ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002190-87-05/F Helsinki, 15.10.2012

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

For Dilauroyl peroxide, CAS No. 105-74-8 (EC No. 203-326-3), 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 dilauroyl peroxide, CAS No. 105-74-8 (EC No. 203-326-3), submitted by [redacted] (Registrant), latest submission number [redacted], for [redacted].

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 rats by the oral route according to OECD test guideline 408. In addition to the standard parameters of the 90 day study there is a proposal to investigate additional parameters within the proposed study: histopathology of the testes, weights of reproductive organs and accessory glands (i.e. testis, epididymis, prostate, seminal vesicle) and sperm parameters.;
- Pre-natal developmental toxicity study in the rat by the oral route according to OECD test guideline 414;
- Long-term toxicity to sediment organisms according to OECD test guideline 225 (Sediment-Water *Lumbriculus* Toxicity Test Using Spiked Sediment).

The examination of the testing proposals was initiated on 2 March 2011.

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 information from third parties.

On 23 January 2012 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.
On 1 February 2012 ECHA received comments from the Registrant agreeing to ECHA's draft decision.

ECHA considered the Registrant's comments received and did not amend the draft decision.

On 14 June 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 of the receipt of the notification.

Subsequently, Competent Authorities of the Member States submitted proposals for amendment to the draft decision.

On 18 July 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 for amendment within 30 days of the receipt of the notification.

ECHA reviewed the proposals for amendment received.

On 30 July 2012 ECHA referred the draft decision to the Member State Committee.

On 6 August 2012, the Registrant provided comments on the proposed amendments. ECHA decided to amend the draft decision. The Member State Committee took the comments of the Registrant into account.

After discussion in the Member State Committee meeting on 19-21 September 2012, a unanimous agreement of the Member State Committee on the draft decision as referred to MSC was reached on 20 September 2012. 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 proposed tests using the indicated test method(s) and the registered substance:

1. Sub-chronic repeated dose toxicity study (90-days) in rats, oral route (Annex IX, 8.6.2., test method: EU B.26/OECD 408)
2. Pre-natal developmental toxicity study in the rat by the oral route (Annex IX, 8.7.2., test method: EU B.31/OECD 414)
3. Long-term toxicity to sediment organisms (Annex X, 9.5.1., test method OECD 225)

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **15 October 2014** an update of the registration dossier containing the information required by this decision.

Data from a second pre-natal developmental toxicity study on another species is a standard information requirement according to Annex X, 8.7.2 of the REACH Regulation. 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. If

the Registrant considers that testing is necessary to fulfill this information requirement, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species.

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.

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant for the registered substance.

1. Sub-chronic repeated dose toxicity

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 generate the data for this endpoint.

The Registrant proposed to extend the sub-chronic toxicity study (90-day) by including additional examinations/parameters concerning reproductive toxicity. ECHA notes, that it is at the Registrant's discretion to perform the intended additional examinations during the testing program and use the results to ensure the safe use of the substance. However, the Registrant is reminded that the proposed extension of this study to include additional examinations concerning reproductive toxicity does not fulfil the standard information requirements in the registration dossier for reproductive toxicity set out in Annex X, 8.7.3 unless Annex X, 8.7 column 2 adaptation is applied.

A proposal for amendment was received from a Member State Competent Authority for rejection of the 90-day sub-chronic repeated dose toxicity study on the grounds that, on the basis of the information contained in the registration dossier, the following adaptation to the information requirement set out in column 2 of Annex IX, 8.6.2. could be applied *"the substance should be unreactive, insoluble and not inhalable, and there is no evidence of absorption and no evidence of toxicity in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure."*

In its comments to this proposal for amendment the Registrant agreed that on this basis the testing proposal should be rejected.

In light of the proposal for amendment and the Registrant's comment ECHA has assessed whether this adaptation to the information requirement is possible. ECHA has concluded that on the basis of the information available in the registration dossier this adaptation of the information requirement cannot be applied. In particular:

- The substance is chemically reactive and reported to be so within the dossier. The substance is an initiator of chemical reactions and producer of free radicals.
- The substance has some reported evidence on possible toxicity e.g. in the blood parameters, where statistically significant findings were observed in the reticulocyte maturity indices and large unstained cells which were also out of the range of the

historical control data. Therefore, it cannot be concluded that there is no evidence of absorption and no evidence of toxicity.

- The exposure scenarios within the CSR indicate widespread [redacted] incorporating at least 15 PROCs, many of which indicate exposure potential. This is not indicative of "*limited human exposure*".
- The substance is reported within the CSR to be used for both [redacted] and although there is evidence the substance itself may not contain a significant respirable fraction, deposition may still be expected in the upper respiratory tract with subsequent possibility of impact on those surfaces and, additionally, the potential for subsequent exposure through ingestion. The CSR reports the [redacted] to be of a liquid, in which case [redacted] may be anticipated.

Accordingly, the proposal for amendment has not been accepted.

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, oral route (test method: EU B.26/OECD 408) using the registered substance, dilauroyl peroxide.

2. Pre-natal development toxicity study in the rat

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. 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.

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, oral route (test method: EU B.31/OECD 414) using the registered substance, dilauroyl peroxide.

When considering the need for a testing proposal for a prenatal developmental toxicity study in a second species, 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.

3. Long-term toxicity to sediment organisms

A long-term toxicity to sediment organisms study is a standard information requirement as laid down in Annex X, section 9.5.1. of the REACH Regulation. Long-term toxicity to sediment testing shall be proposed by the registrant if the results of the chemical safety assessment indicate the need to investigate further the effects of the substance and/or relevant degradation products on sediment organisms. The information on this endpoint is not available for the registered substance. The Registrant concludes that in the environment, due to the high adsorption coefficient of the substance, the vast majority of the substance would be found in the sediment. Consequently the Registrant proposes to perform a long-term toxicity to sediment organisms study according to OECD 225 Guidelines Sediment-water *Lumbriculus* toxicity test using spiked sediment.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study: Sediment-water *Lumbriculus* toxicity test using spiked sediment (test method OECD 225) using the registered substance, dilauroyl peroxide.

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 new studies meet real information needs. Within this context, the Registrant's dossier was sufficient to confirm the identity of the substance to the extent necessary for evaluation of the testing proposal. The Registrant must note, 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 joint registrants of the same substance to agree to the tests proposed (as applicable to their tonnage level) 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 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 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 registered to enable the relevance of the studies to be assessed.

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

ECHA reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP).

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.

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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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