EUROPEAN CHEMICALS AGENCY

Helsinki, 21 August 2020

Addressees
Registrant(s) of JS_1902936-62-2 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
7 October 2019

Registered substance subject to this decision ("the Substance")
Substance name: Reaction products of N6,N6'-hexane-1,6-diylbis[N2,N4-dibutyl-N2,N4,N6-tris(2,2,6,6-tetramethylpiperidin-4-yl)-1,3,5-triazine-2,4,6-triamine] and allylbromide, subsequently reacted with ethaneperoxoic acid, hydrogenated
EC number: 812-927-5
CAS number: 1902936-62-2

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 ***28 February 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. Skin sensitisation (Annex VII, Section 8.3.)

   i. *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E)(Annex VII, Section 8.3.1.); and

   ii. only if the *in vitro/in chemico* test methods specified under point 1.i.) are not applicable for the Substance, or the results obtained are not adequate for classification and risk assessment, *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429);

2. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method EU B.13/14. / OECD TG 471).

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

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

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- 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 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.

Authorised[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.

ECHA
EUROPEAN CHEMICALS AGENCY

Appendix on Reasons common to several requests

1. Assessment of your read-across approach under Annex XI, Section 1.5.

You seek to adapt the following standard information requirements by applying a read-across approach in accordance with Annex XI, Section 1.5:

- Skin sensitisation (Annex VII, Section 8.3);
- In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.).

ECHA has considered the scientific and regulatory validity of your read-across approach in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

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 the ECHA RAAF document.

A. Predictions for toxicological properties

You have provided a read-across justification in the Chemical Safety Report.

You predict the properties of the Substance from information obtained for the source substance: Reaction product of N2,N2'-1,6-hexanediylbis[N4,N6-dibutyl-N2,N4,N6-tris(2,2,6,6-tetramethyl-4-piperidinyl)-1,3,5-triazine-2,4,6-triamine and hydrogen peroxide and butanal (EC: 700-878-1; CAS: 1395069-30-3).

You have provided the following reasoning for the prediction of toxicological properties: you state that both substances are structurally similar, consist of the same major components but the Substance has a higher average O-alkylation grade [redacted] source). You claim that the difference in relative amounts of the substituents has no influence on the toxicological properties. Furthermore, you state that the source substance has '*lower molecular weight components*' (MW [redacted]) compared to the Substance (MW [redacted]). Therefore, you claim that the source substance has higher potential of systemic uptake and possibility of skin penetration.

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. You predict that the properties of your Substance are based on a worst-case approach.

You have not established a reliable basis for predicting toxicological properties for the following reasons.

A. Characterisation of the source substance

Annex XI, Section 1.5 of the REACH Regulation provides that "*substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as group.*"

According to the ECHA Guidance, "*the purity and impurity profiles of the substance and the structural analogue need to be assessed*", and "*the extent to which differences in the purity and impurities are likely to influence the overall toxicity needs to be addressed, and where technically possible, excluded*". The purity profile and composition can influence the overall toxicity/properties of the Substance and of the source substance(s).[2] Therefore, qualitative and quantitative information on the compositions of the Substance and of the source substance(s) should be provided to allow assessing whether the attempted predictions are compromised by the composition and/or impurities.

Furthermore, whenever the Substance and/or the source substance(s) are UVCB (Unknown or Variable composition, Complex reaction products or of Biological materials) substances qualitative compositional information of the individual constituents of the category members needs to be provided; as well as quantitative characterisation in the form of information on the concentration of the individual (or group) constituents of these substances; to the extent that this is measurable.[3]

Your read-across justification contains limited compositional information for the source and target substances. You state that the source substance and the Substance '*consist of the same major components. They differ in their relative content, noting that it is not possible to quantify these. Minor components should also be identical, but this is difficult to prove*". You also state that the Substance has an higher O-alkylation rate than the source substance.

ECHA agrees that the Substance and the source substance have similar '*structural components*'. However, when comparing the composition of the substances it is the constituents/groups of constituents of each substance, not the '*structural components*' within the constituents that are of interest. In this context, ECHA notes that the Substance has constituents/group of constituents with a N-OH functionality [redacted] while the source substance has constituents/group of constituents with a N-H functionality [redacted] You did not explain why this difference in functionality will not affect the prediction. Without this information, no qualitative or quantitative comparative assessment of the compositions of the source substance and of the Substance can be completed. In the absence of this information, the extent to which differences in the compositions of the substances influence the overall toxicity cannot be assessed. Therefore, it is not possible to assess whether the attempted predictions are compromised by the composition of the source substance.

B. Missing information to support your worst-case claim

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

[2] ECHA Guidance R.6, Section R.6.2.3.1
[3] ECHA Guidance R.6, Section R.6.2.5.5
[4] ECHA Guidance R.6, Section R.6.2.2.1.f

establish that the properties of the Substance can be predicted from the data on the source substance(s).

As indicated above, your read-across hypothesis is based on the assumption that the source substance constitutes a worst-case for the prediction of the property under consideration of the Substance. 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 a conservative prediction of the properties of the Substance from the data on the source substance(s). Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

You have not provided such information that allows comparison of the properties under consideration between the Substance and the source substance.

In the absence of such information, you have not established that the source substance constitutes a worst-case for the prediction of the property under consideration of the Substance. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

B. Conclusion on the read-across approach

As explained above, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. Therefore, your adaptation is rejected and it is necessary to perform testing on your Substance.

Further, endpoint-specific considerations are addressed under the individual endpoints.

Appendix A: Reasons to request information required under Annex VII of REACH

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

1. Skin sensitisation (Annex VII, Section 8.3.)

Skin sensitisation is a standard information requirement in Annex VII, Section 8.3. to REACH. Column 1 of Section 8.3. requires the registrants to submit information allowing a conclusion whether the substance is a skin sensitiser and whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and risk assessment, where required.

You have adapted this information requirement by using a read-across approach under Annex XI, Section 1.5. In this context, you have adapted the information requirement according to Annex VII, Section 8.3.2, column 2, third paragraph with statement "*A valid LLNA (OECD 429) was performed prior to the amendment of the REACH annexes in 2016.*".

You have provided the following information with the source substance: Reaction product of N2,N2'-1,6-hexanediylbis[N4,N6-dibutyl-N2,N4,N6-tris(2,2,6,6-tetramethyl-4-piperidinyl)-1,3,5-triazine-2,4,6-triamine and hydrogen peroxide and butanal (EC: 700-878-1; CAS: 1395069-30-3):

(i) *In vivo* (LLNA) (according to OECD TG 429, GLP, 2013).
(ii) *In vitro* direct peptide reactivity assay (no guideline, non-GLP, 2012).
(iii) *In vitro* myeloid U937 skin sensitization test (MUSST) (no guideline, non-GLP, 2012).

Based on this information you have concluded that the source substance is not a skin sensitiser.

We have assessed the provided information and have identified the following issues:

As already explained in the Appendix on general considerations above, your adaptation based on Annex XI, Section 1.5. is rejected.

In addition, ECHA also observe the following deficiencies in the data provided:

A. According to Article 13(3) of REACH, tests on substances must be conducted in accordance with the applicable OECD test guidelines or other recognised international test methods. For *in vivo* skin sensitisation studies to be considered reliable, the study must follow the principles of the test method (OECD TG 429).

OECD TG 429 states in paragraph 19 that "*The vehicle should not interfere with or bias the test result and should be selected on the basis of maximising the solubility in order to obtain the highest concentration achievable while producing a solution/suspension suitable for application of the test substance. Recommended vehicles are acetone: olive oil (4:1, v/v), N,N-dimethylformamide, methyl ethyl ketone, propylene glycol, and dimethyl sulphoxide (19) but others may be used if sufficient scientific rationale is provided.*"

The submitted *in vivo* study under item i) was performed with very low concentrations due to the irritating effects noted in higher test concentrations. The Substance itself is not predicted to be irritating or corrosive to the skin and the organic solvent (methyl ethyl ketone (MEK))

used in the study appears to affect the Subtance properties, as indicated by you in the dossier "*If applied in organic solvent, the substance becomes a sticky paste which then causes irritation to the skin.*"

No scientific rationale has been provided why MEK was selected as a vehicle for the study, albeit it was recognised that the selected vehicle will change the properties of the Substance that does not reflect substance under physiological conditions/real life exposure. Due to the vehicle effect, the results obtained from the *in vivo* study under item i) cannot be considered valid.

For the reasons noted above, this study does not provide information required by OECD TG 429 (2013). Therefore this study cannot be used to adapt this information requirement according to Annex VII, Section 8.3.2, column 2, third paragraph.

B. ECHA further notes that in relation to the provided *in vitro* data, Annex VII, Section 8.3.1, column 1 (a to c) specifies that *in vitro/in chemico* information needs to be generated for three key events.

You have provided the information on skin sensitisation under items (ii) and (iii) above indicating that the source substance is a skin sensitiser. You did not submit any informaton on the key event of inflammatory response in keratinocytes set by REACH Annex VII, Section 8.3.1., point (b).

ECHA also notes that the dossier or the Chemical Safety Report does not contain any consideration why the positive results of the two above mentioned *in vitro* skin sensitisation studies have been disregared when making the final conclusions on skin sensitisation potential of the Substance i.e. that the Substance is not a skin sensitiser.

In conclusion, in absence of all this information, the information on skin sensitisation under items (ii) and (iii) does not allow classification and risk assessment.

On this basis, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance for skin sensitisation, *in vitro/in chemico* studies (OECD TG 442C, 442D and 442E) are considered suitable. In case the *in vitro/in chemico* method are not suitable for the Substance or the results cannot be used for classification and risk assessment, an *in vivo* skin sensitisation study must be performed and the murine local lymph node assay (LLNA) (OECD TG 429) is considered suitable.

Please also note that due to the problems noted in the LLNA study performed with the source substance, another *in vivo* method must be considered, in case no suitable vehicle can be identified for the LLNA. In case a non-LLNA *in vivo* method is used for testing, justification for the use of such method must be provided in the dossier.

2. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.)

An *in vitro* gene mutation study in bacteria is a standard information requirement in Annex VII to REACH.

You have adapted this information requirement by using a read-across approach under Annex XI, Section 1.5. You have provided the following information with the source substance;

Reaction product of N2,N2'-1,6-hexanediylbis[N4,N6-dibutyl-N2,N4,N6-tris(2,2,6,6-tetramethyl-4-piperidinyl)-1,3,5-triazine-2,4,6-triamine and hydrogen peroxide and butanal (EC: 700-878-1; CAS: 1395069-30-3):

> *In vitro* gene mutation study in bacteria (according to OECD TG 471, [redacted] 2012); *S. typhimurium* TA 1535, TA 1537, TA 98, TA 100 and *E. coli* WP2 bacteria, with and without metabolic activation.

As explained in the Appendix of general considerations, your adaptation in accordance with Annex XI, Section 1.5. is rejected. Therefore, the information requirement is not fulfilled.

Appendix B: 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 stating that *"a sub-chronic toxicity study (90 days) does not need to be conducted because the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day 'limit test' and human exposure is limited"*.

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

The standard information requirement can be adapted if several cumulative conditions are met (Section 8.6.2., Column 2, fourth indent, Annex IX to REACH), including the condition that the substance is unreactive.

However, ECHA observes that the Substance may contain a number of non-alkylated N-OH groups (i.e. [redacted] moiety). These functional groups can react further. In addition, one of the technical functions of the Substance is UV-light stabilizer in plastics. The Substance is a hindered amine which do not generally absorb UV-light but help removing free radicals, produced by photo-oxidation in the polymer. Through this process the amine functionality on the tetramethylpiperidine ring (hindered amine) will react and be converted to alkoxy amine functionality. For all these reasons ECHA concludes that the Substance can not be considered as unreactive.

Therefore, your adaptation is rejected and the information provided does not fulfil the information requirement.

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[5]. The Substance is a granulated powder, with particle size > 100 microns, which does not raise concern for 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.

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

Appendix C: Procedural history

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 4 November 2019.

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: 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

1. *Selection of the Test material(s)*

   The Test Material used to generate the new data must be selected taking into account the following:

   a) the boundary composition(s) of the Substance,
   b) 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*

   a) 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.
   b) The reported composition must include The reported composition must identify all the constituents as far as possible as well as their concentration (OECD GLP (ENV/MC/CHEM(98)16) and EU Tests Methods Regulation (EU) 440/2008 (Note, Annex). Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods,

With that detailed information, ECHA can confirm 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 dossiers[7].

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

Appendix E: List of references - ECHA Guidance8 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.

[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

OECD Guidance documents[10]

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.

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

Appendix F: 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.