EUROPEAN CHEMICALS AGENCY

Helsinki, 28 May 2019

Addressee: [redacted]

Decision number: TPE-D-2114471591-47-01/F
Substance name: Slags, silicomanganese-manufg.
EC number: 273-733-9
CAS number: 69012-33-5
Registration number: [redacted]
Submission number: [redacted]
Submission date: 15 February 2018
Registered tonnage band: Over 1000

DECISION ON A TESTING PROPOSAL

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

Your following testing proposal is rejected:

> **Pre-natal developmental toxicity study (Annex X, Section 8.7.2., test method: EU B.31./OECD TG 414) in a second species (rabbit), using the analogue substance Slags, ferromanganesemanufg, (EC 273-728-1).**

You are requested to provide

> **A justification for adaptation of the Pre-natal developmental toxicity endpoint (Annex X, Section 8.7.2) in accordance to Annex XI, Section 1.2 of the REACH Regulation (as further described below).**

You have to submit the requested information in an updated registration dossier by **4 September 2019**. You also have to update the chemical safety report, where relevant.

The reasons for this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and 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, has to 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 Wim De Coen, Head of Unit, Hazard Assessment

[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 submitted by you.

1. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2., column 2) in a second species**

Pursuant to Article 40(3)(d) of the REACH Regulation, ECHA may reject a proposed test.

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 and Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The dossier contains a pre-natal developmental toxicity study in rats as first species with an analogue substance Slags, ferromanganesemanufg. (EC 273-728-1), which was submitted in order to satisfy the request for a PNDT study in a first species with the registered substance under Decision CCH-D-2114288754-34-01/F.

You have submitted a testing proposal for a pre-natal developmental toxicity study in rabbits according to EU B.31./OECD TG 414 with the analogue substance Slags, ferromanganesemanufg.

ECHA has evaluated your proposal to perform the test with the analogue substance Slags, ferromanganesemanufg.

ECHA has also evaluated the new studies and information submitted in the technical dossier which are listed below:

- 90-day oral toxicity study with the registered substance; 2016; GLP; OECD 408; doses: 10, 100 and 1000 mg/kg bw/day; treatment related effects: ulceration with inflammation and oedema in the non-glandular stomach and foveolar hyperplasia associated with eosinophilic globules and inflammatory cell infiltrate in the glandular stomach (all effects were attributed to the physical properties of the test material); NOAELsystemic= 1000mg/kg bw/day, NOAEL local=100mg/kg bw/day.
- Basic toxicokinetics *in vivo*: in the context of the 90-day oral toxicity study presented above, blood samples were taken in weeks 7 and 13 to determine if any absorption took place; no guideline study; results: plasma manganese, aluminium, barium and silicon concentration were found to be less than the limit of quantification (LOQ) in all groups, indicating that no quantifiable absorption had occurred.
- 43 days oral toxicity study in rats with the analogue substance, 2016, GLP, no guideline, doses 10, 100 and 1000 mg/kg bw/day, 4 animals/sex/group, during the study, toxicokinetics, clinical condition, bw and food consumption investigations were undertaken; results: with the exception of one mid dose male which had quantifiable concentrations of aluminium at 1 and 24 hrs post dose, there were no quantifiable levels of manganese, silicon, aluminium and barium; conclusion: under the conditions of the study there was no evidence of any absorption of the test material.
- PNDT oral study in rat with the source substance, in accordance with OECD 414, GLP, 2016, doses: 100, 300 and 1000 mg/kg/day; results: no adverse treatment

related effects were observed, NOAEL maternal=1000 mg/kg/bw, NOAEL developmental=1000mg/kg/bw.

On the basis of the available information ECHA evaluated whether the conditions for a weight of evidence adaptation pursuant to Annex XI, Section 1.2. are met.

ECHA's observations:

- The registered and the analogue substances are inorganic UVCB substances with the same metallic elements and oxides as constituents. The manufacturing process of the registered substance (alloying Mn ore with iron) produces the analogue substance as by-product. A comparison of the compositions of target and analogue substance shows that the elemental and oxide constituents are the same, however, the constituent concentrations vary widely. The main principle difference between the compositions is that the registered substance contains silicon [redacted] whereas the analogue substance contains manganese oxide [redacted]. According to you, the analogue substance is regarded as worst case due to the presence of manganese oxide, potentially regarded as an additional toxic constituent.
- The results for the analogue substance in the repeated dose toxicity study, the PNDT study in rat and the toxicokinetic measurements are consistent with the results obtained with the registered substance indicating lack of systemic toxicity and poor uptake.
- ECHA considers that the lack of developmental effects in the PNDT study in rats with the analogue substance is supportive of the lack of developmental toxicity for the registered substance as well in any species, rat or rabbit, as poor oral absorption of the registered substance will occur in the rabbit as well.
- Based on the information on particle size distribution of the registered substance in the technical IUCLID dossier (inhalable particles sizes less than 100 pm below [redacted] and [redacted]), the potential for inhalation exposure and uptake is low;
- Due to its physical inorganic nature (crystalline solid), the registered substance is unlikely to be absorbed through the skin.

Overall, ECHA concludes that the information available in the technical dossier on potential of systemic exposure, absorption and developmental toxicity is adequate to address the developmental toxicity potential of the registered substance in a second species (rabbit).

Hence, ECHA concludes that the information provided in the technical dossier is sufficient support for an adaptation pursuant to Annex XI, Section 1.2. derived from the afore-mentioned sources and leading to the assumption/conclusion that the registered substance does not have pre-natal developmental toxicity properties with respect to the information requirement for a PNDT study in a second species.

In your comments to the draft decision, you agreed to provide the requested information.

Therefore, pursuant to Article 40(3)(d) of the REACH Regulation, your proposed test for Pre-natal developmental toxicity study (Annex X, Section 8.7.2., column 2; test method: EU B.31./OECD TG 414) in a second species (rabbit), using the analogue substance Slags, ferromanganesemanufg, (EC 273-728-1) is rejected. You are requested to update the technical dossier by developing an adaptation to this endpoint in accordance to Annex XI, Section 1.2 of the REACH Regulation.

Appendix 2: Procedural history

ECHA received your registration containing the testing proposals for examination in accordance with Article 40(1) on 27 April 2017.

ECHA held a third party consultation for the testing proposals from 25 October 2017 until 11 December 2017. ECHA did not receive information from third parties.

This decision does not take into account any updates after **1 October 2018**, 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.

In your comments you agreed to the draft decision. ECHA took your comments into account 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 adopted the decision under Article 51(3) 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 requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.