Helsinki, 01 September 2020

Addressees
Registrant(s) of JS_567868 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
28 May 2013

Registered substance subject to this decision ("the Substance")
Substance name: Reaction mass of 1H-Benzotriazole-1-methanamine, N,N-bis(2-ethylhexyl)-6-methyl- and 2H-Benzotriazole-2-methanamine, N,N-bis(2-ethylhexyl)-5-methyl- and N,N-bis(2-ethylhexyl)-4-methyl-1H-benzotriazole-1-methylamine and 2H-Benzotriazole-2-methanamine, N,N-bis(2-ethylhexyl)-4-methyl- and N,N-bis(2-ethylhexyl)-5-methyl-1H-benzotriazole-1-methylamine
List number: 939-700-4
CAS number: NS

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

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***6 June 2022***.

Requested information must be generated using the Substance unless otherwise specified.

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

1. Water solubility (Annex VII, Section 7.7.; test method: EU A.6./OECD TG 105/OECD GD 29);

2. Partition coefficient n-octanol/water (Annex VII, Section 7.8.; using an appropriate test method).

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487);

2. Hydrolysis as a function of pH (Annex VIII, Section 9.2.2.1.; test method: EU C.7./OECD TG 111).

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

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit).

Reasons for the request(s) are explained in the following appendices:
- Appendices entitled "Reasons to request information required under Annexes VII to IX of REACH", respectively.

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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- 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, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

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 VII of REACH

1. Water solubility

Water solubility is a standard information requirement in Annex VII Section 7.7 to REACH.

You have adapted this information requirement based on the Substance being hydrolytically unstable.

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

According to Annex VII, Section 7.7, Column 2, the study does not need to be conducted if the Substance is hydrolytically unstable at pH 4, 7 and 9 (half-life less than 12 hours).

You claim that the study cannot be conducted because the Substance is hydrolytically unstable at pH 4, 7 and 9. To support your claim you have provided a hydrolysis study.

However, as explained under Appendix B, section 2 of this decision, the hydrolysis study is rejected. Therefore your claim that the Substance is hydrolytically unstable is unsupported.

Your adaptation is rejected and the information requirement is not fulfilled.

2. Partition coefficient n-octanol/water

Partition coefficient n-octanol/water is a standard information requirement in Annex VII Section 7.8 to REACH.

You have provided an adaptation for this information requirement based on the Substance being hydrolytically unstable.

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

Under Annex VII, Section 7.8, Column 2, the study may be omitted if the test cannot be performed (e.g. the Substance decomposes), and a calculated value for partition coefficient as well as details of the calculation method are provided.

According to ECHA Guidance[2], in case of rapid hydrolysis, the evidence in the form of a hydrolysis endpoint study record (study summary) must be provided. Testing for the hydrolysis products instead may be considered, as information on the properties of relevant degradation products is needed for the risk assessment of the Substance.

You have claimed that the Substance is hydrolytically unstable at pHs 4, 7 and 9 and you have provided hydrolysis study.

You have not provided calculated value on partition coefficient n-octanol/water for the Substance.

Furthermore, you have provided calculated partition coefficient n-octanol/water (logKow) values of identified and theoretical hydrolysis products and the result of an experimental logKow study for substance diethylhexylamine, EC 203-372-4 (potential hydrolysis poduct).

You have neither provided details of the calculation method nor study summaries.

[2] ECHA Guidance R.7a, section R.7.1.8.4

The dossier does not contain any information, in form of study summary, to support your claim that an experimental study to determine the logKow of the Substance is not feasible. In particular, and as explained under Appendix B, section 2 of this decision, the hydrolysis study is rejected and there is no evidence on the hydrolysis rate at environmentally relevant pH values. Therefore your claim that the Substance is hydrolytically unstable is unsupported. Nevertheless, the logKow calculation for the Substance is not provided, as required in Annex VII, Section 7.8, Column 2.

With respect to the provided information on theoretical hydrolysis products, as the provided hydrolysis study is rejected, there is no evidence on the actual hydrolysis products. Hence, you have not demonstrated whether the logKow studies provided for the assumed hydrolysis products are relevant for the risk assessment of your Substance.

In addition, without the details of a calculation method and a study summary for the reported logKow values of the assumed hydrolysis products, the validity of the provided data cannot be confirmed.

Based on the above, the information you provided for this endpoint is rejected and the information requirement is not fulfilled.

Appendix B: Reasons to request information required under Annex VIII of REACH

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

In vitro cytogenicity study in mammalian cells is a standard information requirement in Annex VIII to REACH.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. using the following study:

- *in vitro* mammalian chromosome aberration test ([redacted] 2005) performed according to the OECD TG 473, with Benzotriazole, 1(or 2)-[1-(cyclohexyloxy)heptyl]methyl- (CAS No. 866625-93-6.

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

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6 and related documents.

You have provided a read-across justification in IUCLID Section 7.1 and your reasoning for the prediction of toxicological properties is: *"Metabolic behaviour is supposed to be similar for a structural analogue (see chapter 7.6.1 for details on molecule). It is postulated that this substance yields to the main metabolite methylbenzotriazole after gastro-intestinal and/or liver cleavage. This substance provides the data of the genotoxicity testing for potential clastogenicity (chromosome aberration)."*

Under section 7.6.1 in IUCLID (Genetic toxicity in vitro), you specify the structural analogue as the source substance, Benzotriazole, 1(or 2)-[1-(cyclohexyloxy)heptyl]methyl- (CAS No. 866625-93-6.

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

ECHA notes the following shortcomings with regards to the prediction of toxicological properties:

Read-across hypothesis

A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the substances[3]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

[3] ECHA Guidance, Chapter R.6

Your read-across hypothesis is that the structural similarity between the source substance(s) and your Substance is a sufficient basis for predicting the properties of your Substance.

While structural similarity is a prerequisite for applying the grouping and read-across approach, it does not necessarily lead to predictable or similar human health properties. You have not provided a well-founded hypothesis to establish a reliable prediction for a toxicological property, based on recognition of the structural similarities and differences between the source substance(s) and your Substance.

Missing supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[4]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include bridging studies to compare the toxicity profile of the Substance and source substance(s).

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substance cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design (and duration) for the Substance and of the source substance(s).

The data set reported in the technical dossier does not include information for the Substance and of the source substance(s) to support your prediction of the properties of the Substance.

In the absence of such information, you have not established that the Substance and the source substance(s) are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

Therefore, the information requirement is not fulfilled.

Information on the study design

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. Hydrolysis as a function of pH

Hydrolysis as a function of pH is a standard information requirement in Annex VIII to REACH.

You have provided the following information:

- OECD TG 111 key study ([redacted], 2013) with the Substance.

[4] ECHA Guidance R.6, Section R.6.2.2.1.f

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

To fulfil this information requirement, a study must comply with the OECD TG 111/EU method C.7. Therefore the following requirements must be met:

- a main hydrolysis testing (tier 2) is performed if more than 10 % hydrolysis occurs after 5 days in the preliminary test (tier 1)
- tier 2 test must be conducted at three temperatures in the range of 10-70°C (preferably with at least one temperature below 25°C utilised)
- hydrolysis rate and half-life (or DT50) must be determined for 20/25°C
- identification of hydrolysis products (tier 3) using appropriate analytical method must be performed for major hydrolysis products (present at least ≥ 10 % of the applied dose)

Your registration dossier contains an OECD TG 111 study showing the following:

- preliminary test (tier 1) indicating fast hydrolysis of the Substance at pHs 4, 7 and 9 at 50 ± 0.5 °C;
- analytically identification of one hydrolysis product (methyl-1 H-benzotriazole).

However you did not perform a main hydrolysis testing (tier 2 test).

Therefore, you have not provided relevant information on hydrolysis at environmentaly relevant conditions (temperature below 25°C) and you have not determined the hydrolysis rate nor the half-life (or DT50) at 20/25°C. In addition, while you have analytically identified one hydrolysis product (methyl-1 H-benzotriazole), you report two additional theoretical hydrolysis products (formaldehyde and diethylhexylamine) without analytical identification of the actual hydrolysis products.

Therefore, the provided study does not fulfil the information requirement.

Appendix C: Reasons to request information required under Annex IX of REACH

1. Pre-natal developmental toxicity study in one species

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

In your dossier, you have provided

(i) a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD TG 422) conducted with the Substance ([redacted] 2013); and
(ii) an adaptation according to Column 2 of Annex IX, Section 8.7 third indent due to low toxicological activity.

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

A. To comply with this information requirement, the provided study must be an OECD TG 414 study.

The provided OECD TG 422 study is not the study required under REACH. In addition, the provided OECD TG 422 study does not address the key parameters of OECD TG 414, such as structural malformations and variations.

Therefore the information provided is rejected.

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

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

You have justified your adaptation by referring to the marginal treatment related effects observed in the OECD TG 422 screening study and the lack of classification for reproduction and developmental toxicity of the hydrolysis products: "*recent hydrolysis data suggest that the test article rapidly hydrolyses to formaldehyde (CAS No. 50-00-0), bis(2-ethylhexyl)amine (CAS No. 106-20-7) and tolyltriazole (CAS No. 29385-43-1), none of which is classified for reproduction and developmental toxicity.*"

In your adaptation, you have not substantiated your claim on no toxicity and you have not provided any toxickokinetic data to show that there is no systemic absorption. On the contrary, the information on the dose range finding (DRF) study provided in the endpoint study record of the OECD TG 422 indicates that evidence of systemic toxicity, and therefore of systemic absorption, was observed for the Substance. In the OECD TG 422 study (WIL Research, 2013), the dose levels used in the study (15, 45, 150 mg/kg bw/d) were selected based on mortality observed at 300 and 1000 mg/kg bw/d of the Substances reported at in the DRF study.

These observations constitute evidence of systemic absorption and of toxicity of the Substance after oral administration.

Moreover, your claim of rapid hydrolyses is not valid. As explained in Appendix B, Section 2, your hydrolysis study has been rejected. In addition, the lack of classification for reproduction and developmental toxicity does not indicate lack of toxicity in general.

Finally, the uses of the Substance indicate that there is significant human exposure. The Substance has reported professional and consumer uses in lubricants, greases and related products.

As a conclusion, you have not demonstrated that the Substance has no toxicity, no absorption and no significant human exposure. Therefore, your adaptation is rejected.

Information on study design

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[5] administration of the Substance.

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

Appendix D: 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[6].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

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 variation in compositions reported by all members of the joint submission,
   - 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 and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[7].

[6] https://echa.europa.eu/practical-guides
[7] https://echa.europa.eu/manuals

Appendix E: Procedure

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

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 20 August 2019.

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

ECHA took into account your comments and amended the deadline.

Deadline to submit the requested information in this decision

In the draft decision communicated to you, the time indicated to provide the requested information was 12 months from the date of adoption of the decision.

In your comments on the draft decision you requested ECHA to extend the standard granted time to a total of 36 months. Your request was based on the proposal of 2-tiered testing.

You proposed a 2-tiered testing approach where you intend to conduct the requested hydrolysis as a function of pH (Appendix B, section 2) test (Tier 1) before conducting the other requested physico-chemical and toxicological studies (Tier 2). You requested a total of 18 months to conduct the hydrolysis test. In addition, you requested a total of 18 months subsequent to the hydrolysis test to conduct the mammalian toxicity studies; pre-natal developmental toxicity study (OECD TG 414; Appendix C, section 1) and the concurrently requested sub-chronic toxicity (90-day) study (OECD TG 408; communication number TPE-D-2114504298-49-01/D).

Regarding the timeline for the hydrolysis test, you justified your request stating that a total of 18 months are needed to conduct the study because of the challenges in the development of a suitable analytical method to determine the hydrolysis rate and identify the hydrolysis products due to the predicted low water solubility of the Substance. ECHA considers that a total of 12 months are sufficient: 6 months for the development of the analytical method and 6 months for conducting the study and interpreting the results.

Regarding your proposed 2-tiered testing approach, ECHA notes the following:

You justified the tiered testing for physico-chemical studies by indicating that information on the hydrolysis rate and hydrolysis products is "*essential to identify the proper approach to generate the information required on A.1. water solubility and/or A.2. partition coefficient*". ECHA agrees that physico-chemicals studies can be performed subsequent to the hydrolysis test, in order to determine whether they are technically feasible with the Substance and/or whether it is more relevant to test the hydrolysis products. ECHA considers that additional 6 months to allow for sequential testing for the physico-chemical studies subsequent to the hydrolysis test are sufficient (a total of 18 months).

You justified the tiered testing for mammalian toxicity studies by indicating that "*the information on hydrolytic stability of the registered substance is essential for choosing the suitable vehicle(s) and preparing the dosing solutions in the mammalian toxicity studies*". However, as evidenced by the oral OECD TG 422 Screening study conducted with the Substance ([redacted] 2013) and provided in the registration dossier, you can test the Substance in mammalian toxicity studies using solution of 0.5% carboxymethyl cellulose and

0.1% Tween-80 in water as a vehicle (including analytical verification of doses). Therefore, ECHA has rejected the tiered approach for mammalian toxicity studies and no additional time is granted for choosing the suitable vehicle(s) and preparing the dosing solutions.

In addition to the tiered testing, you requested an additional 6 months for conducting the mammalian toxicity studies requested in the current decision and in the concurrent testing proposal evaluation draft decision (TPE-D-2114504298-49-01/D). To justify your request, you provided documentary evidence from the testing laboratory that a total of 18 months is required for the performance of the studies. ECHA considers that an extension of the timeline to provide the requested information of 6 additional months is justified, making a total of 18 months.

In conclusion, ECHA has partially agreed with your request on deadline extension and a total of 6 months additional time is given for conducting the hydrolsis and mammalian toxicity studies. However, the proposed tiered testing for the mammalian toxicity studies is rejected.

Therefore, ECHA has only partially granted the request and set the deadline to 18 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 F: List of references - ECHA Guidance[8] 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)[9]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[9]

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.

OECD Guidance documents[10]

[8] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[9] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[10] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

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.

Appendix G: 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.