Decision number: CCH-D-0000002304-84-04/F Helsinki, 21 June 2012

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

For Vinyl 2-ethylhexanoate, CAS No 94-04-2 (EC No 202-297-4), 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 (the REACH Regulation).

I. Procedure

Pursuant to Article 41(1) of the REACH Regulation the ECHA has performed a compliance check of the registration dossier for Vinyl 2-ethylhexanoate, CAS No 94-04-2 (EC No 202-297-4) submitted by [redacted] (Registrant). This decision is based on the registration dossier as submitted with the submission number [redacted] for 100-1000 tonnes per year. This decision does not take into account any updates submitted after 20 January 2012, 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.

The compliance check was initiated on 21 June 2010.

On 29 April 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.

On 26 May 2011 ECHA received comments from the Registrant agreeing to most of the requests in ECHA's draft decision.

On 27 May 2011 the Registrant submitted an updated IUCLID file with the above-mentioned submission number to ECHA upgrading the registration tonnage to 100-1000 tonnes per year. A testing proposal was included in the updated dossier. ECHA has considered the information received as well as the Registrant's comments on the draft decision, and subsequently amended the draft decision, targeted to the information requirements subject to the present decision.

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 not to amend 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 within 30 days of the receipt of the notification.

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

On 26 March 2012 the Registrant provided comments on the proposed amendments. The Member State Committee took the comments of the Registrant into account.

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 was reached on 26 April 2012.

Due to the tonnage band update to 100-1000 tonnes per annum and given that there are adaptation possibilities provided to omit the short-term repeated dose toxicity study (28 days) in Annex VIII, 8.6.1., Column 2 and Annex IX, 8.6.1. Column 1 of the REACH Regulation, this decision does not address the Annex VIII, 8.6.1 repeat dose toxicity information requirement as originally foreseen in ECHA's draft decision. This does not imply that the registration dossier is compliant with the information requirement(s) of Annex VIII, 8.6.1. or Annex IX, 8.6.2. of the REACH Regulation respectively.

This compliance check decision does not prevent ECHA to initiate further compliance checks on the present dossier at a later stage.

The present decision relates solely to the compliance check process. The outcome of the testing proposals examination will be addressed in a separate decision.

II. Information required

1) Pursuant to Articles 41(1)(a), 41(3) and 10(a)(ii) as well as Annex VI, Section 2 of the REACH Regulation the Registrant shall submit for the registered substance:

   a. The spectral data: ultra-violet and nuclear magnetic resonance and/or mass spectra (Annex VI, 2.3.5.);
   b. Chromatographic data that enables the composition to be quantified (Annex VI, 2.3.6.). This shall include a description of how the composition of the substance was quantified based on the chromatographic data;
   c. The description of the analytical methods or the appropriate bibliographical references for the identification of the substance and the additive. This information shall be sufficient to allow the method to be reproduced (Annex VI, 2.3.7.).

2) Pursuant to Articles 41(1)(a), 41(3), and 10(a)(vi) and (vii), as well as Annexes VII and VIII of the REACH Regulation the Registrant shall submit the following information using the test methods indicated below while taking in account that there may be an obligation to agree on sharing of information and costs with other registrants at a later stage:

   - Boiling point (Annex VII, 7.3.; EU Method A.2.)
   - Vapour pressure (Annex VII, 7.5.; EU Method A.4.)
   - Water solubility (Annex VII, 7.7.; EU Method A.6.)
   - Partition coefficient n-octanol/water (Annex VII, 7.8.; EU Method; A.8.)
   - Auto-ignition temperature (Annex VII, 7.12.; EU Method A.15.)

- Skin sensitisation (Annex VII, 8.3.; EU Method B.42.)
- *In vitro* gene mutation study in mammalian cells (Annex VIII, 8.4.3; EU Method B.17)
- *In vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study (Annex VIII, 8.4.2; EU Method B.10 or draft OECD guideline 487).

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated IUCLID dossier to ECHA **by 21 June 2013**.

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

Based on the examination of the technical dossier, ECHA concludes that the information therein, submitted by the Registrant for registration of the above mentioned substance for the purpose of registration within the applicable tonnage band of 10 to 100 tonnes per year in accordance with Articles 6 and 11(2) of the REACH Regulation, does not comply with the requirements of Articles 10 and 12, and Annexes VI, VII, and VIII thereof. During the course of this compliance check, the Registrant updated his dossier to a tonnage band of 100-1000 tonnes per year. This compliance check is targeted to compliance with the requirements of Articles 10, 12 and 13 and with Annexes VII and VIII thereof. Consequently, the Registrant is requested to submit the information mentioned above that is needed to bring the registration into compliance with the relevant information requirements.

1) Missing information related to substance identity

Pursuant to Article 10(a)(ii) and Annex VI, Section 2 of the REACH Regulation, the technical dossier of the registration shall include information on the identity of the substance. Annex VI, Section 2 lists information requirements that shall be sufficient to identify the registered substance.

a. The technical dossier contains only an infra-red spectrum of the substance, which alone is not sufficient to verify the substance identity. The technical dossier does not contain ultra-violet, nuclear magnetic resonance, or mass spectra, and does not contain a justification for omitting these spectra. The Registrant shall therefore provide an ultra-violet spectrum in addition to a nuclear magnetic resonance or mass spectrum for the registered substance.
b. The technical dossier contains a gel permeation chromatogram that does not enable the substance composition to be quantified. The Registrant is required to submit chromatographic data that enables the composition to be quantified. The Registrant is required to include a description of how the composition was quantified based on the chromatographic data.
c. The registration did not contain details of analytical methods to determine the main constituent and the additive, which is required by Annex VI, Section 2.3.7 of the REACH Regulation. The Registrant is requested to submit the missing information.

In its comments the Registrant expressed consent to provide this data.

2) Missing information related to endpoints

Pursuant to Articles 10(a)(vi) and (vii), and 12(1)(c) of the REACH Regulation, a registration for a substance produced in quantities of 10-100 tonnes per year shall contain as a minimum the information specified in Annexes VII-VIII of the REACH Regulation.

2.1) Boiling point

The technical dossier contains a study on a qualitative or quantitative structure-activity relationship model (QSAR) performed using the EPISUITE, MPBPWIN v.1.42 model with a Registrant-assigned Klimisch score of 2 (reliable with restrictions). Annex XI, section 1.3 sets out conditions which are prerequisite for the acceptance of a QSAR prediction. These conditions are not met because no information was provided to prove that the substance falls within the applicability domain of the QSAR model, and no adequate and reliable documentation of the applied method has been provided. Therefore it is not possible to evaluate the validity of this QSAR estimate, and this QSAR estimate is not sufficient to fulfil this information requirement.

Therefore, the Registrant is requested to submit the missing information on boiling point, performed with the registered substance, using the test method A.2 according to Commission Regulation (EC) No 440/2008, and to update the technical dossier and the Chemical Safety Report (CSR) with the relevant information.

In its comments the Registrant expressed consent to provide this data.

2.2) Vapour pressure

The technical dossier contains a QSAR study performed using the EPISUITE, MPBPWIN v.1.42 model, with a Registrant-assigned Klimisch score of 2. Annex XI, section 1.3 sets out conditions which are prerequisite for the acceptance of a QSAR prediction. These conditions are not met because no information was provided to prove that the substance falls within the applicability domain of the QSAR model, and no adequate and reliable documentation of the applied method has been provided. Therefore it is not possible to evaluate the validity of this QSAR estimate, and this QSAR estimate is not sufficient to fulfil this information requirement.

Therefore, the Registrant is requested to submit the missing information on vapour pressure, performed with the registered substance, using the test method A.4 according to Commission Regulation (EC) No 440/2008, and to update the technical dossier and the Chemical Safety Report (CSR) with the relevant information.

In its comments the Registrant expressed consent to provide this data.

2.3) Water solubility

The technical dossier contains two QSAR studies performed using the OECD Toolbox, EPISUITE WSKOWWIN v.1.67 model with a Registrant-assigned Klimisch score of 2, and the EPISUITE WATERNT v.101 model with a Registrant-assigned Klimisch score of 2. Annex XI, section 1.3 sets out conditions which are prerequisite for the acceptance of a QSAR prediction. These conditions are not met because no information was provided to prove that the substance falls within the applicability domain of the QSAR model, and no adequate and reliable documentation of the applied method has been provided. Therefore it is not possible

to evaluate the validity of this QSAR estimate, and this QSAR estimate is not sufficient to fulfil this information requirement.

Therefore the Registrant is requested to submit the missing information on water solubility, performed with the registered substance, using the test method A.6 according to Commission Regulation (EC) No 440/2008, and to update the technical dossier and the Chemical Safety Report (CSR) with the relevant information.

In its comments the Registrant expressed consent to provide this data.

2.4) Partition coefficient

The technical dossier contains two QSAR studies performed using the OECD Toolbox, LogP Multicase model with a Registrant-assigned Klimisch score of 2, and the EPISUITE KOWWIN v.1.67 with a Registrant-assigned Klimisch score of 2. Annex XI, section 1.3 sets out conditions which are prerequisite for the acceptance of a QSAR prediction. These conditions are not met because no information was provided to prove that the substance falls within the applicability domain of the QSAR model, and no adequate and reliable documentation of the applied method has been provided. Therefore it is not possible to evaluate the validity of this QSAR estimate, and this QSAR estimate is not sufficient to fulfil this information requirement.

Therefore, the Registrant is requested to submit the missing information on partition coefficient, performed with the registered substance, using the test method A.8 according to Commission Regulation (EC) No 440/2008, and to update the technical dossier and the Chemical Safety Report (CSR) with the relevant information.

In its comments the Registrant expressed consent to provide this data.

2.5) Auto-ignition temperature

The technical dossier contains statements for the use of a read-across approach from a supporting substance (structural or analogue surrogate). The Registrant proposes to read-across the results of an auto-ignition temperature test from the analogue vinyl neodecanoate based on the structural similarity of this substance to the registered substance.

Annex VIII, second introductory paragraph, requires the Registrant to clearly state reasons for adapting the standard information requirements according to the rules in Annex XI. As insufficient justification was provided for read-across, the requirements of Annex XI, Section 1.5 in conjunction with Annex VIII, second introductory paragraph, of the REACH Regulation were not met. Specifically, although the substance shares common functional groups to the read-across substance, the read-across substance differs from the target substance in both branching and length of the carbon chain. Furthermore the identity of the read-across substance is unclear; the read-across substance appears to be a Chemical of Unknown or Variable Composition, Complex Reaction Product and Biological Materials (UVCB) composed of different isomers with different branching. Finally, read-across is not appropriate for this endpoint at all as the self-ignition temperature can vary significantly based on small changes in the substance's structure. Based on the structural differences between the registered and read-across substances, the auto-ignition temperatures can be expected to differ significantly between, and can affect the risk assessment for this substance. Consequently, the read-across fails the criteria of Annex XI, section 1.5, and the information requirement for auto-ignition temperature is not fulfilled.

Therefore, the Registrant is requested to submit the missing information on auto-ignition temperature, performed with the registered substance, using the test method A.15 according to Commission Regulation (EC) No 440/2008 and to update the technical dossier and the Chemical Safety Report (CSR) with the relevant information.

In its comments the Registrant expressed consent to provide this data.

2.6) Skin sensitisation

The technical dossier does not contain the results of a skin sensitisation study on the registered substance. Instead, it contains statements on the use of a read-across approach for a supporting substance (structural or analogue surrogate). The technical dossier contains the results of a skin sensitisation study performed using OECD guideline 206 on vinyl neodecanoate.

Annex VIII, fourth introductory paragraph, requires the Registrant to clearly state reasons for adapting the standard information according to the rules in Annex XI. As insufficient justification was provided for read-across, the requirements of Annex XI, Section 1.5 in conjunction with Annex VIII, fourth introductory paragraph, of the REACH Regulation were not met. In addition to the lack of justification for the read-across, ECHA concludes that the read-across is insufficient for the following reasons:

- The registered substance vinyl 2-ethyl hexanoate is a mono-constituent substance, whereas the read-across substance appears be a UVCB composed of different isomers with different branching. In addition, information on the substance identity, including the proportion of different isomers of the read-across substance is lacking. Therefore structural similarity between the read-across and registered substances has not been established.

- The registered substance has a distinct spectrum and potency of toxicological effects, compared to the read-across substance in other toxicological endpoints. Therefore toxicological similarity between the registered and read-across substances has not been established.

Consequently, the read-across fails the criteria of Annex XI, section 1.5, and the information requirement for skin sensitisation is not fulfilled.

In its comments to the draft decision as well as in the updated dossier the Registrant provided further justification to the originally submitted read-across argumentation. The argumentation includes a comparison of the structure as well as the physico-chemical, and (eco)toxicological properties of three substances, vinyl 2-ethylhexanoate, as well as the read-across substances vinyl neononanoate and vinyl neodecanoate. However this is not sufficient to justify the read-across because the available information on the registered substance indicates it has a distinct spectrum and potency of toxicological effects compared to the read-across substances, and these differences are not explained satisfactorily. For example, in a 14 day repeated dose toxicity study, the registered substance showed different potency and organ-specific effects (neurotoxicity, haematotoxicity, absence of renal hyaline droplets) to that observed with the read-across substances. These effects are not addressed by the read-across argument.

Therefore, the Registrant is requested to submit the missing information on skin sensitisation, performed with the registered substance, using the test method B.42

according to Commission Regulation (EC) No 440/2008, and to update the technical dossier and the Chemical Safety Report (CSR) with the relevant information.

2.7) *In vitro* gene mutation study in mammalian cells

The technical dossier does not contain the results of an *in vitro* gene mutation study in mammalian cells on the registered substance. Instead, it contains statements on the use of a read-across approach for a supporting substance (structural or analogue surrogate). The technical dossier contains the results of an *in vitro* gene mutation study in mammalian cells performed according to OECD Guideline 476.

Annex VIII, fourth introductory paragraph, requires the Registrant to clearly state reasons for adapting the standard information according to the rules in Annex XI. As insufficient justification was provided for read-across, the requirements of Annex XI, Section 1.5 in conjunction with Annex VIII, fourth introductory paragraph, of the REACH Regulation were not met. In addition to the lack of justification for the read-across, ECHA concludes that the read-across is insufficient for the following reasons:

- The registered substance vinyl 2-ethyl hexanoate is a mono-constituent substance, whereas the read-across substance appears be a UVCB composed of different isomers with different branching. In addition, information on the substance identity, including the proportion of different isomers of the read-across substance is lacking. Therefore structural similarity between the read-across and registered substances has not been established.

- The registered substance has a distinct spectrum and potency of toxicological effects, compared to the read-across substance in other toxicological endpoints. Therefore toxicological similarity between the registered and read-across substances has not been established.

Consequently, the read-across fails the criteria of Annex XI, section 1.5, and the information requirement for "in vitro gene mutation study in mammalian cells" is not fulfilled.

In its comments to the draft decision as well as in the updated dossier the Registrant provided further justification to the originally submitted read-across argumentation. The argumentation includes a comparison of the structure as well as the physico-chemical, and (eco)toxicological properties of three substances, vinyl 2-ethylhexanoate, as well as the read-across substances vinyl neononanoate and vinyl neodecanoate. However this is not sufficient to justify the read-across because the available information on the registered substance indicates it has a distinct spectrum and potency of toxicological effects compared to the read-across substances, and these differences are not explained satisfactorily. For example, in a 14 day repeated dose toxicity study, the registered substance showed different potency and organ-specific effects (neurotoxicity, haematotoxicity, absence of renal hyaline droplets) to that observed with the read-across substances. These effects are not addressed by the read-across argument

Therefore, the Registrant is requested to submit the missing information on *in vitro* gene mutation in mammalian cells, performed with the registered substance, using the test method B.17 according to Commission Regulation (EC) No 440/2008, and to update the technical dossier and the Chemical Safety Report (CSR) with the relevant information.

2.8) *In vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study

The technical dossier does not contain the results of an *in vitro* gene micronucleus study on the registered substance. Instead, it contains statements on the use of a read-across approach for a supporting substance (structural or analogue surrogate). The technical dossier contains the results of an *in vitro* mammalian chromosome aberration test according to OECD Guideline 473.

Annex VIII, fourth introductory paragraph, requires the Registrant to clearly state reasons for adapting the standard information according to the rules in Annex XI. As insufficient justification was provided for read-across, the requirements of Annex XI, Section 1.5 in conjunction with Annex VIII, fourth introductory paragraph, of the REACH Regulation were not met. In addition to the lack of justification for the read-across, ECHA concludes that the read-across is insufficient for the following reasons:

- The registered substance vinyl 2-ethyl hexanoate is a mono-constituent substance, whereas the read-across substance appears be a UVCB composed of different isomers with different branching. In addition, information on the substance identity, including the proportion of different isomers of the read-across substance is lacking. Therefore structural similarity between the read-across and registered substances has not been established.

- The registered substance has a distinct spectrum and potency of toxicological effects, compared to the read-across substance in other toxicological endpoints. Therefore toxicological similarity between the registered and read-across substances has not been established.

Consequently, the read-across fails the criteria of Annex XI, section 1.5, and the information requirement for skin sensitisation is not fulfilled.

In its comments to the draft decision as well as in the updated dossier the Registrant provided further justification to the originally submitted read-across argumentation. The argumentation includes a comparison of the structure as well as the physico-chemical, and (eco)toxicological properties of three substances, vinyl 2-ethylhexanoate, as well as the read-across substances vinyl neononanoate and vinyl neodecanoate. However this is not sufficient to justify the read-across because the available information on the registered substance indicates it has a distinct spectrum and potency of toxicological effects compared to the read-across substances, and these differences are not explained satisfactorily. For example, in a 14 day repeated dose toxicity study, the registered substance showed different potency and organ-specific effects (neurotoxicity, haematotoxicity, absence of renal hyaline droplets) to that observed with the read-across substances. These effects are not addressed by the read-across argument.

Therefore, the Registrant is requested to submit the missing information on *in vitro* cytogenicity study in mammalian cells or the *in vitro* micronucleus study, performed with the registered substance, using the test method B.10 according to Commission Regulation (EC) No 440/2008 or draft OECD guideline 487, and to update the technical dossier and the Chemical Safety Report (CSR) with the relevant information.

In its comments the Registrant expressed consent to provide this data using OECD guideline 473 (EU Method B.10).

IV. 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 ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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.

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://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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