Helsinki, 30 March 2017

Addressee: [redacted]

Decision number: CCH-D-2114358335-47-01/F
Substance name: TRIFLUOROACETIC ACID
EC number: 200-929-3
CAS number: 76-05-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 04.12.2015
Registered tonnage band: 1000+T

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. **Sub-chronic toxicity study (90-day), oral route (Annex IX, Section 8.6.2.; test method: EU B.26./OECD TG 408) in rats with the registered substance adjusted to physiological pH;**

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 with the registered substance adjusted to physiological pH;**

3. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a second species (rabbit or rat), oral route with the registered substance adjusted to physiological pH;**

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 adjusted to physiological pH, 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.**

5. **Identification of PNEC and risk characterisation (Annex I, Section 3.3.1. and 6.): revise PNECs for freshwater, marine water, freshwater sediment and marine sediment using the study giving rise to the highest concern according to Annex I, Section 3.1.5 and revise the risk characterisation accordingly *or* provide a detailed justification for not using the recommendations of ECHA guidance in PNEC derivation.**

6. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment.**
   - **(1) Revise the exposure assessment to provide a detailed justification, including related risk management measures, for using non-default release factor in the exposure estimation for exposure scenarios ES1 and ES2 *or* to apply default release factors according to ECHA Guidance R.16;**
   - **Revise the exposure assessment to apply a "fraction of the main source" of 100% for exposure scenarios ES3, ES4 and ES6 in accordance with the recommendations of ECHA Guidance R.16 *or* to provide adequate justification for any deviation from these recommendations.**
   - **The risk characterisation shall be revised accordingly.**

7. **Exposure assessment (Annex I, Section 5.1.1.) for human health: provide documentation for the recommended personal protective equipment, i.e. hand and skin protection, respiratory protection and eye/face protection;**
   - **specify the type of glove material, thickness and breakthrough times;**
   - **specify the filter type/class for the respiratory protective equipment;**
   - **specify the type and quality of protective clothing.**

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 **7 January 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 **9 July 2018**. You may only commence the extended one-generation reproductive toxicity study as requested under point *4* after **8 October 2018**, 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 Kevin Pollard, 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

0. Grouping of substances and read-across approach

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests. Such other means include the use of information from structurally related substances (grouping of substances and read-across), "provided that the conditions set out in Annex XI are met".

In the registration, you have adapted, inter alia, the standard information requirements for

- Sub-chronic repeated dose toxicity study (Annex IX, Section 8.6.2.)
- Extended one-generation reproduction toxicity study (Annex X, Section 8.7.3.)

by applying a read-across adaptation following REACH Annex XI, Section 1.5.

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 an property-specific context.

0.1 Description of the grouping and read-across approach proposed by the Registrant

You have provided a document attached to IUCLID section 13 named "[redacted]".

In this report you indicate that "*This report addresses the analogue approach for the read-across of the environmental fate, genotoxicity and ecotoxicological properties of trifluoroacetic acid (TFA) from its structural analogue sodium trifluoroacetate (TFANa) and some human toxicological properties of trifluoroacetic acid (TFA) from its structural analogue potassium trifluoroacetate (TFAK). These substances have trifluoracetate as the common functional group, with the anions being either potassium, sodium, or hydrogen. The environmental fate, ecotoxicity, and human toxicity of the substances is expected to be mostly governed by the presence of the trifluoroacetate anions formed upon dissociation. Experimental data of sodium trifluoroacetate are available for the following ecotoxicological and toxicological endpoints:*

- *Environmental fate properties (biodegradation, bioavailability)*
- *Short-term toxicity to fish*
- *Short-term toxicity to aquatic invertebrates*
- *Toxicity to aquatic algae and cyanobacteria*
- *Toxicity to microorganisms*
- *Toxicity to terrestrial plants*
- *Genetic toxicity in vitro*

Experimental data of potassium trifluoroacetate are available for the following human endpoints:

- *Repeated dose toxicity*
- *Toxicity to reproduction"*

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

You proposed a first read-across approach using information from the source substances sodium trifluoroacetate and potassium trifluoroacetate for endpoints investigating not only local effects of the acid. ECHA does not address these endpoints in this decision.

However, for the endpoints "Repeated dose toxicity" and "Toxicity to reproduction", you have provided a "combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test" (OECD TG 422) performed with the source substance "Reaction mass of potassium trifluoroacetate and potassium trifluoromethanesulphinate" (EC 911-467-3).

In the following, ECHA is addressing the read-across to this substance for the endpoints sub-chronic toxicity (Annex IX, Section 8.6.2.) and extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.).

ECHA notes that you did not provide any justification for the read-across adaptation for the source substance "reaction mass of potassium trifluoroacetate and potassium trifluoromethanesulphinate" (EC 911-467-3).

You provided the following information on this substance: *"Analytical purity: 37.9% - Impurities (identity and concentrations): Sulfates 0.14%; sulfites 0.34%; dimethylformamide 0.24%; fluorures 39 ppm - Composition of test material, percentage of components:* [redacted]*".*

In your comments on the draft decision according to REACH Article 50(1) you specify further the remaining constituent to be "[redacted]."

You further specify that *"In the screening study the test material was dosed at concentrations of 100, 300 and 1000 mg/kg based on active ingredient which corresponds to ca. 50; 150 and 500 mg/kg potassium trifluoroacetate. Since no adverse effects were after repeated exposure at the highest dose tested, it was concluded that the presence of TFSK did not significantly contribute to the toxicity of the mixture. "*

ECHA notes that the substance characterisation of the source substances needs to be sufficiently detailed in order to assess whether the attempted prediction is not compromised by the composition and/or impurities. ECHA observes that the analytical purity of the source substance is 37.9% containing [redacted]. ECHA notes that the reported fraction of the registered substance in the mixture after removal of the solvent ([redacted]% out of summarised [redacted]%, see above) is [redacted]%.

ECHA observes further that you report doses that have been re-calculated based on the active ingredient. However, ECHA notes inconsistencies (see above paragraph, calculating a sum of [redacted]% instead of [redacted]%) in the reported percentages of constituents in the technical dossier, including impurities.

Therefore, the provided data do not demonstrate that the test was conducted with a top dose of the registered substance equivalent to the limit dose of 1000 mg/kg bw/d as required by OECD TG 422, but instead with a mixture of inconsistently reported constituents, of which the registered substance could constitute a total of [redacted]%.

In addition, you have not addressed the obvious structural differences between the source substance, more specifically of the constituent potassium trifluoromethanesulphinate (TFSK), and the target substance. Furthermore, you did not explain why those differences would not lead to differences in the toxicity profile of target and source substances.

In your comments, you did not specifically explain how the presence of the other constituent TFSK would contribute to the toxicity of the tested mixture, other than "*no significant contribution*". In other words, you did not provide evidence or an explanation why mixture effects could be excluded.

Furthermore, you did not provide supporting evidence to substantiate the read-across to this source substance. More specifically, you did not provide reliable *in vivo* information to demonstrate similarities or differences regarding the toxicological profile of source and target substance. ECHA considers that structural similarity alone is not sufficient. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. In particular, the structural similarities must be linked to a scientific explanation of how and why a prediction is possible. Therefore, it cannot be verified that the proposed read-across can be used to predict properties of the registered substance.

0.3 Conclusion on the read-across approach

The adaptation of the standard information requirements for the endpoints sub-chronic toxicity and extended one-generation reproductive toxicity study in the technical dossier are based on the proposed read-across approach examined above. As also further explained under sections 1 and 4 below, ECHA does not consider the proposed read-across to be a reliable basis to predict the properties of the registered substance for the reasons set out above. Thus, the adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. Therefore, ECHA rejects the adaptations for those endpoints in the technical dossier that are based on Annex XI, Section 1.5.

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

Pursuant to Articles 10(a) and 12(1) 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 information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

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

In the technical dossier you have provided study records of several mechanistical studies flagged as "not assignable" or "not reliable". ECHA acknowledges that those studies do not provide reliable information to address the standard information requirement.

You have also provided a study record for a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (OECD TG 422) with the analogue substance "Reaction mass of potassium trifluoroacetate and potassium trifluoromethanesulphinate" (EC 911-467-3) which you have flagged as "reliable with restrictions". However, this study does not provide the information required by Annex IX, Section 8.6.2., because exposure duration is less than 90 days and not all tissues/organs are histopathologically investigated and not necessarily with the same statistical power as a study according to OECD TG 408 would require. Furthermore, as explained above in Appendix 1, section 0 of this decision, your adaptation of the information requirement according to Annex XI, Section 1.5., read-across, is rejected.

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.

ECHA has evaluated the most appropriate route of administration for the study. Based on the information provided in the technical dossier and/or in the chemical safety report, ECHA considers 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, even though the information indicates that human exposure to the registered substance by the inhalation route is likely, an acute inhalation study was provided that investigated the local effects of the substance in the respiratory tract. Hence, the sub-chronic toxicity study shall be performed by the oral route using the test method EU B.26./OECD TG 408.

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.

ECHA considers that to identify the systemic hazard of the substance, testing with the registered substance adjusted to physiological pH is most appropriate to avoid local irritative effects at the site of administration.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD TG 408) in rats with the registered substance adjusted to physiological pH.

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

Pursuant to Articles 10(a) and 12(1) 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 information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method EU B.31./OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. 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.

In the technical dossier you have provided study records for three non-guideline studies

1) *"Postnatal hepatic and renal consequences of in utero exposure to halothane or its oxidative metabolite trifluoroacetic acid in the rat"* ([redacted] 1996; flagged as key study and as reliable with restrictions);
2) *"Whole-embryo culture study Comparative effects of haloacetic acids in whole embryo culture"* ([redacted]. 1996; flagged as disregarded study and as reliable with restrictions);
3) *"Fetal morphology in mice exposed to halothane" ([redacted] 1979; flagged as "not assignable").*

You have also sought to adapt this information requirement. You provided the following justification for the adaptation: *"Trifluoroacetic acid (TFA) is corrosive based on the pH (0.45) and the alkali reserve (35 g NaOH/g substance). Therefore, considering these properties, it is scientifically unjustified to perform a developmental study to detect effects at doses recommended by the guidelines since strong corrosive effects would be observed in the dams. Moreover, no effect would be detected at low doses where no corrosivity may occur in the animals. This justification was corroborated by the [redacted] study (1996, Kr. 2) in which no effects were observed on development when TFA was orally administered at doses of 150 mg/kg bw/d to female rats from gestation day (GD) 10 to GD 20. In addition, a combined repeated dose/reproduction study according to OECD 422 with the structural analogue Potassium trifluoroacetate did no show any adverse effect on developmental parameters at the highest dose level. A No Observed Adverse Effect Level (NOAEL) of 375 mg TFA/kg was derived for reproduction/developmental effects. In the absence of a concern for developmental toxicity of TFA at non-corrosive concentrations, it is not considered appropriate to propose further developmental testing with trifluoroacetic acid."*

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.2., 'weight of evidence' with the conclusion that the registered substance does not have developmental effects at non-corrosive concentrations.
ECHA has examined your provided individual sources of information:

- ECHA notes that study (2) was disregarded due to major methodological deficiencies, and can not therefore be a reliable source of information.

- ECHA notes that study (3) has been characterised as of reliability 4 (not assignable), and is under any circumstances conducted on an analogue substance (2-bromo-2-chloro-1,1,1-trifluoroethane) for which no read-across justification has been provided. In view of the reliability of the study, and the failure to meet the requirements of Annex XI, 1.5 for adequate and reliable documentation in respect of the read-across, ECHA considers that this study cannot meet the information requirement by itself.

- ECHA considers that the provided post-natal developmental toxicity study (study (1), [redacted] 1996) as well as the provided OECD TG 422 screening study ("combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (OECD TG 422) with the analogue substance "Reaction mass of potassium trifluoroacetate and potassium trifluoromethanesulphinate" (EC 911-467-3)) do not have reliable coverage of the key parameters of the test method EU B.31./ OECD TG 414.

More specifically, these studies do not cover key parameters of pre-natal developmental toxicity effects *in vivo,* because no skeletal and visceral examination of foetuses is performed. In studies with post-natal examination of the offspring (study (1), the OECD TG 422 study), the dams are allowed to deliver naturally and malformed offsprings are frequently cannibalised. Hence, malformation might remain undetected in a post-natal study. In addition, the read-across approach for the OECD 422 screening study is rejected (see section 0 above).

Thus the individual sources of information in the dossier do not provide the information required for this endpoint.

Next, ECHA has examined your justification for considering that the information as a whole would be a sufficient weight of evidence.

- ECHA notes that your weight of evidence argument does not attempt to identify the strengths and weaknesses of the individual sources of the individual sources of information, and explain how these studies taken together can provide a sufficient weight of evidence. Rather, you assert that "*no effect would be detected at low doses where no corrosivity may occur in the animals.*"

- ECHA considers that testing with the registered corrosive substance for identification of systemic hazards is possible and scientifically justified when adjusting the pH of the registered substance to a physiological value. ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015) indicated the following with respect to administration of substance for reproductive toxicity studies: "*In certain cases, testing of neutral salts of alkaline or acidic substances may be appropriate and allows investigation of intrinsic properties at adequate dose levels*". Therefore, by using a buffered solution, the dose-limitations are removed, and the toxicity of the deprotonated form can be assessed.

- Additionally, ECHA considers your assertion that "no effect would be detected" is not supported by information in the dossier.

In summary, ECHA considers that you have not provided an adequate justification why there is sufficient weight of evidence, and ECHA considers that there is not sufficient weight of evidence from several independent sources of information which would allow to assume/ conclude that the substance does not have a particular dangerous property, i.e., pre-natal developmental toxicity as investigated in a study according to OECD 414 and required following Annex XI, Section 1.2., weight of evidence. Consequently, your adaptation is rejected.

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.

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 assumption ECHA considers testing should be performed with 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 corrosive liquid, ECHA concludes that testing should be performed by the oral route.

ECHA considers that to identify the systemic hazard of the substance, testing with the registered substance adjusted to physiological pH is most appropriate to avoid local irritative effects at the site of administration.

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 first species (rat or rabbit) by the oral route with the registered substance adjusted to physiological pH.

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

Pursuant to Articles 10(a) and 12(1) 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 information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

Pre-natal developmental toxicity studies (test method EU B.31./OECD TG 414) 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).

However, there is no information provided for a pre-natal developmental toxicity study in a second species. Furthermore, the justification for waiving a pre-natal developmental toxicity study in a first species could not be accepted and, for the same reasons, cannot be used for waiving a pre-natal developmental toxicity study in a second species.
Therefore, 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.

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 rabbits or rats as a second species, depending on the species tested in the first pre-natal developmental toxicity study.

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 corrosive liquid, ECHA concludes that testing should be performed by the oral route.

ECHA considers that to identify the systemic hazard of the substance, testing with the registered substance adjusted to physiological pH is most appropriate to avoid local irritative effects at the site of administration.

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 (rabbit or rat) by the oral route with the registered substance adjusted to physiological pH.

Notes for your consideration

You are reminded that before performing a pre-natal developmental toxicity study in a second species you must 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 enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement.

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

Pursuant to Articles 10(a) and 12(1) 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 information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

The basic test design of an extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443 with 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.

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

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 "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (OECD TG 422) with the analogue substance "Reaction mass of potassium trifluoroacetate and potassium trifluoromethanesulphinate" (EC 911-467-3) which you have flagged as "reliable with restrictions". In addition, you have provided a study record for an *in vivo* fertility study with single oral administration of trifluoroacetic acid to male rats and subsequent histopathological investigation of the testes. You have flagged this study as "not assignable".

You have also sought to adapt this information requirement by providing the following justification: *"For TFA limited information on reproduction toxicity in experimental animals is available. According to the introductory paragraph 4 of Annex IX and X of the REACH Regulation "in vivo testing with corrosive substances at concentration/dose levels causing corrosivity shall be avoided". TFA is highly corrosive to biological tissues and for this reason it is scientifically unjustified to perform a reproduction study to detect any effects on the reproduction at doses recommended by the guidelines since strong corrosive effects of TFA would be observed. Moreover, based on the available data from the structural analogue Potassium trifluoroacetate, it would be unlikely for effects to occur at low doses where corrosivity is not already observed in the animals. Furthermore, TFA did not induce any effect on the fertility of male rats both in vivo and in vitro studies using testes target cells such as Sertoli cells (Weight of evidence approach). For this reason it is not considered appropriate to propose further reproduction testing with trifluoroacetic acid."*

First ECHA notes your argument based on the introductory paragraph 4 of Annex IX and X of the REACH Regulation that further testing is unjustified due to the corrosivity of the registered substance. ECHA acknowledges that *in vivo testing with corrosive substances at concentration/dose levels causing corrosivity shall be avoided".* ECHA considers that testing with the registered corrosive substance for identification of systemic hazards is possible and scientifically justified when adjusting the pH of the registered substance to a physiological value. ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.1, October 2015) indicated the following with respect to administration of substance for reproductive toxiicty studies: *"In certain cases, testing of neutral salts of alkaline or acidic substances may be appropriate and allows investigation of intrinsic properties at adequate dose levels*". Therefore, by using a buffered solution, the dose-limitations are removed, and the toxicity of the deprotonated form can be assessed.

Furthermore, you have sought to adapt this information requirement according to Annex XI, Section 1.2., 'weight of evidence' with the conclusion that the registered substance does not have effects on fertility of male rats.

ECHA has examined your provided individual sources of information within you weight of evidence approach:

- ECHA considers that the provided OECD TG 422 screening study ("combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (OECD TG 422) with the analogue substance "Reaction mass of potassium trifluoroacetate and potassium trifluoromethanesulphinate" (EC 911-467-3)) does not have reliable coverage of the key parameters of the test method EU B.56./OECD TG 443. More specifically, this study does not cover key elements, such as exposure duration, life stages and statistical power of an extended one-generation reproductive toxicity study. The main missing key elements are: 10 weeks pre-mating exposure duration, at least 20 pregnant females per group, and an extensive postnatal evaluation of the F1 generation. In addition, the read-across approach for the OECD 422 screening study is rejected (see section 0 above).

- ECHA notes that you flagged the *in vivo* fertility as "not assignable". Furthermore, ECHA notes that this study has relevant limitations. It was performed with a single oral administration of trifluoroacetic acid (adjusted to pH 7) to 10 male rats per dose groups with two exposure group with highest dose of 25 mg/kg bw/d leading to no histopathological effects in the testis. However, higher doses were not investigated and the limit dose of 1000 mg/kg bw/d was not used. In view of the reliability of the study and since the study investigated only one of many aspects of fertility, ECHA considers that this study cannot meet the information requirement by itself.

Thus the individual sources of information in the dossier do not provide the information required for this endpoint.

Next, ECHA has examined your justification for considering that the information as a whole would be a sufficient weight of evidence. However, ECHA notes that your weight of evidence argument does not attempt to identify the strengths and weaknesses of the individual sources of information, and explain how these studies taken together can provide a sufficient weight of evidence. Rather, you assert "*no effect on fertility of male rats.*"

In summary, ECHA considers that you have not provided an adequate justification why there is sufficient weight of evidence, and ECHA considers that there is not sufficient weight of evidence from several independent sources of information which would allow to assume/ conclude that the substance does not have a particular dangerous property, i.e., reproductive toxicity as investigated in a study according to OECD 443 and required following Annex XI, Section 1.2., weight of evidence. Consequently, your adaptation is rejected.

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

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

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 existing relevant data to be used for dose level setting, it is recommended that results from a conducted 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.

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 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a corrosive liquid, ECHA concludes that testing should be performed by the oral route.

ECHA considers that to identify the systemic hazard of the substance, testing with the registered substance adjusted to physiological pH is most appropriate to avoid local irritative effects at the site of administration.

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 with the registered substance adjusted to physiological pH, 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;

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 **9 July 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 **8 October 2018** (i.e. within three months after expiry of the 15-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 **8 October 2018** 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 **7 January 2021**.

Notes for your consideration

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.

5. Identification of PNEC and risk characterisation (Annex I, Section 3.3.1. and 6.)

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report (CSR) which shall document the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Annex I, Section 3.3.1. of the REACH Regulation requires to establish a PNEC for each environmental sphere based on the available information and to use an appropriate assessment factor to the effect values. Annex I, Section 3.1.5. of the REACH Regulation further requires that the study or studies giving rise to the highest concern shall normally be used to derive PNECs. If a study giving rise to the highest concern is not used, then this shall be fully justified.

You have proposed a PNEC value of 1 mg/L for freshwater and of 0.1 mg/L for marine water. You have calculated PNECs for freshwater sediment and marine sediment from those values using the equilibrium partitioning method.

You have provided the following justification:
"Among all the species tested, a toxic effect (growth inhibition) was found only for the algae Selenastrum capricornutum which lead to a R52 classification for the environment. Therefore it is proposed to take the lowest value of the range of EC50 that lead to such a classification, 10 mg/L, to derive the PNEC. This value is in line with the ErC50 for Selenastrum capricornutum calculated at 8.6 mg/L. Ten other algae species and three aquatic plants have been tested without showing any toxicity at the highest tested concentrations (up to 1997 mg/L TFA). The other organisms, invertebrates and fish are much less sensitive to TFA than Selenastrum capricornutum based on chronic test with daphnia and an acute fish limit test showing no effect. Therefore, it is postulated that the most sensitive species has been examined with high probability and an assessment factor of 10 could be applied to the lowest value in the range of toxicity consistent with a R52 classification".

ECHA notes that you have used the value of 10 mg/L as a starting point for deriving the PNECs. However, this does not correspond to the result giving rise to the highest concern. In particular, the PNEC you have proposed for freshwater is 5 times higher than the lowest available NOEC, which is 0.2 mg/L for *Selenastrum capricornutum*. This PNEC will therefore not protect the most sensitive species. ECHA acknowledges that *Selenastrum capricornutum* was the only tested algae species presented in the dossier showing such toxic effects.

Some hypotheses for explaining why *Selenastrum capricornutum* is much more sensitive than the other tested algae species have been proposed in the literature (e.g. Boutonnet et al. 1999, Human and Ecological Assessment, Vol.5, No 1, pp. 59-124). However it is not possible to definitively conclude that no other algae species will show the same range or even higher sensitivity to the registered substance and therefore that the functionality of the ecosystems would not be disrupted if the PNECs proposed by the registrant were accepted. ECHA considers that the result giving rise to the highest concern, i.e. the NOEC of 0.2 mg/L for *Selenastrum capricornutum*, shall be used to derive the PNECs for the aquatic environment.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to revise PNECs for freshwater, marine water, freshwater sediment, marine sediment using the result giving rise to the highest concern, i.e. the NOEC of 0.2 mg/L for *Selenastrum capricornutum*, according to Annex I, Section 3.1.5 and revise the risk characterisation accordingly or provide a full justification for not using the study giving rise to the highest concern.

6. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation the registration shall contain a chemical safety report (CSR) which shall document the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

According to Article 14(4) of the REACH Regulation, if the substance fulfils the criteria for any of the hazard classes of Annex I to Regulation (EC) No 1272/2008 listed in Article 14(4) of the REACH Regulation or is assessed to be a PBT or vPvB, the chemical safety assessment shall include an exposure assessment and risk characterisation.

ECHA notes that the registered substance has a harmonised classification and labelling as Skin Corr. 1A, Acute Tox. 4 and Aquatic Chronic 3. Therefore an exposure assessment and risk characterisation shall be included in the chemical safety assessment.

The exposure assessment shall be carried out according to section 5 of Annex I and shall include exposure scenarios and exposure estimations for the registered substance. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards. Annex I, section 6 of the REACH Regulation requires you to characterise the risk for each exposure scenario and to consider the environmental spheres for which exposure to the substance is known or reasonably foreseeable, under the assumption that the risk management measures described under exposure scenario in Section 5 of the same Annex have been implemented. In addition, the overall environmental risk caused by the substance shall be reviewed by integrating the results for the overall releases, emissions and losses from all sources to all environmental compartments.

The seven following exposure scenarios (ES) are presented in the dossier:

ES1: Manufacture - Manufacturing of TFA on the plant of [redacted]
ES2: Manufacture - Manufacture on the plant of [redacted]
ES3: Formulation - Formulation and Re-packing
ES4: Use at industrial site - Use as intermediate at industrial site
ES5: Use at industrial site - Use as solvent at industrial site
ES6: Use at industrial site - Use for surface treatment glass at industrial site
ES7: Use by professional worker - Laboratory professional use

The environmental exposure assessment and risk characterisation provided contain several deficiencies as indicated below.

a) Missing information on the risk management measures for ES1 and ES2

Pursuant to Annex I, section 5.1.1 of the REACH Regulation, exposure scenarios (ES) shall include, where relevant, a description of operational conditions (OCs) and of risk management measures (RMMs). As indicated in Annex I, section 5.2.2. of the REACH Regulation, emission estimation shall be performed under the assumption that the risk management measures and operational conditions described in the exposure scenario have been implemented. These RMMs and OCs should be included in the exposure scenarios provided in a CSR.

Operational conditions consist of a set of actions, tools, parameters such as amount of substance, process temperature and pH, duration and frequency of release, type of use (e.g. indoor or outdoor), containment of process (open or closed), continuous or batch process (leading to an intermittent release), capacity of surroundings, etc. having, as a side effect, an impact on the release and the exposure. Risk management measures consist of technologies and procedures aimed at either reducing the releases and/or preventing a release pathway. Examples of risk management measures intended to reduce release are filters, scrubbers, biological or physico-chemical wastewater treatment plants. Both OCs and RMMs have an impact on the type and amount of release and the resulting exposure. ECHA Guidance on information requirements and chemical safety assessment Chapter R.16: Environmental Exposure Estimation (ECHA, version: 3.0, February 2016) specifically provides default release factors associated with different Environmental Release Categories (ERCs).

These default release factors can be used for a first tier assessment of the emissions. However, better information may be available that could then be used instead. In particular, release factors can be refined by taking into account RMMs and OCs. In this case, it is important to explicitly link such RMMs and OCs to the release factors and communicate them properly in the exposure scenarios.

For exposure scenario ES1 (Manufacturing of TFA on the plant of [redacted]), the assessment is based on release data measured at the manufacturing site. ECHA notes that risks are not controlled for the aquatic compartment (for freshwater and marine water, freshwater sediment and marine water sediment) as RCRs were calculated to be above 1 for this compartment and this exposure scenario. You indicated that "*actions for the improvement of environmental impact of the site are ongoing, with the objective to obtain a RCR < 1*". You further indicated the following:

"*The releases of the substance into the waste water of the manufacturing site are measured daily. A project for environmental improvement of the site started in 2013 and has enabled a significant reduction of the aqueous releases of TFA. This project and the impact on the aqueous releases of TFA are described in a technical and economic study which has been provided to the local authorities. The objective of this project is to reduce the release of TFA to a monthly mean of 4 kg/d in 2018. In 2015, the monthly mean measured releases from January to September are equal of below 45 kg/d. This monthly mean should decrease at the end of the year 2015 because two investments are under implementation. Therefore, for the environmental exposure assessment, the objective for 2015 described in the technical and economic study is applied (i.e. 30 kg/d)".*

However ECHA notes that the release rate assumed for the assessment (i.e. 30 kg/d) is hypothetical as it is not supported by actual data. Furthermore, this release rate does not ensure that the risks are controlled. You have not provided any detail on the risk management measures you intend to implement in order to have the risks adequately controlled.

For exposure scenario ES2 (Manufacture on the plant of [redacted]), you have assumed the following factors: 0.1%, 0.3%, 0% for air, water and soil respectively. By comparison, the default release factors recommended for ERC1 by ECHA Guidance R.16 are: 5%, 6% and 0.01%, respectively for air, water and soil. You claim that the release factors you have applied are based on A and B tables of the TGD (2003). No further justification is provided for using these release factors, in particular, the exposure scenario does not specify any RMM. According to ECHA guidance, use of release factors from A and B tables without justification is not acceptable. Specific information on RMM and OC must be provided when using A and B tables of the TGD, otherwise they are considered insufficient to meet the REACH requirements (ECHA guidance R.16.2.3.3).

b) Deviations on the assumed fraction used at main source (i.e. annual use amount at a site)

Pursuant to Annex I, section 5.2.1 of the REACH Regulation the exposure estimation as part of the exposure assessment entails three elements: emission estimation, assessment of chemical fate and pathways and estimation of exposure levels. Pursuant to Annex I, section 5.2.2. of the REACH Regulation, emission estimation shall consider the emissions during all relevant parts of the life-cycle of the substance resulting from the manufacture and each of the identified uses.

For point sources, a protective estimation of the emissions requires that the capacity of the largest point source for the particular stage of the life cycle should be estimated. The main source thus represents the emission source where the largest fraction of the production volume or market volume of the substance is handled. If this information is not known, it has to be estimated from the registered total annual tonnage.

For exposure scenarios ES3, ES4 and ES6, you have assumed that the fraction of the main local source is 10% of the registered total annual tonnage. However, the Guidance on information requirements and chemical safety assessment Chapter R.16: Environmental Exposure Estimation (ECHA, version: 3.0, February 2016, page 38) recommends that, for an industrial site, the annual use amount at the site should be set, by default, to 100% of the total annual tonnage for the use, i.e. that the fraction of the main source should be set to 100%. Exposure scenarios ES3, ES4 and ES6 all apply to industrial sites, and therefore by default the annual use amount at a site should have been assumed to be 100% for these 3 exposure scenarios. This default value of 100% is a worst case to cover situations where the total registered tonnage is processed by at a single site. By assuming lower values, you may have underestimated the local exposure. The default value of 100% may be overwritten on the basis of site specific information or of information on the actual amount used by the largest downstream user. However no such information is provided in your dossier, and you have not provided any justification for deviating from the default recommendation of the guidance.

c) Outcome

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation, you are requested:
- to provide justification for the release factors applied for exposure scenarios ES1 and ES2 and in particular to specify the risk management measures or to apply default release factors in exposure scenarios 1 and 2 according to ECHA Guidance R.16;
- to apply a "fraction of the main source" of 100% for exposure scenarios ES3, ES4 and ES6 in accordance with the recommendations of ECHA Guidance R.16 or to provide adequate justification for any deviation from these recommendations;
- to revise the risk characterisation accordingly.

7. Exposure assessment and risk characterisation (Annex I, Section 5.1.1.) for human health

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation the registration shall contain a chemical safety report (CSR) which shall document the chemical safety assessment (CSA) conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

Article 14(6) as well as Annex I, 0.1., 5.1.1., 5.2.4. and 6.2. of the REACH Regulation require registrants to identify and apply appropriate measures to adequately control the risks identified in a CSR. The exposure shall be estimated and risks shall be characterised in the CSR under the assumption that relevant risk management measures have been implemented.

According to Annex I, 0.3., 0.5. and 5.1.1. the applied Risk Management Measures (RMM) have to be described in the CSR. The CSR needs to contain sufficient information to allow ECHA to gain assurance that the risks are adequately controlled and that appropriate RMMs can be prescribed by actors in the supply chain.

Accordingly, the supplier is required to describe the relevant RMM in detail in the Safety Data Sheet in order to minimise the exposure for workers handling the registered substance (e.g. the type of gloves to be worn, protection equipment for parts of the body other than the hand or respiratory protection shall be clearly specified based on the hazard of the substance or mixture and potential for contact and with regard to the amount and duration of exposure in accordance with Annex II, section 8.2.2.2.(b)(i), (ii) and 8.2.2.2.(c) respectively). The information provided in the Safety Data Sheet (SDS) shall be consistent with information in the Chemical Safety Report (Annex II, section 0.1.2. of the REACH Regulation).

In the CSR, you have provided non-specific advice about personal protective equipment. For instance you state in the conclusion on risk characterisation that "*The substance is corrosive, therefore dermal and ocular contact should be avoided. The use of personal protective equipment (PPE) and appropriate risk management measures (RMMs) enable the control of risks. Eye irritancy and dermal corrosivity is controlled by use of face shields or goggles and acid resistant gloves. Details of the RMMs are given in the ES.*" However, ECHA notes, there is no detailed information of the PPE in the ES.

You have provided some information of PPE in the Section 11 (Guidance on safe use) in the technical dossier (IUCLID): "*Personal protective equipment :*
- Respiratory protection: Self-contained breathing apparatus. If the ventilation is suitable, it is not essential to wear respiratory equipment.
- Hand protection: Protective gloves made of PVC.
- Eye protection: Safety spectacles and a face shield.
- Skin and body protection: Light overall made of PVC. Boots made of PVC."

The registered substance has been classified as very corrosive to skin (Skin Corr. 1A; H314: Causes severe skin burns and eye damage). The use of PPE may be needed when the substance is handled, even though the RCR<1 in the ESs. Also you have mentioned in the qualitative risk characterisation that PPE should be used.

ECHA notes that specific detailed information on the recommended personal protective equipment is missing both from the CSR and from the information on safe use within the IUCLID dossier. The glove material is not enough in this case, as some acids may permeate or degrade the PVC material. It is especially important to know the breakthrough time for the material that is used for the skin and body protection to ensure it is used within safe limits.

To ensure the safe use of a substance, Annex I, Section 5.1.1. requires a description of the risk management measures to reduce or avoid direct and indirect exposure of humans.

Gloves are reported in the CSR and IUCLID Section 11 as required personal protective equipment to prevent dermal exposure to the substance. Generally, gloves that are capable of preventing exposure to the skin for a pre-determined duration shall be specified. Typically, this information, as a minimum, has to specify the glove material and, depending on the exposure scenarios, may also need to include the breakthrough time and thickness of the glove material. Gloves need to be manufactured and tested according to CEN standard EN 374:2003 – Gloves giving protection from chemicals and micro-organisms.
Respiratory protection is reported in the CSR and IUCLID Section 11 as required personal protective equipment to prevent inhalation exposure to the substance.

Typically, this information, as a minimum, has to specify the type/class of filters that are capable of preventing inhalation exposure for a pre-determined duration and delivering the assessment protection factor specified by you.

Where protective clothing is specified as a mean to reduce exposure to the registered substance it has to be capable of providing the required barrier properties. This can only be assured through provision of clothing that has been tested to ensure a minimum performance against splash/spray/jet challenge. The minimum standard for liquid chemicals is "Type 6" protective clothing that meets the standard of EN 13034:2005 – Chemical protective clothing offering limited protection against liquid chemicals (type 6 and type PB [6] equipment), typically disposable coveralls. If the working space is confined, and the worker may need to lean on contaminated surfaces or the chemical may splash, better protection may be needed. "Type 3 or 4" protective clothing requirements are defined in EN 14605: 2005 – Type 3 or 4 Protective Clothing Performance requirements for clothing with liquid-tight (Type 3) or spray tight (Type 4) connections, including items providing protection to parts of the body only (Type PB 3 and PB 4). Unspecified workwear that has not been tested according to the appropriate standards for permeation and penetration resistance is not chemical protective clothing, as defined, and is unlikely to provide any demonstrable protection.

Therefore, pursuant to Article 41(1) you are requested to provide documentation for the recommended personal protective equipment, i.e. skin protection (hand and body protection) and respiratory protection:
- further specify the type of glove material, thickness and breakthrough times;
- further specify the filter type/class for the respiratory protective equipment;
- further specify the type and quality of protective clothing.

DEADLINE TO SUBMIT THE REQUESTED INFORMATION IN THIS DECISION

In the draft decision communicated to you the time indicated to provide the requested information for the sub-chronic toxicity study was 12 months from the date of adoption of the decision. In your comments on the draft decision, you requested an extension of the timeline to 24 months. You sought to justify this request by the documentation of two different CRO's timeframe plans by concluding that the necessary time required for conducting the OECD TG 408 study in rats is 13 - 16 months. However, based on the information from the CRO's, timelines of 12 and 15 months (including 2 months for updating the registration) were indicated. Therefore, your arguments for extending the deadline to 24 months, including uncertainties regarding the availability of resources, were not sufficiently substantiated. However, ECHA took into account the documentation of the study plans you provided. Therefore, ECHA has partially granted the request and set the deadline to 15 months.

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 1 June 2016.

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 amended the deadline.

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

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.