ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002102-92-05/F Helsinki, 14 June 2012

DECISION ON A TESTING PROPOSAL SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006

For 2-ethylhexyl nitrate, CAS No. 27247-96-7, (EC No. 248-363-6), 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 40(1) of the REACH Regulation, ECHA has examined testing proposals set out in the registration dossier for 2-ethylhexyl nitrate, CAS No. 27247-96-7, (EC No. 248-363-6), submitted by [redacted] (Registrant), latest submission number [redacted] for 1000 tonnes or more per year.

In accordance with Articles 10(a)(ix) and 12(1)(e) of the REACH Regulation, the Registrant submitted the following testing proposals as part of the registration dossier to fulfil the information requirements set out in Annexes IX and X:

- Sub-chronic repeated dose toxicity study (90-days) in the rat by the inhalation route and according to OECD test guideline 413
- Pre-natal developmental toxicity study initially in the rat by the inhalation route according to OECD test guideline 414
- Developmental toxicity study in the rabbit by the inhalation route according to OECD test guideline 414
- Two-generation reproductive toxicity study in the rat by inhalation and according to OECD test guideline 416.

The present decision relates solely to the examination of the testing proposal for a sub-chronic toxicity study (90-day), a pre-natal developmental toxicity study and a developmental toxicity study. The testing proposal for the two-generation reproductive toxicity study is addressed in a separate decision although all testing proposals were initially addressed together in the same draft decision.

The examination of the testing proposals was initiated on 23 November 2010.

ECHA opened a third party consultation for the testing proposals including testing on vertebrate animals that was held from 29 April 2011 until 13 June 2011. ECHA did not receive any comments by the deadline from third parties.

On 23 November 2011 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

By 23 December 2011 the Registrant did not provide any comments on the draft decision to ECHA.

On 20 January 2012 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 to amend the draft decision within 30 days. Subsequently, Competent Authorities of the Member States submitted proposals for amendment to the draft decision. ECHA reviewed the proposals for amendment received and decided to modify the draft decision.

On 23 February 2012 ECHA notified the Registrant of proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on those proposals within 30 days of the receipt of the notification.

On 5 March 2012 ECHA referred the draft decision to the Member State Committee.

On 26 March 2012 the Registrant provided comments on the proposals for amendment. The Member State Committee took the comments of the Registrant into account.

The draft decision was split into two draft decision documents: one relating to the testing proposal for a two-generation reproductive toxicity study and one relating to the testing proposals for a sub-chronic repeated dose toxicity study, a pre-natal developmental toxicity study in the rat and a developmental toxicity study in the rabbit.

On 25 April 2012, in the discussion at the Member State Committee meeting, the representatives of the Registrant provided comments on the most appropriate route for testing indicating a possible reconsideration of the oral route as being the most appropriate. However, these comments were counter to the arguments formulated by the Registrants in the registration dossier subject to the ongoing testing proposal evaluation (latest submission number [redacted]). Therefore these new comments were not taken into account when reaching unanimous agreement on the draft decision in the Member State Committee meeting.

After discussion in the Member State Committee meeting on 24-27 April 2012, the Member State Committee modified the draft decision and a unanimous agreement of the Member State Committee on the draft decision relating to the testing proposals for a sub-chronic repeated dose toxicity study, a pre-natal developmental toxicity study in the rat and a developmental toxicity study in the rabbit was reached on 25 April 2012 and ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the requirements of the REACH Regulation. The decision does not prevent ECHA to initiate a compliance check on the present dossier at a later stage.

II. Testing required

Pursuant to Article 40(3)(a) of the REACH Regulation the Registrant shall carry out the following tests using the indicated test method:

1. Sub-chronic toxicity study (90-day) in rats, inhalation route (Annex IX, 8.6.2., test method: EU B.29/OECD 413)
2. Pre-natal developmental toxicity study in rats, inhalation route (Annex IX, 8.7.2., test method: EU B.31/OECD 414)
3. Developmental toxicity study in rabbits, inhalation (Annex X, 8.7.2., test method: EU B.31/OECD 414).

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA **by 14 June 2015** an update of the registration dossier containing the information required by this decision.

The Registrant shall determine the appropriate order of the studies taking into account the possible outcomes and considering the possibilities for adaptations of the standard information requirements according to column 1 or 2 provisions of the relevant Annexes of the REACH Regulation.

At any time, the Registrant shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other registrants.

III. Statement of reasons

Pursuant to Article 40(3)(a) of the REACH Regulation ECHA may require the Registrant to carry out the proposed test. In accordance with that provision ECHA decided to accept all the tests proposed by the Registrant for the reasons set out below.

The decision of ECHA is based on the examination of the testing proposal of the Registrant for the registered substance.

1. Sub-chronic repeated dose toxicity

A sub-chronic toxicity study (90 days) 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 generate the data for this endpoint.

The Registrant has provided justification for the study and particularly related to the choice of the inhalation route. This was considered appropriate because exposure to humans via inhalation is likely taking into account vapour pressure. The oral route was rejected by the Registrant due to liver first-pass metabolism possibly detoxifying the substance. It is also considered by the Registrant that there is "no possibility" of oral exposure of workers and general public. ECHA accepts the justification for the study and choice of route.

Therefore pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Sub-chronic toxicity study (90-day) in rats, inhalation route (test method: EU B.29/OECD 413) using the registered substance, 2-ethylhexyl nitrate.

2. Pre-natal developmental toxicity study in the rat

Pre-natal developmental toxicity studies are part of the standard information requirements as laid down in Annexes IX and X, section 8.7.2 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 generate the data for this endpoint.

The inhalation route has been proposed by the Registrant based on arguments of vapour pressure, route of human exposure, and rejection of the oral route due to possible detoxification and it being unlikely that workers or the general public will be exposed by the oral route. ECHA accepts the justification for the study and choice of route.

Therefore pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Pre-natal developmental toxicity study in rats, inhalation route (test method: EU B.31/OECD 414), using the registered substance, 2-ethylhexyl nitrate.

3. Developmental toxicity study in the rabbit

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, section 8.7.2. of the REACH Regulation. According to section 8.7.2 of Annex X subject to the Annex IX, 8.7.2, column 2 requirements of the REACH Regulation, a further pre-natal developmental toxicity study performed in a second species is required to fulfil the standard information requirements. The information available on this endpoint for the registered substance in the technical dossier does not meet these information requirements. Consequently there is an information gap and if Annex X 8.7, Column 2 or Annex XI provisions do not apply, it will be necessary to generate the information for this endpoint.

The inhalation route has been proposed by the Registrant based on arguments of vapour pressure, route of human exposure, and rejection of the oral route due to possible detoxification and it being unlikely that workers or the general public will be exposed by the oral route. ECHA accepts the justification for the study and choice of route.

Therefore pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Pre-natal developmental toxicity study in rabbits, inhalation route (test method: EU B.31/OECD 414) using the registered substance, 2-ethylhexyl nitrate. Prior to performing this study, a prenatal developmental toxicity study in a second species, in the rabbit, the Registrant should take into account the outcome of the pre-natal developmental toxicity study on the first species and all 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".

IV. Adequate identification of the composition of the tested material

The process of evaluation of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the generation of information is tailored to real information needs in order to prevent unnecessary testing. The information submitted in the registration dossier was sufficient to confirm the identity of the substance for the purpose of assessing the testing proposal. It is noted, however, that this information, or the information submitted by other registrants of the same 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 proposed tests, 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 the joint registrants of the same substance to agree with the tests proposed in the testing proposal (as applicable to their tonnage level) and to document the necessary information on its composition. The substance identity information of the registered substance and of the sample tested must enable ECHA to confirm the relevance of the testing for the substance actually registered by each joint registrant. Finally, the studies must be shared by the joint registrants concerned.

V. General requirements for the generation of information and Good Laboratory Practice

ECHA always reminds registrants of the requirements of Article 13(4) of the REACH Regulation that reads:

"Ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice provided for in Directive 2004/10/EC or other international standards recognised as being equivalent by the Commission or the Agency and with the provisions of Directive 86/609/EEC, if applicable."

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

National authorities monitoring good laboratory practice (GLP) maintain lists of test facilities indicating the relevant areas of expertise of each facility.

VI. 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 appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the ECHA's internet page at http://echa.europa.eu/appeals/app_procedure_en.asp. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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