~~Confidential~~

Helsinki, 12 November 2021

Addressees
Registrant(s) as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
08/11/2012

Registered substance subject to this decision ("the Substance")
Substance name: 4,4',4''-(ethan-1,1,1-triyl)triphenol
EC number: 405-800-7

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 the deadline of ***20 November 2023***.

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

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

1. 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

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

1. In vivo mammalian erythrocyte micronucleus test (Annex IX, Section 8.4., column 2)

   The study requested above (Mammalian erythrocyte micronucleus test (1991)[1]) is already available in the other registrations for the Substance. Under Article 26(3) of REACH, you must not repeat a study involving vertebrate animals conducted on the same substance.

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

3. 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)

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

5. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

[1] https://echa.europa.eu/registration-dossier/-/registered-dossier/13161/7/7/3/?documentUUID=65d37f98-d882-4160-82f7-a6d1ab0c76ae

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendices entitled "Reasons to request information required under Annexes VIII of REACH" and "Reasons to request information required under Annexes IX of REACH".

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH, the information specified in Annexes VII, VIII and IX to REACH, for registration at [redacted].

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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[2] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[2] 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 on Reasons common to several requests

1. **Assessment of your adaptation under Annex XI, Section 3 (Substance-tailored exposure-driven testing)**

You seek to adapt the following information requirements by applying an exposure based approach under Annex XI, Section 3.2(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.)

ECHA has considered the scientific and regulatory validity of your exposure based approach(es) in general before assessing the specific standard information requirements in the following appendices.

As stated in Annex XI, Section 3, testing in accordance with Sections 8.6 and 8.7 of Annex VIII and in accordance with Annexes IX and X may be omitted based on the exposure scenario(s) developed in the CSR, by providing an adequate and scientifically-supported justification based on a thorough and rigorous exposure assessment in accordance with Section 5 of Annex I and by communicating the specific conditions of use through the supply chain. Any one of the following criteria 3.2.(a), (b) or (c) shall be met.

For an adaptation under the Annex XI, 3.2(b), where the substance is not incorporated in an article the manufacturer or the importer demonstrates and documents for all relevant scenarios that throughout the life cycle strictly controlled conditions as set out in Art 18(4)(a) to (f) apply.

In your CSR you provide numerous exposure scenarios and develop exposure estimations using ECETOC TRA, version 2. You describe manual interventions that require the use of personal protective equipment to control exposure e.g. exposure scenario 9.1.1, page 30.

ECHA assessed this information according to the requirements of Annex XI, Section 3 of the REACH Regulation and identified the following issues:

The criterion 3.2(b) requires a demonstration that "*throughout the life cycle strictly controlled conditions as set out in Article 18(4)(a) to (f)*" apply. As you have indicated that the prevention of exposure is based on the use of personal protective equipment in some tasks related to the use of the Substance, the Substance does not appear to be handled under strictly controlled conditions. Additionally, you estimate exposures of [redacted] mg/m^3 for Industrial polymerisation. You also include manual loading of powder into a mixer with a predicted inhalation exposure of [redacted] mg/m^3. These indicate exposure and are hence not indicative of strictly controlled conditions. Therefore, criterion 3.2(b) for exposure-based adaptation is not satisfied. 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.

Therefore, the adaptation you provided is not in line with the conditions specified in Annex XI, Section 3.2.(b) and the exposure based adaptation under Appendix XI, section 3 is rejected.

Appendix A: Reasons to request information required under Annex VIII of REACH

1. Screening for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or in vitro methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted this information requiement according to Annex XI, section 3 (Substance-tailored exposure-driven testing) and state that "*Section 3.2 of Annex XI stipulates that the omission may be justified if criterion (b) is met: "(b) where the substance is not incorporated in an article the manufacturer or importer demonstrates and documents for all relevant scenarios that throughout the life cycle strictly controlled conditions as set out in Article 18(4)(a) to (f) apply." In addition Section 3.3 of Annex XI requires that specific conditions of use be communicated through the supply chain. All of these requirements are deemed to be met for this registrant*.".

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

As explained under Appendix on 'Reasons common to several requests', your adaptation under the Annex XI, section 3 is rejected.

Therefore, the information you provided does not fulfil the information requirement.

Information on the study design

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 with oral[3] administration of the Substance.

[3] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix B: Reasons to request information required under Annex IX of REACH

1. In vivo mammalian erythrocyte micronucleus test

Under Annex IX, Section 8.4, column 2 of REACH, the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered if 1) there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and 2) there are no appropriate results already available from an *in vivo* somatic cell genotoxicity study.

In relation to the first condition, your dossier contains positive results for the *in vitro* cytogenicity test which raise concerns for chromosomal aberration.

In relation to the second condition, your dossier contains no data from an *in vivo* somatic cell genotoxicity study.

Therefore, the conditions set out in Annex IX, Section 8.4, column 2 are met and the information requirement for an appropriate *in vivo* somatic cell genotoxicity study is triggered.

Test selection

According to the ECHA Guidance Chapter R.7a, Section R.7.7.6.3, the mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) or the mammalian bone marrow chromosomal aberration test ("CA test", OECD TG 475) are suitable to follow up a positive *in vitro* result on chromosomal aberration if the Substance or its metabolite(s) will reach the target tissue. Alternatively, the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) is a suitable test to be performed. Therefore, the MN test, the CA test and the comet assay are suitable tests to follow up the chromosomal aberration concern identified for the Substance.

However, the *in vitro* chromosomal aberration test showed that the Substance induced both structural and numerical chromosomal aberrations, indicating that the Substance may cause both clastogenicity and aneuploidy. The *in vivo* MN test has the advantage of detecting both structural chromosomal aberrations (resulting from clastogenicity) and numerical chromosomal aberrations (resulting from aneuploidy). On the other hand, neither the *in vivo* CA test nor the *in vivo* comet assay is suitable to detect aneugens. Therefore, the *in vivo* MN test is the most appropriate follow up test for the Substance.

Test design

According to the test method OECD TG 474, the test must be performed in mice or rats. As regards the route, we note that the anticipated route of human exposure should be considered when designing the MN test .

Regarding the exposure of the target tissue, the applicable test guideline (OECD TG 474) states "If there is evidence that the test substance(s), or its metabolite(s), will not reach the target tissue, it may not be appropriate to use this test". Additionally, a negative test result can be considered reliable if "Bone marrow exposure to the test substance(s) occurred". Accordingly, if the Substance is negative in this test, but it is not possible to demonstrate that bone marrow exposure to the Substance occurred, then ECHA will consider any remaining uncertainty concerning the mutagenic potential of the Substance and whether to request any further information.

Information regarding data sharing obligations

The other registrations for the Substance contain a Mammalian erythrocyte micronucleus test (1991), intraperitoneal injection, with the Substance, 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 (ECHA Guidance on data-sharing[4]).

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

A Sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX to REACH.

You have provided following key study conducted with the Substance:

i. Repeated dose 28-day oral toxicity Study in Rodents conducted according to OECD TG 407 ([redacted], 1990)

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

To be considered compliant and enable concluding whether the Substance has dangerous properties and supports the determination of a No-Observed Adverse Effect Level (NOAEL), a study has to meet the requirements of the OECD TG 408. The following key parameter(s) of this test guideline include, among others:

- at least 10 female and 10 male animals should be used at each dose level (including control group); and
- dosing of the Substance daily for a period of 90 days until the scheduled termination of the study.

The provided study:

- was conducted with 5 animals per sex per test dose group. The statistical power of the information provided is not sufficient because it does not fulfil the criterion of 20 animals (10 males + 10 females) for each test group set in the OECD TG 408; and
- does not have the required exposure duration of 90 days as required in the OECD TG 408, because you indicated an exposure duration of 28 days.

Therefore, the information you provided does not fulfil the information requirement.

Information on the study design

Referring to 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, because the Substance is a solid and the fraction of inhalable particles is low.

3. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

You have adapted this information requiement according to Annex XI, section 3 (Substance-tailored exposure-driven testing) and state that "*Section 3.2 of Annex XI stipulates that the omission may be justified if criterion (b) is met: "(b) where the substance is not incorporated in an article the manufacturer or importer demonstrates and documents for all relevant scenarios that throughout the life cycle strictly controlled conditions as set out in Article 18(4)(a) to (f) apply." In addition Section 3.3 of Annex XI requires that specific conditions of use be communicated through the supply chain. All of these requirements are deemed to be met for this registrant*.".

[4] ECHA Guidance on data sharing: https://echa.europa.eu/documents/10162/23036412/guidance_on_data_sharing_en.pdf/545e4463-9e67-43f0-852f-35e70a8ead60

We have assessed this information and identified the following issue(s):
As explained under Appendix on 'Reasons common to several requests', your adaptation under the Annex XI, section 3 is rejected.

Therefore, the information you provided does not fulfil the information requirement.

Information on the study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[5] administration of the Substance.

4. Long-term toxicity testing on aquatic invertebrates

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

You have provided the following information:

i. a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification: "*In accordance with column 2 of REACH annex IX, testing of the long-term toxicity to aquatic invertebrates does not need to be conducted as the chemical safety assessment does not indicate a need for further investigation"*.

We have assessed this information and identified the following issue:

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.

On this basis, the information requirement is not fulfilled.

Study design

The Substance is difficult to test due to the low water solubility (25 mg/L) and adsorptive properties (log Koc 3.6-6) of the Substance, which have resulted in presence of undissolved test material in the test media of the submitted short-term toxicity studies. 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.

[5] ECHA Guidance R.7a, Section R.7.6.2.3.2.

5. Long-term toxicity testing on fish

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

You have provided the following information:

i. a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification: *"In Annex IX of Regulation (EC) No 1907/2006, it is laid down that long-term toxicity testing shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic organisms. The registrant's CSR does not indicate a need for such further testing"*.

We have assessed this information and identified the following issue:

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 long-term toxicity to fish 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.

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

The OECD TG 210 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 Appendix B.4.

Appendix C: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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[6].

B. 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 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[7].

[6] https://echa.europa.eu/practical-guides
[7] https://echa.europa.eu/manuals

Appendix D: 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 11 December 2020.

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

ECHA did not receive any comments within the commenting period.

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 E: List of references - ECHA Guidance[8] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[9]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[10]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[11]

[8] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[9] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[10] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[11] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix F: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

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.