

Helsinki, 11 April 2019

Addressee: [REDACTED]

Decision number: TPE-D-2114466011-62-01/F

Substance name: (6R-trans)-7-amino-8-oxo-3-[[[(1,2,5,6-tetrahydro-2-methyl-5,6-dioxo-1,2,4-triazin-3-yl)thio]methyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid

EC number: 261-491-7

CAS number: 58909-56-1

Registration number: [REDACTED]

Submission number: [REDACTED]

Submission date: 03/05/2018

Registered tonnage band: 100-1000

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 proposals are accepted and you are requested to carry out:

- 1. Dissociation constant (Annex IX, Section 7.16.; test method: OECD TG 112) using the registered substance;**
- 2. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: OECD TG 408, version 25 June 2018) in rats using the registered substance.**
- 3. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414, version 25 June 2018) in a first species (rat or rabbit), oral route using the registered substance.**

You are required to submit the requested information in an updated registration dossier by **19 April 2021** except for the information requested under points 1 and 2 for Dissociation constant and Sub-chronic toxicity study (90-day) which shall be submitted in an updated registration dossier by **20 April 2020**. For each deadline, you shall also 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.

This decision does not address the information requirement of the Extended one-generation reproductive toxicity study according to Annex IX, Section 8.7.3. of the REACH Regulation. The results of the Sub-chronic toxicity study (90-day) will be used, among other relevant information, to decide on the study design of the Extended one generation reproductive toxicity study. Therefore, your testing proposal for Extended one-generation reproductive toxicity study will be addressed after having received the results of the Sub-chronic toxicity study (90-day).

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>.

Authorised¹ by Ofelia Bercaru, Head of Unit, 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 1: Reasons

The decision of ECHA is based on the examination of the testing proposals you submitted.

1. Dissociation constant (Annex IX, Section 7.16.)

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

Dissociation constant is a standard information requirement as laid down in Annex IX, Section 7.16. to the REACH Regulation. You have submitted a testing proposal for a Dissociation Constants in Water (OECD TG 112) for the registered substance.

ECHA considers the proposed test appropriate and testing should be performed with the registered substance.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed test using the registered substance: Dissociation constants in water (test method: OECD TG 112).

2. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)

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

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. to the REACH Regulation.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to OECD TG 408 "*newest version*". ECHA understands that you refer to the version adopted on 25 June 2018.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Sub-chronic toxicity (90-day): oral. ECHA notes that 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.

You proposed testing by the oral route, in rats. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA agrees that the oral route - which is the preferred one as indicated in ECHA Guidance on information requirements and chemical safety assessment (version 6.0, July 2017) Chapter R.7a, Section R.7.5.4.3 - is the most appropriate route of administration. In addition, according to the test method OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

Therefore, ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex IX, Section 8.6.2. of the REACH Regulation.

Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: Sub-

chronic toxicity study (90-day) in rats, oral route (test method OECD TG 408, version 25 June 2018).

Notes for your considerations

You submitted a testing proposal for an Extended one-generation reproductive toxicity study (Annex IX, 8.7.3.), as per a defined "testing strategy [...]": *1. The 90-day toxicity study according to OECD 408 will be performed (after decision of ECHA); 2. If the results of this OECD 408 study indicate adverse effects on reproductive organs or tissues, the OECD 443 EOGRTS will be started in its basic test design [...], one species; 3. If the results of this OECD 408 study indicate no adverse effects on reproductive organs or tissues, the OECD 421 reproduction toxicity screening test will be started."*

This testing proposal is not addressed in this decision because the results of the sub-chronic toxicity study (90-day) are considered crucial to inform on the study design of the Extended one-generation reproductive toxicity study. Therefore, you are required to perform the sub-chronic toxicity study (90-day) first, and submit the results by the deadline indicated above.

Together with providing the results for the requested sub-chronic toxicity study (90-day), you may also update your testing proposal for the Extended one-generation reproductive toxicity study. The updated testing proposal should include a justification for the design of the Extended one-generation reproductive toxicity study following ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017), taking into account the results of the sub-chronic toxicity study (90-day).

3. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

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

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. to the REACH Regulation.

You have submitted a testing proposal for a pre-natal developmental toxicity study in rats according to OECD TG 414 "newest version" by the oral route. ECHA understands that you refer to the test guideline version adopted on 25 June 2018.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (pre-natal developmental toxicity). ECHA notes that 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 performed with the registered substance is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

You proposed testing with the rat as a first species, by the oral route. According to the test method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with the rat or rabbit as a first species. In addition, ECHA agrees that the oral route is the most appropriate route of administration for substances except gases

to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a solid, ECHA concludes that testing should be performed by the oral route.

Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in a first species (rats or rabbits), oral route (test method: OECD TG 414, version 25 June 2018).

Notes for your consideration

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017), Chapter R.7a, Section R.7.6.2.3.2.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 1 June 2018.

ECHA held a third party consultation for the testing proposals from 10 August 2018 until 24 September 2018. ECHA did not receive information from third parties.

This decision does not take into account any updates after **3 January 2019**, 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 did not receive any comments by the end of the commenting period.

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 carrying out the tests required by the present decision, it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new tests must be suitable to assess these.

Furthermore, 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.