ECHA
EUROPEAN CHEMICALS AGENCY

Helsinki, 25 September 2019

Addressee: [redacted]

Decision number: CCH-D-2114482453-46-01/F
Substance name: Cobalt zinc aluminate blue spinel
EC number: 269-049-5
CAS number: 68186-87-8
Registration number: [redacted]
Submission number subject to follow-up evaluation: [redacted]
Submission date subject to follow-up evaluation: 2 May 2017

DECISION TAKEN UNDER ARTICLE 42(1) OF THE REACH REGULATION

By decision CCH-D-0000003730-80-05/F of 4 July 2014 ("the original decision") ECHA requested you to submit information by 9 May 2017 in an update of your registration dossier.

Based on Article 42(1) of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA examined the information you submitted with the registration update specified in the header above, and concludes that

Your registration still does not comply with the following information

Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a first species (rat or rabbit), oral route

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.

The respective Member State competent authority (MSCA) and National enforcement authority (NEA) will be informed of this decision. They may consider enforcement actions to secure the implementation of the original decision and exercise the powers reserved to them under Article 126 of Regulation No 1907/2006 (penalties for non-compliance) for the period during which the registration dossier was not compliant[1].

[1] See paragraphs 61 and 114 of the judgment of 8 May of the General Court of the European Court of Justice in Case T-283/15 Esso Raffinage v. ECHA

Appeal

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[2] by Wim De Coen, Head of Unit, Hazard Assessment

[2] 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

Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

In decision CCH-D-0000003730-80-05/F ("the original decision") you were requested to submit information derived with the registered substance for Pre-natal developmental toxicity endpoint.

In the updated registration subject to follow-up evaluation, you have provided an adaptation according to the Annex IX, Section 8.7, Column 2, and according to the Annex XI, Section 1.2.

Regarding the Annex IX, Section 8.7, Column 2 adaptation *"The studies do not 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."* As further explained below, ECHA considers that none of the criteria are met.

With regards to *"low toxicological activity"*, ECHA notes that in the newly generated 28-day limit dose test the following findings were observed at 1000 mg/kg bw/day. You reported statistically significant differences in haematological and clinical biochemistry parameters, namely increased platelet counts in females and decreased absolute basophilic granulocytes in males; and statistically significantly increased bilirubin levels in males. Furthermore, you reported statistically significant organ weight changes in males (decreased relative and absolute spleen weight). Gross pathology revealed a green discoloured content of the stomach or the intestines which was linked to the presence of granular green-coloured material in the intestine-lumen. The histopathological analysis also showed inflammatory lesions in different organs. You considered the findings not test item related, however ECHA is of the opinion that this does not support a conclusion of *"no evidence of toxicity seen in any of the tests available"*.

With regards to *"absence of systemic absorption via relevant routes of exposure"*, ECHA notes that in the non-guideline single dose mass balance study with the registered substance, you reported recoveries of 97.4 % cobalt, 105% aluminium and 100% zinc via urine and faeces. Further, you reported measurable quantities of zinc (0.01%) and cobalt (<0.006%) in urine during the first day in the single dose mass balance study. You also reported that 24 hour urine and plasma sampling in the 28-day limit dose test showed negligible uptake of the registered substance. For example, you reported following concentrations of cobalt in male rat plasma: for test group the concentration was 0.053 µg/L, whereas for the control group, the concentration was 0.003 µg/L. Regarding the cobalt excreted via urine in males, you reported, for test group 1.42 µg, whereas for the control group 0.07 µg. ECHA is of the opinion that the data demonstrate absorption via oral route which is, based on the particle size distribution, a relevant route of exposure together with inhalation route due to ingestion of larger particles cleared from the respiratory tract. Based on the information provided, ECHA is of the opinion that it cannot be concluded that there is *"no systemic absorption via relevant routes of exposure"*.

With regards to *"no or no significant human exposure"*, ECHA notes that you reported a Mass median aerodynamic diameter (MMAD) of 49.04 µm as particle size distribution of the registered substance. Therefore, ECHA observes that the registered substance is inhalable (particles that enter the respiratory system via the nose or mouth, D <100 µm). ECHA notes also that although based on the concurrent particle size analysis via inhalation deposition modelling with MPPD (Multiple Path Particle Dosimetry) an important fraction of the deposition occurs in the extra thoracic region, it is also predicted by the model that a fraction of the airborne material is deposited in the pulmonary alveoli (0.7%) and tracheo-bronchial region (0.6%). Additionally, ECHA observes that in the report on the occupational exposure assessment attached to IUCLID Section 13 [redacted] you describe spraying applications of the registered substance by downstream users. ECHA notes that spraying application are normally connected to a certain degree of exposure and while in table 17 of the document you describe the industrial spraying in enclosed settings, the professional spraying applications involve a worker directly working over the article which indicates inhalation exposure to the registered substance. ECHA is of the opinion that it cannot be concluded that there is *"no or no significant human exposure"*.

With respect to the adaptation according to the Annex XI, Section 1.2, ECHA observes that the sources of information do not allow concluding whether or not the registered substance has a particular dangerous property (i.e. developmental toxicity). In particular, none of the sources of information provides evidence about the potential of the registered substance to cause pre-natal developmental toxic effects, as the only repeated dose toxicity study available does not examine pre-natal developmental endpoints. Also, as already pointed above, in ECHA's view, it cannot be concluded that the registered substance would show such general absence of toxicological activity and absorption, which would allow to conclude an absence of developmental toxicity as well.

In summary, ECHA observes that the information provided does not fulfil the adaptation requirements of the Annex IX, 8.7. Column 2 or Annex XI, Section 1.2.

In your comments to the draft decision you provided comments for each of the conditions of the above mentioned adaptation according to Annex IX, Section 8.7, Column 2.

As regards *"no or no significant human exposure"*, you firstly commented on the property of the substance of being inhalable stating that, based on the dustiness testing, only 10% of the sample has the propensity to become airborne under physical agitation. Additionally, you indicated that the (MPPD model prediction indicates that the total deposition in the human respiratory tract will be approx. 60.9%. When sub-categorising into the different regions of the respiratory tract, only a small fraction of the particles will deposit into the respiratory tract while the remaining portion will deposit into the tracheobronchial and extra-thoracic region, thus the majority of inhaled particles will be rapidly cleared to the gastrointestinal tract either by swallowing or by mucociliary escalation. Secondly, you also indicated that the professional spraying applications are niche applications and conducted for R&D purposes. You stated that they are conducted on a very infrequent and short-time basis in dedicated spray booths and the workers wear personal protective equipment. You stated that these activities are conducted for 15 minutes per shift/once a month and the percentage of the pigment is maximum [redacted]

ECHA underlines that, as reported in the ECHA Guidance R.8.R.7.1.14, dustiness is a relative term and is dependent on the method chosen, the condition and properties of the tested bulk material, and various environmental variables in which the tests are carried out. Thus, different methods may provide different results. While the dustiness indicates the propensity of a material to become airborne under workplace conditions, the numeric value of dustiness does not give information on the particle size distribution. Additionally, in the report on the occupational exposure assessment (IUCLID Section 13) it is stated that the total dustiness of cobalt zinc aluminate blue spinel corresponds to high dustiness and the emission potential of the pigment as such does not allow supporting the claim of "*absence of exposure*" or "*no significant exposure*". In the report it was concluded that such dust emissions needs to be further examined with monitoring data. The mass median aerodynamic diameter (MMAD) of the airborne fraction determined during the dustiness test (49.04 µm (GSD 7.72)) indicates that it is inhalable. In relation to the MPPD inhalation deposition modelling, ECHA underlines that the predicted total deposition in the human respiratory tract (43.8%) does not provide information in defining whether the different work tasks are showing no or no significant exposure.

ECHA underlines that in the report on the occupational exposure assessment (IUCLID Sect 13) the duration of exposure corresponds to 4h/shift and notes that a concentration of [redacted] of pigment in the spraying application cannot be considered low. Overall, although ECHA understands that these uses are marginal compared to industrial ones, ECHA notes that also short-term and infrequent activities give an opportunity to the worker to be exposed to the aerosol generated during spraying tasks. Additionally, there are no exposure estimates or monitoring data available for such activities.

Furthermore, ECHA notes that you provided the exposure levels for inhalable dust obtained at different workplaces in table 15 of the report on the occupational exposure assessment (the highest estimation is [redacted] during milling/mixing) and introduced a bioaccessibility factor for one constituent (i.e. Co). ECHA underlines that the bioavailability is not relevant in this case since the internal exposure shall not be considered when assessing the external exposure via inhalation. The bioavailability is not relevant since the occupational exposure assessment is performed for external exposure and the DNELs and OELs are generally expressed as external values. If internal exposure is assessed then bioavailability is taken into account. In such situation biomonitoring data shall be provided together with a DNEL expressed as internal value ($DNEL_{biomarker}$) (ECHA Guidance R.8, R.8.1.2.7). The estimated occupational exposure levels are below the OEL for general inhalable dust (10 mg/m^3) but the levels demonstrate that the exposure via inhalation is possible. Therefore, ECHA considers that it cannot be concluded that there is "*no or no significant human exposure*".

With regards to "*low toxicity activity*", you provided new information from a newly generated 28-day limit dose test to demonstrate that the values of the main findings are within the historical control ranges. That information, which is not provided in the IUCLID dossier, would allow to consider those observations as non-adverse. ECHA notes that this information seems to indicate "*no evidence of toxicity in a 28-day 'limit test'*". However, as stated above, several other conditions of the adaptation according to column 2 of section 8.7 of Annex IX are not met.

ECHA also notes that further to comparions with historical control values comparsions with internal controls of the 28-day limit test are relevant. Therefore, the presence of several

changes, compared with the internal controls, in haematological and clinical biochemistry parameters, as well as in spleen weight, seems to indicate that the substance is absorbed and enters into the systemic circulation to a certain extent. This is relevant for the determining if systematic absorption via relevant routes of exposure takes place, as discussed above.

Regarding the "*absence of systemic absorption via relevant routes of exposure*", ECHA already addressed that information, please see above.

Besides ECHA's comments on the criteria "*insoluble*" and as explained above, the particles, which will deposit extrathoracicly and subsequently swallowed, will be absorbed to a certain extent.

Finally, ECHA notes that in your comments to the draft decision you proposed an adaptation based on a read-across approach according to Annex XI, section 1.5 of REACH Regulation. The provided read-across hypothesis is based on the bioavailability and toxicity of the three main compounds of the registered substance, cobalt(II), zinc(II) and aluminium(III). However, you only listed several studies which '*will be assessed further*'. Annex XI, Section 1.5 of the REACH Regulation states that "*adequate and reliable documentation of the applied method shall be provided*". Within this documentation "*it is important to provide supporting information to strengthen the rationale for the read-across*" (ECHA Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of chemicals; section R.6.2.2.1 Read-across). The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the target substance can be predicted from the data on the source substances. Therefore, in the absence of such documentation and only referring to your future assessment of the listed studies, ECHA cannot verify that the properties of cobalt zinc aluminate blue spinel can be predicted from the data on the source substances.

As already stated in the original decision, 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.

As detailed above, the request in the original decision was not met, and you are still required to provide the pre-natal developmental toxicity study (Annex IX, 8.7.2.; test method: EU B.31./OECD 414) in rats or rabbits, oral route.

Appendix 2: Procedural history

In accordance with Article 42(1) of the REACH Regulation, the Agency examined the information submitted by you in consequence of decision CCH-D-0000003730-80-05/F. The Agency considered that this information did not meet one or more of the requests contained in that decision. Therefore, a new decision-making process was initiated under Article 41 of the REACH Regulation.

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 of this decision was notified to the Member States Competent Authorities according to Article 51(1) of the REACH Regulation.

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 within 30 days of the notification.

ECHA took into account your comments and did not amend the request(s).

ECHA notified the draft decision to the competent authorities of the Member States for proposals 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 decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

2. The Article 42(2) notification for the original decision is on hold until all information requested in the original decision has been received.