Helsinki, 5 April 2019

Addressee: [redacted]

Decision number: TPE-D-2114465819-31-01/F
Substance name: 1,2,3,4-tetrahydronaphthalene
EC number: 204-340-2
CAS number: 119-64-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 20/11/2017
Registered tonnage band: Over 1000

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation ((EC) No 1907/2006) (the REACH Regulation), ECHA examined your testing proposal(s) and decided as follows.

Your testing proposal is accepted and you are requested to carry out:

1. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route with the registered substance 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 have to submit the requested information in an updated registration dossier by **12 April 2021**. You also have to update the chemical safety report, where relevant.

The reasons for this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

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.

Authorised[1] by Ofelia Bercaru, Head of Unit, Hazard Assessment IV

[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

The decision of ECHA is based on the examination of the testing proposals you submitted and information submitted by third parties.

1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

The basic test design of an extended one-generation reproductive toxicity study (EOGRTS) is a standard information requirement as laid down in column 1 of Section 8.7.3., Annex X of the REACH Regulation, whereas column 2 defines when the study design needs to be expanded.

The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for an EOGRTS according to OECD TG 443 by the oral route in rats, to be performed with the registered substance. You have provided the following justification:
*"Materials and methods: OECD TG 443; basic test design (Cohorts 1A, and 1B without extension). It is proposed to conduct the study with rats by using oral exposure. Justification: In mice, uterus atrophy and atrophy of the ovary were found in a 13 weeks inhalation study. No such effects were found in a corresponding 13 weeks inhalation study with rats. In the 2-years inhalation study with mice no uterus atrophy and no ovary atrophy was observed at the same doses that are used in the 13 week inhalation study. Therefore, it can be concluded that these may be mice specific and transient effects. However a 2 year inhalation study with rats showed effects on the uterus (incidences of stromal polyp and endometrium hyperplasia in the high dose group [redacted] mg/m³ were significantly greater than those in the chamber controls; see Chapter 7.7 "Carcinogenicity" of IUCLID and Chapter 5.8 of this CSR). Therefore, an effect of the substance on reproduction (fertility) cannot be excluded.
Furthermore it is proposed to conduct the study by using oral exposure because according to the toxicokinetic results the substance will be readiliy resorbed into the body and hence it is systemic available after oral gavage. Other exposure routes like nose-only inhalation exposure is technically not feasible especially because very young and hence very small animals have to be used in this study."*

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (extended one-generation reproductive toxicity study). 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 considers that the proposed study design needs further specification to fulfil the information requirement. The following refers to the specifications of this required study.

Premating exposure duration and dose-level setting

You did not specify the premating exposure duration. 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[3].

Therefore, the requested premating exposure duration is ten weeks.

The highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of effect levels and effects of reproductive toxicity with those of systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

If there is no relevant data to be used for dose-level setting, it is recommended that a range-finding study (or range finding studies) is performed and that its results are reported with the main study. This will support the justifications of the dose-level selections and interpretation of the results.

Species and route selection

You proposed testing by oral route in rats. The provided information does not indicate that the rat is an inadequate species. Therefore, ECHA agrees with your proposal.

b) Consideration of the information received during third party consultation

ECHA received third party information during the third party consultation. For the reasons explained below the information provided is not sufficient to fulfil this information requirement.

ECHA received third party information concerning the testing proposal during the third party consultation.

The third party provided their considerations of the study design and stated that the basic study design (Cohorts 1A and 1B without extension) "*is considered to be appropriate in the absence of any triggers or conditions necessitating the inclusion of additional cohorts or a further generation*". However, the third party did not provide any scientific data which would fulfil this information requirement.

Notes for your consideration

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 information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the available information, together with the new information, shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA Guidance[3]. You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented.

In your comments to the draft decision you agreed to conduct the requested study, while disagreeing with the 10-week premating exposure duration. You argued that ECHA did not justify the length of premating exposure duration.

ECHA stresses that in order to ensure that the study design adequately addresses the

fertility endpoint, the duration of the premating exposure period (as well as the selection of the highest dose level) is a key aspect to be considered. According to ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility. This is not fully achieved after two weeks. In addition, no substance-specific information is present in the dossier to support a shorter premating exposure duration. Consequently, ECHA maintains the 10 weeks premating exposure duration.

Furthermore, in your comments to the draft decision you asked for the extension of the deadline of 24 months to 30 months. ECHA considers that you have not provided sufficient documentary evidence from the selected test laboratory indicating their expert opinion and scheduling timelines for the study in question in order to justify the extension, as requested by ECHA. Also you have not provided a substance-related justification as to why more time is required. Therefore, ECHA did not extend the deadline in the draft decision.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 20 November 2017.

ECHA held a third party consultation for the testing proposals from 26 March 2018 until 11 May 2018. ECHA received information from third parties (see Appendix 1).

This decision does not take into account any updates after **7 November 2018**, 30 calendar days after the end of the commenting period.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

ECHA took into account your comments and did not amend the request(s) or the deadline.

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

2. Failure to comply with the requests in this decision will result in a notification to the enforcement authorities of the Member States.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition.

   In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.