~~Confidential~~

Helsinki, 22 October 2020

Addressees
Registrants of BPA-2PO_JS listed in the last Appendix of this decision

Date of submission of the dossier subject of a decision
01/04/2020

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: 1,1'-isopropylidenebis(p-phenyleneoxy)dipropan-2-ol
EC number: 204-137-9
CAS number: 116-37-0

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

DECISION ON TESTING PROPOSAL(S)

Based on Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***28 July 2023***.

The requested information must be generated using the Substance unless otherwise specified.

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

1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) by oral route, in rats, specified as follows:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce systemic toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;

You must report the study performed according to the above specifications. Any expansions of the study design must be scientifically justified.

Reasons for the request(s) is explained in the following appendix:

- Appendix entitled "Reasons to request information required under Annexes X of REACH", respectively.

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 to X to REACH, for registration at more than 1000 tpa.

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 can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Approved[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[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 A: Reasons to request information required under Annex X of REACH

This decision is based on the examination of the testing proposal you submitted.

1. Extended one-generation reproductive toxicity study

The basic test design of an extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement under Annex X to the REACH Regulation. Furthermore, column 2 of Section 8.7.3. defines when the study design needs to be expanded.

You have submitted a testing proposal for an EOGRTS according to OECD TG 443 by the oral route with 10-week premating exposure duration. You have provided the following justification and specification of the study design according to the criteria described in Column 2 of Section 8.7.3, Annex X, and detailed in ECHA Guidance R.7a:

"Name of the substance on which testing is proposed to be carried out : 1,1'-[propane-2,2-diylbis(4,1- phenyleneoxy)]dipropan-2-ol / CAS No 116-37-0 / EC No 204-137-9
[...]
it is considered that the basic design for the extended-one generation is sufficient to address the requirements for Annex X as:
- the uses of 1,1'-isopropylidenebis(p-phenyleneoxy)dipropan-2-ol are restricted to professional uses;
- no genotoxic potential has been recorded following the experimental studies performed,
- unexpected severity or occurrence of findings was not encountered compared with studies with shorter exposure;
- there were no indication of endocrine disruptor in the experimental studies available, including in in vitro assays to detect Estrogen receptor agonists or antagonists (perez et al, 1998, Environmental Health Perspectives 106(3): 167-174; and also in a study in progress);
- No particular concern for neurotoxicity or immunotoxicity or developmental immunotoxicity have been identified after repeated exposures whatever the type of the study (subacute and subchronic, fertility or developmental studies).

Therefore, the basic design (i.e. without the extension of cohort 1B and without cohorts 2A, 2B and 3) seems appropriate and in agreement with Annex XI requirement in order to avoid unnecessary animal testing. Although, in the 90-day toxicity study, spermatic staging profiles, estrous cycle determination and reproductive organs parameters have already been evaluated and revealed no changes, it is proposed to extend the pre-mating period to ten weeks to adequately assess the fertility as recommend in ECHA guidance R7.A (December 2016)."

You provided your considerations and proposed to test the Substance but also proposed to consider a read-across adaptation once an EOGRTS on a related substance under Substance Evaluation (SEv) decision is available. ECHA has taken these considerations into account.

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

As provided in Annex XI, Section 1.5., you may adapt the information requirement, provided you fulfil the identified criteria, and submit a scientifically supported justification and supporting information.

You explain your approach as follows: *"[...] at this time, no extended one-generation study or equivalent is available with a substance whose data could be used for read-across. Experimental studies related to a corap evaluation final decision are running on the grade 4 of 4,4'-isopropylidenediphenol, propoxylated (1-4 .5 propoxylated moles), CAS 37353-75-6, including an one-extended generation study by oral route. The evaluation of the overall data*

of theses studies will allow to assess if data could be used for readacross towards 1,1'-isopropylidenebis(p-phenyleneoxy)dipropan-2-ol".

You have not provided any supporting information or justification for conducting testing with the analogue substance. Your adaptation of this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. is therefore rejected and testing should be conducted using the Substance.

The proposed study design fulfils the information requirement.

The following refers to the specifications of this required study.

Premating exposure duration and dose-level setting

You proposed *"it is proposed to extend the pre-mating period to ten weeks to adequately assess the fertility as recommend in ECHA guidance R7.A (December 2016)."* ECHA considers that ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA Guidance R.7a

In order to be compliant and not to be rejected due to too low dose levels, the highest dose level must aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels. A descending sequence of dose levels should be selected in order to demonstrate any dose-related effect and to establish NOAELs.

If there is no existing relevant data to be used for dose level setting, it is recommended that results from a range-finding study (or range finding studies) are reported with the main study.

You must provide a justification with your study report that demonstrate that the dose level selection meets the conditions described above.

Cohorts 1A and 1B

Cohorts 1A and 1B belong to the basic study design and shall be included.

Species and route selection

You proposed testing by oral route. ECHA agrees with your proposal.

You did not specify the species for testing. According to the test method OECD TG 443, the rat is the preferred species.

In your comments you agree to perform the study. For your deadline extension request, see Appendix C, below.

Outcome

Under Article 40(3)(a) of REACH, you are requested to carry out the proposed test with the Substance.

Further expansion of the study design

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3

(developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if relevant information becomes available from other studies or during conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3., Annex X. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in ECHA Guidance[2].

[2] ECHA Guidance R.7a, Section R.7.6.

Appendix B: 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[3].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test material) which must be relevant for all the registrants of the Substance.

1. Selection of the Test material(s)

   The Test material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test material must contain that constituent/ impurity.

2. Information on the Test material needed in the updated dossier
   - You must report the composition of the Test material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test material and their concentration values 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 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[4].

[3] https://echa.europa.eu/practical-guides
[4] https://echa.europa.eu/manuals

Appendix C: Procedure

ECHA held a third party consultation for the testing proposal(s) from 26 March 2018 until 11 May 2020. ECHA did not receive information from third parties.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

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

ECHA took into account your comments and amended the deadline.

Extension of deadline
In your comments to the draft decision you request a deadline extension from 24 to 30 months as you consider the deadline of 24 months is not reasonable to perform such study considering the overload of laboratories able to perform OECD 443 study. Whilst you did not substantiate your extension request in this decision, you substantiated your request in your compliance check draft decision (CCH-D-2114468459-32-01/D) on the same registration dossier. ECHA has considered your evidence and has amended the deadline of 24 months to 30 months.

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 D: List of references - ECHA Guidance5 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)[6]

RAAF - considerations on multi-constituent substances and UVCBs (RAAF UVCB, March 2017)**Error! Bookmark not defined.**

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.

[5] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[6] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

OECD Guidance documents[7]
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.

[7] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix E: Addressees of this decision and the corresponding information requirements applicable to them

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]
[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.