EUROPEAN CHEMICALS AGENCY

Decision number: TPE-D-0000002436-75-07/F Helsinki, 30 July 2013

DECISION ON A TESTING PROPOSAL SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006

For Silver, CAS No 7440-22-4 (EC No 231-131-3), 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 40(1) of the REACH Regulation, ECHA has examined the following testing proposal submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(e) thereof for Silver, CAS No 7440-22-4 (EC No 231-131-3), by [redacted] (Registrant).

- Long term toxicity to soil macroorganisms: OECD Guideline 222 (Earthworm Reproduction Test, (*Eisenia fetida/Eisenia andrei)*) using the analogue substance Silver nitrate.
- Long term toxicity to terrestrial plants: Test protocol based on ISO 11269-1 (1993), ISO 11269-2 (1995) and OECD guideline 208 using the analogue substance Silver nitrate.
- Toxicity to soil micro-organisms: OECD Guideline 216 (Soil Microorganisms: Nitrogen Transformation Test) using the analogue substance Silver nitrate.

This decision is based on the registration dossier 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 after 18 January 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 decision does not imply that the information provided by the Registrant in his 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.

On 29 February 2012, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposals set out by the Registrant in the registration dossier for the substance mentioned above.

On 19 October 2012 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 14 November 2012 ECHA received comments from the Registrant.

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

On 18 January 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, Competent Authorities of the Member States submitted proposals for amendment to the draft decision.

On 21 February 2013 ECHA notified the Registrant of proposals 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.

ECHA reviewed the proposals for amendment received and amended the draft decision according to one of them.
On 4 March 2013 ECHA referred the draft decision to the Member State Committee.

On 21 March 2013, the Registrant provided comments on the proposed amendments. The Member State Committee took the comments of the Registrant into account.

A unanimous agreement of the Member State Committee on the draft decision was reached on 8 April 2013 in a written procedure launched on 27 March 2013. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Testing required

The Registrant has requested to carry out the required tests using an analogue substance. ECHA emphasises that any final decision on the validity of the read-across, including the grouping approach proposed by the Registrant would be premature at this point in time. The eventual validity of the read-across hypothesis and grouping approach will be reassessed once the requested studies become available. Nevertheless, based on the information already submitted, ECHA considers that the approach proposed by the Registrant is plausible. In addition, ECHA notes that the present decision is taken with the understanding that the analogue test substance, silver nitrate, is proposed by the Registrant to cover the non-nanomaterial form of silver only. In the light of this assessment ECHA has taken the following decision:

The Registrant shall carry out the following proposed tests pursuant to Article 40(3)(a) of the REACH Regulation using the indicated test methods and the analogue substance, Silver nitrate:

1. Long-term toxicity on terrestrial invertebrates (Annex X, 9.4.4.; test method: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*), OECD 222);
2. Effects on soil micro-organisms (Annex IX, 9.4.2.; test method: Soil microorganisms: nitrogen transformation test, EU C.21/OECD 216);
   and
3. Long-term toxicity testing on plants (Annex X, 9.4.6.; test method: Test protocol based on ISO 11269-1 (1993), ISO 11269-2 (1995) and OECD guideline 208);
   or

Long-term toxicity testing on plants (Annex X, 9.4.6.; test method: Terrestrial plants, growth test, OECD 208, with at least six species tested (and as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD 208 guideline)).

Pursuant to Articles 40(4) and 22 of the REACH Regulation, the Registrant shall submit to ECHA by **30 April 2014** an update of the registration dossier containing the information required by this decision.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposals submitted by the Registrant for the registered substance.

In relation to the testing proposals subject to the present decision, the Registrant has proposed to use a read-across and grouping approach, in accordance with Annex XI, 1.5, and to perform the tests on an analogue substance. To the extent that the proposed testing relies upon an identical read-across hypothesis, and that all required tests address endpoints for terrestrial toxicity, ECHA has first considered the scientific validity of the proposed read-across and grouping approach (preliminary considerations), before assessing the testing proposed (Sections 1, 2 and 3, below).

Read-across and grouping approach (preliminary considerations)

Article 13(1) of the REACH Regulation stipulates that information on intrinsic properties of substances may be generated by means other than tests, provided that the conditions set our in Annex XI are met. This includes information from structurally related substances (grouping or read-across).

According to the Registrant, the read-across hypothesis is based on silver (Ag) ion toxicity since the silver ion is "*the species of silver considered to be of greatest toxicity*". Therefore since "*Silver nitrate dissociates readily in aqueous solution to liberate Ag^+ ions*" the Registrant has proposed to test silver nitrate, CAS No 7761-88-8 (EC No 231-853-9), a highly soluble silver substance, on the basis that this substance can be regarded as a worst case for the proposed read across to other less soluble silver substances such as the registered substance.

Although ECHA considers the proposed read-across and grouping approach as plausible, based on the conclusions drawn, a final decision on the validity of the approach will only be possible when the conditions set out in Annex XI are eventually met for each relevant endpoint. As long as the results of the tests proposed by the Registrants are not available, ECHA considers that the read-across and grouping approach, although plausible, is still under development.

ECHA emphasises that it is the Registrants responsibility to amend and substantiate the read-across justification according to Annex XI, 1.5. and to use all relevant available data.

Following the update of the dossier based on the present decision, ECHA will determine whether the documentation provided is sufficient to satisfactorily address the information requirement of Annex X for the registered substance as proposed by the Registrant. If, upon further consideration, the proposed approach does not satisfy the conditions set out in Annex XI, ECHA reserves the right to request the information necessary to fulfil the information requirements.

1. Long-term toxicity on terrestrial invertebrates

a) Examination of the testing proposal

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

Long-term toxicity on terrestrial invertebrates is a standard information requirement as laid down in Annex X, 9.4.4. of the REACH Regulation. Column 2 of section 9.4.4. of Annex X further indicates that this information requirement must be fulfilled unless the chemical safety assessment leads to the conclusion that the test is not needed.

While, information on this endpoint is available (OECD 222) in the registration dossier for an analogue substance (Silver nitrate) the Registrant has concluded that there is a need to perform further testing since:

"The toxicity of silver ion (Ag+) and silver nanoparticles (Ag NPs) in soils is poorly understood at present compared to other metals in soils (e.g. copper, zinc). The silver ion has been found to be toxic to both plants (Wallace et al. 1977) and soil microbial processes (Johansson et al. 1998; Throback et al. 2007). While the Ag+ ion is highly bactericidal and fungicidal, on addition to soil the ion is sorbed to organic matter and clays and its bioavailability is significantly reduced (Hou et al. 2005)."

and

"the amount of information available for Ag is very small and there are no models of soil bioavailability, ageing processes, or leaching factors, and even toxicity data are limited. Data on behaviour of other metals in soil cannot be used to infer reactions for Ag+ due to the different chemistry of Ag+ compared to other metals – for example, Ag+ retention in soil (Kd value) is much harder to predict from soil properties than, for example, Zn as noted in the very recent GEMAS partitioning studies (Janik et al. 2010). Furthermore, Ag+ is affected to a greater extent by complexation reactions in soils than many other metals e.g. chloride in saline soils, which complexes Ag+ and increases mobility – effects on bioavailability in soils are unknown. This project aims to address these knowledge gaps by examining Ag+ ion behaviour across a range of soils, and determine toxicity of Ag+ to key soil microbial processes, plants and soil invertebrates."

Given the properties of the registered substance, ECHA considers that the further testing on different soil types is justified since soil properties can have a pronounced impact on the observed effects. The justifications provided are sufficient to support the testing proposed.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study:

- Long-term toxicity on terrestrial invertebrates (Annex X, 9.4.4.; test method: Earthworm reproduction test (Eisenia fetida/Eisenia andrei), OECD 222).

using the analogue substance, Silver nitrate.

2. Effects on soil micro-organisms

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

Effects on soil micro-organisms is a standard information requirement as laid down in Annex IX, section 9.4.2 of the REACH Regulation. Column 2 of Section 9.4. of Annex IX of REACH specifies that in the absence of toxicity data for soil organisms, the equilibrium partitioning method may be applied to assess the hazard to soil organisms. However, ECHA considers that the intrinsic properties of soil microbial communities are not addressed through the equilibrium partitioning extrapolation method. Thus, the hazard to soil microbial communities needs to be evaluated as a standard information requirement under Annex IX, 9.4.2. Therefore, ECHA concludes that the effects on soil micro-organisms need to be ascertained by performing a relevant test.

The Registrant proposed a nitrogen transformation test (OECD 216). According to ECHA *Guidance on information requirements and chemical safety assessment* (May 2008), Chapter R.7C, R.7.11.3.1. p112, the nitrogen transformation test (OECD 216) is considered sufficient for most non-agrochemicals.

While, information on this endpoint is available (OECD 216) in the registration dossier for an analogue substance (Silver nitrate) the Registrant has concluded that there is a need to perform further testing and has provided justifications as outlined in section III.1. above.

Given the properties of the registered substance, ECHA considers that the further testing on different soil types is justified since soil properties can have a pronounced impact on the observed effects. The justifications provided are sufficient to support the testing proposed.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to carry out the proposed study:

- Effects on soil micro-organisms (Annex IX, 9.4.2.; test method: Soil microorganisms: nitrogen transformation test, EU C.21/OECD 216)

using the analogue substance, Silver nitrate.

3. Long-term toxicity testing on plants

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

Long-term toxicity testing on terrestrial plants is a standard information requirement as laid down in Annex X, section 9.4.6. of the REACH Regulation. Column 2 of section 9.4.4. of Annex X further indicates that this information requirement must be fulfilled unless the chemical safety assessment leads to the conclusion that the test is not needed.

Although information on toxicity testing in plants is available in the registration dossier for the analogue substance, Silver nitrate, ECHA understands that the Registrant proposes to generate data on the long-term toxicity of the substance to plants (Annex X, section 9.4.6.). The OECD 208 test detailed in the registration dossier was carried out using only two different plant species. The OECD test guideline 208 reflects on the need to choose the number of species to be tested depending on relevant regulatory requirements and on the need for a reasonably broad selection of species to account for interspecies sensitivity

distribution. For long-term toxicity testing (Annex X, 9.4.6) ECHA considers six species as the minimum to achieve a reasonably broad selection. Furthermore, long term toxicity testing shall be conducted as a minimum with two monocotyledonous species and four dicotyledonous species from different groups, selected according to the criteria indicated in the OECD 208 guideline. Consequently there is an information gap and it is necessary to generate the data for this endpoint.

Regarding the test method, the Registrant initially proposed a seedling root elongation and seedling growth test protocol based on ISO 11269-1 (1993), ISO 11269-2 (1995) and OECD Test 227 (2000).

However, in formal comments received by ECHA on 14 November 2012 the Registrant clarified that the reference to OECD 227 test guideline was proposed in error and that toxicity testing on plants is proposed to be performed according to OECD guideline 208. Furthermore, the Registrant indicated that a higher tier risk assessment methodology is to be employed.

ECHA notes that the minimum requirement for six plant species in the OECD 208 test, as explained above in this section, to cover the long term testing requirement is based on the assumption that a standard terrestrial risk assessment is to be performed where toxicity data for a limited number of taxonomic groups is to be used. Under such assumptions, it is appropriate to carry out the OECD 208 long-term test on plants using the minimum six plant species. However, if the Registrant intends to use higher tier assessment methodology this implies that a more robust risk assessment will be performed and hence the requirement for six species in the OECD 208 test may not apply. In this instance it may be appropriate to carry out the testing as proposed by the Registrant using a test protocol based on ISO 11269-1 (1993), ISO 11269-2 (1995) and OECD guideline 208.

Therefore, pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is required to perform one of the following studies:

- Long-term toxicity testing on plants (Annex X, 9.4.6.; test method: Test protocol based on ISO 11269-1 (1993), ISO 11269-2 (1995) and OECD guideline 208);

or

- Long-term toxicity testing on plants (Annex X, 9.4.6.; test method: Terrestrial plants, growth test, OECD 208 using at least six species (and as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD 208 guideline))

using the analogue substance, Silver nitrate.

Once the results of the test become available it is the responsibility of the Registrant to assess the use of the test results to fulfil data requirements of the REACH Regulation and the use of the test results in the chemical safety assessment.

If the current OECD 208 data in the registration dossier is to be used to fulfil the long-term toxicity testing on terrestrial plants information requirement in the context of a standard terrestrial risk assessment with toxicity data from three taxonomic groups, a minimum of 4 additional species shall be tested using the same soil type as in the available study. The Registrant shall ensure that a minimum of two monocotyledonous species and four dicotyledonous species from different groups are selected according to the criteria indicated in the OECD 208 guideline.

IV. Adequate identification of the composition of the tested material

The process of evaluation of testing proposals set out in Article 40 of the REACH Regulation aims at ensuring that the new studies meet real information needs. Within this context, the Registrant's dossier was sufficient to confirm the identity of the substance to the extent necessary for evaluation of the testing proposal. The Registrant must note, however, that this information, or the information submitted by other registrants of the same substance, has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the proposed tests, the sample of substance used for the new studies must be suitable for use by all the joint registrants. It is the responsibility of all joint registrants of the same substance to agree to the tests proposed (as applicable to their tonnage level) 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, irrespective of 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 hazards corresponding to these grades.

Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the studies to be assessed.

V. General requirements for the generation of information and Good Laboratory Practice

ECHA reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP).

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

VI. 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 appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the 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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Geert Dancet
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