EUROPEAN CHEMICALS AGENCY

Helsinki, 31 January 2017

Addressee: [redacted]

Decision number: CCH-D-2114352349-44-01/F
Substance name: Ethanol, 2,2'-oxybis-, reaction products with ammonia, morpholine derivs. residues
EC number: 272-712-1
CAS number: 68909-77-3
Registration number: [redacted]
Submission number: [redacted]
Submission date: 20.12.2013
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;**

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;**

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

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);**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;**

5. **Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25./OECD TG 309) at a temperature of 20 °C with the registered substance;**

6. **Identification of degradation products (Annex IX, 9.2.3.) using an appropriate test method with the registered substance;**

7. **Exposure assessment (Annex I, Section 5.1.1.) for human health:**
   - provide documentation for the recommended personal protective equipment (hand protection);
   - specify the type of glove material, and breakthrough times;
   - reassess risk management measures at outdoor tasks;
   - rephrase use of local exhaust ventilation (LEV) for closed processes (PROC1).

8. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment:**
   - use default release factors and revise the risk characterisation accordingly for water compartment for ES1 and ES 2 *or* provide a detailed justification for not using the default release factors, for instance based on risk management measures, operational conditions or substance properties; the risk characterisation shall be revised accordingly.

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 **8 February 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 **7 February 2018**. You may only commence the extended one-generation reproductive toxicity study as requested under point 4 after **7 May 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 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

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 a study record for a "repeated dose 28-day oral toxicity study" (test method: OECD TG 407). 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 the number of animals per dose group is significantly lower. Therefore, the sensitivity of a 28-day study is much lower than that of a 90-day study.

The technical dossier does not contain an adaptation in accordance with column 2 of Annex IX, Section 8.6.2. or with the general rules of Annex XI for this standard information requirement.

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.
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, the exposure concentrations reported in the chemical safety report for the inhalation route are limited. Further, a relatively high systemic exposure after oral administration is expected according to the technical dossier. Hence, the test shall be performed by the oral route using the test method EU B.26./OECD TG 408. Hence, the test 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 acknowledges that in the comments on the draft decision, you agreed to perform the requested study.

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: Repeated dose 90-day oral toxicity study (test method: EU B.26./OECD TG 408) in rats.

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 a study record for a "reproduction/ developmental toxicity screening test" (test method: OECD TG 421). However, this study does not provide the information required by Annex IX, Section 8.7.2., because it does not cover key parameters of a pre-natal developmental toxicity study, such as examinations of foetuses for skeletal and visceral alterations. Therefore, your adaptation of the information requirement is rejected.

The technical dossier does not contain an adaptation in accordance with column 2 of Annex IX, Section 8.7.2. or with the general rules of Annex XI for this standard information requirement.

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 rats or rabbits as a first species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

ECHA acknowledges that in the comments on the draft decision, you agreed to perform the requested study within a sequential testing strategy to avoid unnecessary testing. 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 (rats or rabbits) by the oral route.

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).

The technical dossier does not contain information on a pre-natal developmental toxicity study. Furthermore, the technical dossier does not contain an adaptation in accordance with column 2 of Annex X, Section 8.7.2. or with the general rules of Annex XI for this standard information requirement.

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

ECHA acknowledges that in the comments on the draft decision, you agreed to perform the requested study within a sequential testing strategy to avoid unnecessary testing.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a second species (rabbits or rats) by the oral route.

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 in 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 requirements*

In the technical dossier you have provided a study record for a "reproduction/developmental toxicity screening test" (test method: OECD TG 421).

You have also sought to adapt this information requirement. 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.

The provisions of Annex XI Section 1.2. stipulate that the weight of evidence needs to lead to the assumption or conclusion that the substance has or has not the particular dangerous property under investigation.

You provided the following justification for the adaptation:
"A two-generation reproduction study is not required as there is sufficient weight of evidence from the OECD 421 screening study. In this study rates were exposed to very high dosis (1000 mg/kg/day). No systemic, reprotoxic or developmental effects were observed over the course of the study in either the F0 parental animals (males or females), or the F1 progeny. Moreover, as the substance is only used in closed systems: no relevant long-term exposure will be observed. Based on these results it can be concluded that this endpoint has been adequately tested through the use of the screening study and that no additional studies are required."

However, ECHA notes that your adaptation does not meet the general rules for adaptation of Annex XI, Section 1.2., because the OECD TG 421 screening study does not provide the information required by Annex X, Section 8.7.3., more specifically, it does not cover key elements, such as exposure duration, life stages and statistical power of an extended one-generation reproductive toxicity study. More specifically, 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. Hence, it is not possible to assume or conclude based on the provided information whether the registered substance has or has not a hazardous property on sexual function and fertility and post-natal development. Therefore, your adaptation of the information requirement is rejected.

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 3.2.(a). Annex XI, Section 3.2.(a) requires that you can demonstrate (i) no significant exposure, (ii) the DNEL is relevant and appropriate, and (iii) exposures are well below the DNEL covering all relevant exposures.

Your adaptation does not meet the general rules for adaptation of Annex XI, Section 3 either, because there is not sufficient evidence in your technical dossier to demonstrate that human exposure is absent or not significant. For example, inhalation exposure of workers above [redacted] mg/m^3 has been estimated. Also, the DNELs derived for reproductive toxicity are based on the results from a screening test for reproductive/developmental toxicity.

As indicated in the footnote to subparagraph 3.2(a)(ii) of Annex XI, a DNEL derived from a screening test for reproductive/developmental toxicity shall not be considered appropriate to omit reproductive toxicity information required at Annex IX and X, Sections 8.7.2 and 8.7.3. Consequently, the DNELs derived for reproductive toxicity in your dossier cannot be used for adopting information requirement of an extended one-generation reproductive toxicity study.

Therefore, your adaptation of the information requirement 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.

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

Species and route selection

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

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, 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.

c) Outcome

ECHA acknowledges that in the comments on the draft decision, you agreed to perform the requested study within a sequential testing strategy to avoid unnecessary testing.

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

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

Currently, it has not been decided whether to include or exclude **the extension of** Cohort 1B, Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) in the EOGRTS design. 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 **7 February 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 **7 May 2018** (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 **7 May 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 **8 February 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. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.)

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.

"Simulation testing on ultimate degradation in water" is a standard information requirement as laid down in Annex IX, section 9.2.1.2. of the REACH Regulation. Column 2 of Section 9.2.1.2 of Annex IX further indicates that the study needs to be conducted if the chemical safety assessment (CSA) according to Annex I indicates the need to investigate further the degradation of the substance and its degradation products and that the choice of the appropriate test(s), which may include simulation degradation tests in appropriate media, depends of the results of the CSA. Column 2 indicates that the study does not need to be conducted if the substance is highly insoluble in water or if the substance is readily biodegradable. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

You provided the following justification for the adaptation*: "From a regular and an enhanced CO2 evolution test it was concluded that the substance is not readily biodegradable, although limited biodegradation was observed. No further simulation testing is deemed necessary as it will not improve the current conclusion on biodegradation. Furthermore, the chemical safety assessment showed safe uses for all environmental compartments when assuming no biodegradation."*

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 IX, Section 9.2.1.2., column 2. However, ECHA notes that your adaptation does not meet the specific rules for adaptation of Annex IX, Section 9.2.1.2., column 2 because the substance is neither readily biodegradable nor highly insoluble in water.

Furthermore, ECHA notes that you have provided information that could be seen as an attempt to adapt the information requirement according to Annex IX, Section 9.2., column 2 as you have claimed that based on the CSA there is no need for further testing. ECHA acknowledges your claim of all uses being shown safe when assuming no biodegradation. However, ECHA notes that the exposure assessment and risk characterization for environment are to be revised as per request in section (8) of the present decision. Thus,

the chemical safety assessment (CSA) cannot currently be used to justify why there is no need to investigate further the degradation of the substance and its degradation products.

Furthermore, ECHA notes that neither in your CSA nor in the technical dossier you have provided any information on the degradation products, nor justified that there is no need to investigate further the degradation products of the registered substance. ECHA considers that the study requested is needed to obtain information on the degradation products, as specified further below in this section and in section (6) of this draft decision

In the comments you provided to the proposals for amendments (PfAs) made by the Member States Competent Authorities (MSCAs), you have indicated that there is no experimental data available on the possible formation of degradation products from simulation testing in water, sediment or soil. You have provided QSAR predictions for ready biodegradability using EPISUITE BIOWIN v4.10 for 13 of the 14 identified constituents reported in the technical dossier of the registered UVCB substance. ECHA acknowledges that valid (Q)SAR predictions could be used to identify the representative constituents of a UVCB substance for second tier testing, as indicated in ECHA Guidance R.11, section R.11.4.2.2.

However, you have not provided adequate documentation, including information that the predictions are within the applicability domain of BIOWIN models. Thus, ECHA cannot estimate the validity of the predictions. In addition, for those constituents that were predicted to be not ready biodegradable, you have provided aquatic toxicity predictions using ECOSAR v1.11 and concluded that all these constituents are not T. However, ECHA notes that you have not provided adequate documentation for these predictions. In addition, ECHA notes that you have not provided any conclusions on the PBT assessment of the registered substance or the possible degradation products. In your comments on the PfAs, you also proposed to perform an additional tier one biodegradation test (i.e. one of the inherent biodegradability tests according to test guideline OECD 302) to draw conclusions on the P assessment. If the inherent biodegradability test shows no evidence of primary degradation, you have proposed that this would be sufficient to conclude that the chemical is persistent. ECHA acknowledges your comment and points out that an inherent biodegradability test would not meet the information requirement of Annex IX, Section 9.2., nor can it be used for the identification of degradation products, the main purpose for this request as identified above. Results obtained from an inherent biodegradation study would also not be acceptable for the purpose of the PBT/vPvB assessment.

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

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to ECHA *Guidance on information requirements and chemical safety assessment, Chapter R.7b* (version 3.0, February 2016) Aerobic mineralisation in surface water – simulation biodegradation (test method EU C.25. / OECD TG 309) is the preferred test to cover the standard information requirement of Annex IX, Section 9.2.1.2.

One of the purposes of the simulation test is to provide the information that must be considered for assessing the P/vP properties of the registered substance in accordance with Annex XIII of the REACH Regulation to decide whether it is persistent in the environment. Annex XIII also indicates that "*the information used for the purposes of assessment of the PBT/vPvB properties shall be based on data obtained under relevant conditions*". The

Guidance on information requirements and chemical safety assessment R.7b (version 3.0, February 2016) specifies that simulation tests "attempt to simulate degradation in a specific environment by use of indigenous biomass, media, relevant solids [...], and a typical temperature that represents the particular environment".
The Guidance on information requirements and chemical safety assessment Chapter R.16 on Environmental Exposure Estimation, Table R.16-9 (version 2.1 October 2012) indicates 12°C (285K) as the average environmental temperature for the EU to be used in the chemical safety assessment. For this specific case, ECHA requires the test to be conducted at 20°C as the main reason for this request is the identification of degradation products. Conducting the study at 20°C would result in faster degradation rate and would therefore enhance the formation of degradation products.

In the OECD TG 309 Guideline two test options, the "pelagic test" and the "suspended sediment test", are described. ECHA considers that the pelagic test option should be followed as that is the recommended option for P assessment and is most suitable for the identification of degradation products.

ECHA notes that if technical difficulties prevent testing from being completed, you should provide information on why the requested test was not technically possible within the technical dossier.

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: Aerobic mineralisation in surface water – simulation biodegradation test (test method: EU C.25./OECD TG 309) at a temperature of 20 °C.

Notes for your consideration

Before conducting the requested test you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R7b, Sections R.7.9.4 and R.7.9.6 (version 3.0, February 2016) and Chapter R.11, Section R.11.4.1.1 (version 2.0, November 2014) on PBT assessment.

Due to the substance being a UVCB, you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R.11, Section R.11.4.2.2 (version 2.0, November 2014) on P assessment of multi-constituent substances.

In accordance with Annex I, Section 4, of the REACH Regulation you should revise the PBT assessment when results of the test detailed above is available. You are also advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11, Section R.11.4.1.1. and Figure R. 11-3 on PBT assessment for the integrated testing strategy for persistency assessment in particular taking into account the degradation products of the registered substance.

6. Identification of degradation products (Annex IX, 9.2.3.)

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 identification of the degradation products is a standard information requirement according to column 1, Section 9.2.3. of Annex IX of the REACH Regulation. Column 2 of

Section 9.2.3. of Annex IX further states that the information does not need to be provided if the substance is readily biodegradable.

ECHA observes that you have not provided information concerning the identity of degradation products. Furthermore, there is no valid adaptation of this standard information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

ECHA notes further that as already discussed in section (5) above, you have neither in your Chemical safety Assessment (CSA) nor in your technical dossier justified that there is no need to investigate further the degradation products of the registered substance.

ECHA has address the comments you provided on the MSCAs PfAs in section (5) above. For the reasons outlined in section (5) above, ECHA considers that the information provided cannot be seen to fulfill the information requirement for the identification of degradation products.

ECHA notes further that the OECD 309 Test Guideline features the formation and identification of the degradation products. The identification of degradation products should therefore be included in the degradation simulation test requested above under section 5.

Regarding appropriate and suitable test methods, the methods will have to be substance specific. When analytically possible, identification, stability, behaviour, molar quantity of metabolites relative to the parent compound should be evaluated. In addition degradation half-life, log Kow and potential toxicity of the metabolite may be investigated. Furthermore, ECHA notes that if technical difficulties prevent testing from being completed, you should provide information on why the requested test was not technically possible within the technical dossier.

Therefore, pursuant to Article 41(1)(a) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision:

Identification of the degradation products (Annex IX, Section 9.2.3.) by using an appropriate and suitable test method, as explained above in this section.

Notes for your consideration

Before providing the above information you are advised to consult the ECHA *Guidance on information requirements and chemical safety assessment* (version 3.0, February 2016), Chapter R.7b., Sections R.7.9.2.3 and R.7.9.4. These guidance documents explain that the data on degradation products is only required if information on the degradation products following primary degradation is required in order to complete the chemical safety assessment. Section R.7.9.4. further states that when substance is not fully degraded or mineralised, degradation products may be determined by chemical analysis.

Due to the substance being a UVCB, you are advised to consult the ECHA Guidance on information requirements and chemical safety assessment, Chapter R.11, Section R.11.4.2.2 (version 2.0, November 2014) on P assessment of multi-constituent subtances.

In accordance with Annex I, Section 4, of the REACH Regulation you should revise the PBT assessment when the information detailed above is available. You are also advised to consult the ECHA Guidance on information requirements and chemical safety assessment (version 2.0, November 2014), Chapter R.11, Section R.11.4.1.1. and Figure R. 11-3 on PBT assessment for the integrated testing strategy for persistency assessment in particular taking into account the degradation products of the registered substance.

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, 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 exposure scenario 1 that *"workers wear gloves, boots, helmets and goggles",* and in exposure scenario 2 that *"Workers wear all appropriate PPE according to guidance on the MSDS and local risk assessments: rubber gloves, rubber footwear, goggles and protective overalls".* You have also provided some information of RMMs in the Section 11 (Guidance on safe use) in the technical dossier (IUCLID): *"Hand protection: Chemical-resistant, impervious gloves complying with an approved standard should be worn at all times when handling chemical products if a risk assessment indicates this is necessary".* 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.

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.

In the CSR you state that the substance is manufactured outside (ES 1), however for the transfer operation LEV is required. You use the ECETOC TRA for the exposure assessment. According to the technical report No. 107 of ECETOC TRA for outside activities, the "addition" of LEV is not provided as an option, as the effectiveness of extraction ventilation in outdoor settings is notoriously dependent on local conditions. Recalculation shows that the use of the default values of ECETOC TRA would yield RCRs > 1 for PROC 8b and PROC 9. Therefore, you are requested to reassess the tasks which are performed outdoors.

In ES 2 "the use of amine C8 as an intermediate" you state that LEV is present for all processes. The combination of a closed system (PROC 1) with LEV is not intended according to ECETOC TRA. However, recalculation shows that the exposure reduction effect of the LEV was not taken into account in the exposure assessment for PROC 1. To prevent misinterpretation you are asked to rephrase the relevant section as follows: "LEV is assumed to be present for all processes, except for PROC 1."

Therefore, pursuant to Article 41(1) you are requested to provide documentation for the recommended personal protective equipment for hand protection by further specifying the type of glove material and breakthrough times. You are also requested to revise the exposure assessment and risk characterisation to take account of the valid options for the use of local exhaust ventilation in the exposure modelling.

8. 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.

Pursuant to Annex I, Section 5.2.1 of the REACH Regulation the exposure estimation entails three elements: emission estimation, assessment of chemical fate and pathways and estimation of exposure levels. Emission estimation shall be performed under the assumption that the risk management measures (RMMs) and operational conditions (OCs) described in the exposure scenario (ES) have been implemented. These RMMs and OCs should be included in the ESs provided in a CSR.

According to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.16 (version: 2.1, 2012) the exposure scenario should contain information about operational conditions and risk management measures based on which the assumed release factors and daily use rates can be justified. Exposure scenarios making reference to non-standard release factors (ERC based) without providing more specific information on the conditions of use or risk management measures are considered insufficient to meet the REACH requirements according to ECHA Guidance R.16 Section %.16.3.1.4.
In the present case, in the CSR you have provided two ESs: 1) manufacturing of the substance; 2) use as intermediate. For ES 1 you have provided non-default release factors for water and air compartment that are considerably lower than recorded for the

representative ERC. For ES 2 you have provided non-default release factors for water and soil compartment that are lower than recorded for the representative ERC's.

ECHA notes that, in order to cover any exposures that may be related to the identified hazards, you have provided the following justification for the release factors used for the exposure estimation for ES 1: "*Emission factor to waste water is set to 2.59E-06, as indicated by industry experts of* [redacted]. *The emission factors to air and soil could be set to 0, as explained in section 9.1.1. However, the default EUSES value of 0.0001 was used for both air and soil emissions, to reflect a reasonable worst case situation. Given the low vapour pressure, the default release factor to air of 0.05 is regarded as highly overestimated and is therefore not used.",* but you did not provide any further justification (supported by OC's and/or RMM's) of these assumptions for water compartment. For release factors used for ES2 you provided the following justification: "*When using EUSES, the default release fractions to air, water and soil are 0, 0.02 and 0.0001, respectively. In view of the low vapour pressure, the ERC's highly overestimate the release to air, and therefore the release fraction from EUSES is used. As the substance is an expensive product, it can be assumed that spillages to industrial soil or emission to wastewater will not occur. Furthermore, the substance will completely react away, and consequently cleaning of the reactors will not result in the substance being present in the cleaning liquid. Therefore a release fraction to soil of 0.0001 (similar to EUSES) and to water of 0.0001 (based on worst-case estimate from the industry) are proposed.",* but you did not provide any further justification (supported by OC' and/or RMM's) of these assumptions for water compartment.

ECHA considers that an adequate and detailed justification (e.g. based on RMMs and/or OCs and/or substance properties) of release factors used in exposure estimation, other than the default ERC release factors, is not provided in the CSR. Where internal measures of releases are available, the summary of results of these measurements is needed. This summary should be detailed enough to understand whether or not it covers relevant scenarios for possible releases from the substance processing according to the relevant ES.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are requested to use default release factors and other recommendations of ECHA Guidance R.16 for water compartment for both ES1 and ES2 and revise the risk characterisation accordingly *or* provide a detailed justification (e.g. based on RMMs and/or OCs and/or substance properties) for not using the default release factors as recommended in ECHA Guidance R.16 for estimation of environmental exposure.

Deadline to submit the requested information in this decision

In the draft decision communicated to you, the time indicated to provide the requested information was 42 months from the date of adoption of the decision. In your comments on the draft decision, you requested an extension of the timeline to 48 months. You justified this request by explaining that if sequential testing could be done there would be a possibility to make a decision whether rats or rabbits should be tested as the first species in the pre-natal developmental test.

In case no effects were seen in the 90-day repeated dose toxicity study and the extended one generation study in rats, rabbit could be chosen as the first species for the pre-natal developmental toxicity study and the study in the second species (rat) could be waived if the test in rabbits did not show any effects on pre-natal developmental toxicity. ECHA agrees that in this case sequential testing introduces a possibility to reduce animal testing with the registered substance.

Therefore, ECHA has granted the request and set the deadline to 48 months (except for the sub-chronic toxicity study (90-day); see above). A decision on whether rats or rabbits should be selected as the first species in the pre-natal developmental test should be taken when results from the tests requested under endpoints 1 and 4 of this decision are available.

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 20 April 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.

In your comments to the requests number 1 and 5-8 you agreed to the draft decision. ECHA took your comments on the other requests into account and amended the deadline.

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

ECHA received proposal(s) for amendment and modified the draft decision.

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

ECHA referred the draft decision to the Member State Committee.

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

In addition, you provided comments on the draft decision. These comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

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

Appendix 3: Further information, observations and technical guidance

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

2. Failure to comply with the 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 carrying out the test(s) required by the present decision it is important to ensure that the particular sample of substance tested is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported. If the registration of the substance covers different grades, the sample used for the new test(s) must be suitable to assess these. Furthermore, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.