Decision number: CCH-D-2114307484-53-01/F Helsinki, 30 September 2015

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

For Slags, ferromanganese-manufg., CAS No 69012-28-8 (EC No 273-728-1), 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 Slags, ferromanganese-manufg., CAS No 69012-28-8 (EC No 273-728-1), submitted by [redacted] (Registrant).

The scope of this compliance check is limited to the standard information requirements of 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 05 March 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 30 May 2013.

On 5 December 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 21 January 2014 ECHA received comments from the Registrant on the draft decision, concerning the information requirements of Annex IX and X, Sections 8.6.2., 8.7.2. and 8.7.3.

Subsequently, on 5 March 2014 the Registrant updated his registration dossier with the submission number [redacted].

The compliance check requirement to submit information of a two-generation reproductive toxicity study (EU B.35, OECD TG 416) or an extended one-generation reproductive toxicity

study (EU B.56, OECD TG 443) has been removed from this draft decision due to the legislative amendments to the REACH Regulation regarding Annex X, Section 8.7.3. In light of this, ECHA Secretariat did not consider further the Registrant's comments and update concerning the information requirement of Annex X, Section 8.7.3. However, ECHA Secretariat did consider further the Registrant's comments and update concerning the information requirements of Annex IX and X, Sections 8.6.2., 8.7.2. On the basis of all this information and change of scope, Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

On 5 March 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.

Subsequently, proposals for amendment to the draft decision were submitted.

The ECHA Secretariat reviewed the proposals for amendment received and did not amend the draft decision.

On 10 April 2015 ECHA notified the Registrant of the proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on the proposals for amendment within 30 days of the receipt of the notification.

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

On 20 April 2015 ECHA referred the draft decision to the Member State Committee.

By 11 May 2015, in accordance to Article 51(5), the Registrant provided comments on the proposals for amendment. The Member State Committee took the comments of the Registrant on the proposals for amendments into account.

A unanimous agreement of the Member State Committee on the draft decision was reached on 26 May 2015 in a written procedure launched on 13 May 2015.

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 Annexe 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: EU B.26./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;

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 **9 October 2017**.

Notes for consideration by the Registrant:

In light of the comments made by the Registrant, ECHA points out that the Registrant may adapt the testing requested above according to the specific rules outlined in Annexe IX 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 sound 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 Authorities of the Member States for enforcement.

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.

Pursuant to Articles 10(a)(vii), 12(1)(e) of the REACH Regulation, a technical dossier for a substance manufactured or imported by the Registrant in quantities of 1000 tonnes or more per year shall contain as a minimum the information specified in Annexes IX and X of the REACH Regulation.

1. Sub-chronic toxicity study (90-day), oral route (Annex IX, 8.6.2.)

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 not provided any study record of a Sub-chronic toxicity study (90-day) in the dossier that would meet the information requirement of Annex IX, Section 8.6.2.

Instead, the Registrant has proposed to adapt the information requirement of Sub-chronic toxicity. The Registrant has justified the proposal for adaptation with a reference Annex XI, section 3.1, according to which testing "...may be omitted, based on exposure scenario(s) developed in the Chemical Safety Report."

ECHA points out that paragraph 3.1. shall be regarded as introduction to paragraph 3.2. that specifies which criteria need to be met by the Registrant in order to adapt the relevant information requirements. In the dossier the Registrant has not justified nor documented that any of the adaptation possibilities indicated in Section 3.2.(a) to (c) of Annex XI of the REACH Regulation applies.

Therefore, since the Registrant has not provided sufficient data to show that (any) one of the criteria given in Annex XI, 3.2 of the REACH Regulation is met, the adaptation of the information requirement suggested by the Registrant cannot be accepted.

Furthermore, the Registrant has justified the proposal for adaptation with a reference to absence of systemic toxicity observed in the acute oral toxicity study, non-significant absorption and low exposure via oral and inhalation route. According to Annex IX, 8.6.2., Column 2, 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 adequately shown 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. It has not been documented that there is "no systemic absorption via relevant routes". On the contrary, according to IUCLID 7.1., the substance is bioavailable.

In his comment the Registrant has proposed to adapt the information requirements and referred to read-across. ECHA points out that pursuant to Annex XI, section 1.5. of the REACH Regulation it is a prerequisite of read-across that there is structural similarity between the source and the target substance of the read-across.
In the updated dossier, the Registrant has provided some relevant data on the read-across substance MnCl2, which is more bioavailable than MnO and Mn. Data on 90-day inhalation toxicity, within a two-generation reproductive toxicity study on manganese chloride has also been provided.

However, a two-generation reproduction toxicity study does not sufficiently cover key parameters of a sub-chronic toxicity study (90-days). Manganese and inorganic manganese compounds are neurotoxic for humans after repeated exposure. An occupational exposure limit (8 h TWA) for manganese and inorganic manganese compounds was derived with 0.2 mg/m3 (inhalable fraction) and 0.05 mg/m3 (respirable fraction) (see SCOEL/SUM/127 June 2011 Recommendation from the Scientific Committee on Occupational Exposure Limits for manganese and inorganic manganese compounds).

From the toxicokinetics and toxicodynamic point of view, there are some supportive elements in the read-across proposed, e.g. since it is likely that MnCl2 is more available and hence potentially more toxic than MnO and Mn, and no difference of the mode of action between the source and the target substance of the read-across is anticipated. Also it is a "worst case" or precautionary approach to use a more bioavailable compound of manganese for the hazard assessment and NOAEL estimation. However, there are toxicological studies, in particular on neurotoxicity of manganese which the Registrant has not included in his update.

Moreover, the registered substance consists of [redacted] % of manganese and manganese oxide and in addition, [redacted]% of silicon dioxide and [redacted]% of aluminum oxide. These two substances have not been considered in the read-across justification and no data on this endpoint has been provided for these substances. There are also small amounts of barium oxide and magnesium oxide in the registered substance. The Registrant has not explained why the presence of the other constituents, in addition to manganese, does not matter for the read-across he proposes. Consequently, there is a concern whether the selection of the source substances of the read-across has been appropriate. Because all the components of the target substances of the read-across have not been covered by the source substance of the read-across, an adequate comparison of the toxicokinetics of the source and target substance of the read-across is missing.

ECHA points out as well that the mechanistic basis, i.e. the read-across hypothesis is missing. Finally, the Registrant did not explain how human health effect of the registered substance (target substance) can be predicted from the reference (source) substances of the group.

Therefore, the proposed adaptation which is only based on read-across from manganese chloride to manganese and manganese oxide is not acceptable. Since the Registrant has not provided sufficient information to show that conditions of an adaptation in Annex XI, 1.5. or Column 2 of Annex IX, 8.6.2 are met, the adaptation of the information requirement suggested by the Registrant cannot be accepted.

Concerning the adequate route of exposure, ECHA finds that manganese chloride which was used in the 90-day study is rather soluble, while inhalation of the slag (which includes manganese) results in rather insoluble particles entering the lungs. This difference is relevant for the local effects. The chloride may rapidly dissolve and be immediately absorbed, whereas the manganese in slag may stay for a long time in the lungs. Moreover, major differences in distribution may occur. The Registrant did not take into account that a relatively large part of the inhaled slag will not reach the alveoli, but will be swallowed after clearance through the mucociliary transport. In the stomach, the acidity may mobilize the Mn. Due to particle size distribution (3.3% < 100 µm) and based on reasoning above, and taking into account the information provided on the uses and human exposure, ECHA considers oral route to be most appropriate in this case.

One Member State proposal for amendment indicates that the read-across (according to Section 1.5. of Annex XI) proposed by the Registrant has not been adequately justified, although according to the proposal for amendment it may have some merits. The Member State proposed ECHA to encourage the Registrant to develop a robust read-across to an appropriate manganese salt.

In their comments to the proposals for amendment, the Registrant has proposed an alternative source substance for the read-across and provided a more robust justification for their read-across approach. Instead of MnCl2 the Registrant proposes to use Slags, silicomanganese as the source substance for the read-across to Slags, ferromanganese. The Registrant has provided data on the composition of these two substances, and shown similarity of the compositions. Both substances contain Silicon, Aluminium, Calcium and Magnesium oxides and Manganese in relatively similar proportions, whereas only FeMn slags contains manganese oxide. Thereby, chemical and structural similarity of the source and target substance has been considered.

The Registrant has also compared the relevant physico-chemical properties of the two substances and documented similarities in e.g. vapour pressure, water solubility, density, partition coefficient and particle size. While the bioavailability of both substances is low, and the Registrant has performed bioaccessibility studies, full comparison of the absorption parameters has not been done and therefore, the Registrant is advised to follow a worst case scenario, especially concerning the systemic uptake of manganese, when predicting the bioaccessibility and toxicity of the target substance of the read-across.

The Registrant has also provided lower tier toxicological data on the source and target substances and shown similarity. It is noted that no repeated dose toxicity studies or reproductive toxicity studies are available, which brings remaining uncertainly to the read-across approach. ECHA notes that the sub-chronic toxicity study on the source substance is on-going. Furthermore, the read-across hypothesis has not been formulated by the Registrant. In ECHA's understanding, the Registrant proposes that the prediction of the toxicity of the target susbtance is based on a worst case scenario, within the one-to-one read-across.

It is recognised that the Registrant has strengthened his read-across justification with the comments made and the documentation made available. Provided that the Registrant

develops his read-across justification further in regard of the evaluation given above, ECHA considers that the read-across may become plausible and therefore, the data on the source substance of the read-across could potentially be used to meet the information requirement for the target substance.

However, in the original dossier submission or in the comments to the draft decision, a justification of the read-across adaptation, based on the above and other adequate and reliable documentation was not provided. As specified in the chapter I "Procedure" above, this decision does not take into account any updates submitted after 4 March 2015.

Therefore, since the Registrant has not provided adequate reasoning to support the fulfilment of the criteria pursuant of an adaptation according to Column 2 of Annex IX, 8.6.2. or according to Annex XI, 1.5, 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 appropriate route of administration, the Registrant agreed in their comment that oral route is used in the sub-chronic toxicity study.

According to the test method EU B.26/OECD 408 the rat is the preferred rodent species. ECHA considers this species as being appropriate.

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 90-day oral toxicity study (test method: EU B.26./OECD 408) in rats.

2. Pre-natal developmental toxicity study (Annex IX, 8.7.2.)

A "Pre-natal developmental toxicity study" for a first species 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 not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex IX, Section 8.7.2. Instead, the Registrant has sought to adapt the information requirement for a prenatal developmental toxicity study. The Registrant has justified the proposal for adaptation with a reference Annex XI, section 3.1, according to which testing "...may be omitted, based on exposure scenario(s) developed in the Chemical Safety Report".

As the Registrant has not demonstrated and documented that strictly controlled conditions indeed apply throughout the whole life cycle (see Section III.1. above), nor provided sufficient information to show that conditions of an adaptation in Column 2 of Annex IX, 8.7 are met, the adaptations suggested by the Registrant are not justified.

The Registrant has sought to adapt the current information requirement on the basis of Annex XI, Section 1.1. governing the use of existing data. The justification of the adaptation given by the Registrant was the low bioavailability of the registered substance in the artificial lung and gastric fluid. Moreover, the Registrant suggest that "Available literature dating back 50 years on human and animal data on reproductive toxicity (all aspects) to inorganic manganese-based compounds (included in the updated dossier) showed equivocal evidence with no specific inhalation nor oral studies on FeMn slag." However,

ECHA notes that the only study record provided is the pre-natal developmental toxicity study made with manganese chloride (Sanchez 1993). Also it remains unclear whether and to what extent the available data can be related to the registered substance, which consists of manganese, manganese oxide and other substances not addressed in the dossier.

In his comment the Registrant has proposed to adapt the information requirements and referred to read-across. ECHA points out that pursuant to Annex XI, 1.5. of the REACH Regulation it is a prerequisite of read-across that there is structural similarity between the source and the target substance of the read-across.

The Registrant has provided in the updated registration some relevant data on a read-across substance MnCl2, which is more bioavailable than MnO and Mn. A "Maternal and developmental toxicity" study on manganese chloride has been provided. From the toxicokinetics and toxicodynamic point of view, there are some supportive elements in the read-across proposed, e.g. since it is likely that MnCl2 is more available and hence potentially more toxic that MnO and Mn, and no difference of the mode of action between the source and the target substance of the read-across is anticipated. Also it is a "worst case" or precautionary approach to use a more bioavailable compound of manganese for the hazard assessment and NOAEL estimation. However, the quality and reliability this study is considered not to be sufficient, since not all relevant parameters and endpoints have been reported, and also because in the IUCLID executive summary the conclusion made ignores several statistically significant developmental toxicity findings simply by referring to maternal toxicity.

ECHA also notes that the pre-natal developmental study was done by subcutaneous injection. The Registrant has not sufficiently justified why that is considered as an appropriate route. Under the REACH Regulation intraperitoneal route is not usually applied, which may compromise the use of that type of test data for the read-across.

Moreover, the registered substance consists of [redacted] % of manganese and manganese oxide and in addition, [redacted]% of silicon dioxide and [redacted]% of aluminium oxide. These two substances have not been considered in the read-across justification and no data on this endpoint has been provided for these substances. There are also small amounts of barium oxide and magnesium oxide in the registered substance. The Registrant has not explained why the presence of the other constituents, in addition to manganese, does not matter for the read-across he proposes. Consequently, there is a concern whether the selection of the source substances of the read-across has been appropriate. Because all the components of the target substances of the read-across have not been covered by the source substance of the read-across, a full comparison of the toxicokinetics of the source and target substance of the read-across is missing.

ECHA points out as well that the mechanistic basis, i.e. the read-across hypothesis is missing. Finally, the Registrant did not explain how human health effect of the registered substance (target substance) can be predicted from the reference (source) substances of the group.

One Member State proposal for amendment indicates that the read-across (according to Section 1.5. of Annex XI) proposed by the Registrant has not been adequately justified, although according to the proposal for amendment it may have some merits. The Member State proposes ECHA to encourage the Registrant to develop a robust read-across to an appropriate manganese salt.

In their comments to the proposals for amendment, the Registrant has proposed an

alternative source substance for the read-across and provided a more robust justification for their read-across approach. Instead of MnCl2, the Registrant proposes to use Slags, silicomanganese as the source substance for the read-across to Slags, ferromanganese. The Registrant has provided data on the composition of these two substances, and shown similarity of the compositions. Both substances contain Silicon, Aluminium, Calcium and Magnesium oxides and Manganese in relatively similar proportions, whereas only FeMn slags contains manganese oxide. Thereby, chemical and structural similarity of the source and target substance has been considered.

The Registrant has also compared the relevant physico-chemical properties of the two substances and documented similarities in e.g. vapour pressure, water solubility, density, partition coefficient and particle size. While the bioavailability of both substances is low, and the Registrant has performed bioaccessibility studies, full comparison of the absorption parameters has not been done and therefore the Registrant is advised to follow worst case scenarios, especially concerning the systemic uptake of manganese, when predicting the bioaccessibility and toxicity of the target substance of the read-across.

The Registrant has also provided lower tier toxicological data on the source and target substances and shown similarity. It is noted that no repeated dose toxicity studies or reproductive toxicity studies are available, which brings remaining uncertainly to the read-across approach. Also the read-across hypothesis has not been formulated by the Registrant. In ECHAs understanding the Registrant proposes that the prediction of the toxicity of the target substance is based on worst case scenarios, within the one-to-one read-across.

It is recognised that the Registrant has strengthened the read-across justification with his comments made and the documentation made available. Provided that the Registrant develops his read-across justification further in regard of the evaluation given above, ECHA considers that the read-across may become plausible and therefore, the data on the source substance of the read-across could potentially be used to meet the information requirement for the target substance.

However, in the original dossier submission or in the comments to the draft decision, a justification of the read-across adaptation, based on the above and other adequate and reliable documentation was not provided. As specified in the chapter I "Procedure" above, this decision does not take into account any updates submitted after 4 March 2015.

Therefore, since the Registrant has not provided adequate reasoning to support the fulfilment of the criteria pursuant of an adaptation according to Column 2 of Annex IX, Section 8.7.2. or according to Annex XI, 1.5, 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 8.7.2.

Concerning the appropriate route of administration, the Registrant agreed in their comment that oral route is used in the pre-natal developmental toxicity study.

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) 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: Pre-natal developmental toxicity study (test method: EU B.31./OECD 414) in rats or rabbits by the oral route.

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 the conditions for these adaptations are not fulfilled, 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 the conditions for these adaptations can be fulfilled, he should update his technical dossier by clearly stating the reasons for adapting the standard information requirement of Annex X, 8.7.2. of the REACH Regulation.

3. Deadline for submitting the required information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 36 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also contained a two-generation reproductive toxicity study (EU B.35, OECD TG 416) or an extended one-generation reproductive toxicity study (EU B.56, OECD TG 443) (Annex X, Section 8.7.3.). As these studies are not addressed in the present decision, ECHA Secretariat considers that a reasonable time period for providing the required information in the form of an updated IUCLID5 dossier is 24 months from the date of the adoption of the decision. The section II of this decision was therefore modified accordingly.

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

Authorised[1] by Guilhem de Seze, Head of Unit, Evaluation

[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.