ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 13 December 2016

Addressee: [redacted]

Decision number: CCH-D-2114350695-43-01/F
Substance name: glyoxal
EC number: 203-474-9
CAS number: 107-22-2
Registration number: [redacted]
Submission number: [redacted]
Submission date: 17.10.2016
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. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: generate an exposure assessment for all relevant exposure scenarios and revise the risk characterisation 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 **20 June 2017**. You shall also update the chemical safety report, where relevant.

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

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

Authorised[1] by Kevin Pollard, Head of Unit, Evaluation E1

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons

1. 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 Article 14(4), if the substance fulfils the criteria for any of the hazard classes listed in that provision or is assessed to be a PBT or vPvB, the CSA shall include exposure assessment and risk characterisation.

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 reasonablely 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*".

In the CSR you provided, the exposure assessment for the environment is missing. You claimed that no exposure assessment is necessary for the environment by stating for each exposure scenario that '*As no environmental hazard was identified no environmental-related exposure assessment and risk characterisation was perfomed*".

ECHA notes that you have classified the substance as Acute Tox. 4 (H302), Skin Irrit. 2 (H315), Eye Irrit. 2 (H319), Skin Sens. 1B (H317), Muta. 2 (H341), and STOT Single Exp. 3 (H335) and thus, fulfilling the criteria set out in Article 14(4) of the REACH Regulation to require an exposure assessment and a risk characterisation in the chemical safety assessment.

Additionally, ECHA notes that effects were observed in some environmental toxicity studies and for example, in the long-term aquatic invertebrate (*Daphnia*) study, a NOEC value of 3.19 mg of active ingredient/L was reported for the registered substance. This value was considered for the calculation of the PNECfreshwater.

In your comments to the draft decision you acknowledge the Decision of the Board of Appeal in case A-015-2014 that the scope of the exposure assessment and associated risk characterisation provided for by Article 14(4) is not limited to hazards which lead to classification under the CLP Regulation. However you seem to question the way the hazard is to be identified in accordance with the REACH Regulation and you claim that *"it is hardly impossible to identify an environmental hazard in the meaning of Article 14(4) REACH for all ecotoxicological study data provided in the present dossier."* You also question the ecological relevance of standardised toxicity tests. Furthermore, you consider that no hazard for the environment has been identified as the "*effects seen in the Daphnia study are within natural variation and do not constitute a biological significant effect nor a hazard*" and that they "*should NOT be regarded as an adverse effect nor as a hazard below the threshold concentration of 10 mg/L as recommended in OECD testing guideline 211".*
ECHA responds to your comments in detail below:

Firstly, as provided by the REACH Regulation and stated by the Board of Appeal in the above mentioned Decision, the identification of the hazards posed by a substance is based on all the information available to the registrant for the purpose of fulfilling the standard information requirements laid down in Annexes VII to XI (paragraphs 39 and 88).

The standardised toxicity tests which are prescribed for the above purpose are internationally accepted and validated, and their applicability and usefulness in the regulatory context is widely recognised, including in the REACH Regulation. They are designed to study effects of chemicals in a harmonised way that allows evaluating the impact of chemicals in absence of additional stressors. In addition, standard tests allow comparison of effects caused by different chemicals and coordinated chemicals management.

Furthermore ECHA notes that as widely acknowledged and also stated in ECHA Guidance, "*it is considered most likely that ecosystems will be more sensitive to the chemicals than individual organisms in the laboratory. Therefore, results of tests are not used directly for the risk assessment but used as a basis for extrapolation of the PNEC*" (ECHA's Guidance on information requirements and chemical safety assessment, Part B: Hazard Assessment, Section B.7.2. (page 37) (version 2.1, December 2011)). For this reason, results from toxicity studies are not used directly in risk assessment but rather the effect value obtained is divided by an assessment factor to account for uncertainty and to extrapolate to the natural populations, leading to a lower PNEC value to be used in risk assessment. Therefore ECHA notes that an effect observed in an ecotoxicity test cannot be ignored nor considered to not to be biologically relevant when, in general, it is agreed that the natural populations may be more sensitive to chemicals than the test organisms exposed in standardised toxicity tests. ECHA notes also that chronic studies are designed to study exposures determined in relation to the life-cycle of the organisms to increase their biological relevance.

Furthermore, tests assessing effects on reproduction are considered as one of the most useful measures of evaluating long-term effects on populations. As also indicated in the OECD 211 guideline "*The primary objective of the test is to assess the effect of chemicals on the reproductive output of Daphnia magna*", and that "*..the ecologically most relevant response variable is the total number of living offspring produced per parent animal..*"..

Secondly, in your comments you indicate that testing guidelines used to derive data for glyoxal do not provide judgement on what and which level of effect should be considered as adverse and a cut off value is needed to determine what is an adverse effect.

ECHA considers that contrary to what you indicate, the REACH standard information requirements and guidelines provide sufficient information on what is considered as an adverse effect, with respect to the concentration tested and the effects seen. In particular, in the OECD 211 guideline *Daphnia magna* Reproduction Test it is indicated that 10 mg/L may be the highest concentration that needs to be tested at the chronic study described in the guideline, whereas in OECD 208 Terrestrial Plant Test: Seedling Emergence and Seedling Growth Test it is described that 1000 mg/kg dry soil may be the maximum concentration to be tested. In your comments you also state that you consider the 10 mg/L to be a threshold value for hazard/adverse effects in the chronic *Daphnia* study. Furthermore, ECHA notes that with regards to effects and adverse effects in particular the OECD 211 guideline denotes that "*In general, adverse effects of the test substance compared to the control are investigated using one-tailed hypothesis testing at $p \leq 0.05$*". In other words, a statistically significant effect is considered an adverse effect. In another guideline, based on which a study in your dossier has been conducted, the EPA Guideline OPPTS 850.1035 Mysid Acute Toxicity Test, the NOEC is defined as "*the highest tested concentration in an acceptable toxicity test which did not cause the occurrence of any specified adverse effect (statistically different from the control at 95 percent level)".* It is hence clearly indicated that any effect above the NOEC is considered adverse. ECHA considers these interpretations appropriate and also notes that using statistical significance to denote an effect is a scientifically accepted principle, even if you in your comment question its relevance.

The above scientific principles are recognised in ECHA's Guidance on information requirements and chemical safety assessment, Part B: Hazard Assessment, Section B.8.4. (page 48) (version 2.1, December 2011) when describing the required scope of the exposure assessment. It provides that in addition to the classified hazards for the substance the registrant should consider, for the environmental compartment,"*whether adverse effects have been observed in studies conducted at the highest practicable & biologically-relevant concentration on environmental toxicity e.g. according to OECD and EU Guidelines (e.g. 100 mg/l in OECD guideline as a limit test for acute aquatic toxicity), taking into account the properties of the substance determining the environmental fate*". It also states that "*If no adverse effects have been observed in studies at the highest recommended concentrations/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*". In the footnote (12) on p. 48 it is further defined that "***Please note****: Not always applicable to environmental hazards from substances with low water solubility. Please also note that severe (eco)toxicological effects (e.g. mortality) observed only slightly above the limit dose would still require an exposure assessment*".

Thirdly, in your comments you claim that there are no adverse effects seen in the Daphnia study below the threshold concentration of 10 mg/L, as the changes below 10 mg/L are not statistically significant and should be considered natural variation. However, your assumption seems to disregard the data present in your dossier as corrected for the active ingredient which clearly show adverse effects that are statistically significant, as illustrated in details below.

In the technical dossier endpoint study record (ESR) for Long-term toxicity to aquatic invertebrates (section 6.1.4. of IUCLID), in the table "*Effect concentrations*" you have given the effect values in relation to both the measured concentrations (40 % glyoxal, 60 % water) and as corrected to the active ingredient. You have provided a NOEC value of 3.19 mg/L active ingredient and 7.96 mg/L test material and a LOEC value of 4.85 mg/L active ingredient and 12.1 mg/L test material. In your PNEC derivation you have used the effect

value corrected for the active ingredient. ECHA considers the approach you applied of correcting the effect value for the active ingredient as appropriate. However, in the results under "*Any other information on results incl. tables*" you have reported the results with reference to the measured test material (40 % glyoxal, 60 % water). ECHA acknowledges that based on the data reported in the table "*Any other information on results incl. tables*" the effects seen at the lowest two (nominal) concentrations were not found to be statistically significant whereas a 28 % and 32 % decrease in reproduction was found at the test material concentrations of 12 and 18 mg/L; these concentrations are equal to 4.8 mg/L and 7.2 mg/L active ingredient. ECHA considers the effects at 4.8 mg/L and 7.2 mg/L active ingredient as clear and adverse, they were also found to be statistically significant. ECHA hence notes that statistically significant decrease in reproduction of 28 to 32 % was found at effect concentrations below the 10 mg/L.

Fourthly, your claim of not being possible to identify an environmental hazard in the meaning of Article 14(4) REACH for all ecotoxicological study data provided in your dossier is contrary to the actual findings from such studies, as presented in your dossier. In the initial draft decision ECHA noted the effects observed in the long-term aquatic invertebrate study (as explained above), as an example of effects observed in some environmental toxicity studies for the registered substance. Additionally, in a terrestrial plant study conducted according to OECD 208 effects on biomass of two species of plants were observed below the maximum tested concentration of 1000 mg/L and NOECs of 203 mg active substance/kg (dry soil) were derived (IUCLID section 6.3.3.). You have used this value for the derivation of the terrestrial PNEC. Furthermore, in an acute marine invertebrate study carried out according to the EPA Guideline OPPTS 850.1035 Mysid Acute Toxicity Test, a 96 h NOEC of 17.1 mg/L (active ingredient) and LC50 of 53.2 mg/L (active ingredient) were found (IUCLID section 6.1.3.). These values are below the 100 mg/L given in ECHA guidance as an example for a limit value for acute toxicity, furthermore, the EPA guideline itself states that NOEC denotes the level of adverse effects.

Therefore, there are adverse effects in several environmental studies present in your dossier, which were observed below the relevant threshold concentration.

In conclusion, the arguments provided by you in your comments cannot lead to omit the required data that is needed in order to comply with the REACH Regulation.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to generate an exposure assessment for all relevant uses identified in section 3.5 of IUCLID and in the CSR and revise the risk characterisation accordingly.

Deadline to submit the requested information in this decision

In the draft decision communicated to you, the time indicated to provide the requested 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 and the Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: generate an exposure assessment for all relevant exposure scenarios and revise the risk characterisation accordingly and submit the information results to ECHA in a dossier update was 12 months from the date of adoption of the decision. In your comments on the draft decision, you provided sufficient information for the endpoint of Pre-natal developmental toxicity. Based on the provided information, ECHA has removed this request and set the adequate deadline of 6 months for the remaining request.

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 11 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.

ECHA took into account your comments and amended the request(s).

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

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

Appendix 3: Further information, observations and technical guidance

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

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

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new test(s) is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) must be suitable to assess these grades. Finally, there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.