~~Confidential~~

Helsinki, 29 May 2024

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

Date of submission of the dossier subject to this decision
27 May 2021

Registered substance subject to this decision ("the Substance")
Substance name: Reaction mass of 1-hydroxypropan-2-yl diethylphosphinate and 2-hydroxypropyl diethylphosphinate
EC/List number: 829-436-7

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 ***8 December 2025***.

Requested information must be generated using the Substance unless otherwise specified.

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

1. Short-term repeated dose toxicity (28 days) (Annex VIII, Section 8.6.1.) by oral route, in rats, to be combined with the screening for reproductive/developmental toxicity requested below.

2. Screening study 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 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(s) of the decision and their 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 VIII of REACH

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

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

1.1. Information provided

2 You have adapted this information requirement. You have provided the following arguments in the report [redacted] attached to the endpoint study record provided for this information requirement:

(i) A structure-activity analysis addressing the potential of the Substance to cause neurotoxicity.

(ii) A reference to available repeated dose toxicity data for phosphonates and phosphates identified using the OECD QSAR Toolbox. However you consider that "*these chemicals could not be used as analogues of the target chemicals due to different type of activity with respect to AChE inhibition*".

3 You conclude your analysis assuming that both of the main constituents of the Substance will not cause neurotoxicity and will be non toxic in repeated dose toxicity tests.

1.2. Assessment of the information provided

4 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 VIII, Section 8.6.1., Column 2.

5 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH or Annex VIII, Section 8.6.1., Column 2 and the legal basis you are relying on for your intended adaptation is not apparent to ECHA.

6 Therefore, you have not demonstrated that this information can be omitted and the information requirement is not fulfilled.

1.3. Study design

7 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.).

8 The study design is addressed in request 2.

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

2. Screening study for reproductive/developmental toxicity

10 A screening study for reproductive/developmental toxicity study (OECD 421 or OECD 422) is an information requirement under Annex VIII, Section 8.7.1.

2.1. Information provided

11 You have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence). You have provided the following arguments in the report [redacted] attached to the endpoint study record provided for this information requirement:

(i) a prediction from the OASIS TIMES Androgen receptor-binding and Estrogen receptor-binding models for each of the main constituents of the Substance;

(ii) a prediction from the OASIS TIMES Androgen receptor-binding and Estrogen receptor binding models for structurally similar substances identified using the OECD QSAR Toolbox.

12 You conclude from these predictions that both constituents of the Substance are "not toxic" for androgen receptor-binding and estrogen receptor-binding according to the models of OASIS TIMES used. You consider that the negative predictions obtained from these models for the structurally similar substances confirm the not toxic conclusion derived for the Substance.

2.2. Assessment of the information provided

2.2.1. Weight of evidence adaptation rejected

13 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.

14 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.

15 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.

16 Information that can be used to support weight of evidence adaptation for the information requirement of Annex VIII, Section 8.7.1. includes similar information that is produced by the OECD TGs 421/422. The OECD TGs 421/422 require the study to investigate the following key parameters: 1) sexual function and fertility, 2) toxicity to offspring, and 3) systemic toxicity.

1) Sexual function and fertility

Sexual function and fertility on both sexes must include information on mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, organ weights and histopathology of reproductive organs and tissues, litter sizes, nursing performance and other potential aspects of sexual function and fertility.

2) Toxicity to offspring

Information on pre- and perinatal developmental toxicity reflected by litter sizes, postimplantation loss (resorptions and dead foetuses), stillborns, and external malformations, postnatal developmental toxicity reflected by survival, clinical signs and body weights of the pups (or litters), and other potential aspects related to pre-, peri- and postnatal developmental toxicity observed up to postnatal day 13.

3) Systemic toxicity

Information on systemic toxicity include clinical signs, survival, body weights, food

consumption, haematology, clinical chemistry, organ weights and histopathology of non-reproductive organs and other potential aspects of systemic toxicity in the parental generation up to postnatal day 13.

17 The sources of information (i) and (ii) characterise the potential of substances to bind to estrogen or androgen receptors. The sources of information (i) and (ii) may provide relevant information on some aspects of sexual function and fertility, toxicity to offspring, and systemic toxicity which could be mediated through interaction with the estrogen and/or androgen receptors.

18 However, these QSAR predictions are not informative of the intrinsic reproductive toxicity properties of the Substance which can be mediated via other mechanistic pathways than through binding to the estrogen and/or androgen receptors. Therefore, information on the affinity of a substance to bind to these receptors cannot, on its own, characterise the intrinsic reproductive toxicity properties of a substance including information on the sexual function, fertility, the systemic toxicity in the parental generation and toxicity to the offspring.

19 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for screening for reproductive/developmental toxicity.

20 Based on the above, your weight of evidence adaptation under Annex XI, Section 1.2. is rejected. Therefore, the information requirement is not fulfilled.

2.3. Study design

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

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

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

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

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 14 March 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 agreed to 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[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 and other parameters relevant for the property to be tested.

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