene mutation study in bacteria (1980), performed with Phosphite; Phosphorous acid, diisodecyl phenyl ester EC 247-098-3;
(ii) *in vitro* DNA damage and repair (1971), preformed with Phosphite; Phosphorous acid, diisodecyl phenyl ester EC 247-098-3;
(iii) *in vitro* DNA damage and repair (1981), performed with Phosphorus acid, triisodecyl ester EC 246-998-3;
(iv) *in vitro* gene mutation in bacteria (2014), performed with triisotridecyl phosphite EC 278-758-9;
(v) *in vitro* gene mutation in bacteria (1981), performed with Phosphorus acid, triisodecyl ester EC 246-998-3;
(vi) *in vitro* mammalian cells micronucleus test (2017), performed with Phosphorous acid, triphenyl ester EC 202-908-4; triphenyl phosphate EC 204-112-2;
(vii) *in vitro* gene mutation study in mammalian cells (2018), performed with triisotridecyl phosphite EC 278-758-9;
(viii) *in vivo* erythrocyte micronucleus test (1981), performed with Phosphorus acid, triisodecyl ester EC 246-998-3;
(ix) *in vivo* erythrocyte micronucleus test (2014), performed with triisotridecyl phosphite EC 278-758-9.

3 You have concluded that "All genetic toxicty studies are negative".

4 While you have not identified this information as weight of evidence approach, you have provided multiple sources of information (i) – (ix) for genotoxicity, and therefore, ECHA has evaluated the provided information under Annex XI, Section 1.2. (weight of evidence).

1.2. Assessment of the information provided

5 Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.

6 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.

7 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

8 We have identified the following issues.

1.2.1. Lack of documentation justifying the weight of evidence adaptation

9 Annex XI, Section 1.2. requires that adequate and reliable documentation is provided to describe a weight of evidence approach.

10 You have not included a justification for your weight of evidence adaptation, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude on the information requirements under consideration.

11 Beside this critical deficiency, ECHA has also assessed the other aspects of your adaptation.

12 Information that can be used to support weight of evidence adaptation for the information requirement of Annex VII, Section 8.4.1 includes similar information that is produced by the OECD TG 471. This includes:

- Detection and quantification of reverse point mutations (by base substitutions or frameshift mechanisms on guanine-cytosine (GC) and adenine-thymine (AT) base pairs) in cultured bacteria (*Salmonella typhimurium* and/or *Escherichia coli* strains).

13 The sources of information (vi) – (ix) do not provide relevant information on the detection and quantification of gene mutations (base pairs, substitution or frame shift) in cultured bacteria and they cannot contribute to your weight of evidence.

14 More specifically, *in vitro* chromosomal aberration test (vi) and *in vivo* mammalian erythrocyte micronucleus tests (viii and ix) provide information on cytotoxicity and the frequency of cells with structural chromosomal aberrations or frequency of micronuclei, respectively, in mammals, but do not inform on gene mutations. The source of information (vii) provides information on detection and quantification of gene mutations (point mutations, frame-shift mutations, small deletions, etc.) including data on the frequency of mutant colonies in cultured mammalian cells.

15 The sources of information (ii) and (iii) provide information on bacteria (*E. coli*), however, the strains used (W3110 (pol A+) and p3478 (pol A-)) differ to the ones recommended in OECD TG 471 (*E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101). You did not clarify if the test system used, detects the gene mutation in bacteria as regards to AT base pairs, according to OECD TG 471. Therefore, they cannot be considered as relevant sources of information that could contribute to the conclusion on the key parameter investigated by the required study.

16 The sources of information (i) and (v) include four strains of *S. typhimurium*, which all have GC base pairs at the primary reversion site. Therefore, these sources of information may provide relevant information on gene mutation in bacteria (as regards GC base pairs). The source of information (iv) provides relevant information on all key elements. However, the sources of information (i), (iv) and (v) have deficiencies affecting the reliability of their contribution to the weight of evidence adaptation.

1.2.2. Reliability of the contribution of the information on analogue substances (sources of information (i), (iv), (v))

17 You intend to predict the toxicological properties of the Substance for the above listed information requirements from the information obtained with analogue substances in a read-across approach as part of your weight of evidence adaptation. For this information to be considered reliable, it would have to meet the requirements for Grouping of substances and read-across approach.

18 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.

19 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).

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

- source substance 1: Phosphorous acid, diisodecyl phenyl ester EC 247-098-3
- source substance 2: Phosphorus acid, triisodecyl ester EC 246-998-3
- Source substance 3: triisotridecyl phosphite EC 278-758-9

21 ECHA understands that your read-across hypothesis assumes that different compounds have the same type of effects. You predict the properties of your Substance to be quantitatively equal to those of the source substances.

22 We have identified the following issues with the prediction of toxicological properties:

1.2.2.1. Absence of read-across documentation

23 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 a an explanation why the properties of the Substance may be predicted from information on the source substance(s).

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

25 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substances.

26 As a conclusion, due to the issues identified above in the read-across approach, the information from the analogue substances do not reliably contribute to a weight of evidence intended to identify the properties of the Substance.

1.2.2.2. Methodological deficiencies of sources of information (i) and *(v)*

27 The evaluation of the reliability of the contribution of each relevant line of information to the weight of evidence approach includes an assessment of each source of information against the specifications of the test guideline followed.

28 Studies (i) and (v) are reported as *in vitro* gene mutation study in bacteria and has been performed according to a test protocol similar to the OECD TG 471. This test guideline requires that:

a) triplicate plating is used at each dose level;

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

29 In the sources of information (i) and (v) you reported "ambiguous" results with metabolic activation in four tested strains (TA98, TA100, TA1535, TA1537, and TA 1538). You did not provide any further information, in particular:

a) triplicate plating at each dose level;

b) the mean number of revertant colonies per plate for the treated doses and the controls is not reported;

30 Therefore, the sources of information (i) and (v) do not cover all the specifications of the OECD TG 471 which hampers the independent assessment of the results, hence they have significant reliability issues.

1.2.2.3. Conclusion on the weight of evidence

31 Taken together, only source of information (iv) provides relevant information on detection and quantification of reverse point mutations in cultured bacteria, that addresses base substitutions or frameshift mechanisms on GC and AT base pairs. However, the reliability of the contribution of the information obtained from source (iv) is hampered by the deficiencies identified, related to the use of information on analogue substances.

32 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for in vitro gene mutation study in bacteria.

33 Based on the above, your adaptation is rejected and the information requirement is not fulfilled.

1.3. Study design

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

2. Long-term toxicity testing on aquatic invertebrates

35 Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII, Column 1, Section 9.1.1. However, under Column 2, long-term toxicity testing on aquatic invertebrates may be required by the Agency if the substance is poorly water soluble, i.e. solubility below 1 mg/L.

2.1. Triggering of the information requirement

36 In the provided QSAR estimation (2020), the saturation concentration of the Substance in water was determined to be less than 1 mg/L.

37 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

2.2. Information requirement not fulfilled

38 As you have not provided information on long-term toxicity on aquatic invertebrates for the Substance, the information requirement is not fulfilled.

2.3. Study design

39 The Substance is difficult to test due to the low water solubility (< 1 mg/L). The OECD TG 211 specifies that, for difficult to test substances, you must consider the approach described in the 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 the 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.

3. Growth inhibition study aquatic plants

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

3.1. Information provided

41 You have adapted this information requirement and provided the following justification: "*This phosphite substance has a very low water solubility limit and what does dissolve in water rapidly hydrolyses to phenol, isodecanol and phosphorous acid. The environmental assessment has focused on the fate and toxicity of the hydrolysis products*".

3.2. Assessment of the information provided

42 A registrant may only adapt this information requirement based on the general rules set out in Annex XI or the specific rules set out in Annex VII, Section 9.1.2., Column 2.

43 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH or Annex VII, Section 9.1.2., Column 2.

44 You have not demonstrated that this information can be omitted. Therefore, the information requirement is not fulfilled.

3.3. Study design

45 The OECD TG 201 specifies that, for difficult to test substances, the 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.

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 04 May 2023.

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 6 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.

In your comments you indicated that you had no specific comments on the draft decision. ECHA took your comments into account and did not amend the request(s).

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]

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

(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/group of constituents on the test results for the endpoint to be assessed. For example, if a constituent/group of constituents of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/group of constituents.

(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 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.

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).