EUROPEAN CHEMICALS AGENCY

Helsinki, 30 May 2017

Addressee: [redacted]

Decision number: TPE-D-2114361229-47-01/F
Substance name: COBALT DICHLORIDE
EC number: 231-589-4
CAS number: 7646-79-9
Registration number: [redacted]
Submission number: [redacted]
Submission date: 26.10.2015
Registered tonnage band: 100-1000T

DECISION ON A TESTING PROPOSAL

Based on Article 40 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA examined your testing proposal(s) and decided as follows.

1. **Your testing proposal is accepted and you are requested to carry out:Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: EU B.31./OECD TG 414) in a second species (rabbit, oral route) using the registered substance.**

You 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 and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **6 June 2018**. You shall also update the chemical safety report, where relevant.

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.

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[1] by Ofelia Bercaru, Head of Unit, Evaluation E3

[1] 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

The decision of ECHA is based on the examination of the testing proposal(s) submitted by you.

1. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species**

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

You have submitted a testing proposal for a pre-natal developmental toxicity study in a second species (rabbits) according to EU B.31./OECD TG 414 by the oral route.

The technical dossier contains a pre-natal developmental toxicity study in rats which establishes a NOAEL for maternal toxicity at 25 mg/kg/day and a NOAEL for developmental toxicity at 100 mg/kg/day.

ECHA observes that the information requirement of a pre-natal developmental toxicity study in a second species is not a standard information requirement applying to the substance subject to this decision, as it is registered in the tonnage band of 100 to 1000 tonnes per year.

However, ECHA notes that cobalt dichloride is proposed to be tested with the intention of being used as the source substance for the grouping of substances and read-across approaches aimed at fulfilling the information requirements of Annex X, Section 8.7.2 for other cobalt containing substances registered at a tonnage band of above 1000 tonnes or more per year. Pre-natal developmental toxicity studies on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

In your comments on the draft decision, you agreed to perfom the test.

Based on a Member State Competent Authority proposal(s) for amendment, ECHA revised the reasoning of the read-across approach.

The read-across hypothesis you provide is based on cobalt ion toxicity. For systemic effects following oral administration, your hypothesis is based on that systemic toxicity is driven by exposure to the cobalt ion. *Invitro* bioaccessibility data is used to predict cobalt ion release from the substances included in the approach. Based on the results of the bioaccessibility, the substances are divided into three groups: soluble inorganic cobalt substances, poorly soluble inorganic cobalt salts and inorganic cobalt substances with an organic ligand. For the soluble inorganic cobalt substances, cobalt dichloride is proposed as the test material because it is highly water soluble (*i.e.* 586 g/L). This is consistent with the results of the *in vitro* bioaccessibility study available in the registration dossier which shows a very high rate of cobalt ion release.

The purpose of a pre-natal developmental toxicity study is to identify hazards caused by systemic exposure to the test material. Under the current hypotheses ((1) toxicity is governed by the cobalt ion and (2) bioavailability of cobalt correlates with the release of cobalt in the gastric environment) cobalt dichloride is considered an approprate candidate to perform a prenatal developmental toxicity study.

ECHA considers that your proposal to use information obtained from the proposed test as a conservative estimate for developmental toxicity effects caused by the cobalt ion applicable to all cobalt releasing substances is plausible. However, depending on the nature of the counter ion and further factors eventually influencing absorption/toxicity (*e.g.* role of transporters, nutritional state, feedback mechanisms) there may be additional effects which should be considered in the hazard identification. In addition, ECHA notes that currently there are no internationally accepted test guideline for *in vitro* bioassessability.

In your comments on the proposal for amendment, you highlight that:

- The proposed testing is part of a previously submitted testing strategy based on a read-across approach;
- There is no internationally agreed test guidelines for *in vitro* bioaccessibility/bioelusion. However, there are a number of different protocols available and *in vitro* bioaccessibility/bioelution and these protocols have been used for regulatory purposes, *e.g.* restrictions under the REACH Regulation. Furthermore, the ECHA Guidance R.6 refers to bioaccessibility as a possible approach to support grouping of substances and read-across approaches; You clarify the reasoning for using cobalt dichloride as a conservative estimate of systemic cobalt ion toxicity; and
- You clarify that *in vitro* bioaccessibility in the current read-cross approach provides the first tier of the grouping for the oral route of exposure; and you agree that *in vitro* bioaccessibility is not to be used as a basis for grouping for the inhalation route.

ECHA has considered your comments on the proposal for amendment and revised the reasoning for accepting the proposed testing (as outlined above). ECHA considers the read-across approach as plausible, and that testing cobalt dichloride is considered approprite with regard to systemic toxicity caused by the cobalt ion following oral administration. ECHA considers that bioaccessibility is a useful basis for grouping inorganic cobalt salts.However, given that there is currently no internationally agreed test guideline, detailed descriptions of the study protocol used have to be provided including limitations in the applicability of the applied method.

Irrespective of the limitations of the method, ECHA considers that the results of the proposed test can servein a way that still needs to be defined for each substance – if justified – as a conservative estimate of the hazard caused by the cobalt ion; and will thus be useful for a quantitative risk assessment for cobalt salts.

Hence, with a view to the intended read-across to substances registered in the tonnage band of 1000 tonnes or more per year, ECHA considers that testing the cobalt dichloride in a second species for pre-natal developmental toxicity, and reading across the results from this test in order to meet the information requirements of Annex X, Section 8.7.2 applicable to other members of the group, can be considered as plausible.

ECHA requested your considerations for alternative methods to fulfil the information requirement for Reproductive toxicity (pre-natal developmental toxicity). ECHA notes that you provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

ECHA considers that the proposed study is appropriate to fulfil the information requirement of Annex X, Section 8.7.2. of the REACH Regulation.

You proposed testing with the rabbit as a second species. According to the test method EU B.31./OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default consideration and available studies, ECHA considers testing should be performed with the rabbit as a second species, taking into account the species tested in the first pre-natal developmental toxicity study was the rat.

You proposed testing by the oral route.

ECHA agrees that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a highly water soluble salt, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, you are thus requested to carry out the proposed study with the registered substance subject to the present decision: Pre-natal developmental toxicity study in a second species (rabbit), oral route (test method: EU B.31./OECD TG 414).

Notes for your consideration

Before performing a pre-natal developmental toxicity study in a second species you should consider the specific adaptation possibilities of Annex X, Section 8.7.2., column 2 and general adaptation possibilities of Annex XI. If the results of the test in the first species or any other new information enable such adaptation, testing in the second species should be omitted and the registration dossier should be updated containing the corresponding adaptation statement and underlying scientific justification.

For the selection of the appropriate species you are advised to consult ECHA *Guidance on information requirements and chemical safety assessment* (version 4.1, October 2015), Chapter R.7a, section R.7.6.2.3.2.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposal(s) for examination pursuant to Article 40(1) on 1 March 2016.

ECHA notes that the tonnage band for the joint submission is 100 to 1000 tonnes per year. However, the proposed testing is part of a testing strategy to fulfil the information requirements for a group of substance by means of read-across. The tonnage band for several other group members is 1000 tonnes or more per year.

ECHA held a third party consultation for the testing proposal(s) from 18 July 2016 until 1 September 2016. ECHA did not receive information from third parties.

This decision does not take into account any updates after **4 January 2017**, 30 calendar days after the end of the commenting period.

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.

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 proposal(s) for amendment.

ECHA received proposal(s) for amendment and modified the reasoning of the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-53 meeting and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This decision does not imply that the information provided in your registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

2. 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.

3. In relation to the information required by the present decision, the sample of the substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported 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 the substance tested in the new test(s) 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 or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) 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 test(s) to be assessed.