ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-2114303248-57-01/F Helsinki, 30 June 2015

DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006

For Fatty acids, C16-18 and C18-unsatd., Me esters, distn. residues, CAS No 68604-41-1 (EC No 271-692-1), registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration for Fatty acids, C16-18 and C18-unsatd., Me esters, distn. residues, CAS No 68604-41-1 (EC No 271-692-1, submitted by [redacted] (Registrant).

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation). The scope of this compliance check is limited to the standard information requirement of Annex X, Sections 8.7.2, and 8.7.3 of the REACH Regulation. ECHA stresses that it has not checked the information provided by the Registrant and other joint registrants for compliance with requirements regarding the identification of the substance (Section 2 of Annex VI).

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 1000+T per year. This decision does not take into account any updates submitted after 05 March 2015, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

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

The compliance check was initiated on 27 June 2013.

On 27 September 2013 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt fo the draft decision.

On 4 October 2013 ECHA received comments from the Registrant on the draft decision, concerning the information requirements of Annex X, Sections 8.7.2, and 8.7.3. The compliance check requirement to submit information of a two-generation reproductive toxicity study (EU B.35, OECD TG 416) or an extended one-generation reproductive toxicity study (EU B.56, OECD TG 443) has been removed from this draft decision due to the legislative amendments to the REACH Regulation regarding Annex X, Section 8.7.3. In light

of this, ECHA Secretariat did not consider further the Registrant's comments concerning the information requirement of Annex X, Section 8.7.3. However, ECHA Secretariat did consider further the Registrant's comments concerning the information requirements of Annex X, Sections 8.7.2. On the basis of this information and change of scope, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

On 5 March 2015 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals for amendment of the draft decision within 30 days of the receipt of the notification.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Information required

A. Information in the technical dossier derived from the application of Annexes VII to XI

Pursuant to Articles 41(1)(a),(b) 41(3), 10(a)(vii), 12(1)(e), 13 and Annex X of the REACH Regulation the Registrant shall submit the following information using the indicated test method and the registered substance subject to the present decision:

1. Pre-natal developmental toxicity study (Annex X, 8.7.2.; test method: EU B.31./OECD 414) in rats or rabbits, oral route;

B. Deadline for submitting the required information

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated registration to ECHA by **7 July 2016**.

Notes for consideration by the Registrant:

In light of the comments made by the Registrant, ECHA points out that the Registrant may adapt the testing requested above according to the specific rules outlined in Annexes VIII to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a sound scientific justification, referring to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Authorities of the Member States for enforcement.

III. Statement of reasons

Pursuant to Article 41(3) of the REACH Regulation, ECHA may require the Registrant to submit any information needed to bring the registration into compliance with the relevant information requirements.

Pursuant to Articles 10(a)(vii), 12(1)(e) of the REACH Regulation, a technical dossier for a

substance manufactured or imported by the Registrant in quantities of 1000 tonnes or more per year shall contain as a minimum the information specified in Annex X of the REACH Regulation.

1. Pre-natal developmental toxicity study (Annex IX, 8.7.2.)

A "Pre-natal developmental toxicity study" for a first species is a standard information requirement as laid down in Annex X, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

The Registrant has not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex X, Section 8.7.2. Instead, the Registrant has proposed to adapt the information requirement for a prenatal developmental toxicity study (Annex X, 8.7.2.). The Registrant has justified the proposal for adaptation with reference to low toxicological activity, toxicokinetic data and no or no significant human exposure, without specifying the adequate adaption possibility given in the respective column 2 of that section of Annex X.

According to Annex IX, 8.7., Column 2, third indent (and Annex X, Section 8.7, third indent), the study does not need to be conducted if *"the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure."*

The Registrant has however not adequately documented that the conditions of one of the adaptation possibility foreseen in column 2 of Annex IX / X, section 8.7 are fulfilled. While the sub-acute study submitted shows relatively low toxicity (NOAEL above 250 mg/kg bw), it has not been documented that there is "no systemic absorption via relevant routes". On the contrary, according to what was reported in section 7.1 of IUCLID, the substance is bioavailable. Moreover, according to the process descriptors provided by the Registrant, there is potential for exposure.

Therefore, since the Registrant has not provided sufficient information to show that conditions of an adaptation in Column 2 of Annex X, 8.7 are met, the adaptation of the information requirement proposed by the Registrant cannot be accepted.

Read-across

In his comments to the draft decision, the Registrant has proposed to adapt the information requirement for a pre-natal developmental toxicity study and referred to read-across from 2-Ethylhexyl Stearate for which a pre-natal developmental toxicity study has been published [redacted]. In addition, other source substances (Methyl Oleate, Palmitate Methyl Esters, Ethyl Oleate and Butyl Stearate) have been suggested for the read-across, but for none of these substances has a pre-natal developmental toxicity study been provided. ECHA thus assessed the provided information in the light of the criteria of Annex XI, Section 1.5 of the REACH Regulation.

Structural similarity
ECHA points out that the first prerequisite of the read-across, pursuant to Annex XI, Section 1.5 of the REACH Regulation is structural similarity between the source and the target substances of the read-across. While it is recognized that "Fatty acids, C16-18 and C16-18-unsatd., Me esters" (i.e. the main component of the registered substance) and 2-Ethylhexyl Stearate may have some structural similarities, the registered substance contains several consitituents, i.e. glycerides, polymers, free fatty acids, and methanol. The Registrant has not explained in his comments how these other constituents can be covered by the suggested read-across. The concentrations of the relevant constituents have not been assessed for their relevance in the context of the proposed read-across nor has the toxicity of these constituents been sufficiently covered; and therefore it is not possible to assess whether read-across can at all cover these other constituents.

The main component of the registered substance contains an ester functionality and the only substance with adequate data on pre-natal developmental toxicity is a stearate (i.e. contains a carbonic acid functionality) and therefore they are structurally different. The relevance of the data of the source substance for the prediction of the property of the target substance has not been assessed.

Therefore, ECHA considers that the first prerequisite of the read-across, i.e. structural similarity, has not been demonstrated.

Boundaries and membership in the chemical group used in the read-across
In his comment, the Registrant has provided a matrix, which gives some relevant information on 2-Ethylhexyl Stearate, Methyl Oleate, Ethyl Oleate and Butyl Stearate. However the registered substances has not been included in that matrix. Furthermore, the Registrant has not provided an explicit definition of the substances, which belong to the group for the purpose of read-across and there is no explanation how the registered substance (considering all its constituests) fits within the boundaries of the grouping as intended.

Documentation
The Registrant has referred to four studies on different source substances for his read-across, two were made with "stearates" and three other "related compounds" and two were made using esters. While there may be some relevant structural similarity and some limited data on low systemic toxicity on the substances, the Registrant has not explained the relevance of the information generated with the given source substances for the target substance subject to this decision.

Additionally, the Registrant has not provided a study record for any of these studies thus not fulfilling the requirement to provide adequate and reliable documentation, as requested in Annex XI, Section 1.5 of the REACH Regulation.

Toxicokinetics
Concerning the toxicokinetics of some of the group members, the Registrant has explained that "*Higher molecular weight aliphatic esters are readily hydrolysed to the corresponding alcohol and acid and then generally oxidised to carbon dioxide and water. In addition, there is data from human and animal studies that show rapid absorption in the liver and breakdown of the substance into methanol and fatty acids; there is absence of the substance itself in the plasma/blood and in the urine.*" While this information might be considered relevant, adequate and detailed comparison of the metabolism of the source(s) and target substance of the read-across is missing. As the registrant's conclusions are

inadequately supported and documented, ECHA cannot verify whether the information supports their predicition.

Overall, the Registrant did not provide sufficient data on common precursors and/or breakdown products that the members of this chemical group have (Annex XI, Section 1.5 of the REACH Regulation).

Prediction of the effects
The Registrant did not explain how human health effect of the registered substance (target substance) can be predicted from the reference (source) substances of the group. The Registrant did not explain the mechanistic basis, i.e. failed to provide a read-across hypothesis.

The weakness of the toxicokinetic data specified above adds on the uncertainly of predicting the hazardous properties of the registered substance.

In summary, ECHA considers ECHA cannot verify from the information provided that the differences in structures do not cause any difference in properties or whether the read-across is valid for the endpoint and hence the criterion of predictability of human health and environmental effects of the target substance is not fulfilled, as required under Annex XI, Section 1.5 REACH.

Weight of Evidence

In the dossier update the registrant has also proposed a Weight of Evidence and proposes that the WoE consists of the following cumulative sources of confirmation:

- "The substance is of low toxicological activity.
- The metabolism of the substance does not lead to reprotoxic metabolites.
- Evidence from chronic toxicity studies.
- Evidence from reproductive toxicity studies."

ECHA finds that the reproductive toxicity parameters covered in a pre-natal developmental toxicity study have either not been sufficiently covered in studies that have been provided and/or depend on a read-across also provided by the registrant that has been found inadequately documented and justified, as specified above. Therefore the cumulative evidence provided from these studies does not correspond with the specific REACH information requirement set in Annex X, column two nor satisfy the conditions for Weight of Evidence as indicated in Annex XI, Section 1.2 of the REACH Regulation.

As explained above, the information available on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rat or the rabbit as a first species to be used.

Therefore, pursuant to Article 41(1)(a) and (b) and 41(3) of the REACH Regulation, the Registrant is requested to submit the following information derived with the registered

substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD 414) in rats or rabbits by the oral route.

Notes for consideration by the Registrant

In addition, a pre-natal developmental toxicity study on a second species is part of the standard information requirements as laid down in Annex X, section 8.7.2. for substances registered for 1000 tonnes or more per year (see sentence 2 of introductory paragraph 2 of Annex X).

The Registrant should firstly take into account the outcome of the pre-natal developmental toxicity on a first species and all other relevant available data to determine if the conditions are met for adaptations according to Annex X, 8.7. column 2, or according to Annex XI; for example if the substance meets the criteria for classification as toxic for reproduction Category 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment, or alternatively, if weight of evidence assessment of all relevant available data provides scientific justification that the study in a second species is not needed. If the Registrant considers that the conditions for these adaptations are not fulfilled, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species. If the Registrant comes to the conclusion that the conditions for these adaptations can be fulfilled, he should update his technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex X, 8.7.2. of the REACH Regulation.

2. Deadline for submitting the required information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 30 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also contained a two-generation reproductive toxicity study (EU B.35, OECD TG 416) or an extended one-generation reproductive toxicity study (EU B.56, OECD TG 443) (Annex X, Section 8.7.3.). As these studies are not addressed in the present decision, ECHA Secretariat considers that a reasonable time period for providing the required information in the form of an updated IUCLID dossier is 12 months from the date of the adoption of the decision. The decision was therefore modified accordingly

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted by the Registrant and other joint registrants for identifying the substance has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the information required by the present decision, the sample of substance used for the new studies must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition.

In addition, it is important to ensure that the particular sample of substance tested in the new studies are appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies must be suitable to assess these grades.

Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the studies to be assessed.

V. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on ECHA's internet page at http://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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Claudio Carlon
Head of Unit, Evaluation