EUROPEAN CHEMICALS AGENCY

Helsinki, 21 September 2016

Addressee [redacted]

Decision number: TPE-D-2114344610-59-01/F
Substance name: Isononanoic acid, C16-18 (even numbered)-alkyl esters
EC number: 601-141-6
CAS number: 111937-03-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 28.04.2014
Registered tonnage band: 1000+T

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA examined your testing proposal(s) and decided as follows.

Your testing proposal is accepted and you are requested to carry out:

Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats using the registered substance, including additional examinations to assess potential effects on fertility.

You may adapt the testing requested above according to the specific rules outlined in Annexes VI 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 scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **28 March 2018**. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, shall be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under http://echa.europa.eu/regulations/appeals.

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2

[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 1: Reasons

The decision of ECHA is based on the examination of the testing proposal submitted by you and scientific information submitted by third parties.

Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.)

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to EU B.26./OECD TG 408 with the following justification: "*There are no data available on the subchronic repeated dose toxicity (90 days) of isononanoic acid, C16-18 alkyl esters. In order to meet the standard information requirements of Regulation (EC) 1907/2006, Annex IX, Column 1, 8.6.2, a GLP-compliant subchronic toxicity study in the rat via the oral route following OECD 408 is proposed. The potential effects on fertility will be assessed by extending the standard study protocol to include additional sperm motility parameters and careful examination of reproductive organs/tissues in all the groups. The results of the study will be used to determine the following steps in the testing regime. The study will be conducted after a decision on the requirement to carry out the proposed test has been taken in accordance with the procedure laid down in Regulation (EC) 1907/2006, and a deadline to submit the information required has been set by the Agency. Approximately 15 months will be needed to perform the study and finalise the study report.*"

You proposed testing by the oral route. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA agrees that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of very low vapour pressure and no uses with spray application are reported that could potentially lead to aerosols of inhalable size.

Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

You proposed to extend the sub-chronic toxicity study (90 day) by including additional examinations/parameters as specified above. ECHA notes, that it is at your discretion to perform the intended additional examinations during the testing program and use the results to ensure the safe use of the substance. However, you are reminded that the proposed extension of this study does not fulfil the standard information requirement in the registration dossier for reproductive toxicity set out in Annex X, Section 8.7.3.

Consideration of the information received during third party consultation:

ECHA received third party information concerning the testing proposal during the third party consultation. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

Third party information 1:
A third party has indicated that the substance is a chemical constituent in cosmetics products and included in the European Commission inventory of cosmetic ingredients. The third party has also indicated that no use other than in cosmetic products was identified for the registered substance and therefore no animal testing should be performed according to Article 18, paragraph 2 of Regulation (EC) No 1223/2009.

ECHA acknowledges that the substance is listed in the EU Cosmetic ingredient database (CosIng). However, ECHA notes that, contrary to your obligations according to Article 10(a)(iii) and 10(b) and Annex VI of the REACH Regulation, you have not identified use(s) of the registered substance other than manufacture of the substance neither in section 3.5 of the IUCLID dossier nor in section 2.2 of the CSR and, therefore, the life cycle of the registered substance is unclear and currently only covering the manufacture of the substance.

With regard to the potential only use of the substance in cosmetics, ECHA has recently published a clarification of the interface between REACH and the Cosmetics Regulation (EC) No 1223/2009 (ECHA Factsheet ECHA-14-FS-04-EN, 27 October 2014), in relation to information requirements. In particular, ECHA has clarified that "*registrants of substances that are exclusively used in cosmetics may not perform animal testing to meet the information requirements of the REACH human health endpoints. The exception is any testing required to assess the risks from exposure to workers ("Workers" in this context are to be understood as persons who are actively involved in a particular activity of a production or manufacturing site, where they may be exposed directly or indirectly to chemical substances. On the other hand, professional users who use the cosmetic product as part of their professional activity (e.g. hairdressers) and consumers shall not be considered as "workers").*"

In this particular case, ECHA notes that you have identified PROC scenarios (1, 2, 3, 4, 8a, 8b, 9, 15) based on which it is foreseen that there will be opportunities for workers being exposed to the substance since not all the PROCs rely on closed systems, namely PROCs 4, 8a, 8b, 9 and 15.

Therefore, ECHA concludes that following the clarification provided in the above-mentioned Factsheet, the REACH requirements do apply for the present case in order to assess the risk of workers' exposure because: i) it is not clear if the substance is solely used in cosmetics, and ii) even if solely used in cosmetic products, workers will be exposed to the substance and therefore, testing is required to be able to assess the risks from the exposure to workers.

Third party information 2:
A third party has indicated that based on the results obtained in "all reported studies" the substance appears to display a low toxicity profile. However, ECHA notes that it is your responsibility to consider and justify in the registration dossier any adaptation of the information requirements in accordance with Annex IX, Section 8.6.2., column 2, fourth indent. This adaptation specifies that a sub-chronic toxicity study (90-day) does not need to be conducted if "the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day study, particularly if such a pattern is coupled with limited human exposure". ECHA notes that all criteria need to be met.

ECHA observes that the third party comment addressed only the criterion concerning the lack of evidence of toxicity in a 28-day study. However, an adaptation would also need to demonstrate that the other conditions of the adaptation possibility are fulfilled but the third party did not provide sufficient evidence for the lack of reactivity, solubility or absorption.

Therefore the criteria listed in Column 2 of Annex IX, section 8.6.2., fourth indent are not met and the information requirement for the sub-chronic toxicity study (90-day) cannot be adapted on this basis.

Third party information 3:
ECHA acknowledges that a third party has proposed both a weight of evidence and a read-across approach for you to consider.

ECHA notes that it is your responsibility to consider and justify any adaptation of the information requirements in accordance with the relevant conditions as established in Annex XI, Section 1.2. and/or 1.5. Therefore, you should assess whether you can justify a weight of evidence and/or a read-across as suggested by the third party. If the information requirement can be met by way of adaptation, you should include the adaptation argument with all necessary documentation according to Annex XI, Section 1.2. and/or 1.5. in the registration dossier.

ECHA notes that the information provided by the third party is insufficient for demonstrating that the conditions of Annex XI, Section 1.2. or 1.5. of the REACH Regulation are met.

ECHA observes that the third party has proposed a weight of evidence approach based on a database search. The third party claims that this general weight of evidence approach can be used to predict the sub-chronic toxic properties of a substance based on observed "low toxicity" in a sub-acute (short-term repeated dose) toxicity study if the substance fulfils certain other criteria described as a "low toxicity profile". However, ECHA notes that this predictive weight of evidence approach has shortcomings that prevent its application. First of all, ECHA notes that a weight of evidence approach requires substance-specific justification and cannot be addressed with a generic weight of evidence approach which, amongst other aspects, does not explain whether it is applicable to the registered substance. Secondly, the proposed approach has a limited predictive power. It is based on only eighteen substances with a "low toxicity profile". Thirdly, ECHA notes that the proposed general weight of evidence approach that a substance will or will not have an effect in a sub-chronic toxicity study based on results of a sub-acute toxicity study is not appropriate for the following reasons.

The study design of sub-acute toxicity studies and sub-chronic toxicity studies differ in relevant key parameters, which affect the uncertainty and relevance of the information obtained from these studies. For example, the reduced number of animals used in a sub-acute toxicity study (5 animals per sex and dose) compared to the sub-chronic toxicity study (10 animals per sex and dose) results in a lower statistical power of the sub-acute toxicity study to detect effects. Similarly, the duration of exposure in a sub-chronic toxicity study (90 days) covers a prolonged period of the animals' lifespan as compared to the sub-acute toxicity study (28 days). As a consequence of these differences in the study protocols, a sub-chronic toxicity study (90-day) may detect effects which were not observed in a sub-acute toxicity study (28 days).

ECHA also observes that no read-across justification demonstrating that the condition of Annex XI, Section 1.5. of the REACH Regulation are met has been provided.

Therefore, the information submitted by the third party is not sufficient to adapt the standard information requirement.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the registered substance subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26./OECD TG 408).

Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 5 April 2013.

ECHA held a third party consultation for the testing proposal(s) from 17 September 2014 until 2 November 2014. ECHA received information from third parties (see Appendix 1).

This decision does not take into account any updates after **18 July 2016**, 30 calendar days after the end of the commenting period.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision on 11 May 2016 and invited you to provide comments.

You did not comment on the draft decision by 17 June 2016.

On 21 July 2016, ECHA notified the competent authorities of the Member States of its draft decision and invited them to propose amendment to the draft decision under Article 51 of the REACH Regulation.
As no amendment was proposed, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

2. 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 Enforcement Authorities of the Member States.

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported 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 the substance tested in the new test(s) is 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 or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) 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 test(s) to be assessed.