ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 27 September 2016

Addressee: [redacted]

Decision number: CCH-D-2114340871-51-01/F
Substance name: 2-ethylhexyl acrylate
EC number: 203-080-7
CAS number: 103-11-7
Registration number: [redacted]
Submission number: [redacted]
Submission date: 30.11.2012
Registered tonnage band:>1000 tonnes per year

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA requests you to submit information on

1. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2; test method: EU B.31/OECD TG 414) in rabbits, oral route with the registered substance**

2. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3; test method: OECD TG 443) in rats, oral route with the registered substance; specified as follows:**

   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce some toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation**

3. **Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5; test method: Daphnia magna reproduction test, EU C.20/OECD TG 211) with the registered substance;**

4. **Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1; test method: Fish, early-life stage (FELS) toxicity test, OECD TG 210) with the registered substance;**

5. **Bioaccumulation in aquatic species (Annex IX, Section 9.3.2; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD TG 305) with the registered substance;**

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 **4 October 2019. 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/web/guest/regulations/appeals.

Authorised[1] by Hannu Braunschweiler, Head of Unit, Evaluation E1

[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

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

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

Pre-natal developmental toxicity studies on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The technical dossier contains information on a pre-natal developmental toxicity study in rats by the inhalation route using the registered substance as test material. This study fulfils the standard information requirement for a pre-natal developmental toxicity study in a first species (Annex IX, Section 8.7.2.).

In the technical dossier you have provided a study record for a pre-natal developmental toxicity in rabbits using an analogue substance methyl acrylate.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement based on read-across approach according to Annex XI, Section 1.5.

ECHA notes that there is no hypothesis and justification establishing a basis whereby toxicological properties of the registered substance may be predicted from data for the analogue substance methyl acrylate. In the absence of any justification supporting the proposed grouping/read-across approach, ECHA considers that you have failed to provide an adequate and reliable documentation of the applied method as required by Annex XI, Section 1.5 of the REACH Regulation. Therefore, ECHA is not in a position to conclude on the proposed read-across approach which could allow establishing that relevant properties of the registered substance can be predicted from those of the analogue substance. The proposed read-across has therefore to be rejected as not acceptable.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided 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.

In your comments to the draft decision you propose to address the information requirements listed in the draft decision by using a category approach. Based on the information provided in the read-across justification document (Justification For Acrylate category) ECHA understands that the read-across hypothesis is based on structural similarity (all category members are esters of acrylic acid with increasing carbon chain length), rapid metabolism of the parent compounds to acrylic acid and corresponding alcohols, and similarities in physico-chemical and (eco)toxicological properties and environmental fate among the category member.

In the comments provided you have submitted new data on metabolism and breakdown products of multiple category members, including the substance subject to this decision. In addition, you further indicated that new studies with n-butyl acrylate (OECD 414 in rabbits and OECD 421, a preliminary study for OECD 443) will be available at the end of 2016. This

data will be used in an update of the category approach.

ECHA has assessed the information provided in the comments and while no complete independent assessment could be completed on the basis of the information provided, ECHA makes the following preliminary observations:

- Based on the results of human health studies provided in the read-across justification document, the category members are of low acute toxicity and the NOAEL values obtained from the repeated dose toxicity studies seem to be within similar range. You claim that the substances have similar target organs. The NOAEL values obtained from the developmental toxicity studies conducted with some of the category members in rats are within 25-200 ppm. You conclude that based on this data, there are no indications that the category members are developmental toxicants. ECHA points out that no robust study summaries of the studies forming the basis for your arguments are available for assessment. In the absence of this information, the similarity in the toxicity profiles and your conclusions on absence of developmental toxicity of the substances cannot be verified.

- ECHA notes that the new metabolism data in rat liver S9 fraction and plasma (*Roos Kerstin, 2015)* provided alongside the comments seems to support the claim about rapid hydrolysis of short chain acrylates, as the hydrolysis rates of e.g. n-butylacrylate and 2-ethylhexylacrylate are around 1 minute in S9 and 6-8 minutes in plasma. In addition, the hydrolysis seems to be complete as the parent compound disappears within 5 minutes from S9 and 30 minutes from plasma.

- You claim that since none of the alcohol breakdown products of the category members are classified for reproductive toxicity, it can be concluded that they do not affect fertility. ECHA stresses that "non-classification" alone is not a sufficient evidence for any substance lacking hazardous properties.

- ECHA understands that in case the results of OECD 414 in rabbits, OECD 421 (a preliminary study for OECD 443) with n-butyl acrylate support the category hypothesis, you intend to predict the reproductive and developmental toxicity properties of 2-ethylhexyl acrylate from the data of n-butyl acrylate. Based on the summary of several studies provided in the comments, 2-ethylhexanol and acrylic acid (breakdown products of the registered substance) do not seem to affect fertility and developmental toxicity. ECHA points out that no fertility and developmental toxicity data has been provided for n-butanol, which is one of the breakdown products of n-butyl acrylate.

For the reasons presented above, ECHA is not in a position to conclude based on the information provided by you in your comments on whether the potential updated read-across approach referred to by you will comply with the requirements of Annex XI, section 1.5 of the REACH Regulation. Therefore ECHA did not amend the requests in the draft decision.

ECHA will further assess the information provided in an updated dossier after the deadline for providing the requested information and will come to a conclusion on whether the information provided adequately fulfils the information requirement addressed in the decision.

The test in the first species was carried out by using a rodent species (rats). According to the test method EU B.31/OECD 414, the rabbit is the preferred non-rodent species. On the

basis of this default assumption, ECHA considers that the test should be performed with rabbits as a second species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are 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 TG 414) in a second species rabbits by the oral route.

2. Extended one-generation reproductive toxicity study

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

The basic test design of an extended one-generation reproductive toxicity study (Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

a) The information requirement

In the technical dossier you have provided a study record for a two-generation reproductive toxicity test (OECD 416) conducted with an analogue substance methyl acrylate. In addition, you state that in a sub-chronic toxicity (90-day) study "*animals exposed to the highest dose level of 100 ppm (approx. 0.750 mg/L) by inhalation did not give evidence for any impairment of the investigated reproductive organs of both sexes*".

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement based on read-across approach according to Annex XI, Section 1.5. and Annex X, Section 8.7.3., column 2 (*"Two-generation reproductive toxicity studies (B.35, OECD TG 416) that were initiated before 13 March 2015 shall be considered appropriate to address this standard information requirement."*).

ECHA notes that there is no hypothesis and justification establishing a basis whereby toxicological properties of the registered substance may be predicted from data for the analogue substance methyl acrylate. In the absence of any justification supporting the proposed grouping/read-across approach, ECHA considers that you have failed to provide an adequate and reliable documentation of the applied method as required by Annex XI, Section 1.5 of the REACH Regulation. Therefore, ECHA is not in a position to conclude on the proposed read-across approach which could allow establishing that relevant properties of the registered substance can be predicted from those of the analogue substances. The proposed read-across has therefore to be rejected as not acceptable.
ECHA points out that while the sub-chronic toxicity (90-day) study may provide relevant information on the toxicity of the test material to the reproductive organs/tissues, it does

not provide sufficient information on its own to fulfil the information required by Annex X, Section 8.7.3.

Furthermore, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex X, Section 8.7.3., column 2 because your data has been generated on an analogue substance methyl acrylate and your proposed read-across is rejected, as explained above.

Therefore, your adaptation of the information requirement cannot be accepted.

In your comments to the draft decision, you propose to address the information requirements listed in the draft decision by using a category approach as described in detail above in section 1. ECHA's assessment of the information provided is presented above in section 1.

ECHA is not in a position to conclude based on the information provided by you in your comments on whether the potential updated read-across approach referred to by you will comply with the requirements of Annex XI, section 1.5 of the REACH Regulation. Therefore ECHA did not amend the requests in the draft decision.

ECHA will further assess the information provided in an updated dossier after the deadline for providing the requested information and will come to a conclusion on whether the information provided adequately fulfils the information requirement addressed in the decision.

Hence, the information provided 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. Thus, an extended one-generation reproductive toxicity study according Annex X, Section 8.7.3. is required. The following refers to the specifications of this required study.

b) The specifications for the study design

Premating exposure duration and dose-level setting

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.6 (version 4.0, July 2015).

The highest dose level shall aim to induce some toxicity to allow comparison of effect levels and effects of reproductive toxicity with those of systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

It is recommended that results from a range-finding study (or range finding studies) for the extended one-generation reproductive toxicity study are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented.

Species and route selection

According to the test method EU B.56/ OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

c) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method EU B.56/ OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce some toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

Notes for your consideration

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if new information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the new information shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA guidance. You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented. The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented.

3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

"Long-term toxicity testing on aquatic invertebrates" is a standard information requirement as laid down in Annex IX, Section 9.1.5. 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.

Column 2 of Annex IX, Section 9.1. specifies that long-term aquatic toxicity testing shall be proposed by the Registrant if the chemical safety assessment according to Annex I indicates the need to investigate further effects on aquatic organisms. The choice of the appropriate test(s) will depend on the results of the chemical safety assessment.

ECHA understands that you have sought to adapt this information requirement based on a read-across approach according to Annex XI, Section 1.5 of the REACH Regulation and state the following in the endpoint summary of Aquatic toxicity: "*The aquatic toxicity of the six acrylic esters (methyl, 2-ethylhexyl, ethyl, n-butyl, isobutyl, and tert-butyl acrylate) is evaluated as a category*". You further specify in the endpoint summary of Long-term toxicity to aquatic invertebrates that "*There are no data on long-term toxicity towards invertebrates for 2-Ethylhexyl acrylate. But for the structurally related ethyl acrylate and n-butyl acrylate 21 -day chronic toxicity studies are available ([redacted]).*" In the technical dossier you have provided two key studies: a study record for a Daphnid chronic toxicity (Guideline EPA OTS 797.1330) using an analogue substance ethyl acrylate, and a study record for a *Daphnia magna* reproduction (OECD Guideline 211) using another analogue substance n-butyl acrylate.

ECHA notes that there is no hypothesis and justification establishing a basis whereby ecotoxicological properties of the registered substance may be predicted from data for the analogue substances ethyl acrylate and n-Butyl acrylate. In the absence of any justification supporting the proposed grouping/read-across approach, ECHA considers that you have failed to provide an adequate and reliable documentation of the applied method as required by Annex XI, Section 1.5 of the REACH Regulation. Therefore, ECHA is not in a position to conclude on the proposed read-across approach which could allow establishing that relevant properties of the registered substance can be predicted from those of the analogue substances. The proposed read-across has therefore to be rejected as not acceptable.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided 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.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Daphnia magna reproduction test (test method: EU C.20./OECD TG 211).

4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.1.)

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

"Long-term toxicity testing on fish" is a standard information requirement as laid down in Annex IX, Section 9.1.6. of the REACH Regulation. Adequate information on Fish, early-life stage (FELS) toxicity test (Annex IX, 9.1.6.1.), or Fish, short-term toxicity test on embryo and sac-fry stages (Annex IX, 9.1.6.2.), or Fish, juvenile growth test (Annex IX, 9.1.6.3.)

needs to be present in the technical dossier for the registered substance to meet this information requirement.

Column 2 of Annex IX, Section 9.1. specifies that long-term aquatic toxicity testing shall be proposed by the Registrant if the chemical safety assessment according to Annex I indicates the need to investigate further effects on aquatic organisms. The choice of the appropriate test(s) will depend on the results of the chemical safety assessment.

You have waived long-term toxicity testing on fish using the following justification: "*In accordance with section 3 of REACH Annex XI, the study does not need to be conducted. Based on acute LC/EC50 values, Daphnia magna was the most sensible aquatic organism showing a 48-hour EC50 of 1.30 mg/L. Accordingly, 21-day chronic life-cycle studies with Daphnia magna exposed to the structural analogues n-butyl and ethyl acrylate were conducted. The respective NOECs were 0.136 and 0.19 mg/L, respectively. Since 2-ethylhexyl acrylate is readily biodegradable and has a hydrolysis half-life of 210 h at pH 7, considerable aquatic exposure is not to be expected. The available monitoring data support this prediction. A PEC local of 0.6 µg/L for formulation was calculated as worst case scenario in the EU Risk Assessment (2005), and a PEC local for paper recycling of 0.5 µg/L. These are concentrations far below the NOEC obtained in the long-term study with Daphnia magna.*"

ECHA acknowledges that you have attempted to adapt the information requirements in accordance with the specific adaptation rules in Column 2 of Annex IX, section 9.1. However, you have based the read-across adaptation on 21-day chronic life-cycle studies with *Daphnia magna* exposed to the analogue substances n-butyl and ethyl acrylate. As described in sub-section 3 (above) of this Decision, ECHA notes that the adaptations provided to use the long-term toxicity to aquatic invertebrates for the registered substance by the application of a read-across approach could not be accepted and there is an information gap. Therefore, ECHA considers that these studies on analogue substances cannot be further used as an adequate source of data to support an adaptation of the standard information requirement on long-term toxicity to fish.

Furthermore, based on aquatic acute toxicity studies there is no evidence that any of the three trophic levels would be substantially more sensitive than the others (*Oncorhynchus mykiss* 96-h LC50 = 1.81 mg/L; *Daphnia magna* 48-h EC50 = 1.3 mg/L (CL 95 %: 1.08 - 1.55); *Scenedesmus subspicatus* 72-h ErC50 (Growth rate) = 1.71 mg/L). Therefore, long-term toxicity testing may be required for both, aquatic invertebrates and fish.

As explained above, the information provided 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.

Regarding the long-term toxicity testing on fish pursuant to Annex IX, section 9.1.6.1, ECHA considers that the FELS toxicity test according to OECD TG 210 is the most sensitive of the standard fish tests available as it covers several life stages of the fish from the newly fertilised egg, through hatch to early stages of growth and should therefore be used (see ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b, Figure R.7.8-4). The test method OECD TG 210 is also the only suitable test currently available for examining the potential toxic effects of bioaccumulation (ECHA Guidance Chapter R7b, version 2.0, November 2014). For these reasons, ECHA considers the FELS toxicity test using the test method OECD TG 210 as appropriate and suitable.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Fish, early-life stage (FELS) toxicity test (test method: OECD TG 210).
Notes for your consideration

Before conducting any of the tests mentioned above in points 4-5 you shall consult the ECHA *Guidance on information requirements and chemical safety assessment (version 2.0, November 2014)*, Chapter R7b, Section R.7.8.5 to determine the sequence in which the aquatic long-term toxicity tests are to be conducted and the necessity to conduct long-term toxicity testing on fish.

According to ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R7b (Section R.7.8.5., including Figure R.7.8-4), if based on acute aquatic toxicity data neither fish nor invertebrates are shown to be substantially more sensitive, long-term studies may be required on both. In such case, according to the integrated testing strategy, the Daphnia study is to be conducted first. If based on the results of the long-term Daphnia study and the application of a relevant assessment factor, no risks are observed (PEC/PNEC<1), no long-term fish testing may need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

5. Bioaccumulation in aquatic species (Annex IX, Section 9.3.2.; test method: Bioaccumulation in fish: aqueous and dietary exposure, OECD 305).

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

"Bioaccumulation in aquatic species, preferably fish" is a standard information requirement as laid down in Annex IX, Section 9.3.2. 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.

ECHA understands you have sought to adapt this information requirement by means of a weight of evidence in accordance with Section 1.2. of Annex XI. You provided two lines of evidence. As the first line of evidence, you provided results from a quantitative structure-activity relationship model ((Q)SAR), SRC BCFWIN v2.17. As the second line of evidence, you provided results estimated by calculation (Catalogic v5.10.5 [BCF base-line model v.01.02]). You state in the endpoint summary of Bioaccumulation: aquatic / sediment that "*There are no experimental results on bioaccumulation available*" and that "*BCF values calculated by Q(SAR) models, i.e. Epi Suite SRC BCFWIN v2.17 and OASIS Catalogic v5.10.5, were 282 and 270, respectively.*"

Both lines of evidence are (Q)SAR models, which are based on an estimated Log Kow value of 4.09 (SRC KOWWIN v1.67 ([redacted])).

Regarding both lines of evidence, ECHA notes the following criteria, as described in Section 1.3. of Annex XI to the REACH Regulation, may be considered in assessing quantitative structure-activity relationship models ((Q)SAR):

- results are derived from a (Q)SAR model whose scientific validity has been established,
- the substance falls within the applicability domain of the (Q)SAR model,

- results are adequate for the purpose of classification and labelling and/or risk assessment, and
- adequate and reliable documentation of the applied method is provided.

Furthermore, regarding the criterion for adequate and reliable documentation, the justification for using the (Q)SAR information should be based on the use of the QSAR Reporting Formats described in ECHA *Guidance on information requirements and chemical safety assessment* (May 2008), Chapter R.6 (Section R.6.1.6.):

- the description of a particular (Q)SAR model (i.e. description of the algorithm, its development and validation based on the OECD principles) will be stored in the (Q)SAR Model Reporting Format (QMRF).
- the (Q)SAR Prediction Reporting Format (QPRF) will explain how an estimate has been derived by applying a specific model or method to a specific substance. This should include information on the model prediction(s), including the endpoint, a precise identification of the substance modelled and the relationship between the modelled substance and the defined applicability domain.

These reporting formats would provide a comprehensive description of the use of the (Q)SAR during the classification and safety assessment of a given substance for a specific endpoint, and for justifying any further testing considered necessary to obtain adequate and complete information.

ECHA notes that you have not provided adequate and reliable documentation of the applied methods for the individual lines of evidence. Therefore, the technical dossier does not contain evidence that the provided (Q)SAR models are scientifically valid and the substance would fall within the applicability domain of the models. Accordingly, ECHA considers that the level of information obtained from the different lines of evidence either individually or taken together does not constitute a sufficient evidence to conclude on the bioaccumulation potential of the substance. Therefore, the information as currently provided does not contribute to a weight of evidence approach intended to determine whether the registered substance has or has not a dangerous property for the endpoint under consideration according to Annex XI, section 1.2.

In your comments to the draft decision you propose to update the section 5.3.1 of the registration dossier with a description of the QSAR models applied and the related QSAR Prediction reporting formats.

Regarding applicability domain of the model, you describe in your comments that *"Regarding the Meylan model, despite a global applicability domain index just below 0.9 (see Table 1), the predicted substance is in the applicability domain of the model".* However, you also describe that *"According to the similarity index (SI = 0.793), the prediction is not optimal, only moderately similar compounds with known experimental value in the training set being found."*

ECHA notes that the descriptors, which you use to justify that the substance is in the applicability domain of the model, are molecular weight (184.3 g.mol-1) and the log Kow (4.09). However, you have not provided evidence that the substance would be within the global applicability domain of the model. A full report (e.g. from VEGA platform) and the rest of the parameters used for the applicability domain index of the model should be provided and considered in the assessment of the reliability and adequacy of the prediction.

Furthermore, you have not provided other elements to indicate the validity of the model and

the prediction in your comments. Appropriate measures of goodness-of-fit, robustness and predictivity should be provided and considered in the assessment of the reliability and adequacy of the prediction.

You further justify in your comments the low bioaccumulation potential of the registered substance by metabolic biotransformation. Based on Arnot-Gobas model, *"biotransformation half-life of 2-Ethylhexyl acrylate in fish was 4.152 hours"*. You support this prediction by referring to *in vitro* data on rat liver cells: *"A fast esterase cleavage within the first 10 incubation minutes was observed with a parallel increase of acrylic acid after incubation with S9 fraction of rat liver"*. ECHA acknowledges the information on the potential transformation of the substance. However, ECHA notes that this information does not provide evidence on validity of the models or the predictions on bioaccumulation potential itself.

As described above, ECHA notes that you have not provided in your comments a full documentation of the approach including applicability domain, appropriate measures of goodness-of-fit, robustness and predictivity. In the absence of such documentation, ECHA is not in the position to verify the model validity and their ability to predict hazardous property of the substance. Therefore, ECHA is not also in the position to verify the compliance of the provided documentation with the requirements of Annex XI of the REACH Regulation. Therefore ECHA did not amend the request in the draft decision.

ECHA will further assess the information provided in an updated dossier after the deadline for providing the requested information and will come to a conclusion on whether the information provided adequately fulfils the information requirement of Annex VII-IX.

As explained above, the information provided 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.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Bioaccumulation in fish: aqueous or dietary bioaccumulation fish test (test method: OECD TG 305).

Extension of the deadline

You ask to postpone the final decision until the end of 2016 in order to have time to consider the possibility to update the dossier with new experimental data and an updated read-across justification document.

Having considered your request, ECHA extended by 6 months the deadline for submitting the information requested in the draft decision, to 36 months. This extension will enable you to consider the new expected experimental data on the potential analogue substance and decide whether the new read-across approach can fulfil the requirements of Annex XI, section 1.5 of the REACH Regulation. ECHA will however not postpone the sending of the final decision.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 13 October 2015.

ECHA notified you of the draft decision and invited you to provide comments.
ECHA took into account your comments and did not amend the requests but extended the deadline.

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment(s).
ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation:

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-48 meeting and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to fulfil otherwise the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests 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 tests 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 tests 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 tests to be assessed.