~~Confidential~~

Helsinki, 08 February 2022

Addressees
Registrants of JS-C10-DMA as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
24/10/2018

Registered substance subject to this decision ("the Substance")
Substance name: Decyldimethylamine
EC number: 214-302-7
CAS number: 1120-24-7

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

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

- Appendix/Appendices entitled "Reasons to request information required under Annexes VII 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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 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". 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 Mike Rasenberg, 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. In vitro gene mutation study in bacteria

An in vitro gene mutation study in bacteria is an information requirement under Annex VII to REACH (Section 8.4.1.).

You have provided key studies and one supporting study in your dossier:

i. KEY_471_1996_Huntington with decyldimethylamine / CAS 1120-24-7 in strains S. typhimurium TA 98 and TA 100 which gave negative results
ii. RA_C12-14DMA_KEY_471_1996_[redacted]_96 with Amines, C12-14-alkyldimethyl / CAS 84649-84-3 in strains S. typhimurium TA 98 and TA 100 which gave negative results.
iii. RA_C12DMA_KEY_471_1988_[redacted] with dodecyldimethylamine / CAS 112-18-5 in the strains S. typhimurium TA 1535, TA 1537, TA 98, TA 100 and E. coli WP2 which gave negative results.
iv. RA_C14DMA_KEY_471_1996_[redacted] with dimethyl(tetradecyl) / CAS 112-75-4 in strains S. typhimurium TA 98 and TA 100 which gave negative results.
v. RA_C16DMA_KEY_471_1996_[redacted] with hexadecyldimethylamine / CAS 112-69-6 in strains S. typhimurium TA 98 and TA 100 which gave negative results.
vi. RA_C18DMA_KEY_471_1996_[redacted] with dimantine / N,N-dimethyloctadecan-1-amine / CAS 124-28-7 in strains S. typhimurium TA 98 and TA 100 which gave negative results.
vii. RA_C12DMA_NON KEY_471_1996_[redacted] with dodecyldimethylamine / CAS 112-18-5 in the strains S. typhimurium TA 98 and TA 100 which gave negative results.

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

1) Invalid read- across adaptation

The studies (ii) to (vii.) are perfomed with analogue substances. ECHA has considered the scientific and regulatory validity of your grouping and read-across approach in general before assessing the specific standard information requirements in the following appendices.

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 (addressed under 'Scope of the grouping'). 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 (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6. and related documents[2][3].

In your registration dossier you have formed a group (category) of 'dimethylalkylamines' (DMA Category). You have provided a read-across justification document in IUCLID Section 13 in your CSR.

[2] Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: Read-Across Assessment Framework (https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)
[3] Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: https://doi.org/10.2823/794394

You provide the following reasoning for the grouping the substances: "*all members share a very similar chemical structure, which is the basis for physical-chemical properties that are similar and follow a predictable trend with increasing alkyl chain length"* and "*due to the very similar structure, similar physico-chemical properties, environmental fate, ecotoxicity and mammalian toxicity of the DMAs under discussion, they can be accounted for in one category and fulfilment of data requirements by read-across from one category member to all other category members is justified."*

You define the applicability domain of the category as follows:
'*The category of dimethylalkylamines (DMAs) (i.e. N,N-dimethyl-Cx-(even numbered)-alkyl-1-amines) covers ten DMAs with alkyl chain lengths ranging from C10 to C18*.'

You have provided the following reasoning for the prediction of toxicological properties:
"The actual toxicity profile of a substance is driven by its intrinsic properties and its toxicokinetic behaviour. Based on the close structural similarities of the DMAs under consideration, significant differences in their intrinsic properties as well as in their toxicokinetic behaviour are not to be expected.".

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which is based on the formation of common (bio)transformation products. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

You intend to predict the properties for the category members from information obtained from the following source substances:

- Dodecyldimethylamine / N,N-dimethyldodecan-1-amine /CAS 112-18-5, RA_C12DMA_KEY_471_1988_[redacted] and RA_C12DMA_NON_KEY_471_1996_[redacted]
- Dimethyl(tetradecyl)amine / N,N-dimethyltetradecan-1-amine /CAS 112-75-4, RA_C14DMA_KEY_471_1996_[redacted]
- Hexadecyldimethylamine / N,N-dimethylhexadecan-1-amine /CAS 112-69-6, RA_C16DMA_KEY_471_1996_[redacted]
- Amines, C12-14-alkyldimethyl/N,N-dimethyl-C12-14-(even numbered)-alkyl-1-amines / CAS 84649-84-3, RA_C12-14 DMA_KEY_471_1996_[redacted]
- Dimantine / N,N-dimethyloctadecan-1-amine /CAS 124-28-7, RA_C18DMA_KEY_471_1996_[redacted]

ECHA has assessed your read-across approach and notes the following shortcomings with regards to predictions of toxicological properties.

Specific issue for the read-across within DMA category

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

According to the ECHA Guidance, one of the factors in determining the robustness of a category is the density and distribution of the available data across the category.[4] To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members needs to be available.

[4] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.1.5.

Furthermore in larger categories there may be breaks in trends which could affect the reliability of interpolation.[5] To confirm that there are no such breakpoints, adequate and reliable information needs to cover also substances within a range of homologous series.

For gene mutation in bacterial cells there are seven Ames studies with six diferent substances. However, as explained below under A.1.2, only the study performed with dodecyldimethylamine / CAS 112-18-5 is an adequate study performed with all the strains requested by the testing guideline. All the other studies are performed in only two and same strains (*S. thyphimurium* TA 98 and 100). Therefore, for this endpoint it is considered that there is only one reliable study for the whole category.

Based on these studies you claim that there is a similar toxicity profile for all the members of the DMA category.

Information for one category members is not sufficient to establish a trend across the category consisting of 10 substances. In the absence of information on substances for all ranges of the category (lower border, between the upper and lower borders of the category and upper border of the category), it cannot be confirmed that there is no breakpoint in toxicity trend within the given range of chain length. Therefore, the information provided is not sufficient to conclude that toxicological properties are likely to follow a regular pattern.

2) Non-conformity with the applicable test guideline

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471[6] (1997). One of the key parameters of this test guideline includes that the test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

The reported data for the study (i.) performed with the substance did not include results for the appropriate 5 strains, that is in TA98/TA100/TA1535/TA1537 or TA97a or TA97/the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101). All these studies are performed in only two and same strains (*S. thyphimurium* TA 98 and 100). Only the study iii. performed with analogue dodecyldimethylamine / CAS 112-18-5 is an adequate study performed with all the strains requested by the testing guideline.

In your comments, you state that the *in vitro* gene mutation study in bacteria with C10-DMA is already performed and that C10-DMA is not mutagenic. You also mention that you will provide this information in an updated of your registration dossier. The information in your comments is not sufficient for ECHA to make an assessment because you did not provide the robust study summary of the study. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation").

Therefore, the information requirement is not fulfilled.

Study design

To fulfil the information requirement for the Substance, the *in vitro* gene mutation study in bacteria (OECD TG 471) is considered suitable.

[5] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.2.
[6] ECHA Guidance R.7a, Table R.7.7–2, p.557

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 summaries[7].

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[8].

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

Appendix C: 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 18 November 2020.

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

ECHA took into account your comments and, following the cease of the manufacture of the only Registrant at Annex VIII , amended the requests and the deadline.

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 Guidance[9] 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)[10]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[11]

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[12]

[9] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[10] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[11] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[12] 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 E: Addressees of this decision and their corresponding information requirements

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]
[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.