EUROPEAN CHEMICALS AGENCY

Helsinki, 7 April 2017

Addressee: [redacted]

Decision number: TPE-D-2114356598-33-01/F
Substance name: Ethanol, 2,2'-iminobis-, N-C12-18-alkyl derivs.
EC number: 276-014-8
CAS number: 71786-60-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 09.11.2015
Registered tonnage band: 1000+T

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.

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; it is at the Registrant's discretion to perform the intended additional examinations during the testing program;**
2. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route using the registered substance;**
3. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a second species (in rabbits if first species was rat or rats if first species was rabbits), oral route using the registered substance; and**
4. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: EU B.56./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); and**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.**

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 **14 June 2021** except for the information requested under point *1* for a sub-chronic toxicity study (90-day) which shall be submitted in an updated registration dossier by **14 December 2018**. You may only commence the extended one-generation reproductive toxicity study as requested under point *4* after **14 March 2019**, unless an indication to the contrary is communicated to you by ECHA before that date. 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 Claudio Carlon, Head of Unit, Evaluation E2

[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 and scientific information submitted by third parties.

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

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

a) Examination of the testing proposal

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 "*including the functional observational battery to investigate for evidence of neurotoxic effects and with inclusion of additional reproductive parameters. These reproductive parameters will include, in addition to full histopathological examination of the reproductive organs, staging of spermatogenesis in males and oestrus cycle determination in the females.*"

You proposed testing by the oral route. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA agrees that the oral route - which is the preferred one as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) Chapter R.7a, section R.7.5.4.3 - is the most appropriate route of administration. More specifically, the substance is a liquid of very low vapour pressure and high boiling point. Uses with industrial and non-industrial spray applications are reported in the chemical safety report for the registered substance which is classified as Skin Corr. 1C. However, the reported concentrations are low ([redacted]%). Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408.

You proposed testing in rats. 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.

You proposed to extend the sub-chronic toxicity study (90 day) by "*including the functional observational battery to investigate for evidence of neurotoxic effects and with inclusion of additional reproductive parameters. These reproductive parameters will include, in addition to full histopathological examination of the reproductive organs, staging of spermatogenesis in males and oestrus cycle determination in the females.*" ECHA notes, that it is at your discretion to perform the intended additional examinations during the testing program and use the results to ensure the safe use of the substance. However, you are reminded that the proposed extension of this study does not fulfil the standard information requirement in the registration dossier for reproductive toxicity set out in Annex X, Section 8.7.3.

b) Consideration of the information received during third party consultation]

ECHA received third party information concerning the testing proposal during the third party consultation. For the reasons explained further below the information provided by third parties is not sufficient to fulfil this information requirement.

The third party has referred to the corrosive property of the substance and to the need to adjust the dosing in the planned study for animal welfare reasons.

ECHA acknowledges that – as specified in the general part of Annexes VII-X – *"in vivo testing with corrosive substances at concentration/dose levels causing corrosivity shall be avoided"*. The test methods for repeated dose toxicity and reproductive toxicity specify that the highest dose level should induce *"toxicity but not death or severe suffering"*. Therefore, it is your responsibility to ensure that appropriate dose/exposure levels are used in the requested studies.

c) Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study with the 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).

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

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

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 route.

ECHA considers that the proposed study performed with the registered substance is appropriate to fulfil the information requirement of Annex IX, Section 8.7.2. of the REACH Regulation.

You proposed testing with the rat as a first species. 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.

You proposed testing by the oral route. ECHA agrees 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) of the REACH Regulation, you are requested to carry out the proposed study with the 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).

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.

3. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second 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.

Pre-natal developmental toxicity studies on two species are part of the standard information requirements for 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 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 only submitted a testing proposal for a pre-natal developmental toxicity study in a first species (rats) according to EU B.31./OECD TG 414 by the oral route. As a justification you stated that "*until the proposed OECD414 pre-natal development study in rats, OECD408 90 day study in rats and OECD443 EOGRTS in rats are completed it is not possible to reach a conclusion if the OECD414 study in rabbits required at Annex X is justified or can be waived.*"

However, ECHA notes that a pre-natal developmental toxicity study in a second species is a standard information requirement according to Annex X, Section 8.7.2. Furthermore, your provided explanation does not meet the requirements of any specific adaptation possibility according to column 2 of Section 8.7.2., Annex X nor any general adaptation possibility according to Annex XI. Therefore, ECHA requests as additional test a pre-natal developmental toxicity study in a second species as outlined here below.

ECHA considers that a pre-natal developmental toxicity according to EU B.31./OECD TG 414 performed with the registered substance is appropriate to fulfil the information requirement of Annex X, Section 8.7.2. of the REACH Regulation.
You did not specify the second species to be used for testing. 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 rabbit or the rat as a second species, depending on the species tested in the first pre-natal developmental toxicity study.

You did not specify the route for testing. 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 thus requested to carry out the additional study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in a second species (in rabbits if first species was rat or in rats if first species was rabbit), oral route (test method: EU B.31./OECD TG 414).

Notes for your consideration

Before performing a pre-natal developmental toxicity study in a second species you should consider the specific adaptation possibilities of Annex X, Section 8.7.2., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species or any other new information enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement and underlying scientific justification.

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.

4. Extended one-generation reproductive toxicity study (Annex [IX/X], Section 8.7.3.)

Pursuant to Article 40(3)(a) of the REACH Regulation, ECHA may require the Registrant to carry out the proposed test.

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 of the REACH Regulation. 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. Further detailed guidance on study design and triggers is provided in in ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015).

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 an extended one-generation reproductive toxicity study according to EU B.56./OECD TG 443 with the following justification and specification of the cohorts: "*The basic requirement at Annex X (>1000 tons) level is for the EOGRTS with Cohort 1A and 1B. This is proposed for this study. This is based on the following review of the triggers related to this study and contained in the ECHA Guidance.*

It is proposed to follow the guideline requirement for a 10 week pre-mating dosing period. There is an OECD 422 study which had two weeks premating dosing and did not show any indications of adverse effects on fertility or and other reproductive parameters. Also there were no indications of any adverse histological changes in the reproductive organs or to their weights. This might be considered to be sufficient to argue for a reduction to a two week pre-mating dosing period but in "Appendix R7.6-1, A check list for information that contributes to EOGRTS design" it states the results from a screening study (OECD TGs 421 or 422) may not provide adequate confidence to shorten the premating exposure duration from 10 weeks.

This lack of confidence being due to the shorter two week premating dosing period and the general lower statistical power due to it being a screening study with smaller numbers of litters. None of the additional elements that might support a reduction in the premating dosing period such as very low toxicity, fast elimination etc. can be claimed.

The Conditions/triggers leading to a requirement for an extension of the Cohort 1B to produce an F2 generation have been reviewed. The starting point for such a requirement is "Uses leading to significant exposure of consumers or professionals, taking into account inter alia consumer exposure from articles". There are exposure scenarios which indicate some potential for exposure to professionals and consumers from its use in cleaning products also including via articles form its use as an additive in plastics, but all are shown to be adequately controlled. Also none of the other triggers are applicable, 2, 2'-(C12-18 even numbered alkyl imino)diethanol is not genotoxic so the trigger "Genotoxicity potentially meeting the criteria to Mutagen Category 2" is not activated. Also testing of a related substance 2, 2'-(octadec-9-enylimino)diethanol 25307-17-9 demonstrated the same NOAEL after 28 and 90 days dosing. This indicates that there was no increase in toxicity with increased duration. This together with its ready biodegradability and low log octanol/water partition coefficient of 0.7 do not indicate any potential for bioaccumulation. So the trigger of "Extended exposure to reach steady state kinetics" is not activated. There are no indications from the existing in-vivo studies to suggest any endocrine disrupting modes of action, therefore the third trigger "Indications of action related to endocrine disruption from in-vivo or non-animal approaches" is also not activated.

Based on this review there is no requirement for an extension to Cohort 1B to produce an F2 generation. There were no effects seen in the OECD422 study or in the 28 day and 90 day studies on another member of this substance group 2,2'-(octadec-9-enylimino)diethanol 25307-17-9 to indicate any potential for neurotoxicity that would trigger a requirement to include Cohorts 2A and 2B to investigate the potential for development neurotoxicity. The same applies to immunotoxicity so there is no proposal to include Cohort 3 to investigate the potential for developmental immunotoxicity. The lack of these effects can be confirmed in the proposed 90 day study.

Dose level selection will be based on the doses used in the OECD422 study together with information from the OECD414 study in rats and in particular from the 90 day study, which will help confirm that there is no increased toxicity due to the longer duration compared to the OECD422 study. In any case this will allow us to select the appropriate dose levels for the OECD443 study."
ECHA considers that the proposed study design is appropriate to fulfil the information requirement of Annex X, Section 8.7.3. 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. Thus, an extended one-generation reproductive toxicity study according to column 1 of 8.7.3., Annex X is required. The following refers to the specifications of this required study.

Information from studies to be conducted before the extended-one-generation reproductive toxicity study

The sub-chronic toxicity study shall be conducted before the extended one-generation reproductive toxicity study and the results from that study shall be used, among other relevant information, to decide on the study design of the extended one-generation reproductive toxicity study following ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015).

The sub-chronic toxicity study may provide information on effects that is relevant for triggers (e.g. weight changes and histopathological observations of organs as indication(s) of one or more modes of action related to endocrine disruption which may meet the toxicity-trigger for extension of Cohort 1B or as evidence of specific mechanism/modes of action and/or neurotoxicity and/or immunotoxicity which may meet the particular concern criteria for developmental neurotoxicity and/or developmental immunotoxicity cohorts).

Premating exposure duration and dose-level setting

You proposed "*to follow the guideline requirement for a 10 week pre-mating dosing period.*"

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 4.1, October 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.

If there is no relevant data to be used for dose level setting, it is recommended that results from a range-finding study (or range finding studies) are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

Extension of Cohort 1B

If the column 2 conditions of 8.7.3., Annex X are met, Cohort 1B must be extended, which means that the F2 generation is produced by mating the Cohort 1B animals. This extension provides information also on the sexual function and fertility of the F1 animals.

You proposed not to include an extension of Cohort 1B and provided justifications following the criteria described in column 2 of Section 8.7.3 of Annex X and detailed in ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015).

ECHA agrees that the criteria to extend the Cohort 1B are not met and concludes that Cohort 1B need not be extended to include mating of the animals and production of the F2 generation.

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

Cohorts 2A and 2B

The developmental neurotoxicity Cohorts 2A and 2B need to be conducted in case of a particular concern on (developmental) neurotoxicity as described in column 2 of 8.7.3., Annex X. When there are triggers for developmental neurotoxicity, both the Cohorts 2A and 2B are to be conducted as they provide complementary information.

You proposed not to include Cohorts 2A and 2B and provided justifications following the criteria described in column 2 of Section 8.7.3 of Annex X and detailed in ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015).

ECHA agrees that the criteria to include Cohorts 2A and 2B are not met and concludes that the developmental neurotoxicity Cohorts 2A and 2B need not to be conducted.

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

Cohort 3

The developmental immunotoxicity Cohort 3 needs to be conducted in case of a particular concern on (developmental) immunotoxicity as described in column 2 of 8.7.3., Annex X.

You proposed not to include Cohort 3 and provided justifications following the criteria described in column 2 of Section 8.7.3 of Annex X and detailed in ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015).

Therefore, ECHA agrees that the criteria to include Cohort 3 are not met and concludes that the developmental immunotoxicity Cohort 3 needs not to be conducted.

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

You did not specify the species for testing. According to the test method EU B.56./ OECD TG 443, the rat is the preferred species. On the basis of this default consideration, ECHA considers that testing should be performed in rats.

You did not specify the route for testing. 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.

Outcome

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are requested to carry out the proposed study 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); and
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

Currently, the extension of Cohort 1B and the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) are not requested. However, the sub-chronic toxicity study (90-day) requested in this decision (request *1*) and/or any other relevant information may trigger changes in the study design. Therefore, the sub-chronic toxicity study (90-day) is to be conducted first and the study results submitted to ECHA in a dossier update by **14 Decmber 2018**. If, on the basis of this update and/or other relevant information, a need for changes to the study design is identified, ECHA will inform you by **14 March 2019** (i.e. within three months after expiry of the 12-month deadline to provide the sub-chronic toxicity study (90-day)) of its intention to initiate a new decision making procedure under Articles 41, 50 and 51 of the REACH Regulation to address the design of the extended one-generation reproductive toxicity study. If you do not receive a communication from ECHA by **14 March 2019**, the request of the present decision for the extended one-generation reproductive toxicity study remains effective and you may commence the conduct of the study and the results will need to be submitted by the deadline given in this decision **14 June 2021**.

Note for your considerations:

When submitting the study results of the sub-chronic toxicity study (90-day) you are invited to also include in the registration update your considerations whether changes in the study design are needed (see also *ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.6 (version 4.1, October 2015)*).

Furthermore, after having commenced the extended one-generation reproduction toxicity study in accordance with the ECHA decision, you may also expand this study to address a concern identified during the conduct of it and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the changes in the study design 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.

Deadline to submit the requested Information

In the document entitled "[redacted]" which is attached to the IUCLID dossier of the registered substance you requested a deadline of at least 36 months "*due to the long duration of the OECD443 study and the need to stagger these studies to ensure that if effects are seen that trigger Column 2 criteria allowing the avoidance of any unnecessary animal testing.*"

In this draft decision the time indicated to provide the requested information is 42 months from the date of adoption of the decision. ECHA considers that 42 months is a reasonable time period for providing the required information in the form of an updated registration from the date of the adoption of the decision. However, as a proposal for amendment (PfA) to the draft decision, a Member State Competent Authority (MSCA) suggested to set a shorter deadline, 12 months, for the information requested for a sub-chronic toxicity study (90-day). In your comment on the PfA, you stated that "*12 months from the final decision to having the final report from a 90 day study is not possible*".

You furthermore outlined that "*Reconsiderations of the exposure scenarios based on the new data from the 90-day study (and updating them to CHESAR) may be necessary and thus additional 2 months would be reasonable after the final reporting so in total 20 months from the final decision to the updating of the dossier would be realistic.*" ECHA requested and received documentary evidence from you substantiating your claim of limited laboratory capacity. Based on the documentary evidence received, ECHA considers that a deadline of 20 months is a reasonable time period for providing the required information requested for a sub-chronic toxicity study (90-day). The deadline for providing the remaining information (for two pre-natal developmental toxicity studies and an extended one-generation reproductive toxicity study) has consequently been extended to 50 months.

In your comment on the PfA, you also indicate that you consider it unnecessary in this case to introduce a time limitation on the testing for a sub-chronic toxicity study. You outline that you based on testing of similar substances do not expect to see effects of immunotoxicity or neurotoxicity in the sub-chronic toxicity study, and that the time limitation would create additional work for the registrants (updating of dossiers) and ECHA (reviewing the data within three months). You furthermore indicate that the sub-chronic toxicity study would in any case be carried out first. In relation to your considerations, ECHA emphasises that a re-assessment of the study design of the extended one generation reproductive toxicity study after the submission of the results of the sub-chronic toxicity study is aimed to provide clarity to you as regards the study design needed to meet the standard information requirement.[2]

[2] Further information on this sequential testing can be found in chapter 4 "*Missing relevant information*" of ECHA's technical report "*How ECHA identifies the design for the extended one-generation reproductive toxicity study (EOGRTS) under dossier evaluation*" available in the Internet at https://echa.europa.eu/publications/technical-scientific-reports

Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 12 February 2013.

ECHA held a third party consultation for the testing proposal(s) from 14 August 2014 until 28 September 2014. ECHA received information from third parties (see Appendix 1).

This decision does not take into account any updates after **29 June 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.

In your comments you agreed to the draft decision. ECHA took your comments into account and did not amend the request(s).

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

ECHA received proposals for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendments.

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 Member State Committee reached a unanimous agreement on the draft decision in its MSC-52 written procedure and ECHA took the decision according to Article 51(6) 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 relation to the information required by the present decision, the sample of the substance used for the new test(s) 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 test(s) 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 test(s) 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 test(s) to be assessed.