

Helsinki, 20 January 2021

Addressee

Registrant of N'-(1,3-dimethylbutylidene)-3-hydroxy-2-naphthohydrazide listed in the last Appendix of this decision

Date of submission of the dossier subject of a decision

21/02/2020

Registered substance subject to this decision, hereafter 'the Substance'

Substance name: N'-(1,3-dimethylbutylidene)-3-hydroxy-2-naphthohydrazide

EC number: 435-860-1

CAS number: 214417-91-1

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 **27 July 2022**.

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

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

1. Dissociation constant (Annex IX, Section 7.16.; test method OECD TG 112).
2. Stability in organic solvents and identity of relevant degradation products.
3. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) by oral route, in rats, modified to include urinalysis and immunohistochemical investigation of renal pathology.
4. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) by oral route, in one species (rat or rabbit).

Reasons for the requests are explained in the following appendix:

- Appendix entitled "Reasons to request information required under Annex 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 100-1000 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". 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>.

Approved¹ 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 IX of REACH

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

1. Dissociation constant

Dissociation Constant is an information requirement under Annex IX, Section 7.16. to REACH.

The current registration dossier does not contain a dissociation constant test.

The proposed test OECD TG 112 would meet the information requirement under REACH (Annex IX, section 7.16).

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

2. Stability in organic solvents and identity of relevant degradation products

Stability in organic solvents and identity of relevant degradation products is an information requirement under Annex IX, Section 7.15. to REACH.

The current registration dossier does not contain information on stability in organic solvents and identity of relevant degradation products.

The proposed test for stability of the Substance in formulations to be used in the toxicity studies would meet the information requirement under REACH (Annex IX, section 7.15).

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

3. Sub-chronic toxicity study (90-days)

A sub-chronic toxicity study (90 day) is an information requirement under Annex IX, Section 8.6.2. to REACH.

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 with the Substance.

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. ECHA agrees with your proposal.

In the short-term 28-day oral study (OECD TG 407) you submitted, there was a dose-related increase in incidence and severity in cortical hyaline droplets at all dose levels of the Substance (50, 150 and 1000 mg/kg bw/day). This was observed in the kidneys of male rats and not in male control rats or in any exposed/control female rats. In addition, increased incidence and severity of tubular basophilia and hyaline droplets were observed at the two highest dose levels of the Substance (150 and 1000 mg/kg bw/day) in male rats in a screening study (OECD TG 421) via oral route. Increased incidence and severity of hyaline casts was also observed in female rats at 1000 mg/kg bw/day in the screening study. These findings indicate that the kidney is a target organ of the Substance, which may induce alpha-2u-globulin-mediated nephropathy.

Since this mode of action is considered not relevant to humans, the involvement of alpha-2u-globulin in the kidney effects is a key parameter for establishing the relevance of the kidney effects for risk assessment. Therefore, although optional (as per paragraph 37 of OECD TG 408), a urinalysis is required to investigate further the kidney function after administration of the Substance. Additionally, a full histopathological examination (paragraphs 3, 45 and 47 of OECD TG 408), including immune-histochemical investigation of renal pathology is required to determine if the pathology is mediated by alpha-2u globulin.

Under Article 40(3)(b) of REACH, you are requested to carry out the proposed test under modified conditions, as explained above with the Substance and with inclusion of urinalysis and immune-histochemical investigation of renal pathology, allowing the determination of whether the pathology is mediated by alpha-2u globulin nephropathy.

4. Pre-natal developmental toxicity study

A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX, Section 8.7.2. to REACH.

You have submitted a testing proposal for a PNDT study according to OECD TG 414 with the Substance in the rat.

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.

Species

You proposed testing with the rat as a first species. You may select between the rat or the rabbit because both are preferred species under the OECD TG 414.

Route

You did not specify the route for testing. Based on the ECHA Guidance R.7a, Section R.7.6.2.3.2., the oral route is the most appropriate route of administration to investigate reproductive toxicity.

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

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 summaries².

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 dossiers³.

² <https://echa.europa.eu/practical-guides>

³ <https://echa.europa.eu/manuals>

Appendix C: Procedure

ECHA received your testing proposal(s) on 24 February 2020 and started the testing proposal evaluation in accordance with Article 40(1).

ECHA held a third party consultation for the testing proposals 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 did not receive any comments within the notification 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 D: List of references - ECHA Guidance⁴ 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)⁵

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.

⁴ <https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment>

⁵ <https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across>

⁶ https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316

OECD Guidance documents⁷

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.