~~Confidential~~

Helsinki, 27 January 2021

Addressees
Registrant(s) of AMPHOACETATES C12 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
12 December 2019

Registered substance subject to this decision ("the Substance")
Substance name: Acetic acid, chloro-, sodium salt, reaction products with 4,5-dihydro-2-undecyl-1H-imidazole-1-ethanol and sodium hydroxide
EC number: 271-794-6
CAS number: 68608-66-2

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 the deadline of ***2 November 2021***.

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

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

1. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

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

- Appendix entitled "Reasons to request information required under Annex VIII".

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 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.

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.

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

1. In vitro gene mutation study in mammalian cells

In vitro gene mutation study in mammalian cells is a standard information requirement in Annex VIII to REACH in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

Your dossier contains negative results for both an Ames test and an *in vitro* cytogenicity study. Therefore, the information requirement is triggered.

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 source study:

- *In vitro* gene mutation study in mammalian cells. [redacted] 2010. According to the OECD TG 476 with Reaction products of 1H-Imidazole-1-ethanol,4,5-dihydro-, 2-(C7-C17 odd-numbered, C17-unsatd. alkyl) derivs. and sodium hydroxide and chloroacetic acid, EC No. 931-291-0.

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 (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.

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 document in IUCLID Section 13.

You predict the properties of the Substance from the structurally similar substance: Reaction products of 1H-Imidazole-1-ethanol,4,5-dihydro-, 2-(C7-C17 odd-numbered, C17-unsatd. alkyl) derivs. and sodium hydroxide and chloroacetic acid, EC No. 931-291-0; i.e. the source substance, Amphoacetates C8-C18.

You have provided the following reasoning for the prediction of toxicological properties:
"Only Amphoacetates C8-C18 was tested in a mouse lymphoma assay and was shown to be negative. As ... Amphoacetates C12 have also mainly C12 and C14 mono-acetates... similar to the tested substance, ... Amphoacetates C12 are considered to have a similar genotoxicity and are read-across."

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 predictions of toxicological properties.

Characterisation of the structural similarities and differences between the substances

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*". In order to determine the structural similarities and differences between the substances included in a read-across approach, and in particular in case of UVCB substances (Unknown or Variable composition, Complex reaction products or of Biological materials), qualitative compositional information of the individual constituents of the substances needs to be provided. In addition, quantitative characterisation in the form of concentration values or ranges of the individual constituents of these substances, to the extent that this is measurable, needs to be provided.[2]

You highlighted differences in the composition of the substances relating to the distribution of the alkyl derivative constituents between the substances. You elaborated on the main differences and similarities for the substances as follows:

Table 1. Identification for Amphoacetates C8-C18 and Amphoacetate C12 as provided in the document "[redacted]", section 4.2

	Amphoacetate C12 EC 271-794-6 (target substance)	Amphoacetates C8-C18 EC 931-291-0 (source substance)
[redacted]	[redacted]	[redacted]

A wider range of carbon chain length spanning from [redacted] is included in the composition of the Amphoacetates C8-18 compared with the Amphoacetate C12. The [redacted] are the similar main constituents between the substances. Amphoacetate C12 contains more than [redacted] of [redacted] whereas Amphoacetates C8-C18 contains between [redacted] of [redacted].

Furthermore, you report different "forms", i.e. [redacted] forms for [redacted] (the source substance) and a [redacted] form only for the [redacted]. ECHA understands from this information that there may be two different possible situations/forms of a substance depending on the amount of [redacted] being used in the manufacturing process.

[2] ECHA Guidance R.6, Section R.6.2.5.5

According to the information provided in your technical dossier the source study has been conducted with the [redacted] form of the source substance where [redacted]% of the [redacted] are in the [redacted] form and [redacted] form.

It is unclear whether the percentages reported for each "form" of the substances correspond to average percentages for the entire set of [redacted] constituents or whether these percentages apply to each [redacted] individually. For example, in a [redacted] form, it is unclear whether there is [redacted] of each carbon chain length as [redacted] or if an average of [redacted] chain derivatives with varying percentages of different carbon chain length are [redacted] while these percentages for some constituents are reported to be [redacted] and for others [redacted]

You conducted the study with the source substance Amphoacetates C8-C18 using as a testing material a [redacted] The target substance is reported as a [redacted] only. It is not explained how the information from a [redacted] can be used to predict properties of the target substance with a [redacted] form only.

The information provided on the carbon chain length distribution identifies significant differences in the percentages of the carbon chain lengths. The target substance has [redacted] in much greater concentration than the source substance. It is not explained how the information from a test material used for the study conducted on the source substance containing [redacted] can be used to predict properties of the target substance which contains [redacted].

In order to establish the compositional similarities, it is important to provide a breakdown of of the percentages of [redacted] forms for each carbon chain length for source substance and for the Substance. ECHA notes the technical difficulties mentioned in your dossier in providing an analytical characterisation of the substances. However this level of detail in the composition of the substances is necessary to characterise qualitatively and quantitatively the constituents included in the composition of the substances and to determine the extent of the similarities between the substances. In the absence of this information, no reliable prediction of the properties of the Substance can be made from the data on the source substance.

Conclusion on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

Therefore, the information requirement is not fulfilled.

To fulfil the information requirement for the Substance, both the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) and the thymidine kinase gene (OECD TG 490) are considered suitable.

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[3].

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:

   a) the variation in compositions reported by all members of the joint submission,
   b) the boundary composition(s) of the Substance,
   c) 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 careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods,
   c) The reported composition must also include other parameters relevant for the property to be tested.

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

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 July 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: List of references - ECHA Guidance[4] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[5]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[6]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[7]

[4] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[5] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[6] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[7] 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 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]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]