EUROPEAN CHEMICALS AGENCY

Helsinki, 25 October 2016

Addressee: [redacted]

Decision number: TPE-D-2114346822-48-01/F
Substance name: Esterification products of 4,4'-Isopropylidenediphenol, ethoxylated and prop-2-enoic acid and 3,5,5-trimethylhexanoic acid
EC number: 919-846-5
CAS number: n/a
Registration number: [redacted]
Submission number: [redacted]
Submission date: 09.07.2015
Registered tonnage band: 100-1000T

DECISION ON A TESTING PROPOSAL

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

While your originally proposed test for Sub-chronic toxicity study (90-day), oral route (EU B.26./OECD TG 408) in rats using the analogue substance Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and prop-2-enoic acid, CAS No 64401-02-1 (EC No 613-584-2) is rejected, you are requested to perform:

1. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats using the registered substance modified to include:**
   - **Urinalysis and a full histopathological examination which is to include immunohistochemical investigation of renal pathology to determine if the pathology is mediated by alpha-2u globulin nephropathy; and**
   - **Terminal investigations of bone marrow histology (including bone marrow cellularity). To be included as additional measurements to those described in paragraphs 35 and 36 of OECD TG 408;**
   - **Terminal measurements of immunoglobulins performed by either the plague-forming cell (PFC) assay or the enzyme-linked immunosorbent (ELISA) assay. To be included as additional measurements to those described in paragraph 29 of OECD TG 408; and**
   - **Terminal investigations of lymphocyte subsets distribution including total B- and T-cell counts, T-cell subpopulations (including CD4 and CD8 cells) depending on the previous results of the investigations above. To be included as additional measurements to those described in paragraph 28 of OECD TG 408;**

While your originally proposed test for Pre-natal developmental toxicity study (EU B.31./OECD TG 414) in rats oral route using the analogue substance Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and prop-2-enoic acid, CAS No 64401-02-1 (EC No 613-584-2) is rejected, you are requested to perform:

2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rats or rabbits), oral route using 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 **1 November 2018**. You shall also update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.

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

Appeal

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

Authorised[1] by 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

The decision of ECHA is based on the examination of the testing proposal(s) submitted by you.

0. Grouping of substances and read-across approach

Article 13(1) of the REACH Regulation requires information on intrinsic properties of substances on human toxicity to be generated whenever possible by means other than vertebrate animal tests, including from information from structurally related substances (grouping or read-across), "*provided that the conditions set out in Annex XI are met*".

The decision of ECHA is based on the examination of the testing proposals submitted by you for the registered substance Esterification products of 4,4'-Isopropylidenediphenol, ethoxylated and prop-2-enoic acid and 3,5,5-trimethylhexanoic acid, EC No 919-846-5 (hereafter referred to as *'target (registered) substance'*).

You have proposed to cover the standard information requirements for:

- a sub-chronic toxicity study (90-days; Annex IX, Section 8.6.2.); and
- a pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

by performing the proposed tests with the analoge substance Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and prop-2-enoic acid, CAS No 64401-02-1 (EC No 613-584-2); hereafter referred to as the *'source substance'*).

Annex XI, Section 1.5. requires a structural similarity among the substances within a group or category such that relevant properties of a substance within the group can be predicted from the data on reference substance(s) within the group by interpolation. The following analysis presents your justification for the proposed grouping approach and read-across hypothesis, together with ECHA's analysis concerning the justification in both a generic and property-specific context.

a. Description of the grouping and read-across approach proposed by you

You have provided the following hypothesis:

"*All the substances with a* [redacted] *could be suitable as source chemicals to fill by read-across the registration dossier of the target substance: Ethoxylated bisphenol A, esters with acrylic acid and isononanoic acid (EC n°919-846-5).*
This read-across approach is based on the hypothesis that substances with a close similarity of structure would show similar toxicity which is proved with the toxicological data available on both substances. The read-across approach would be applied for the oral 90-day study and the teratology study in rat."

You concluded the following on the read-across approach:

"To summarise, *the toxicological profiles of the target* [redacted] *and source* [redacted] *substances are quite similar, especially for repeated toxicity, which confirm the reliability of the proposed read-across between* [redacted] *and* [redacted] *for the 90-d repeated toxicity study and the foetal developmental toxicity study in rats.*".

b. Information/documentation submitted to support the grouping and read-across hypothesis

You have provided a read-across justification as a separate attachment in IUCLID section 13. This document outlines the read-across approach, the composition of the source and target substances, and provides a data matrix which allow comparison of available physico-chemical and toxicological information on the *'source substance'* and the *'target (registered) substance'*.

In addition, you provide the following infromation to support the read-across approach:

Studies conducted with the *'target (registered) substance'*:

- Acute oral toxicity (OECD TG423); 2013;GLP; Rel. 1
- Acute dermal toxicity; (OECD TG 402); 2013; GLP; Rel. 1
- Skin irritation (OECD TG 439); 2013; GLP; Rel. 1
- Skin irritation (OECD TG 404); 2013; GLP; Rel. 1
- Eye irritation (OECD TG 405); 2013; GLP; Rel. 1
- Skin sensitisation (OECD TG 429); 2013; GLP; Rel. 1
- Bacterial reverse mutation assay (OECD TG 471); 2013; GLP; Rel. 1
- *In vitro* mammalian cell micronucleus *test* (OECD TG 487); 2013; Rel. 1
- *In vitro* mammalian cell gene mutation test (OECD TG 476); 2013; Rel. 1
- Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test (OECD TG 422); 2014; GLP; Rel. 1

Studies conducted with the *'source substance'*:

- Repeated Dose 28-Day Oral Toxicity in Rodents (OECD TG 407); 2012; GLP; Rel. 1
- Reproduction / developmental toxicity screening test (OECD TG 422); 2013; GLP; Rel. 1

c. ECHA analysis of the grouping approach and read-across hypothesis in light of the requirements of Annex XI, 1.5.

ECHA understands that you base your read-across hypothesis upon the fact that both the *'target (registered) substance'* and the proposed *'source substance'* are structurally similar; *i.e.* both substances have core [redacted]. Because the substances are structurally related have the hypothesis that substances you *"with a close similarity of structure would show similar toxicity"*.

Structural similarity and dissimilarity

You state that both the *'target (registered) substance'* and the *'source substance'* are substances of unknown or variable composition, complex reaction products or biological materials (UVCB), *"however they have a high degree of similarity because of they both contain acrylated BPA structures with a majority of BPA(EO)n monoacrylate and diacrylate."*

In addition, you have in the read-across justification document provided generic chemical structures, chemical name, chemical identifiers, and typical concentrations of the constituents for the *'target (registered) substance'* and the proposed *'source substance'*.
ECHA notes that the *'target (registered) substance'* is a UVCB substance with the following constituents:

[redacted]

[redacted]

ECHA notes that *'source substance'* is a UVCB substance with the following constituents:

[redacted]

ECHA understands that you base your read-across approach on the fact that both the *'target (registered) substance'* and *'source substance'* share common stuctural features (*i.e. "acrylated BPA structures with a majority of BPA(EO)n monoacrylate and diacrylate"*). Furthermore, ECHA understands that the substances differ in several aspects. Firstly, the substances differ in the degree of ethoxylation of [redacted]. ECHA observes that the constituents of the *'target (registered) substance'* are mostly [redacted]. In contrast, the majority of the constituents in the *'source substance'* consists of [redacted]. Secondly, the amount of [redacted] differ between the substances. ECHA observed that the *'target (registered) substance'* consists of [redacted] In contrast, the majority of the constituents in the *'source substance'* consists of [redacted]. Thirdly, the amount of free core structure [redacted] differs between the substances. ECHA observed that the *'target (registered) substance'* consists of [redacted]. In contrast, for the *'source substance'* this constituent is not reported in its technical dossier. Finally, the [redacted] is present in the *'target (registered) substance'* but not in the *'source substance'*.

ECHA considers that you have provided information to demonstrate that both substances have a common structural core consisting of [redacted]. However, the *'target (registered) substance'* and the *'source substance'* also differ in several stuctural aspects (see above). ECHA considers that the toxicological properties of the substances can not be predicted unless all identified stuctural and compositional differences between the *'target (registered) substance'* and the *'source substance'* are taken into account in the prediciton.

Physico-chemical properties

You state that both substances have *"[...]quite close values for three of the major physical-chemical endpoints used to estimate the behaviour of the substances in humans. Both substances belong to a category of substances with the following physical-chemical properties: moderate log Kow: 1.5 – 4.16, low water solubility: 0.04 – 16.39 mg.L^{-1} and very low vapor pressure: 10^{-6} -10^{-7} Pa."*

ECHA observes that based on the data provided it can be concluded that the two substances have similar physico-chemical properties. However, ECHA observes that you have not expained as to why similarity in physico-chemical properties allow for prediction of toxicological properties.

ECHA considers that the fact that physico-chemical parameters are in the same range may support a similar toxicokinetic and toxicity profile, but cannot be used alone to justify a prediction of properties related to human health.

Toxicological data (and Mode of Action)

You claim in your read-across justification document that your "*[...] read-across approach is based on the hypothesis that substances with a close similarity of structure would show similar toxicity which is proved with the toxicological data available on both substances*".

This document also provides a data matrix to allow comparison of the toxicological profiles of the '*target (registered) substance*' and the proposed '*source substance*'.

To support the read-across hypothesis you bring forward the following:

- As no toxicokinetics information is available for neither the 'target (registered) substance' nor the proposed '*source substance*', you provide theoretical considerations on toxicokinetics.

  ECHA notes that since both the '*target (registered) substance*' and the '*source substance*' cause systemic toxicity following oral administration, theoretical considerations on toxicokinetics are of limited value.

- Both the '*target (registered) substance*' and the '*source substance'* are not acutely toxic via the oral and dermal route.

  ECHA notes that both substances have similar acute toxicity.

- Both the '*target (registered) substance*' and the '*source substance'* are not irritating to skin and eyes. However, the '*target (registered) substance*' is a skin sensitizer whereas the '*source substance'* in not a skin sensitizer.

  ECHA notes that the '*target (registered) substance*' and the '*source substance'* differ with respect of skin sensitization.

- With regard to *in vitro* mutagenicity, the '*target (registered) substance*' has negative results in all three *in vitro* mutagenicity tests. In contrast, for the '*source substance*' one of the tests show positive results (*i.e.* the *In vitro* mammalian cell micronucleus test; OECD TG 487).

  ECHA notes that the results in the *In vitro* mammalian cell micronucleus test differ between the '*target (registered) substance*' and the '*source substance*'. ECHA consider that this is not in line with your claim that "*the toxicological profiles of the target [...] and source [...] substances are quite similar*".

- With regard to repeated dose toxicity, ECHA notes that the '*target (registered) substance*' have been tested in a Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test (OECD TG 422); and a NOAEL (P) for systemic toxicity have been established at 300 mg/kg/day (based on "*changes in the kidneys associated with increased in the urine volume, the liver and*

thymus histopathological findings in both genders"). The proposed '*source substance*' have been tested in a Repeated Dose 28-Day Oral Toxicity study (OECD TG 407) and a Reproduction / developmental toxicity screening test (OECD TG 421); a NOAEL for systemic toxicity have been established at 300/250 mg/kg/day (based on increased blood cholesterol, increased liver weight and hepatocellular hypertrophy).

ECHA notes that you argue that the substances have similar toxicity based on that the following toxicological findings have been observed for both substances:

- Both substances caused "*ptyalism at all tested doses*";
- Both substances result in decrease of male body weight and female body weight during gestation;
- The substances cause either hepatocellular or centrilobular hypertrophy;
- Increase of cholesterol in blood in males and females;
- Tubular vacuolisation in the kidneys in males and females;

ECHA notes that both substances causes ptyalism and slightly decreased body weight. ECHA considers these effects to be general signs of toxicity which may be caused by numerous different toxicological mechanisms. In addition, both substances causes liver effects. However, ECHA does not consider hepatocellular hypertrophy and centrilobular hypertrophy to necessarily be caused by the same mechanism.

Furthermore, ECHA notes that for the '*target (registered) substance*' an adverse increased urine volume was observed in both male and female rats. In contrast, this effect was not observed with the '*source substance*'. Furthermore, although hyaline droplet formation in male rats is not considered relevant for humans, this effect was observed (and confirmed by immunohistochemistry) for the '*target (registered) substance*'. In contrast, ECHA notes that this effect was not observed for the '*source substance*'. ECHA considers that the absence of kidney effects with the '*source substance*' contradicts the notion that the toxicological profiles of the substances are similar.

Moreover, ECHA notes that the effects observed for the '*target (registered) substance*' can be indicative of toxicity to the immune system: thymus atrophy and histopathological findings in both genders. In contrast, this effect was not observed with the '*source substance*'. ECHA consider that the absence of thymus effects with the '*source substance*' contradicts the notion that the toxicological profiles of the substances are similar.

- Finally, with regard to toxicity to reproduction, both the '*target (registered) substance*' and the '*source substance*' have been tested in the Reproduction / Developmental Toxicity Screening Test (OECD TG 422 and OECD TG 421, respectively) and for both substances the NOAELs for fertility (P) and developmental toxicity (F1) are 1000 mg/kg/day (based on no effects).

  ECHA does not consider absence of effects in screening test as supportive of a similar mechanism of toxicity.

ECHA concludes that the toxicological information that you have provided do not support the assumption of "*similar toxicity*" between the '*target (registered) substance*' and the '*source substance*'. ECHA therefore considers that there is not an adequate basis for predicting the properties of the registered substance from the data obtained with the source substance.

Toxicokinetic properties

It is unclear to which substances the organism is exposed for the following reasons:

- No hydrolysis data, therefore it is not clear whether the acrylates or the isononanoate, respectively, are available as intact esters for systemic circulation or only hydrolysis products.
- It is also unclear which hydrolysis product is formed at which rate and which one is likely to drive the potential toxicity.
- No information on the toxicity of the [redacted] which are partly already present in the parent substances and further can be formed as hydrolysis products from the [redacted].
- No information on the fate and toxicity of the [redacted], if the [redacted] is indeed hydrolysed completely. [redacted] has a known toxicity profile and it is unclear what impact the ethoxylation has on this toxicity.
- It is not clear whether cleavage of the ethoxy- groups is possible from the [redacted], if formed.
- It is not clear what impact the presence of different ethoxylated species in the UVCB substances has on the formation rates of potential toxic metabolites when compared to the formation rates of such metabolites from the '*target (registered) substance*'. It cannot be excluded that toxicokinetic interactions are only detectable in a sub-chronic toxicity study (90-day) and/or or a pre-natal developmental toxicity study, but not in the screening studies.
- No attempt has been made to assess the possible impact of the variability of the constituents of the source and target substance on the attempted prediction. *E.g.* which '*source substance'* composition will be tested and why and how would this composition be predictive for the range of possible constituent concentrations in the '*target (registered) substance*'. ECHA notes that a significant amount of [redacted] is present in the '*target (registered) substance*'.
- [redacted] may also be formed from the '*source substance'* constituents if hydrolysis occurs; it is not explained how this impacts the prediction. Furthermore, the impact of such variation in the composition is not assessed under the conditions of repeated administration. In particular, it is not clear whether there is a preferential bioaccumulation potential for some constituents which would change the systemic exposure to some constituents at repeated administration over time in comparison to the constituent compositions in the parent substances.

You have proposed that the '*source substance'* has similar toxicity regarding sub-chronic and developmental toxicity and therefore the properties of the '*target (registered)substance*' can be predicted from data obtained from the '*source substance*'. ECHA concludes that the data provided does not provide sufficient evidence to conclude what constituents in the substances or which metabolic products drive the toxicity. In addition, the differences in the toxicity profiles of the '*source substance*' and the '*target (registered) substance'* as explained in the previous section emphasise that the toxicokinetic issues pointed out above need to be addressed for a robust prediction.

ECHA therefore considers that there is not an adequate basis for predicting the properties of the '*target (registered) substance'* from the data obtained with the '*source substance*'.

Selection of the source substance

ECHA notes that you are proposing in a parallel registration to read-across from the same '*source substance*' to another analouge substance [redacted]. This means that the toxicity profiles of the '*source substance*' and the two target substances should all be similar to allow predictions. However

this not the case since the *'target (registered) substance'* shows alpha-2u globulin nephropathy in males, increased urine volumen in males and females, and thymus atrophy effects which are not observed for [redacted]. Furthermore, ECHA notes that you have not explained why the *'source substance'* and not [redacted], is the most appropriate source substance for the proposed predictions. Moreover, ECHA considers that all read-across approaches should be consistent and transparently reported in the concerned technical dossier; i.e. when a source substance is used to read-across to several target substances this should be reported in all concerned dossiers.

ECHA concludes that you have not demonstrated that the most appropriate analogue have been selected as a source substance for the read-across approach. ECHA therefore considers that there is not an adequate basis for predicting the properties of the registered substance from the data obtained with the source substance.

d. Conclusion on the read-across approach

Based on the data submitted by you, ECHA concludes that you have not provided adequate and reliable information to demonstrate that the read-across approach is plausible for the properties under consideration.

ECHA therefore concludes that the criteria of Annex XI, 1.5. are not met, and the read-across approach, as presented by you, cannot be considered plausible to meet the information requirements.

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

Pursuant to Article 40(3)(a) and (c) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test and to carry out additional tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

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

You have submitted a testing proposal for a sub-chronic toxicity study (90 day) in rats by the oral route according to EU B.26./OECD TG 408 with the *'source substance'*.

ECHA has evaluated your proposal to perform the test with the *'source substance'*. For the reasons explained above (see section 0), your proposed read-across approach has been rejected. Concequently, as there is an information gap the proposed test shall be perfomed with the *'target (registered) substance'*.

According to the test method EU B.26./OECD TG 408 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

In the OECD TG 422 study present in your registration dossier, adverse effects were observed in the kidneys of male rats and in female rats (increased urine volume in both

sexes). In this study, immunohistochemical investigation of renal pathology was performed to determine if the pathology is indeed mediated by alpha-2u globulin based on the fact that alpha-2u-globulin-mediated nephropathy is only observed in male rats. This investigation only explains part of the observed kidney toxicity because this effect do not occur in females. However, since you have identified the kidney as a target organ, ECHA accordingly considers that further investigations of the kidneys will be required for establishing the relevance of the kidney effects for risk assessment. For these reasons, ECHA considers that urinalysis of both male and female rats is required to investigate kidney function (which is optional in paragraphs 3, 30 and 32 of OECD TG 408, and the relevant part of Section 1.5.2.2. of EU Method B.26.) Additionally, a full histopathological examination (paragraphs 3, 35 and 36 of OECD TG 408, Section 1.5.2.4. of EU Method B.26.), which is to include immunohistochemical investigation of renal pathology to determine if the pathology is indeed mediated by alpha-2u globulin, is necessary for the same reason. Such investigations will also facilitate the interpretation of the study results and the determination of their relevance to risk assessment.

In a combined repeated dose toxicity study with the reproduction / developmental toxicity screening test (OECD TG 422) conducted with the 'target (registered) substance', effects were seen in the thymus of both males and females (decrease in absolute and relative weight (lymphoid atrophy)). In addition, effects were observed in the mesenteric lymph nodes of both male and female rats. Thus, the OECD TG 422 study raises concern on immunotoxicity that needs to be addressed in the proposed testing.

As part of the EU B.26/OECD TG 408 guideline, the Registrant is requested to include additional measurements in the study protocol concerning:

- Terminal investigations of bone marrow histology (including bone marrow cellularity). To be included as additional measurements to those described in paragraphs 35 and 36 of OECD TG 408;
- Terminal measurements of immunoglobulins performed by either the plague-forming cell (PFC) assay or the enzyme-linked immunosorbent (ELISA) assay. To be included as additional measurements to those described in paragraph 29 of OECD TG 408; and
- Terminal investigations lymphocyte subsets distribution including total B- and T-cell counts, T-cell subpopulations (including CD4 and CD8 cells) depending on the previous results of the investigations above. To be included as additional measurements to those described in paragraph 28 of OECD TG 408.

Therefore, pursuant to Article 40(3)(a) and (c) of the REACH Regulation, you are requested to carry out the additional study with the 'target (registered) substance' subject to the present decision: Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26./OECD TG 408); including additional measurements regarding alpha-2u globulin nephropathy and immunotoxicological parameters shall be carried out (as detailed above); while your originally proposed test for *Sub-chronic toxicity study (90-day) in rats, oral route (test method: EU B.26./OECD TG 408) with the 'source substance'* is rejected according to Article 40(3)(d) of the REACH Regulation.

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

Pursuant to Article 40(3)(a) and (c) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test and to carry out additional tests in cases of non-compliance of the testing proposal with Annexes IX, X or XI.

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 provide information for this endpoint.

You have submitted a testing proposal for a pre-natal developmental toxicity study in rats according to EU B.31./OECD TG 414 by the oral with the *'source substance'*.

ECHA has evaluated your proposal to perform the test with the *'source substance'*. For the reasons explained above (see section 0), your proposed read-across approach has been rejected. Concequently, as there is an information gap the proposed test shall be perfomed with the *'target (registered) substance'*.

According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration, ECHA considers testing should be performed with the rat or rabbit as a first 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 4.1, October 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 40(3)(a) and (c) of the REACH Regulation, you are requested to carry out the additional study with the *'target (registered) substance'* subject to the present decision: Pre-natal developmental toxicity study in a first species (rats or rabbits), oral route (test method: EU B.31./OECD TG 414); while your originally proposed test for Pre-natal developmental toxicity study in a first species (rats or rabbits), oral route (test method: EU B.31./OECD TG 414) with the *'source substance'* is rejected according to Article 40(3)(d) of the REACH Regulation.

Notes for your consideration

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015), Chapter R.7a, section R.7.6.2.3.2.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 9 July 2015.

ECHA held a third party consultation for the testing proposal(s) from 31 August 2015 until 15 October 2015. ECHA did not receive information from third parties.

This decision does not take into account any updates after **8 August 2016,** 30 calendar days after the end of the commenting period.

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

ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and did not amend the request(s).

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

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

3. In carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested 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. If the registration of the substance covers different grades, the sample used for the new test(s) must be suitable to assess these. Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.