EUROPEAN CHEMICALS AGENCY

Helsinki, 7 March 2018

Addressee: [redacted]

Decision number: CCH-D-2114394437-37-01/F
Substance name: Acetophenone
EC number: 202-708-7
CAS number: 98-86-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 17/01/2017
Registered tonnage band: Over 1000

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. **Composition of the substance (Annex VI, Section 2.3.);**
   - **Degree of purity and concentration values;**
2. **Spectral data (Annex VI, Section 2.3.5.) and high-pressure liquid chromatogram, gas chromatogram (Annex VI, Section 2.3.6.);**
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), 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 Sprague Dawley 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;**
   - **Cohorts 2A and 2B (Developmental neurotoxicity);**

5. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: provide a quantitative environmental exposure assessment including exposure scenarios for all the identified uses and revise the risk characterisation accordingly.**

6. **Classification of the registered substance in accordance with Annex VI of Regulation (EC) No 1272/2008.**

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 to the REACH Regulation. 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 adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by **14 September 2020**. You also have to 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 and 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, has to 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

SUBSTANCE IDENTIFICATION

In accordance with Article 10(a)(ii) of the REACH Regulation, the technical dossier must contain information on the identity of the substance as specified in Annex VI, Section 2 to the REACH Regulation. In accordance with Annex VI, Section 2 the information provided has to be sufficient to enable the identification of the registered substance.

1. Composition of the substance (Annex VI, Section 2.3.)

According to chapter 4.2 of the Guidance for identification and naming of substances under REACH and CLP (Version: 2.1, May 2017) – referred to as the "SID Guidance", you shall note that, for well-defined substances, for each constituent (i.e. main constituents, impurities, etc.), the typical, minimum and maximum concentration levels shall be specified regardless of the substance type. In addition, as a rule, the compositional information should be completed up to 100%.

In IUCLID section 1.2 you have reported acetophenone with a degree of purity and a concentration range of 80-100%. This leaves up to 20% of the composition made by impurities. However, you have reported three impurities for which the sum of the upper concentration levels is ca. [redacted]%.

Therefore, the compositional information is not completed up to 100% as almost 20% of the compositional information has not been accounted for.

Consequently, you will need to provide a complete compositional information where the main constituent and the relevant impurities are reported with their typical, minimum and maximum concentration levels (as well as for the degree of purity). Such values should reflect your legal entity composition as manufactured and/or imported. The compositional information of the substance should be completed up to 100%.

In your comments to the draft decision according to Article 50(1) of the REACH Regulation you agreed to provide this information.

The requested information shall be included in section 1.2 of the IUCLID dossier.

2. Spectral data (Annex VI, Section 2.3.5.) and high-pressure liquid chromatogram, gas chromatogram (Annex VI, Section 2.3.6.)

"Spectral data" and "High-pressure liquid chromatogram or gas chromatogram" are information requirements as laid down in Annex VI, Sections 2.3.5. and 2.3.6. of the REACH Regulation, respectively. Adequate information needs to be present in the technical dossier to meet these requirements.

In section 1.4 of the dossier you have included a file named "ACP analytical methods", where the method descriptions for NMR, IR, UV, and GC analyses are provided. In addition, you included a file with the NMR spectrum with relative results. However, the IR and UV spectra (and relative results) are missing, as well as the chromatogram(s) and relative results (i.e. peak table with peak(s) area and peak(s) identification).

Therefore, the information requirements under Annex VI, Section 2.3.5. and 2.3.6 are not fulfilled and without the missing analytical data, it is not possible to verify the composition of the substance and therefore its identity.

Consequently you are requested to provide the missing analytical data (IR and UV spectra, chromatogram(s), and relative results) that support the identification of the substance. You shall ensure that the description of the analytical methods used for recording the spectra and the chromatogram is specified in the dossier in such detail to allow the methods to be reproduced, in line with the requirements under Annex VI Section 2.3.7 of the REACH Regulation. You shall ensure that the information is consistent with the information provided throughout the dossier.

In your comments to the draft decision according to Article 50(1) of the REACH Regulation you agreed to provide this information.

The missing spectral and chromatographic data shall be attached to section 1.4. of the IUCLID dossier.

TOXICOLOGICAL INFORMATION

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

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

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 contains information on a pre-natal developmental toxicity study in rats by the oral route using the registered substance as test material. However, there is no information provided for a pre-natal developmental toxicity study in a second species with the registered substance.

You have sought to adapt this information requirement by providing the following justification:

"*At the time being no additional testing is required, as no significant effect were observed in the first species (rat).*"

In the dossier initially submitted, you have not explicitly claimed an adaptation, and ECHA notes that your adaptation neither meets the specific rules for adaptation of Annex X, Section 8.7.2., column 2, nor the general rules for adaptation of Annex XI. Furthermore, ECHA notes that you based the NOAEL for developmental toxicity of 125 mg/kg body weight in the pre-natal developmental toxicity study in rats on body weight reduction of the pups at 300 mg/kg, and skeletal findings at 750 mg/kg, indicating effects in the first species.

The specific dangerous (hazardous) properties of the registered substance with respect to pre-natal developmental toxicity study in a second species as requested in this decision, *i.e.* information on species differences regarding to prenatal developmental toxicity, has not been covered by the information you submitted. Hence, your adaptation of the information requirement is rejected.

In your comments to the draft decision according to Article 50(1) of the REACH Regulation you showed your intention to explore first a read-across adaptation for this endpoint using data available from a prenatal developmental toxicity study accroding to OECD TG 414 for ethylbenzene (EC No. 202-849-4, CAS No. 100-41-4).

ECHA notes that the read-across justification and the data you are referring to is not available in the current submission of the registration dossier and, as also mentioned in the Appendix 2 to this decision, 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. Thus, an eventual update containing this information will only be examined after the deadline set in the adopted decision has passed.

Nevertheless, ECHA has considered the information provided by you in the formal comments and has the following considerations.

ECHA notes that, although the metabolism you presented for both ethylbenzene and acetophenone could be plausible, you need to prove that indeed the rate of metabolic transformation of ethylbenzene will be fast enough so there will be no systemic exposure to the parent substance and that acetophenone and 1-phenylethanol are indeed readily interconvertible. All the claims made in the read-across should be properly justified and supported by (experimental) scientific data.

Further, ECHA notes that the read-across would become more robust by comparing eco-/ toxicological effects between source- and target-substances. If type and potency of effects are comparable, successful predictions may be possible. Such a comparison could be achieved by *e.g.* conducting a Combined Repeated Dose Toxicity Study with the Reproduction/ Developmental Toxicity Screening Test (OECD TG 422) with the registered substance, and comparing the outcome with (existing) data on the source substance(s).

Finally, you should justify why and how data from an inhalation study can be adequately used to fulfil the data requirement for an oral study, taking differences in route-specific absorption of source- (and target-) substance into account.

ECHA also notes that the ECHA's Guidance and the Read-Across Assessment Framework (RAAF) are available to assist in meeting the adaptation requirement.[2]

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

The test in the first species was carried out by using a rodent species (rat). According to the test method EU B.31./OECD 414, the rabbit is the preferred non-rodent species. On the basis of this default assumption, ECHA considers that the test should be performed with rabbit as a second species.

[2] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

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 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a second species (rabbit) 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., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species with other available information 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.)

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* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

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 provided

You have not provided any study record of an extended one-generation reproductive toxicity study in the dossier that would meet the information requirement of Annex X, Section 8.7.3.

You have sought to adapt the information requirement. While you have not explicitly claimed an adaptation, in the dossier initially submitted, 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. Hence, ECHA has evaluated your adaptation with respect to this provision. You have provided the following for the adaptation: "*an EOGRT study does not need to be conducted as the available repeated dose toxicity studies (see section 7.5.1) do not indicate adverse effects on reproductive organs or tissues and do not reveal other concerns in relation with reproductive toxicity*".

To support your adaptation you have provided the following source of individual information with the registered substance under IUCLID section 7.8.1 and 7.5.1:

- key study: A combined repeated dose toxicity study and reproduction/developmental screening study, Sprague-Dawley rats, oral gavage (OECD TG 422; GLP) with registered substance, [redacted] 2003 (study report); Kapp et al (publication), rel.1.

You have also provided the following sources of individual information with the registered substance under section 7.5.1:

- Key study: sub-chronic repeated dose toxicity study, Wistar rats, oral gavage (OECD TG 408; GLP) with the registered substance, [redacted] 2016 (study report), rel.1.

- Supporting study: "*sub-chronic toxicity: oral*" study, Osborne-Mendel rat, oral feed, (not guideline, not GLP) with the registered substance, Hagan et al 1967 (publication), rel.2.

In addition, you have provided the following individual source of information with the registered substance under section 7.8.2:

- Key study: "developmental toxicity" study, Wistar rat, oral gavage (OECD TG 414; GLP) with the registered substance, [redacted] 2016 (study report), rel.1.

a) ECHA's evaluation and conclusion of the information provided

Evaluation approach/criteria

An adaptation pursuant to Annex XI, Section 1.2., requires sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion.

Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to an extended one-generation reproductive toxicity study (EU B.56./OECD TG 443) as requested in this decision. ECHA considers that this study provides, in addition to information to general toxicity, information in particular on two aspects, namely on sexual function and fertility in P0 and F1 generations (further referred to as 'sexual function and fertility') and on development and toxicity of the offspring from birth until adulthood due to pre- and postnatal and adult exposure in the F1 generation (further referred to as 'effects on offspring').

Relevant elements for 'sexual function and fertility' are in particular functional fertility (oestrous cycle, sperm parameters, mating behaviour, conception, pregnancy, parturition, and lactation) in the parental generation after sufficient pre-mating exposure duration and histopathological examinations of reproductive organs in both P and F1 generations. Relevant elements for 'effects on offspring' are in particular peri- and post-natal investigations of the F1 generation up to adulthood including investigations to detect certain endocrine modes of action, sexual development, and investigations on developmental neurotoxicity. Also the sensitivity and depth of investigations to detect effects on 'sexual function and fertility' and 'effects on offspring' needs to be considered.

Furthermore, the relative values/weights of different pieces of the provided information needs to be assessed as indicated in ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.4., Section 4.4 (version 1.1, December 2011). In particular relevance, reliability and consistency of results/data and coverage (completeness) need to be considered.

Based on the criteria above, ECHA considers the following:

Sexual function and fertility

With respect to the aspect of 'sexual function and fertility', you have provided information on histopathological integrity of the reproductive organs (OECD TG 422, and sub-chronic toxicty studies).

You have also provided reliable information on male and female reproductive performance such as gonadal function, mating behaviour, conception, development of the conceptus and parturition (OECD TG 422 screening study).

However, ECHA notes that the statistical power of OECD TG 422 study is lower than that of the extended one-generation reproductive toxicity study, and certain investigations are not included, such as functional fertility after 10 weeks premating exposure to cover spermatogenesis and folliculogenesis before mating, histopathology of the reproductive organs in F1 animals in adulthood, sexual maturation, oestrous cycle measurements in F1 animals, and investigations related to hormonal modes of action.

Furthermore, you did not provide information on sperm parameters in P and F1 generations.

Thus, the information you provided does not adequately address all relevant elements with respect to sexual function and fertility.

Effects on offspring

ECHA notes that the provided "developmental toxicity" study only provide information on pre-natal effect of the substance. However, the provided information does not address key elements of offspring toxicity observable peri- and postnatlally, such as survival, growth, certain endocrine modes of action and sexual development. Thus, the information you provided does not allow a conclusion on the hazardous property of the registered substance with respect to development and offspring toxicity observable peri- and post-natally.

Based on the currently available information there is concern for potential (developmental) neurotoxicity effect of the substance in adults and consequently there is a concern for developmental neurotoxicity. However, you have not provided information on the potential effect of the substance on developing nervous system. Thus, the information you provided does not allow a conclusion on the hazardous property of the registered substance with respect to developmental neurotoxicity. Consequently, the developmental neurotoxicity cohorts are triggered and included in the extended one-generation study design for the reasons explained under section "*b*" below.

Furthermore, in your comments to the draft decision according to Article 50(1) of the REACH Regulation you showed your intention to explore first a read-across adaptation for this endpoint using data available from a two-generation reproduction toxicity study according to OECD TG 416 and a developmental neurotoxicity study (according to you "*similar to OECD TG 426*") for ethylbenzene (EC No. 202-849-4, CAS No. 100-41-4).

ECHA notes that the read-across justification and the data you are referring to is not available in the current submission of the registration dossier and, as also mentioned in the Appendix 2 to this decision, 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. Thus, an eventual update containing this information will only be examined after the deadline set in the adopted decision has passed.

However, ECHA has considered the information provided by you in the formal comments and has the following considerations.

As mentioned also for the previous endpoint, ECHA notes that, although the metabolism you presented for both ethylbenzene and acetophenone could be plausible, you need to prove that indeed the rate of metabolic transformation of ethylbenzene will be fast enough so there will be no systemic exposure to the parent substance and that acetophenone and 1-phenylethanol are indeed readily interconvertible. All the claims made in the read-across should be properly justified and supported by scientific data.

Further, ECHA notes that you should demonstrate that the biological targets for both substances are also the same, causing the same effects and with similar strength.

Finally, you should justify why data from inhalation studies according to OECD TG 416 and "*similar to OECD TG 426*" can be used to adequately fulfil the data requirement for an oral study according to test method EU B.56./OECD TG 443 with the study design listed below.

ECHA also notes that you should consider ECHA's Guidance and the Read-Across Assessment Framework (RAAF) when assessing the read-across adaptation.

Conclusion

Hence, the information you provided to support your adaptations, considered individually or together, lacks information on critical elements of reproductive toxicity and do not allow to assume/conclude that the substance does not have a particular dangerous (hazardous) property with respect to the information requirement for Annex X, Section 8.7.3.
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. 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.

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

b) The specifications for the study design

Premating exposure duration and dose-level setting

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

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

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.

Cohorts 2A and 2B

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

ECHA notes that existing information on the registered substance derived from available *in vivo* studies show evidence of adverse effects on the adult nervous system. More specifically, the OECD TG 422 study conducted with Sprague Dawley rats showed statistically significant decrease in mean forelimb grip strength and mean motor activity in males, and wobbly gait and decreased activity in both sexes at the high dose level of 750 mg/kgbw/day (Kapp et al 2003, and [redacted] 2003)

In addition, the 90-day study conducted with Wistar rat showed reduced spontaneous activity and increased salivation at the mid (250 mg/kg bw/day) and high dose of 500 mg/kg bw/day (Hagan et al 1967). In this study, the absence of effects on grip strength, and motor activity in comparision to the OECD TG 422 screening study could be explained by the difference species and/or dose level.

However, the concern for neurotoxicity in the developing animals remains because the developing brain is sensitive to chemicals if exposure occurs at critical period during development. Consequently, the developing brain might be vulnerable at lower doses than the adult brain. Therefore, the inclusion of Cohorts 2A and 2B are justified.

ECHA concludes that the developmental neurotoxicity cohorts 2A and 2B need to be conducted, because there is a particular concern on (developmental) neurotoxicity based on the results from the above-identified *in vivo* studies on the registered substance.

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

Species 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.

Furthermore, ECHA notes that the available information shows that the registered substance might be more sensitive to the rat strain of Sprague Dawley than Wistars. More specifically, the OECD TG 422 screening study (Kapp et al 2003, and [redacted] 2003) conducted with Sprague Dawley rats showed effects in the FOB parameters of forelimb grip strength and mean motor activity but not in the 90-day study conducted with Wistar rats (Hagan et al 1967). Hence, ECHA considers that the study shall be performed with Sprague Dawley rats.

Route selection

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 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

c) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443), in Sprague Dawley 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;
- Cohorts 2A and 2B (Developmental neurotoxicity)

Notes for your consideration

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, and/or Cohort 3 if new information becomes available after this decision is issued to justify such an inclusion.

Inclusion is justified if the new information shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented.
The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented.

ENVIRONMENTAL SAFTEY ASSESSMENT

5. 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.

Annex I, Section 5 of the REACH Regulation requires the Registrant to generate 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 the Registrant to characterise the risk for each exposure scenario and to consider the human population (exposed as workers, consumer or indirectly via the environment and if relevant a combination thereof) and 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.

ECHA's Guidance on information requirements and chemical safety assessment, Part B: Hazard Assessment, Section B.8.4. (pages 47 to 48) (version 2.1, December 2011) states that "*if no adverse effects have been observed in studies at the highest recommended concentration/doses tested, this would normally indicate that no hazard has been identified and no DNEL or PNEC can be derived and hence exposure assessment for that route of exposure, type of effect or protection target would not be needed*". Further, in section B.4.2.2. and in Figure B-8-3 it is clarified that if there are ecotoxicity data showing effects and PNECs are derived, a "*quantitative exposure assessment, i.e. derivation of PECs, is mandatory for the water, sediment and soil environmental compartments.*"

With regard to the scope of the required exposure assessment, as stated above and in accordance with Annex I, section 5.0., it has to cover all hazards that have been identified according to sections 1 to 4 of Annex I of REACH Regulation.

ECHA notes that the registered substance has a harmonised classification as Acute Tox. 4 (H302) and Eye Irrit. 2 (H319) and thus, fulfilling the criteria set out in Article 14(4) of the REACH Regulation. Consequently, it is required to conduct an exposure assessment including the generation of exposure scenarios and a risk characterisation in the chemical safety assessment. Furthemore, adverse effects were observed in Freshwater Alga and Cyanobacteria, Growth Inhibition Test [EC50(72h) = 86.4 mg/L, NOEC(72h) = 24.8 mg/L].

ECHA further notes that you have been able to derive PNECs based on the ecotoxicity data and the application of the equilibrium partitioning method (EPM) is possible. Consequently, as explained above, a quantitative exposure assessment is needed. However, ECHA notes that you have failed to provide the corresponding quantitative exposure assessment.

Instead, you have provided a "*Qualitative Environmental Exposure Assessment*" with "*predefined emission scenarios*" "*for acceptable environmental emissions in soil and surface water*". However, no relevant exposure scenarios considering the specified uses identified for the registered substance (including predicted environmental concentrations (PEC)) are described and the risk characterisation (including risk characterisation ratios (RCR)) ihas not been provided.

ECHA also notes that you used non-default site-specific information for the estimation of acceptable environmental emissions. According to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.16 (version 3.0, February 2016) the exposure scenario should contain information about operational conditions and risk management measures based on which site-specific information can be justified.

In your comments to the draft decision according to Article 50(1) of the REACH Regulation you agreed to provide this information.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to provide a quantitative environmental exposure assessment including fully justified exposure scenarios for all the identified uses and revise the risk characterisation accordingly.

6. Classification of the registered substance in accordance with Annex VI of Regulation (EC) No 1272/2008

In accordance with Article 10(a)(iv) of the REACH Regulation, a technical dossier must contain the classification and labelling of the substance as specified in Annex VI, Section 4 of the REACH Regulation. Thus, as laid down *ibidem*, the classification of the substance shall be the result of the application of Titles I and II of Regulation (EC) No 1272/2008, *i.e.* the CLP Regulation, for all hazard classes and categories in that Regulation.

According to Article 4(3) of the CLP regulation "*if a substance is subject to harmonised classification and labelling in accordance with Title V through an entry in Part 3 of Annex VI, that substance shall be classified in accordance with that entry, and a classification of that substance in accordance with Title II shall not be performed for the hazard classes or differentiations covered by that entry*".

Further, for other hazard classes not covered by the entry in Part 3 of Annex VI, "*classification under Title II shall be carried out for those hazard classes or differentiations*", *i.e.* self-classification is required for such other hazard clases not covered by the harmonised classification, which shall be applied as given.

You have provided two classification records in section 2.1 of the IUCLID technical dossier:

- The classification record named "[redacted]" contains the harmonised classification and labelling that is available for the registered substance in Annex VI of the CLP Regulation: Acute Tox. 4 (H302) and Eye Irrit. 2 (H319).

- The classification record named "[redacted]" contains the following classification: Not classified.
  In this record you state in the remarks field: "*Self-classification according to CLP Regulation (1272/2008/EG), after re-evaluation of all data. Attention: as acetophenone is classified as dangerous in Annex VI of CLP Regulation (based on old data), it shall be classified and labelled in accordance with this harmonised classification.*"

ECHA notes that, contrary to your own advice, the information on classification you have provided is not consistent with Annex VI of the CLP Regulation. More specifically, the classification record named "[redacted]" is in breach with the available harmonised classification for the registered substance as Acute Tox. 4 (H302) and Eye Irrit. 2 (H319).

ECHA further notes that in case you have new information based on which you disagree with the available harmonised classification for the registered substance, you may submit a proposal for harmonised classification and labelling to the competent authority in one of the Member States in which the substance is placed on the market (see Article 37(6) of the CLP Regulation). However, in the mean time you are required to comply with the harmonised classification that is currently available for the registered substance.

As explained above, the information provided on classification and labelling for the registered substance in the technical dossier does not meet the information requirement.

In your comments to the draft decision according to Article 50(1) of the REACH Regulation you agreed with this request.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to comply with the harmonised classification and labelling available for the registered substance and to remove the classification record named "[redacted]" from the IUCLID technical dossier. The chemical safety report shall be updated accordingly.

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 17 May 2017.

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

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

ECHA took into account your comments and did not amend the requests.

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

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.