EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002093-83-05/F Helsinki, 02/07/2012

DECISION ON A TESTING PROPOSAL SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006

For Green Liquor, CAS No 68131-30-6 (EC No 268-612-2), registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 40(1) of the REACH Regulation, ECHA has examined the following testing proposals submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12 (1)(e) thereof for Green Liquor, CAS No 68131-30-6 (EC No 268-612-2), by [redacted] (Registrant), latest submission number [redacted] for the tonnage band of 1000 tonnes or more per year:

- Long-term toxicity to aquatic invertebrates (*Daphnia magna* Reproduction test OECD Guideline 211);
- Genetic toxicity *In vivo* (Mammalian Erythrocyte Micronucleus test, OECD Guideline 474).

On 13 December 2010, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposals set out by the Registrant in the registration dossier for the substance mentioned above.

ECHA held a third party consultation for the testing proposal from 31 May 2011 until 15 July 2011. ECHA did not receive information from third parties.

On 29 November 2011 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

On 23 December 2011 ECHA received comments from the Registrant.
ECHA considered the Registrant's comments received and amended the draft decision.

On 2 March 2012 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals to amend the draft decision within 30 days of the receipt of the notification. Subsequently, one Competent Authority of a Member State submitted a proposal for amendment to the draft decision. ECHA reviewed the proposal for amendment received and decided to amend the draft decision accordingly.

On 4 April 2012 ECHA notified the Registrant of proposal for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on that proposal for amendment within 30 days of the receipt of the notification.

On 16 April 2012, the draft decision was referred to the Member State Committee.

The Registrant did not provide comments on the proposed amendment.

A unanimous agreement of the Member State Committee on the draft decision was reached on 21 May 2012 in a written procedure launched on 10 May 2012.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA to initiate a compliance check on the present dossier at a later stage.

II. Testing required

The Registrant shall carry out the following proposed tests pursuant to Article 40(3)(a) of the REACH Regulation using the indicated test methods and the registered substance subject to the present decision:

1. Long-term toxicity testing on aquatic invertebrates (Annex IX, 9.1.5., Test Method EU C.20/OECD TG 211);
2. *In vivo* Mammalian Erythrocyte Micronucleus test (Annex IX, 8.4., Test Method EU B.12/OECD TG 474).

The Registrant may test the substance as manufactured, i.e. with water included. However, the results (as further specified in section III of this decision) of the required tests shall be back-calculated in order to make them correspond to the composition of the substance which contains the minimum amount of water which is necessary to avoid irreversible changes in the substance. The method of calculation shall be clearly reported when updating the registration dossier with the test results.

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **2 July 2013** an update of the registration dossier containing the information required by this decision.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant for the registered substance.

1. Long term toxicity testing on aquatic invertebrates

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

A long-term toxicity study on aquatic invertebrates is a standard information requirement as laid down in Annex IX, section 9.1.5. of the REACH Regulation. The information on this endpoint is not available for the registered substance but needs to be present in the technical dossier to meet the information requirements. Consequently there is an information gap and it is necessary to generate the data for this endpoint.

The Registrant proposes to conduct an OECD Guideline 211 *Daphnia magna* reproduction test stating that "There are no long-term toxicity data available for aquatic invertebrates for any Green liquor. The lack of long-term toxicity test results for aquatic invertebrates is an identified REACH Annex IX data gap. This data gap should be filled by testing under REACH."

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation the Registrant is required to carry out the proposed study: Long term toxicity testing on aquatic invertebrates (Test Method EU C.20/OECD TG 211) using the registered substance Green liquor.

Based on the information provided in the dossier, the substance contains large amounts of water. Article 3(1) of the REACH Regulation defines a substance and explicitly excludes from the definition, any solvent which may be separated without affecting the stability of the substance or changing its composition. ECHA considers water to be a solvent that can largely be removed without affecting the stability of the registered substance or changing its composition. Therefore, only the minimum concentration of water necessary to avoid irreversible changes in the substance composition upon re-addition can be considered part of the registered substance composition and included in the mass balance. While the Registrant is free to test the substance as manufactured (i.e. with water included), the (no)effect concentration(s) in the required test shall be back-calculated to correspond to the appropriate composition of the registered substance as detailed above. The Registrant shall include details of the calculation method when updating the registration dossier with the results of the test.

In his comments on the draft decision, the Registrant provided additional information to support the inclusion of water in the composition of the registered substance. ECHA examined the Registrant's comments and concluded that the available evidence does not demonstrate to which extent – if at all – water is necessary to preserve the stability of the registered substance. In ECHA's opinion, the (no)effect concentration(s) in the required test must reflect those of the substance with the minimum concentration of water necessary to avoid irreversible changes. In reaction to the comments, ECHA therefore decided to amend its draft decision to allow for testing of the substance as manufactured, provided that appropriate back-calculation of the results is performed as described above.

2. *In vivo* Mammalian Erythrocyte Micronucleus test

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

According to section 8.4 of Annex IX of the REACH Regulation, if there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and there are no results available from an *in vivo* study already, an appropriate *in vivo* somatic cell genotoxicity study shall be proposed by the Registrant. As there was a positive result seen in the chromosome aberration study with metabolic activation provided in the registration dossier it follows that an appropriate *in vivo* somatic cell genotoxicity study is required.

The Registrant has acknowledged this requirement and proposes to conduct an OECD Guideline 474 Mammalian Erthrocyte Micronucleus test stating "Since the results from the *in vitro* cytogenicity study in mammalian cells was interpreted as positive a somatic cell *in vivo* test to investigate structural or numerical chromosome aberrations such as mammalian erythrocyte micronucleous test is proposed here".

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation the Registrant is required to carry out the proposed test: *In vivo* Mammalian Erythrocyte Micronucleus test (Test Method EU B.12/OECD TG 474) with the registered substance Green Liquor.

In line with the substance composition issue detailed in section III (1) above, the Registrant is free to test the substance as manufactured (i.e. with water included), but the treatment doses and results of the required test should be back-calculated to correspond to the composition of the substance which contains the minimum amount of water which is necessary to avoid irreversible changes in the substance.

In his comments on the draft decision, the Registrant provided additional information to support the inclusion of water in the composition of the registered substance. ECHA examined the Registrant's comments and concluded that the available evidence does not demonstrate to which extent – if at all – water is necessary to preserve the stability of the registered substance. In ECHA's opinion, the treatment doses and results of the required test must reflect those of the substance with the minimum concentration of water necessary to avoid irreversible changes. In reaction to the comments, ECHA therefore decided to amend its draft decision to allow for testing of the substance as manufactured, provided that appropriate back-calculation of the results is performed as described above.

ECHA notes that the intraperitoneal route of administration may be appropriate for the registered substance due to the probable formation of toxic hydrogen sulphide gas in the acidic environment of the stomach following oral administration. The Registrant is accordingly requested to consider the appropriateness of the intraperitoneal route of administration before performing the required test.

Furthermore ECHA notes that, according to section 8.4. of Annex IX of the REACH Regulation "*If there is a positive result from an in vivo somatic cell study available, the potential for germ cell mutagenicity should be considered on the basis of all available data, including toxicokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, additional investigations shall be considered.*"

At any time, the Registrant shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other Registrants.

IV. Adequate identification of the composition of the tested material

The process of evaluation of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the generation of information is tailored to real information needs in order to prevent unnecessary testing. The information submitted in the registration dossier was sufficient to confirm the identity of the substance for the purpose of assessing the testing proposal. It is note, however that this information, or the information submitted by other Registrants of the same substance, has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the proposed tests, the sample of substance used for the new studies must be suitable for use by all the joint Registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given by the joint Registrants. It is the responsibility of all the joint Registrants of the same substance to agree with the tests proposed in the testing proposal (as applicable to their tonnage level) and to document the necessary information on its composition. The substance identity information of the registered substance and of the sample tested must enable ECHA to confirm the relevance of the testing for the substance actually registered by each joint Registrant. Finally, the studies must be shared by the joint Registrants concerned.

V. General requirements for the generation of information and Good Laboratory Practice

ECHA always reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

VI. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the ECHA's internet page at http://echa.europa.eu/appeals/app_procedure_en.asp. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

[redacted]

Jukka Malm
Director of Regulatory Affairs