EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-2114296644-37-01/F Helsinki, 9 March 2015

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

For disodium [[N,N'-ethylenebis[N-(carboxymethyl)glycinato]](4-)-N,N',O,O',ON,ON']manganate(2-), CAS No 15375-84-5 (EC No 239-407-5), 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 disodium [[N,N'-ethylenebis[N-(carboxymethyl)glycinato]](4-)-N,N',O,O',ON,ON']manganate(2-), CAS No 15375-84-5 (EC No 239-407-5), submitted by [redacted] (Registrant). The scope of this compliance check is limited to the standard information requirement of Annex IX, Section 8.7.2. of the REACH Regulation. ECHA stresses that it has not checked the information provided by the Registrant and other joint registrants for compliance with requirements regarding the identification of the substance (Section 2 of Annex VI).

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more 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.

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 25 April 2013.

On 29 May 2013 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 27 June 2013 ECHA received comments from the Registrant on the draft decision.

On 27 June 2013 the Registrant updated his registration dossier with the submission number [redacted].

The ECHA Secretariat considered the Registrant's comments and update.
The information is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

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.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Information required

Pursuant to Articles 41(1)(a)/(b), 41(3), 10(a)(vii), 12(1)(e), 13 and Annex IX, of the REACH Regulation the Registrant shall submit the following information using the indicated test method and the registered substance subject to the present decision:

- Pre-natal developmental toxicity study in rats or rabbits, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414).

Note for consideration by the Registrant:

The Registrant 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 to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

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 the Member States.

Deadline for submitting the required information

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated registration to ECHA by **16 March 2016**.

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 pre-natal developmental toxicity study is a standard information requirement as laid down in Annex IX, section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

In the technical dossier the Registrant initially provided information with which he sought to fulfil this standard information requirement. The provided information stemmed from a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD 422). The Registrant furthermore argued that he considered it not warranted to perform a pre-natal developmental toxicity study as he assumes that "sufficient information" has been obtained from the submitted study. ECHA stressed that in accordance with the third introductory paragraph of Annex IX the Registrant would have to "clearly state the reasons for any decision to propose adaptations to the standard information under the appropriate headings in the registration dossier referring to the appropriate specific rule(s) in column 2 or in Annex XI". The information provided by the Registrant did not justify any adaptation in accordance with column 2 of Annex IX, Section 8.7.2. or with the general rules of Annex XI for this standard information requirement.

The Registrant did not provide a pre-natal developmental toxicity study with the registered substance and adapted this information requirement by arguing that additional testing on this endpoint would be scientifically unjustified. In the updated dossier and in their comments the Registrant provided a category justification for the "aminocarboxylic acid-based chelant category" ("Justification in support of cross-reading within the Aminocarboxylic acid-based chelants chemical category"). The registered substance is a chelant, complexed with manganese.

The Registrant provided information on the chelating agents ethylenediaminetetraacetic acid (EDTA), hydroxyethylenediaminetriacetic acid (HEDTA), and ethylenediaminetetraacetic acid (DTPA), uncomplexed as acid or salt, or complexed with metal ions, including several endpoint study records on developmental toxicity studies performed with these chelating agents. The submitted studies have been performed either in accordance to guideline OECD 422 (one study), EPA OPP 83-3 (Prenatal Developmental Toxicity Study, two studies) or did not follow a guideline (seven studies). The category approach is mainly based on identical functional groups, metal ion chelating or sequestering properties and thus on a common mechanism of action of the chelants. The information provided does not refer to chelants complexed with manganese.

Only limited information on developmental toxicity of the metal ion, manganese (Mn2+), is provided in the updated dossier: Reference is made to the review of the Dutch Health Council on manganese and its compounds (2001), where the reviewers note "No publications concerning developmental effects in man were found. Manganese induced developmental effects in various animal species by different exposure routes. (...) However these effects were only observed in the presence of maternal toxicity or the maternal toxicity was not clear. For that reason the committee recommends to classify manganese in category 3 ('substances which cause concern for humans owing possible developmental effects that should be regarded as if they cause developmental toxicity in humans') and labelled with R63 (Possible risk of harm to the unborn child)".

Furthermore, the following conclusion is drawn in the endpoint study record of the key study for developmental toxicity (OECD 422) in the dossier: "As there were no differences in toxic effects in the groups at 1500 mg/kg bw with and without additional zinc, it was concluded that the addition of zinc was not necessary to compensate for possible reproductive toxicity of EDTA-MnNa2, if any, due to its chelating, viz. zinc-binding properties. Instead, it was concluded that the reproductive toxicity of EDTA-MnNa2 was most probably directly due to the presence of Mn-ions. However, apparently such effects were only seen at a very high dose of 1500 mg/kg bw EDTA-MnNa2 and not at the next lower level tested of 500 mg/kg bw."

In their justification for data waiving the Registrant stated that "In view of the outcome of the extended OECD 422 study with EDTA-MnNa2 and all data available on the developmental toxicity of other (metal) chelating agents (see also read across document in section 13), we feel that sound data are available, including information on the working mechanism, to conclude about developmental toxicity caused by chelates in general, and as such also by EDTA-MnNa2. Additional testing on this endpoint is therefore scientifically and ethically not justified." ECHA assumes that the Registrant most probably refers to REACH Annex XI, 1.2 (weight of evidence) and to REACH Annex XI, 1.5 (grouping of substances and read-across approach).

The registered substance is a chelant, complexed with manganese. ECHA notes that, with reference to the adaptation possibility of REACH Annex XI, 1.2., weight of evidence, it is required that there is 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, while the information from each single source alone is regarded insufficient to support this notion. Whereas the Registrant has in their category approach provided information on the chelating agents EDTA, HEDTA, and DTPA, uncomplexed as acid or salt, or complexed with metal ions, the Registrant has not provided sufficient information on the metal ion, manganese (Mn2+), as outlined above. ECHA therefore cannot assess whether the registered substance has or has not the particular dangerous property of pre-natal developmental toxicity.

With reference to REACH Annex XI, 1.5. (grouping of substances and read-across approach), ECHA notes that the Registrant has for the metal ion, manganese (Mn2+) also not provided adequate and reliable coverage of the key parameters addressed in test method OECD 414 (e.g. external, soft tissue, and skeletal malformations of the foetuses and other relevant alterations). This is amongst other criteria listed in Annex XI, 1.5. a pre-requisite for applying read-across by means of adaptation and achieve compliance for the respective endpoint of pre-natal developmental toxicity.

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

According to the test method EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit the preferred non-rodent species and the test substance is usually administered orally. ECHA considers these default parameters appropriate and testing should be performed by the oral route with the rat or the rabbit as a first species to be used.

Therefore, pursuant to Article 41(1)(a) and (b) and 41(3) of the REACH Regulation, the Registrant is requested to submit information on Pre-natal developmental toxicity on rats or rabbits, oral route (test method EU B.31/OECD 414) on the registered substance.

Notes for consideration by the Registrant

In addition, a pre-natal developmental toxicity study on a second species is part of the standard information requirements as laid down in Annex X, Section 8.7.2. for substances registered for 1000 tonnes or more per year (see sentence 2 of introductory paragraph 2 of Annex X).

The Registrant should firstly take into account the outcome of the pre-natal developmental toxicity on a first species and all other relevant available data to determine if the conditions are met for adaptations according to Annex X, Section 8.7. column 2, or according to Annex XI; for example if the substance meets the criteria for classification as toxic for reproduction Category 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment, or alternatively, if weight of evidence assessment of all relevant available data provides scientific justification that the study in a second species is not needed. If the Registrant considers that testing is necessary to fulfill this information requirement, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species. If the Registrant comes to the conclusion that no study on a second species is required, he should update his technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex X, Section 8.7.2.

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted by the Registrant and other joint registrants for identifying the substance has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation. The Registrant is reminded of his responsibility and that of joint Registrants to ensure that the joint registration covers one substance only and that the substance is correctly identified in accordance with Annex VI, Section 2 of the REACH Regulation.

In relation to the information required by the present decision, the sample of substance used for the new study 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 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 substance tested in the new study 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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new study 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 study to be assessed.

V. 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://www.echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

[redacted]

Ofelia Bercaru
Head of Unit, Evaluation