ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-0000003729-63-06/F Helsinki, 4 July 2014

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

For Chromium iron oxide, CAS No 12737-27-8 (EC No 235-790-8), 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 Chromium iron oxide, CAS No 12737-27-8 (EC No 235-790-8), submitted by [redacted] (Registrant). The scope of this compliance check is limited to the standard information requirements of Annex VIII, 8.6.1., and Annex IX, Sections 8.6.2. and 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 31 October 2013, 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 5 March 2013.

On 11 June 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.

On 11 July 2013 ECHA received comments from the Registrant.

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

On 31 October 2013 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, a Competent Authority of a Member State submitted a proposal for amendment to the draft decision.

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

On 5 December 2013 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 those proposals for amendment within 30 days of the receipt of the notification.

On 16 December 2013 ECHA referred the draft decision to the Member State Committee.

By 7 January 2014, in accordance to Article 51(5), the Registrant provided comments on the proposal for amendment. The Member State Committee took the comments of the Registrant on the proposal for amendment into account.

A unanimous agreement of the Member State Committee on the draft decision was reached on 21 January 2014 in a written procedure launched on 10 January 2014. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

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

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, 8.6.2.; test method: OECD 408) in rats;

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

3. Short-term repeated dose toxicity study (28 days), oral route (Annex VIII, 8.6.1.; test method: OECD 407) in rats.

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 **5 June 2017**. The timeline has been set to allow for sequential testing as appropriate.

Data from a second pre-natal developmental toxicity study on another species is a standard information requirement according to Annex X, 8.7.2. of the REACH Regulation. 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, 8.7. column 2, or according to Annex XI. If the Registrant considers that testing is necessary to fulfil 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, 8.7.2.

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.

1. Sub-chronic toxicity study (90-day):

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, Section 8.6.2. 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.

The Registrant has proposed to adapt the information requirement of sub-chronic toxicity (Annex IX, Section 8.6.2. of the REACH Regulation).

In the justification of this proposed adaptation the Registrant claims that neither an oral, nor an inhalation study needs to be conducted due to chemical inertness of the registered substance.

However, ECHA notes that neither column 2 of Section 8.6.2. nor general rules for adaptation in Annex XI (such as Section 1 of Annex XI, which the Registrant refers to) include the possibility to adapt the standard information requirement on the basis of the argument made by the Registrant.

The justification of the Registrant most closely relates to the adaptation possibility of Annex IX, 8.6.2. Column 2 according to which no sub-chronic toxicity study needs to be conducted if "the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure."

The Registrant has however not claimed that the cumulative conditions of that adaptation possibility are fulfilled. In addition ECHA notes that no 28-day study record/data was provided in the registration dossier. Moreover, evidence of limited human exposure has not been given.

Therefore, since the Registrant has not provided sufficient information to show that conditions of an adaptation in Column 2 of Annex IX, 8.6.2. or Annex XI are met, the adaptation of the information requirement suggested by the Registrant cannot be accepted. Consequently there is an information gap and it is necessary to provide information for Annex IX, Section 8.6.2.

Concerning the route of administration, the Registrant has indicated that inhaled substance would undergo translocation to the gastrointestinal tract via mucociliary escalation and be swallowed. ECHA agrees that in light of the arguments of the Registrant, the oral route of administration is appropriate. According to the test method the rat is the preferred rodent species. ECHA considers this species as being appropriate.

In his comments to the draft decision, the Registrant proposed a testing strategy that according to his assessment could lead to the possibility of adapting the standard information requirement. However, as the adaptation is currently not justified, ECHA has not amended the testing requirement in Section II of the decision (except for the change of the route of administration).

Therefore, in the absence of a justified adaptation and pursuant to Article 41(1) and (3) of the REACH Regulation, the Registrant is requested to submit information on sub-chronic toxicity (90-day) in rats, oral route (test method OECD 408) (Annex IX, Section 8.6.2.) using the registered substance.

Notes for consideration by the Registrant

In his comments to the draft decision, the Registrant proposed a testing strategy that consists of

- sub-acute (28 day) oral toxicity test at the limit dose (1,000 mg/kg bw/d) to show absence of toxicity,
- generation of toxicokinetic data to document the absence of any quantitatively relevant absorption, and
- reasoning why no significant human exposure occurs during manufacture and uses of the substance.

According to the Registrant, based on the outcome of the above, a decision could be taken whether further testing, i.e. a sub-chronic (90 day) study would be required.

ECHA has considered the solubility and reactivity data submitted, in the light of the relevant CSA Guidance, i.e. R.7.1.1.4.2, R.7.1.7.6. and 7.5.3.4., according to which *e.g. "insoluble and not inhalable can be interpreted as indicators of low exposure potential"*. ECHA notes that the value provided for solubility is below the limit for what ECHA normally considers to be "insoluble".

In the registation dossier, the Registrant has also demonstrated (by means of X-ray diffraction analysis) the low reactivity due to the chrystalline structure to which the metals are bound. The CSA Guidance does not provide a threshold value for reactivity. Taking into account that the cumulative criteria are to be considered jointly, the data on reactivity is considered to be sufficient in this case.

In order to justify the adaptation pursuant to the fourth indent of column 2 of Annex IX, Section 8.6.2., the Registrant would furthermore need to demonstrate that the substance is not inhalable, that there is no evidence of absorption and no evidence of toxicity in a 28-day limit test. The testing strategy outlined by the Registrant is a feasible option for establishing whether the adaptation is justified, except that the testing strategy does not fully address the issue of "non-inhalability". While the Registrant has provided relevant information in his comment, this element would need to be further established in the dossier update.

ECHA also recognises that the testing strategy outlined by the Registrant could pave the way towards a Weight of Evidence (WoE) approach according to Annex XI, 1.2. In the WoE approach, the sub-acute toxicity study, toxicokinetic information and demonstration of no significant human exposure remain relevant. The Registrant should assess the toxicokinetic behavior of the substance as indicated in Annex VIII, 8.8.1. and provide evidence of low absorption by the relevant routes of administration, taking into account, in particular, the

information on the granulometry included in the dossier (the massmedian aerodynamic diameters: MMAD1 = 4.35 µm (20.0%) , MMAD2 = 61.04 µm (80.0%)).

ECHA therefore recognises that the Registrant may seek to justify any adaptation within his own responsibility and to follow an according testing strategy in order to demonstrate that the adaptation is justified.

2. Pre-natal developmental toxicity study:

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.

The Registrant has proposed to adapt the information requirement of pre-natal developmental toxicity (Annex IX, Section 8.7.2. of the REACH Regulation).

The justification of the adaptation given by the Registrant is that "according to section 1 of REACH Annex XI testing for is scientifically not relevant for this substance since this pigment can be considered as chemically inert." Furthermore, the Registrant has provided bioaccessibility data "that indicate very low solubility of the contained elements under physiological conditions: at pH 7.2 in phosphate buffered saline, which is a standard physiological solution that mimics the conditions of human blood serum, in gastric juice (pH 1.5), which mimics the very harsh digestion milieu of high acidity in the stomach."

However, ECHA notes that neither Column 2 of Annex IX, 8.7. nor general rules for adaptation of Annex XI include such possibility to adapt the information requirement.

The justification of the Registrant most closely relates to the adaptation possibility of Annex IX, 8.7. Column 2 according to which no reproductive toxicity studies need to be conducted if the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure.

The Registrant has however not claimed that the cumulative conditions of that adaptation possibility are fulfilled. In addition ECHA notes that signs of toxicity were observed in the acute toxicity inhalation test. Moreover, evidence of no or no significant human exposure has not been given.

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.

Since the Registrant has not provided sufficient information to show that conditions of an adaptation in Column 2 of Annex IX, 8.7. are met, the adaptation of the information requirement suggested by the Registrant cannot be accepted. Consequently there is an information gap and it is necessary to provide information for this endpoint.

In his comments to the draft decision, the Registrant proposed a testing strategy that according to his assessment could lead to the possibility of adapting the standard information requirement. However, as the adaptation is currently not justified, ECHA has not amended the testing requirement in Section II of the decision.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, the Registrant is requested to submit information on pre-natal developmental toxicity (Annex IX, 8.7.2.) on rats or rabbits by the oral route using test method EU B.31/OECD 414 on the registered substance.

Notes for consideration by the Registrant

Firstly, in his comments to the draft decision, the Registrant proposed a testing strategy that consists of

- sub-acute (28 day) oral toxicity test at the limit dose (1,000 mg/kg bw/d) to show absence of toxicity,
- generation of toxicokinetic data to document the absence of any quantitatively relevant absorption, and
- reasoning why no significant human exposure occurs during manufacture and uses of the substance.

As explained above under point III.1, ECHA recognises that the testing strategy outlined by the Registrant could pave the way towards a Weight of Evidence (WoE) approach according to Annex XI, 1.2. In the WoE approach, the sub-acute toxicity study, toxicokinetic information and demonstration of no significant human exposure remain relevant.

ECHA therefore recognises that the Registrant may seek to justify any adaptation within his own responsibility and to follow an according testing strategy in order to demonstrate that the adaptation is justified.

Secondly, when considering the need for a testing proposal for a prenatal developmental toxicity study in a second species, the Registrant should take into account the outcome of the pre-natal developmental toxicity study on the first species and all available data to determine if the conditions are met for adaptations according to Annex IX, 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.

3. Short-term repeated dose toxicity study (28 day), oral route (Annex VIII, 8.6.1.)

A "short-term repeated dose toxicity study (28 days)" is a standard information requirement as laid down in Annex VIII, Section 8.6.1. 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.

This standard information requirement was not included under the original scope of the targeted compliance check. The Registrant – in his comments on the other two endpoints – however brought this standard information requirement within the scope of the present decision-making. ECHA subsequently evaluated the information provided to fulfil the standard information requirement of Annex VIII, 8.6.1.

The Registrant has not provided any study record of a short-term repeated dose toxicity study (28 days) in the dossier that would meet the information requirement of Annex VIII, Section 8.6.1.

The Registrant has in the dossier sought to adapt this information requirement. In the justification of this proposed adaptation, the Registrant claims that neither an oral, nor an inhalation study needs to be conducted due to chemical inertness of the registered substance. ECHA notes that neither Column 2 of Annex VIII, 8.6.1. nor general rules for adaptation of Annex XI include such possibility to adapt this information requirement. Therefore, the adaptation of the information requirement suggested by the Registrant cannot be accepted.

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.

In light of the properties of the substance and the information provided on the uses and human exposure, ECHA considers that testing by the oral route is most appropriate. According to the test method OECD 407 the rat is the preferred species. ECHA considers this species as being appropriate and testing should be performed with the rat.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, the Registrant is requested to submit the following information derived with the registered substance subject to the present decision: Repeated dose 28-day oral toxicity study (test method: OECD 407) in rats.

4. Extension of the timeline

In the draft decision communicated to the Registrant pursuant to Article 50(1), ECHA had foreseen a timeline of 24 months for submitting the required information. In order to enable the Registrant to follow the testing strategy he outlined in his comments on the draft decision and to carry out the tests required pursuant to in the event that he cannot justify the adaptations, ECHA has extended the timeline from 24 to 36 months.

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 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 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 studies 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 studies 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 studies 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://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.

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