EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-2114294461-47-01/F Helsinki, 23 March 2015

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

**For tetrasodium (1-hydroxyethylidene)bisphosphonate, CAS No 3794-83-0 (EC No 223-267-7 ), 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 tetrasodium (1-hydroxyethylidene)bisphosphonate, CAS No 3794-83-0 (EC No 223-267-7), submitted by [redacted] (Registrant).

This decision is based on the registration as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more tonnes per year. This decision does not take into account any updates submitted after 24 July 2014, 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 4 June 2013.

On 29 November 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. That draft decision was based on submission number [redacted].

On 13 January 2014 ECHA received comments from the Registrant. On 27 February 2014 the Registrant updated his registration dossier (submission number [redacted]).

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

On 24 July 2014 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.

On 29 August 2014 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 8 September 2014 ECHA referred the draft decision to the Member State Committee.

By 29 September 2014, in accordance to Article 51(5), the Registrant provided comments on the proposal for amendment. The Member State Committee took the comments of the Registrant on the proposal for amendment into account.

A unanimous agreement of the Member State Committee on the draft decision was reached on 13 October 2014 in a written procedure launched on 2 October 2014.

ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

**A. Information in the technical dossier related to the identity of the substance**

Pursuant to Articles 41(1), 41(3), 10(a)(ii) and Annex VI, Section 2 of the REACH Regulation the Registrant shall submit the following information for the registered substance subject to the present decision:

1. Composition of the substance (Annex VI, 2.3): Information which is suitable and necessary to allow ECHA to establish and verify the composition and the identity of the registered substance, as specified under section III.A.1 below.

**B. Information in the technical dossier derived from the application of Annexes VII to XI**

Pursuant to Articles 41(1), 41(3), 10(a)(vi) and/or (vii), 12(1)(e), 13 and Annexes VII to X 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:

2. *In vitro* gene mutation study in bacteria (Annex VII, 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. /OECD 471) using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102, as specified in section III.A.1 below
3. *In vitro* cytogenicity study in mammalian cells (Annex VIII, 8.4.2., test method: EU B.10./OECD 473) or *in vitro* micronucleus study (Annex VIII, 8.4.2., test method: OECD 487);
4. Effects on terrestrial organisms – Long-term toxicity testing on terrestrial invertebrates (Annex X, 9.4.4.; test method: Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*) (test method: OECD 222), or Enchytraeid reproduction test (test method: OECD 220)

**C. Information related to chemical safety assessment and chemical safety report**

Pursuant to Articles 41(1), 41(3), 10(b), 14 and Annex I of the REACH Regulation the Registrant shall submit in the chemical safety report:

1. A revised Predicted no effects level (PNEC) for aquatic toxicity (Annex I, section 3.3.1. of the REACH Regulation) using appropriate assessment factors recommended by ECHA and re-assessment of related risks. Additionally, the study giving rise to the highest concern shall be used to recalculate the PNEC. In the alternative, the Registrant shall provide a full justification why the study giving rise to the highest concern is not used and a justification for why he has not followed ECHA's Guidance recommendations for the assessment factors.

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 **30 March 2016**.

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.

**A. Information in the technical dossier related to the identity of the substance**

Pursuant to Article 10(a)(ii) of the REACH Regulation, the technical dossier shall contain information on the identity of the substance as specified in Annex VI, Section 2 of the REACH Regulation. In accordance with Annex VI, Section 2 the information provided shall be sufficient to enable the identification of the registered substance.

1. Composition of the substance (Annex VI, 2.3)

The substance composition corresponds to the chemical representation of what the substance consists of and is therefore an essential part of substance identification and the cornerstone of all the REACH obligations. ECHA notes that the Registrant has not included sufficient information on the composition of the substance to enable the identity of the registered substance to be verified, as required under Annex VI, Section 2.3. of the REACH Regulation.

Specifically, the Registrant has reported the composition in Section 1.2 of the dossier identifing one main constituent with the same reference substance as in IUCLID section 1.1 "tetrasodium (1-hydroxyethylidene)bisphosphonate" and with a concentration range ≥[redacted]% and ≤[redacted]% w/w. The typical concentration has not been reported. The Registrant has reported, inconsistently, the degree of purity with a concentration range >[redacted]% and <[redacted] % w/w. In addition, the composition of the registered substance includes also an impurity, namely water with a concentration range ≥[redacted]% and ≤[redacted]%.

ECHA considers that the water included in the updated composition is regarded as a solvent. Article 3(1) of the REACH Regulation specifies that a substance shall not include a solvent which may be separated without affecting the stability of the substance or changing its composition.

Although the Registrant indicates in the remark field that "the substance sample analysed for identity cannot be isolated from water", the Registrant has not provide any justification that the substance tetrasodium (1-hydroxyethylidene)bisphosphonate would not be stable in the absence of water. Moreover, on the contrary to the Registrant's remark, the analytical report attached in IUCLID section 1.4 indicates that some of the analytical results (i.e. XRF and IR) have been recorded on the solid sample (after desiccation), while other results (i.e.

acquisition of a H-NMR) have been recorded on the substance dissolved in $D_2O$. In addition, in section 4.1 the Registrant has stated that the substance is a white, odourless, organic solid in powder form and the melting point (>500°C, 1013 mbar) the Registrant has provided in section 4.2 of the IUCLID file indicates that the substance is a solid in powder form.

Therefore, based on the informations included in the dossier ECHA understands that the solvent (water, $H_2O$) can be removed from the substance without affecting its stability.

Therefore, the Registrant is requested to remove water from the composition listed in section 1.2 of the dossier. If a solvent cannot be removed completely, only the minimum amount of solvent necessary for maintaining the substance stability should be included in section 1.2 in the stabiliser section. However in this case the Registrant should provide a robust scientific justification (including evidence) on the stabilising effect of the solvent. It should be noted that any supporting evidence in respect of the role of water as a stabiliser will be assessed for its validity.

If the Registrant considers that the removal of water from the substance will significantly change the composition and nature of the substance, he may report in section 1.2 a composition which excludes water, but where the identity(-ies) and structure(-s) of the constituent(s) is (are) reported as they are present in the aqueous solution and revealed by suitable analytical methods. The concentrations of the constituent(s) can in this case be obtained by back-calculation from the composition of the aqueous solution.

The information provided in the composition shall be sufficient to enable the specific constituents of the substance registered by this legal entity to be identified and shall be consistent with the information included in Section 1.1 on the "name and other identifiers" for the substance. Further technical details on how to report details on the constituents of a substance in IUCLID are available in the "Data Submission Manual – Part 18: How to report the substance identity in IUCLID 5 for registration under REACH".

## B. Information in the technical dossier derived from the application of Annexes VII to XI

Pursuant to Articles 10(a)(vi) and/or (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 Annex X of the REACH Regulation.

1. *In vitro* gene mutation study in bacteria

An "*In vitro* gene mutation study in bacteria" is a standard information requirement as laid down in Annex VII, Section 8.4.1. 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.

According to Article 13(3) of the REACH Regulation, tests required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods recognised by the Commission or ECHA. Other tests may be used if the conditions of Annex XI are met. More specifically, Section 1.1.2 of Annex XI provides that existing data on human health properties from experiments not carried out according to GLP or the test methods referred to in Article 13(3) may be used if the following conditions are met:

(1) Adequacy for the purpose of classification and labelling and/or risk assessment;

(2) Adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3);
(3) Exposure duration comparable to or longer than the corresponding test methods referred to in Article 13(3) if exposure duration is a relevant parameter; and
(4) adequate and reliable documentation of the study is provided.

According to paragraph 13 of the current OECD 471 test guideline (updated 1997) at least five strains of bacteria should be used. These should include four strains of *S. typhimurium* (TA1535; TA1537 or TA97a or TA97; TA98; and TA100) that have been shown to be reliable and reproducibly responsive between laboratories. These four *S. typhimurium* strains have GC base pairs at the primary reversion site and it is known that they may not detect certain oxidising mutagens, cross-linking agents and hydrazines. Such substances may be detected by *E.coli* WP2 strains or *S. typhimurium* TA102 which have an AT base pair at the primary reversion site.

ECHA notes that the Registrant has provided a test from the year 1979 equivalent or similar to OECD 471 and GLP with an assigned reliability score of 2. The test used four different strains of *S. typhimurium* TA [1535, TA 1537, TA 1538, TA 98 and TA 100]. However, since the test was conducted, significant changes have been made to OECD guideline 471 and this means that the study does not meet the current guidelines, nor can it be considered as providing equivalent data according to the criteria in point 2 of Annex XI, Section 1.1.2 of the REACH Regulation. ECHA also points out that another study provided by the Registrant with etidronic acid, equivalent or similar to OECD 471 (Bacterial Reverse Mutation Assay), with an assigned reliability score 4 does not, contrary to point 2 of Annex XI, Section 1.1.2 , use the recommended combination of strains either.

ECHA concludes that a test using *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102 has not been submitted by the Registrant and that the test using one of these strains is required to conclude on *in vitro* gene mutation in bacteria.

Following the draft decision the Registrant agreed to perform the requested study.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, the Registrant is requested to complete following information derived with the registered substance subject to the present decision, identified in accordance with the request in Section II.A., i.e. the registered substance 'in dry state', after removal of water: Bacterial reverse mutation test (test method: EU B.13/14. / OECD 471) using one of the following strains: *E. coli* WP2 uvrA, or *E. coli* WP2 uvrA (pKM101), or *S. typhimurium* TA102.

2. *In vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study

An "*In vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study" is a standard information requirement as laid down in Annex VIII, Section 8.4.2. 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. According to column 2 of Annex VIII, Section 8.4.2, the study does not usually need to be conducted if adequate data from an *in vivo* cytogenicity test are available, or if the substance is known to be carcinogenic category 1A or 1B or germ cell mutagenic category 1A, 1B or 2. The registrant may also seek to adapt the information requirement according the general rules for adaptation laid down in Annex XI to the REACH Regulation, such as existing equivalent data governed by Section 1.1.2, as described under section III.A.1 above.

ECHA notes that for this endpoint in the submission [redacted] on which the initial decision is based, the Registrant has provided an *in vivo* micronucleus assay with (1

hydroxyethylidene)bisphosphonic acid, disodium salt, equivalent or similar to OECD Guideline 474 (Mammalian Erythrocyte Micronucleus Test).

However, ECHA pointed out that the test provided has several deviations, such as: 4 animals per sex per dose; one sample of bone marrow collected at 6h; only 2 doses, whereas the guideline recommends at least 5 animals/sex/dose and 3 doses. Two intraperitoneal doses were administered at 0 and 24 h. According to the guideline if 2 or more treatments at 24 h intervals are done, the samples should be collected once between 18 and 24h following the final treatment for the bone marrow and once between 36 and 48 h following the final treatment for the bone marrow. The Registrant collected only one sample at 6 hours. Therefore, this test was not sufficient to meet the information requirement.

Following the draft decision the Registrant revised the information for this endpoint and in the updated dossier (submission number [redacted]) as well as in their comments, the Registrant built a weight of evidence (WoE) for this endpoint including:

- *"Firstly, reliable (although not Guideline standard) in vivo genotoxicity tests are available in the registration data set. These are a micronucleus study and a reliable rodent dominant lethal assay."*
- *"Secondly, reliable and guideline-standard data on analogous organophosphonate substances and salts were negative for in vitro cytogenicity. In particular, the disodium salt of HEDP (CAS: 7414-83-7) did not induce mutations in an up to date mouse lymphoma thymidine kinase locus assay using the cell line L5178Y in the presence and absence of metabolic activation. This is important for the assessment of chromosomal aberrations because - in case of a positive result - the ratio of small versus large colonies is used to differentiate point mutations from clastogenic effects."*
- *"Thirdly, there are no structural indicators of genetic toxicity in HEDP or analogous organophosphonate substances. None of these organophosphonates has any functional groups that are associated with genetic toxicity"*

As committed by the Registrant in the comments, the dossier was updated with a dominant lethal assay study included in a WoE approach. However, the dominant lethal assay (not a REACH requirement) is less sensitive than the *in vivo* comet assay and micronucleus (MN) tests and it is not appropriate for covering (possible) cytogenetic effects in somatic cells if the result is negative. In addition there is no proving that the tested substance even reached the germ cells.

As a second argument for the WoE, the Registrant argues that *"reliable and guideline-standard data on analogous organophosphonate substances and salts were negative for in vitro cytogenicity"* However, for the *in vitro* cytogenicity endpoint the dossier contains no data but a waver that "According to REACH Annex VIII, column 2, an In vitro cytogenicity study in mammalian cells or in vitro micronucleus study does not need to be conducted if adequate data from an in vivo cytogenicity test are available. With regard to the induction of cytogenicity, information from two in vivo tests (dominant-lethal-assay, Klimisch 2; micronucleus test, Klimisch 4) and from the colony sizing information derived from the mammalian mutagenicity in vitro study (mouse lymphoma assay, Klimisch 1) is available. Furthermore, a combined chronic toxicity / carcinogenicity study performed with the disodium salt of HEDP gave no rise for concern regarding mutagenic / carcinogenic effects." The *in vitro* data refered are in fact from a mammalian mutagenicity *in vitro* study. While it is true that colonies size may be an indicator in case of postive results for a clastogenic effect this test cannot replace the *in vitro* mammalian chromosome aberration test for the *in vitro* cytogenetic endpoint. As mentioned in the evaluation and interpretation of the results from the OECD TG 476 *"Negative results indicate that, the test substance does not induce*

*gene mutations in the cultured mammalian cells used"* but does not suggest a negative results for cytogenetic effects as well. Also the fact that the carcinogenicity data were negative does not exclude that the substance may be genotoxic.

Another argument was that "*there are no structural indicators of genetic toxicity in HEDP or analogous organophosphonate substances* ". The absence of structural alerts does not necessarily mean that the substance does not show toxicity but could mean also that no information could be found in the searched database. In fact the chemical profiling done for this substance with QSAR Toolbox revealed micronucleus alerts by Benigni/Bossa (H-acceptor-path3-H-acceptor).

Consequently, taking into account all the arguments above, the proposed WoE based on the deficient MN *in vivo* test and the rodent dominant lethal assay, negative *in vitro* gene mutation and presumed lack of structural alerts is not sufficient to conclude for the presence or absence of cytogenetic effects as requested by Annex XI 1.2.

As explained above, the information available on this endpoint for the registered substance in the technical dossier does not meet the information requirement within the meaning of section 1.2 of Annex XI to the REACH Regulation. Consequently there is an information gap and it is necessary to provide information for this endpoint. As for the test method, ECHA considers that either OECD 473 or OECD 487 are suitable and appropriate methods to test chromosomal mutations in mammalian cells.

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, identified in accordance with the request in Section II.A., i.e. the registered substance 'in dry state', after removal of water: *In vitro* cytogenicity study in mammalian cells (test method: EU B.10./OECD 473) or *in vitro* mammalian cell micronucleus study (test method: OECD 487).

3. Effects on terrestrial organisms: Long-term toxicity testing on terrestrial invertebrates

"Effects on terrestrial organisms" is a standard information requirement as laid down in Annex X, section 9.4. of the REACH Regulation. Adequate information on effects on long-term toxicity to invertebrates (Annex X, section 9.4.4.) and long-term toxicity to plants (Annex X, section 9.4.6.) needs to be present in the technical dossier for the registered substance to meet the information requirements. According to column 2 of Annex X, section 9.4., these studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely. The registrant may also seek to adapt the information requirement according the general rules for adaptation laid down in Annex XI to the REACH Regulation

ECHA Guidance R.7C provides information on the possibility to implement an integrated testing strategy in the evaluation of terrestrial toxicity. Specifically, Table R.7.11-2 identifies four hazard categories based on the physico-chemical properties and hazard profile for the substance. In the present case, results for the registered substance show evidence of persistence in the environment, thus the substance should be recognized as a Hazard Category 3 or above, according to Table R.7.11-2. Inclusion into a higher Hazard Class is dependent on the evaluation of the toxicity of the substance to aquatic organisms. ECHA Guidance prescribes that for a Hazard Category 3 substance, the Registrant should provide a screening $PNEC_{soil}$, based on EPM calculation, together with a long-term confirmatory study with the most sensitive organism group, as indicated from aquatic toxicity data.

In the original registration dossier, submission number [redacted], the Registrant had waived testing for all terrestrial toxicity endpoints using the following justification:" *In accordance with Column 2 of REACH Annex IX, the effects on terrestrial organisms studies (required in Section 9.4) do not need to be conducted as the chemical safety assessment according to Annex I indicates that this is not necessary.*"

In the CSR the Registrant has also mentioned that "*$PNEC_{soil}$ has been calculated from $PNEC_{aquatic\text{-}freshwater}$ on the basis of the equilibrium partitioning method* [EPM]*; the risk characterization ratio (RCR) based on $PNEC_{soil}$ is <* [redacted]." However, since the Registrant did not apply an appropriate assessment factor when calculating the $PNEC_{aquatic}$ (see Section III. B. 1.), the RCR on which the Registrant bases their justification is inappropriate. In addition to this, the use of EPM should have been duly justified, since the binding mechanism is not related to binding to organic matter but rather to the ability of the substance to bind to inorganic matter. This point was highlighted by the Registrant in relation to the effects observed in algal toxicity studies, whereby '*The phosphonates possess multiple metal-binding capacities, and pH will affect the number of binding sites by altering the ionisation state of the substance. However, the phosphonate ionisation is extensive regardless of the presence of metals*'. Thus, complexation or chelation of essential oligonutrients is expected to also occur in the soil, in preference to binding of the substance to organic matter.

ECHA pointed out in the original draft decision that the data provided by the Registrant (surrogate PNEC based on EPM) is not sufficient to establish the risk associated with a substance belonging to Hazard Category 3 or above. Also, in view of the identified uses for the substance, exposure of the terrestrial compartment cannot be excluded.

For the reasons outlined above, the justification for waiving provided by the Registrant in the original submission (submission number [redacted]) did not meet the criteria of the specific adaptation rules of Column 2 of Annex X, section 9.4, nor the general adaptation rules of Annex XI. Specifically, the Registrant did not demonstrate that direct or indirect exposure of the soil compartment is unlikely. Because exposure cannot be excluded, the Registrant also failed to provide sufficient evidence (i.e. $PNEC_{soil}$ only based on EPM) to demonstrate that risk to the terrestrial compartment is effectively managed. Therefore, the adaptations could not be accepted.

Following ECHA's draft decision, the Registrant has submitted an updated dossier (submission number [redacted]) where they indicated that a test for long term toxicity to earthworms according to OECD 222 will be carried out in the first half of 2014. Nevertheless, given that this test was requested in a compliance check draft decision, the Registrant should wait until the decision becomes final before proceeding. At this stage, no testing proposal submission would be applicable for this endpoint.

As explained above, the information available on this endpoint for the registered substance in the technical dossier does not meet the information requirements. Consequently there is an information gap and it is necessary to provide information for this endpoint.

Due to the fact that the affinity of the substance towards soil is not mediated by lipophilicity, but rather to its ability to chelate inorganic soil components, the study to fulfil the requirements for this endpoint should be preferably on invertebrates such soil ingesting organisms like earthworms (Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*) test method: OECD 222) or enchitraeids (Enchytraeid reproduction test,test method: OECD 220).

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, identified in accordance with the request in Section II.A., i.e. the registered substance 'in dry state', after removal of water:

Earthworm reproduction test (*Eisenia fetida/Eisenia andrei*) (test method: OECD 222).

or

Enchytraeid reproduction test (test method: OECD 220).

The Registrant should also justify the partition coefficient values selected for the calculation of EPM, taking into consideration the fact that binding to inorganic matter in the soil may be more relevant than binding to organic matter and that this may influence the ability to correctly apply the EPM. The Registrant should then apply the revised $PNEC_{aquatic}$ values requested under Section III, B.1 of this decision. The Registrant has failed to provide an adequate justification in their comments and in the subsequent dossier update. Therefore, the obligation remains. The Registrant should refer to ECHA Guidance R.10.5.2 for the provisions relating to the calculation of EPM for binding behaviour not triggered by lipophylicity of the substance but rather by other binding mechasms.

## C. Information related to the chemical safety assessment and chemical safety report

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation the registration shall contain a chemical safety report which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

1. Predicted no effects levels (PNEC) for aquatic toxicity

Pursuant to Annex I, section 3.3.1 and 3.3.2 of the REACH Regulation, based on the available information, the PNEC for each environmental compartment shall be established. According to Annex I, section 3.1.5, when there is more than one study addressing the same effect, the study or studies giving rise to highest concern shall be used to draw a conclusion. The PNEC may be calculated by applying an appropriate assessment factor to the effect values. An assessment factor expresses the difference between effect values derived for a limited number of species from laboratory tests and the PNEC for the environmental sphere. If the study or studies giving rise to the highest concern are not used, this shall be fully justified and included as part of the technical dossier.

According to ECHA's Guidance on information requirements and chemical safety assessment (Version of May 2008), Chapter R.10, section R.10.3.1.2., pages 17 to 20, the recommended assessment factor to apply when calculating PNEC aquatic using only one long-term study is 100.

In the present case, ECHA notes that the Registrant has waived both algae and fish long-term toxicity testing and used *Daphnia* study ([redacted]) to derive the PNEC aquatic with an assessment factor of 50. In their comments to the draft decision, the Registrant stated that "*based on the available data on the other categories (submitted in 2010 and 2013) there is evidence that the metal chelating properties are the predominant feature of the substances. Based on knowledge of the common properties of the substances it proposed that a weight of evidence approach based on all categories is used to more fully justify use of an AF of 50*". However, this justification is not in line with the provision of ECHA guidance, Chapter R.10 and cannot be considered valid. ECHA Guidance states clearly that in the presence of one long term toxicity study, an AF of 100 would be applicable where the test provider refers to the most sensitive species. ECHA observes that the Registrant did

not use the available data from the categories or category members they indicated to provide a PNEC estimation for the category as a whole. The Registrant rather opted for describing general chelation behaviours of the registered substance in order to provide adaptation to the standard method of PNEC derivation. ECHA concludes that, while information on chelating behaviour may be applied when evaluating the need to conduct or not a study, it does not warrant deviation from the provision of Guidance chapter R.10 in relation to PNEC calculations.

ECHA guidance Chapter R.10 gives no provisions for the adaptation of AF based on chelating properties of a substance. Furthermore, table R.10-4 indicates that, '*in the case of long-term results, an AF of 100 applies to cases when only one single long-term study is available, if this was generated for the trophic level showing the lowest L(E)C50 in the short term tests.*'. Therefore, the justification provided by the Registrant is not sufficient to warrant the application of a AF of 50. The Registrant further indicate in their justification for applying an AF of 50 that '*The alternative to apply an assessment factor of 1000 to the effect concentration from a test on acute toxicity (here fish 96h LC50 of 195 mg/L etidronic acid) as mentioned in REACH R.10 is not recommended. This would lead to a PNEC of 0.195 mg/L (etidronic acid) which is higher than the PNEC derived from the NOEC for Daphnia magna. According REACH R.10 the resulting PNEC based on short-term data may not be higher than the PNEC based on the long-term result available. The PNEC has therefore been derived by dividing the (28 d) NOEC of 6.8 mg/L for Daphnia magna by an assessment factor of 50 (REACH R.10)*'. Although the statement of the Registrant is correct in relation to ECHA guidance Table R10-4, this does not preclude the application of AF 100 in this case, which would result in a PNEC of 0.068 mg L.

Therefore, pursuant to 41(1) and (3) of the REACH Regulation, the Registrant is requested to use the appropriate assessment factors to recalculate the PNEC for aquatic in the CSR. In the alternative, the Registrant shall provide a full justification why he has not followed ECHA's Guidance recommendations for the assessment factors.

The Registrant is reminded that according to ECHA Guidance chapter R.7C prescribes that for a Hazard Category 3 substance, the Registrant should provide a screening $PNEC_{soil}$, based on EPM calculation, together with a long-term confirmatory study with the most sensitive organism group, as indicated from aquatic toxicity data. The PNEC for terrestrial toxicity is based on EPM calculation derived from *Daphnia* toxicity studies. Nevertheless, since the Registrant needs to recalculate the PNEC for aquatic toxicity using correct AF of 100, the derived EPM is expected to change and therefore the calculation shall be adjusted accordingly. In addition to this, the Registrant is also reminded that the use of EPM for the registered substance subject to this decision must be fully justified as the binding mechanism is not related to binding to organic matter in the soil, but it is rather related to binding to inorganic soil components.

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted by 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.
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. Furthermore the substance used should not contain any solvent (e.g. water) which may be separated without affecting the stability of the substance or changing its composition.

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://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.

[redacted]
Ofelia Bercaru
Head of Unit, Evaluation