ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-2114300158-61-01/F Helsinki, 12 June 2015

DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006

For citral, CAS No 5392-40-5 (EC No 226-394-6), 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 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration for citral, CAS No 5392-40-5 (EC No 226-394-6), submitted by [redacted] (Registrant). ECHA notes that in the joint submission covering the current registration, the Chemical Safety Report (CSR) is not provided by the lead registrant on behalf of the member registrants. The scope of this compliance check is limited to the standard information requirements of Annex I and Section 2 of Annex VI, while the compliance check concerning the information requirements laid down in Annexes VII to X was done on the lead registrant dossier of this joint submission.

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 100 to 1000 tonnes per year. This decision does not take into account any updates submitted after 15 January 2015, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for start of substance evaluation in 2015.

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

The compliance check was initiated on 2 June 2014.

On 15 September 2014 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision. That draft decision was based on submission number [redacted]

On 15 October 2014 ECHA received comments from the Registrant on the draft decision.
On 15 October 2014 the Registrant updated his registration dossier with the submission number [redacted]

The ECHA Secretariat considered the Registrant's comments and update.
On basis of this information, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

On 15 January 2015 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 for amendment of the draft decision within 30 days of the receipt of the notification.

Subsequently, proposals for amendment to the draft decision were submitted.

On 20 February 2015 ECHA notified the Registrant of the proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposals for amendment within 30 days of the receipt of the notification.

The ECHA Secretariat reviewed the proposals for amendment received and amended the draft decision.

On 2 March 2015 ECHA referred the draft decision to the Member State Committee.

By 23 March 2015, in accordance to Article 51(5), the Registrant provided comments on the proposals for amendment. The Member State Committee took the comments on the proposals for amendment of the Registrant into account. In addition, the Registrant provided comments on the deadline indicated in the draft decision.

A unanimous agreement of the Member State Committee on the draft decision was reached on 7 April 2015 in a written procedure launched on 26 March 2015.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

A. Information related to chemical safety assessment and chemical safety report

Pursuant to Articles 41(1), 41(3), 10(b), 14 and Annex I of the REACH Regulation the Registrant shall submit in the chemical safety report:

1. A reassessment of the skin sensitisation hazard information on the basis of the study giving rise to highest concern
   or
   A full justification for why the study giving rise to the highest concern was not chosen to draw conclusions for skin sensitisation and a robust study summary for the study chosen (Annex I, 3.1.5. of the REACH Regulation);

2. Revised DNELs for workers and for the general population using the assessment factors recommended by ECHA
   or
   A full justification for not using the recommended assessment factors in the DNEL derivation (Annex I, 1.4.1 of the REACH Regulation);

3. Exposure assessment and risk characterisation to demonstrate that the risk to the environment can be considered to be adequately controlled (Annex I, Sections 5 and 6 of the REACH Regulation);

4. The description of the use "use of cleaning agents – industrial" shall be revised.

5. A qualitative assessment of likelyhood that skin irritation is avoided when implementing exposure scenarios (Annex I, 6.5 of the REACH Regulation).;

B. Deadline for submitting the required information

Pursuant to Articles 41(4) and 22(2) of the REACH Regulation the Registrant shall submit to ECHA by **21 December 2015**.

III. Statement of reasons

Pursuant to Article 41(3) of the REACH Regulation, ECHA may require the Registrant to submit any information needed to bring the registration into compliance with the relevant information requirements.

A. Information related to the chemical safety assessment and chemical safety report

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

1. A reassessment of the skin sensitisation hazard information on the basis of the study giving rise to highest concern or a full justification why the study giving the highest concern was not chosen to draw conclusions for skin sensitisation and a robust study summary for the study chosen (Annex I, Section 3.1.5. of the REACH Regulation)

Annex I, Section 3.1.5. of the REACH Regulation requires that the study giving rise to the highest concern shall be used and a robust study summary shall be prepared for that study or studies and included in the technical dossier. In addition, Annex I, Section 3.1.5. stipulates that if a study giving rise to the highest concern is not used, then this shall be fully justified.

In the technical dossier, the Registrant has chosen the Local Lymph Node Assay (LLNA) and two Guinea Pig Maximisation Studies (GPMT) as key studies. Another LLNA, another GPMT study, and a review article on skin sensitisation are included as supporting studies. However, no robust study summary is available for the Human Repeated Insult Patch Test (HRIPT) which was used in the CSR for the derivation of the DNEL for local effects. There is no published standard testing guideline for HRIPT and, in addition, the HRIPT method was not described sufficiently. Therefore, it is not possible to assess with which method and under which conditions the test was carried out.

Human data will normally take preference over animal data in DNEL derivation *(see: Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health, version 2.1, November 2012).* However, the reporting of the studies must be sufficient to allow for the assessment of such human data. In this case, the reliability of the HRIPT could not be assessed, since the HRIPT test was not sufficiently described and since there is no validation study that would have assessed the reliability of the test.

According to the CSR, both the LLNA and the HRIPT studies lead to similar dose descriptor (NOAEL of about 1400 µg/cm^2). However, the DNEL based on the LLNA would be significantly lower than the DNEL based on the HRIPT, since according to the LLNA model, interspecies variation is taken into account as an assessment factor. Therefore, the LLNA study gives rise to the highest concern.

The Registrant, in his comments submitted according to Article 51(1) of the REACH

Regulation, notes that "The lead registrant has responded in detail to additional requirements on skin sensitization assessment and on the derivation of the DNEL based on human data. Aggregated information has been provided in section 7.4 (endpoint summary: sensitization), and supplementing experimental study details have been given in sections 7.10.xx of the lead's IUCLID dossier as well as in section 5.5.3 of the CSR." ECHA notes that even the updated lead Registranty's dossier does not have robust study summary for the HRIPT, only a "critical reevaluation of existing studies". In fact, the endpoint study record has not been modified at all after the draft decision was sent (latest modification in 2010). Therefore, ECHA does not modify section II of the draft decision.

Based on the above, and in accordance with Annex I, Section 3.1.5 of the REACH Regulation, the Registrant is requested to reassess the skin sensitisation using the LLNA study, or in the alternative to justify the fact that the study giving rise to the highest concern was not chosen and to prepare a robust study summary for the study.

2. Revised DNELs for workers and for the general population using the recommended assessment factors by ECHA or a full justification for not using the recommended assessment factors in DNEL derivation (Annex I, 1.4.1. of the REACH Regulation)

Annex I, 1.4.1 of the REACH Regulation requires that the following factors shall, among others, be taken into account when deriving DNELs:

- the uncertainty arising, among other factors, from the variability in the experimental information and from intra- and inter-species variation;
- the nature and severity of the effect;
- the sensitivity of the human (sub-)population to which the quantitative and/or qualitative information on exposure applies.

The ECHA "Guidance on information requirements and chemical safety assessment" (Volume 8, R8, version 2.1, November 2012) provides further details and specifically provides default factors which should be applied to derive DNELs in the absence of substance specific information.

The assessment factors (AF) applied by the Registrant and the default assessment factors recommended in the above mentioned ECHA Guidance are given in detail in Annex I attached to this decision. A Competent Authority Member State submitted a proposal for amendment to include the default assessment factors recommended in the ECHA Guidance for workers - systemic long term - dermal route and for workers - systemic long term - inhalation route. ECHA has inserted these default assessment factors and in view of the proposal for amendment and corrected other default assessment factors to reflect ECHA's Guidance R.8. In his response to this proposal for amendment, the Registrant states that "We need to point out that the lead registrant has already received a final decision in which the relevant default assessment factors have been specified by ECHA. The specified default assessment factors are identical to those provided in the draft decision to [redacted]. In case ECHA decides to take into account the proposals from Competent Authorities, this would supposedly result in differing final decisions, while substance and underlying database are identical. It is our understanding that in the case of co-registrations ECHA's final decisions need to be aligned by ECHA with regard to the content and outcome of the CSR as long as the underlying database and considered uses are identical. This actually is the case as outlined under "general comments"".

ECHA considers that the accepted proposal for amendment revising Annex I attachment of this draft decision accurately reflects the default assessment factors recommended in the ECHA Guidance R.8. ECHA agrees that it is unfortunate that the Annex I attachment in the lead Registrant's decision contains some editorial errors that were not noted. Thus, the Annex I attachments of the two decisions will be slightly different, however within both decisions,

ECHA draws the attention of the Registrants to the default assessment factors recommended in the ECHA Guidance R.8.

ECHA observes that the Registrant has not followed the recommendations of ECHA's Guidance R.8 and has not provided a full justification for the derivation of DNELs in line with Annex I, 1.4.1. In particular, ECHA notes that for the systemic DNELs for inhalation route interspecies variation is not addressed at all and for systemic DNELs for dermal route, only allometric scaling is taken into account, whereas the remaining difference has not been addressed.

Furthermore, ECHA notes that for long-term local DNELs derived for dermal route based on skin sensitisation (LLNA), the exposure duration (subacute to chronic) was not taken into account at all as an assessment factor.

Thus the Registrant shall revise his DNELs by applying the recommended assessment factors apropriate in this case.

In the alternative, the Registrant shall, in accordance with Annex I, 1.4.1, provide a full justification for the current DNEL derivation for workers and for the general population provided in the chemical safety report.

The Registrant, in his comments submitted according to Article 51(1) of the REACH Regulation, notes that "The annexes of the draft decisions addressed to [redacted] (amended draft decision dated Aug 29, 2014) and addressed to [redacted] (dated Sep 15, 2014) differ with regard to the assessment factors summarized therein. In case of the lead registrant the assessment factors described in draft decision of Aug 29, 2014 do not represent the current CSR update."

ECHA underlines that in this joint submission, each registrant is submitting his own CSR. Furthermore, ECHA notes that the draft decision reflects the information in the addressee's CSR.

Based on the above, the Registrant shall revise his DNELs and reassess related risks. The results of the studies requested under section II.X shall be taken into account when revising the DNELs. If DNELs are not revised, this shall be fully justified. The chemical safety report shall be amended accordingly.

3. Exposure assessment and risk characterisation to demonstrate that the risk to the environment can be considered to be adequately controlled (Annex I, 5. and 6. of the REACH Regulation))

According to Annex I, Section 0.6, the Registrant is required to perform a Chemical Safety Assessment (CSA) for the registered substance. The CSA shall cover 1) human health hazard assessment, 2) human health hazard assessment of physicochemical properties, 3) environmental hazard assessment and 4) PBT and vPvB assessment. The CSA shall also consider exposure assessment and risk characterisation if as a result from these steps, the substance is assessed to be a PBT or vPvB or meets the criteria for any of the hazard classes or categories set out in Annex I to Regulation (EC) No 1272/2008 (CLP Regulation).

Furthermore, according to Annex I, Section 5.0 of the REACH Regulation, the objective of the exposure assessment is to make a quantitative or qualitative estimate of the dose/concentration of the substance to which humans and the environment are or may be exposed. Pursuant to the same paragraph the assessment shall cover any exposures that may relate to the hazards identified in Section 1 to 4 of Annex I of the REACH Regulation.

The Registrant has waived the exposure assessment and risk characterisation for the environment based on the following statement: "*In the chemical safety assessment performed according to Article 14(3) in connection with Annex I section 3 (Environmental Hazard Assessment) and section 4 (PBT/vPvB Assessment) no hazard was identified. Therefore according to REACH Annex I (5.0) an exposure estimation is not necessary. Consequently all identified uses of the substance are assessed as safe for the environment.*"

It is apparent from the CSA that the Registrant has self-classified the substance as R38 (irritating to skin) and R43 (may cause sensitisation by skin contact) according to Annex I of Directive 67/548/EEC, and as Skin Irrit. 2 (H315: Causes skin irritation), Eye Irrit. 2 (H319: Causes serious eye irritation) and Skin Sens. 1 (H317: May cause an allergic skin reaction) according to Regulation (EC) 1272/2008. Therefore the substance is hazardous regarding skin corrosion/irritation (hazard class 3.2), serious eye damage/eye irritation (hazard class 3.3) and respiratory or skin sensitisation (hazard class 3.4) according to the definition given in Annex I to Regulation (EC) No 1272/2008. Consequently, the chemical safety assessment of the registered substance shall also include exposure assessment, exposure estimation, and risk characterisation.

Moreover, the CSA explicitly states that substance related effects were detected in short-term toxicity to fish (96h-LC50: 6.78 mg/L; 96h-NOEC: 4.6 mg/L, based on mortality), short-term toxicity to aquatic invertebrates (48h-EC50: 6.8 mg/L; 48h-NOEC: 3.13 mg/L, based on mobility) and toxicity to algae (72h-EC10: 3 mg/L, based on growth rate). Therefore, hazard is identified in aquatic toxicity and, thus an exposure assessment should be carried out for the environment.

In view of ECHA, Annex I, section 0.6 of the REACH Regulation, requires that a substance that meets the criteria for hazard class 3.1 to 3.6 set out in Annex I to Regulation (EC) No 1272/2008 shall be subjected to exposure assessment and risk characterisation. In addition, the Registrant has in the present case identified environmental hazards as short term toxicity to fish, short-term toxicity to aquatic invertebrates and toxicity to algae, which according to Annex I, section 5.0 of the REACH Regulation, shall be taken into account in the exposure assessment.

Therefore, the Registrant is requested to perform a complete exposure assessment for the environment covering all life-cycle stages of the registered substance originating from manufacture and identified uses, and subsequently perform a risk characterisation for each exposure scenario to demonstrate the safe use of the substance. The Registrant is requested to update the dossier accordingly.

4. The description of the use "use of cleaning agents – industrial" shall be revised.

The technical dossier in section 3.5 (and also the CSR in the corresponding section) contains a scenario for the "use of cleaning agents – industrial". For use description of this scenario the Registrant assigned an Environmental release category "ERC 8a: Wide dispersive indoor use of processing aids in open systems". Following the rationale of this specific ERC as defined in Guidance R.12 and R.16, it is intended for uses by the public at large (consumers) or professional users. For industrial uses the corresponding descriptor is ERC 4 – the use of the related release factors might result in wrong calculations.

Therefore the Registrant shall review the description of this use. In case of missing information for distribution figures within the supply chain the Registrant has to calculate the environmental exposure for industrial and wide dispersive uses based on worst case assumptions regarding tonnages used as indicated in guidance R.16. This would mean that for industrial uses the complete EU tonnage has to be assumed for local exposure estimation. Deviations from this assumption need to be supported by a sound justification.

5. A qualitative assessment of likelihood that skin irritation is avoided when implementing exposure scenarios (Annex I, 6.5 of the REACH Regulation)

Annex I, Section 6.5. of the REACH Regulation requires that for those human effects for which it is not possible to determine a DNEL, a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario shall be carried out. In this case, DNELs have been derived for threshold effects. However, no qualitative assessment has been carried out for local effects on skin due to irritancy, even though the substance is classified for skin irritation. More specifically, there are no risk management measures for skin protection other than gloves. Therefore, it is possible that skin irritation is not avoided by the risk management measures in other parts of the body than hands. The ECHA practical Guide "How to undertake a qualitative human health assessment and document it in a chemical safety report" (Practical Guide 15, version 1.0, November 2012) provides further details on how to carry out a qualitative assessment.

Therefore, the Registrant is requested to perform a qualitative assessment of likelihood that skin irritation is avoided when implementing exposure scenarios.

Notes for consideration by the Registrant

According to Annex I, 0.3., 0.5. and 5.1.1. the applied Risk Management Measures (RMM) have to be indicated in the CSR. Annex II, section 8.2.2.2. (b)(i), requires the Registrant to describe the relevant RMM in detail (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 dermal exposure) in order to minimise the exposure for workers handling the registered substance. In particular, the following requirements for hand protection in order to avoid dermal exposure need to be provided consistently in the SDS and CSR:

- The type of material and its thickness,
- The typical or minimum breakthrough times of the glove material.

ECHA notes that in section 11 of the technical registration dossier in the part for Exposure controls/personal protection, the Registrant specifies the material and minimum breakthrough time of the glove material. However, thickness of the glove is not mentioned either in the CSR or in IUCLID section 11 (Guidance on safe use). Therefore, ECHA recommends that also glove thickness is documented in the CSR and in IUCLID section 11.

IV. 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 an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on ECHA's internet page at http://echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

[redacted]
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Annex I.

Assessment factors (AF) applied by the Registrant:

For workers - systemic long term – inhalation route:
- intraspecies: 3
- exposure duration: 2
- quality of the database: 2
  (overall AF: 12)

For workers - systemic long term – dermal route:
- interspecies: 7
- intraspecies: 3
- exposure duration: 1
- dose response: 3
  (overall AF: 63)

For workers – local long term –dermal route:
- intraspecies: 10
- exposure duration: 1
  (overall AF: 10)

For the general population - systemic long term – inhalation route:
- intraspecies: 5
- exposure duration: 2
- quality of the database: 2
  (overall AF: 20)

For the general population - systemic long term – dermal route:
- interspecies: 7
- intraspecies: 5
- dose response 3
- exposure duration: 1
  (overall AF: 105)

For the general population – local long term –dermal route:
- intraspecies: 10
- exposure duration: 1
  (overall AF: 10)

For the general population - systemic long term – oral route:
- interspecies: 7
- intraspecies: 5
- exposure duration: 1
- dose response: 3
  (overall AF: 105)

The default assessment factors recommended in the ECHA Guidance[1]:

For workers - systemic long term – inhalation route:
- interspecies: 2.5 (remaining differences between species non related to allometry)
- intraspecies: 5 (workers)
- exposure duration: 2 (sub-chronic to chronic)
  (overall AF: 25)

[1] Link to ECHA guidance document R.8 is: http://echa.europa.eu/documents/10162/17224/information_requirements_r8_en.pdf

For workers - systemic long term – dermal route:
- interspecies - allometric correction: 7 (mouse to human)
- interspecies - remaining differences: 2.5 (non-related to allometry)
- intraspecies: 5 (workers)
- exposure duration: 1 (chronic)
- dose response relationship - (LOAEL starting point): 3 (majority of cases)
  (overall AF: 262.5)

For workers – local long term –dermal route:
- intraspecies: 5
- exposure duration: depends on the length of the study

For the general population - systemic long term – inhalation route:
- interspecies: 2.5 (remaining differences between species non related to allometry)
- intraspecies: 10 (general population)
- exposure duration: 2 (sub-chronic to chronic)
  (overall AF: 50)

For the general population - systemic long term – dermal route:
- interspecies - allometric correction: 7 (mouse to human)
- interspecies - remaining differences: 2.5 (non-related to allometry)
- intraspecies: 10 (general population)
- exposure duration: 1 (chronic)
- dose response relationship - (LOAEL starting point): 3 (majority of cases)
  (overall AF: 525)

For the general population – local long term –dermal route:
- intraspecies: 10
- exposure duration: depends on the length of the study

For the general population - systemic long term – oral route:
- interspecies - allometric correction: 7 (mouse to human)
- interspecies - remaining differences: 2.5 (non-related to allometry)
- intraspecies: 10 (general population)
- exposure duration: 1 (chronic)
  (overall AF: 175)