EUROPEAN CHEMICALS AGENCY

~~Confidential~~

Helsinki, 6 May 2021

Addressees
Registrants of Pt_cpd_EC701-315-2_EPMF2019 listed in the last Appendix of this decision

Date of submission of the dossier subject of a decision
30/08/2019

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: 1,3-diethenyl-1,1,3,3- tetramethyldisiloxane and its platinum(0) complexes
EC number: 701-315-2
CAS number: NS

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 ***14 August 2023***.

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

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

1. Extended one-generation reproductive toxicity study (Annex VIII, Section 8.7.1., column 2; test method: EU B.56./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.

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) are explained in the following appendix:

- Appendix entitled "Reasons to request information required under Annex VIII 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 and VIII to REACH, for registration at 10-100 tpa;

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". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations 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 VIII of REACH

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

1. Extended one-generation reproductive toxicity study

According to Annex VIII, 8.7.1., Column 2, at the tonnage level of 10 to 100 tonnes per annum, the Registrant may propose an extended one-generation reproductive toxicity study (EOGRTS, OECD TG 443) (Annex IX, section 8.7.3) instead of a screening study in cases where there are serious concerns about the potential for adverse effects on fertility or development.

Your dossier contains a screening study ([redacted] 2017; OECD TG 422) with the Substance. In this study, increased post-implantation loss, decreased live birth index, depression of pup body weight and reduced viability index were observed. Consequently, you have self-classified the substance as Repr. 2 (H361d: Suspected of damaging the unborn child).

Based on these effects, you have identified a serious concern. To clarify the reproductive/developmental toxicity profile of the Substance, and the most appropriate classification, you propose to conduct an EOGRTS to evaluate specific life stages.

1.1. Information provided to fulfil the information requirement

You have identified a need to perform an EOGRTS and submitted a testing proposal for an EOGRTS according to OECD TG 443 with the Substance.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Toxicity to reproduction. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

ECHA has evaluated your proposal to perform an EOGRTS according to OECD TG 443 at Annex VIII.

ECHA considers that increased post-implantation loss, decreased live birth index, depression of pup body weight and reduced viability index reported in the screening study (OECD TG 422) study raise serious concerns about the potential for adverse effects on reproduction/development. The mere fact that a screening study is already available cannot be considered a valid reason why the adverse effects should not be followed up.

Pursuant to Article 12(1) and Annex VI of the REACH Regulation the standard information requirements listed in Annex VII to X of the REACH Regulation are considered minimum requirements. Annex VI, step 4 of the 'Guidance note on fulfilling the requirements of Annexes VI to XI' provides that the rules set out in Annexes VII to XI may require certain tests to be undertaken earlier than or in addition to the standard requirements. Furthermore, in accordance with Annex I of the REACH Regulation, certain additional information may have to be generated if it is necessary for producing the chemical safety report (CSR). According to the last subparagraph of Section 0.5. of Annex I of REACH, if the manufacturer or importer considers that further information is necessary for producing his CSR and that this information can only be obtained by performing tests in accordance with Annex IX and X, he shall submit a proposal for a testing strategy, explaining why he considers that additional information is necessary and record this in the CSR under the appropriate heading.

This means that when justified, higher tier/further studies may be conducted for substances where the tonnage level would not normally require this as a standard requirement. In order to understand the toxicological properties of the registered substance in light of the adverse effects observed, it is necessary to investigate further so that appropriate risk management measures can be put in place and safe use of the substance can be ensured.

ECHA agrees that an EOGRTS is necessary to address the identified concerns in relation with reproductive/developmental toxicity.

1.2. Specification of the study design

Species and route selection

You proposed testing in the rat. ECHA agrees with your proposal because the rat is the species preferred by OECD TG 443.

You proposed testing by oral gavage route in rats. ECHA agrees with your proposal. The oral route is the most appropriate route of administration to investigate reproductive toxicity[2].

Pre-mating exposure duration and dose-level setting

You proposed ten weeks pre-mating exposure duration. ECHA agrees with your proposal. Ten weeks pre-mating exposure duration is required because there is no substance specific information in the dossier supporting shorter pre-mating exposure duration (ECHA Guidance R.7a, Appendix R.7.6-3). Ten weeks exposure duration is supported also by the lipophilicity of the Substance (log Kow 6.5) to ensure that the steady state in parental animals has been reached before mating.

You proposed to "*to employ identical dose levels to the OECD TG 422 study (30, 125 and 500 mg/kg bw/day), as (not excessive) toxicity was seen in the high dose males and females in this study.*"

ECHA agrees that no (excessive) toxicity was seen in the OECD TG 422 study. Especially, the effects in P0 females were considered to be related to stress only (e.g. changes in adrenal weight).

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.

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

In your comments on the draft decision, you agreed to conduct the study on the Substance.

1.3. Outcome

Your testing proposal is accepted under Article 40(3)(a) and you are requested to conduct the test with the Substance, as specified above.

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 IX/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 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

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[4].

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

Appendix C: Procedure

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 22 January 2020, following the necessary clarification of the identity of your substance.

ECHA held a third party consultation for the testing proposal(s) from 25 May 2020 until 9 July 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.

In your comments on the draft decision, you requested an extension of the deadline to provide information from 24 to 36 months from the date of adoption of the decision.

Upon request, you provided documentary evidence from two CROs, highlighting the importance of sufficient experimental expertise and historical control database in choosing the test facility. ECHA notes that both CROs estimate that 27 months is sufficient for the preliminary study and the main OECD TG 443 study.

On this basis, ECHA has extended the deadline to 27 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 Guidance[5] 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)[6]

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]

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.