Helsinki, 21 February 2020

Addressees
Registrant of [redacted] listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
5 December 2014

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Reaction products of N,N'-ethane-1,2-diylbis(1,3-propanediamine), cyclohexane, peroxidized 4-butylamino-2,2,6,6-tetramethylpiperidine and 2,4,6-trichloro-1,3,5-triazine
EC number: 425-020-0
CAS number: not specified

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

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***28 February 2022.***

A. Requirements applicable to all the Registrants subject to Annex IX of REACH

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method OECD TG 408) in rats with the Substance.

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method OECD TG 414) in a first species (rat or rabbit), oral route with the Substance;

Conditions to comply with the requests

You are bound by the requests for information corresponding to the REACH Annexes applicable to your own registered tonnage of the Substance at the time of evaluation. Therefore you have to comply with the requirements of Annexes VII, VIII and IX of REACH, if you have registered a substance at 100-1000 tpa.

The Appendices state the reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH. The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information. The timeline has been set to allow for sequential testing where relevant.

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 for the requests to comply with Annex IX of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 100 to 1000 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII to IX to REACH.

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.)

A Sub-chronic toxicity study (90 day) is a standard information requirement in Annex IX to REACH.

You have provided an adaptation according to Column 2 of Annex IX, Section 8.6.2 first paragraph, fourth indent in your dossier.

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

As provided in Annex IX, Section 8.6.2, Column 2, you may adapt the information requirement, provided you fulfil the following criteria: the Substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and of toxicity in a 28-day 'limit test', particularly if it is coupled with limited human exposure.

You stated that *"All of the above mentioned conditions are met. The test substance is expected to be absorbed poorly and to be not bioavailable as demonstrated by the lack of systemic toxicity in several acute and subchronic toxicity studies.".* You further refer to the physico-chemical properties of the Substance and consider on that basis that *"poor absorption of the test article during GI passage is expected"*. You conclude that *"the experimental chemical analytics and the physico-chemical data do not suggest absorption through gastrointestinal tract, skin and by inhalation and as a result, systemic availability of the test substance is expected to be low. This is strongly supported by the findings of the available toxicity studies, which could not detect any adverse effects up to the highest doses tested (limit dose of 1000 mg/kg in the subacute study) and gave therefore no indications for systemic availability after oral and dermal exposure. Overall, it can be concluded that the substance is not absorbed and not bioavailable."*

You have not demonstrated that there is no evidence of absorption. On the contrary, evidence of systemic toxicity, and therefore of absorption, was observed in the screening study for reproductive and developmental toxicity (OECD TG 421) conducted with the Substance and included in your dossier ([redacted] 2013). More specifically, in that study increased absolute and relative ovaries weights were observed in high-dose group females, swollen liver was noted in high dose males and reduced size of the testis, epididymidis and prostate was detected in males from unspecified dose groups. These observations constitute evidence of absorption of the Substance after oral administration. Therefore, your adaptation is rejected.

In your comments on the draft decision, you acknowledge that the information requirement is not fulfilled for this endpoint and you agree to perform the requested study.

Information on the design of the study to be performed (species/route)

Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity[2]. The Substance is a powder, with particle size (53 % ≤75µm) which does not raise concern for

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

inhalation. Therefore, the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

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

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX to REACH.

You have provided an adaptation according to Annex IX, Section 8.7, column 2 first paragraph, third indent in your dossier.

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

According to Annex IX, Section 8.7., Column 2, first paragraph, third indent, the study does not need to be conducted if the substance is of low toxicological activity. This needs to be demonstrated with three concomitant criteria, two of them being:

- there is no evidence of toxicity seen in any of the tests available; and
- it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure.

You stated that "*the substance is expected not to be systemically available*". In order to support this claim, you refer to the physico-chemical properties of the Substance and to "*the available toxicity data of the test article which indicate poor absorption resulting in low bioavailability*". You indicate that "*As shown in a 28-day repeated dose toxicity study (OECD 407) and in a Reproduction / Developmental Toxicity Screening Test (OECD 421), no toxicological relevant effects were reported up to the highest dose tested (1000 mg/kg/day)*". You concluded that "*Taken together, the physico-chemical characteristics and the available repeated dose toxicity data strongly indicate that the substance is not systemically available. It is unlikely that adverse effects will be detected in an additional study.*"

As explained under A.1 above, you have not demonstrated that there is no evidence of toxicity and no evidence of systemic absorption. On the contrary, evidence of systemic toxicity, and therefore of absorption, was observed in the screening study for reproductive and developmental toxicity (OECD TG 421) conducted with the Substance and included in your dossier ([redacted] 2013). More specifically, in that study increased absolute and relative ovaries weights were observed in high-dose group females, swollen liver was noted in high dose males and reduced size of the testis, epididymidis and prostate was detected in males from unspecified dose groups. These observations constitute evidence of absorption and of toxicity of the Substance after oral administration. Therefore, your adaptation is rejected

In your comments on the draft decision, you acknowledge that the information requirement is not fulfilled for this endpoint and you agree to perform the requested study.

Information on study design

A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species with oral[3] administration of the Substance.

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

Appendix B: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of REACH.

The compliance check was initiated on 28 May 2019.

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 within 30 days of the notification.

ECHA took into account your comments and did not amend the requests.

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 C: Observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.

3. Test guidelines, GLP requirements and reporting

   Under Article 13(3) of REACH, all new data generated as a result of this decision needs to be conducted according to the test methods laid down in a European Commission Regulation or according to international test methods recognised by the Commission or ECHA as being appropriate.

   Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses shall be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

   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: 'How to report robust study summaries'[4].

4. Test material

   Selection of the test material(s)

   While selecting the test material you must take into account 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. Any constituents that have harmonised classification and labelling according to the CLP Regulation (Regulation (EC) No 1272/2008) must be identified and quantified using the appropriate analytical methods.

   The OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 11 [ENV/MC/CHEM(98)16] requires a careful identification of the test material and description of its characteristics. In addition, the Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "*if the test method is used for the testing of a* [...] *UVCB* [...] *sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents*".

   In order to meet this requirement, all the constituents of the test material used for each test must be identified as far as possible.

   Technical reporting of the test material

   The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values. Without such detailed

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

reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

Technical instructions are available in the manual "How to prepare registration and PPORD dossiers" on the ECHA website (https://echa.europa.eu/manuals).

5. List of references of the ECHA Guidance and other guidance/ reference documents[5]

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 in this decision.

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 in this decision.

ECHA Read-across assessment framework (RAAF, 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.

OECD Guidance documents[7]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.

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

Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD43.

Appendix D: List of the registrants to which the decision is addressed and the corresponding information requirements applicable to them

Registrant Name	Registration number	(Highest) Data requirements to be fufilled
[redacted]	[redacted]	[redacted]