~~Confidential~~

Helsinki, 14 February 2024

Addressee(s)
Registrant(s) of Guanidine Carbonate as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
03 June 2016

Registered substance subject to this decision ("the Substance")
Substance name: Diguanidinium carbonate
EC/List number: 209-813-7

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***19 November 2026***.

Requested information must be generated using the Substance unless otherwise specified.

Information required from all the Registrants subject to Annex VIII of REACH

1. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

2. Adsorption/desorption screening (Annex VIII, Section 9.3.1.; test method: EU C.18/OECD TG 106)

Information required from all the Registrants subject to Annex IX of REACH

3. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: EU C.25/OECD TG 309) at a temperature of 12°C.

4. Identification of degradation products (Annex IX, Section 9.2.3.; test method: EU C.25/OECD TG 309)

The reasons for the request(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You

must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the request(s)
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 for the request(s)

Reasons related to the information under Annex VIII of REACH

1. *In vitro* gene mutation study in mammalian cells

1 An *in vitro* gene mutation study in mammalian cells is an information requirement under Annex VIII, Section 8.4.3., in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

1.1. Triggering of the information requirement

2 Your dossier contains negative results for both an *in vitro* gene mutation study in bacteria and an adequate *in vivo* cytogenicity study.

3 Therefore, the information requirement is triggered.

4 You have not submitted any information for this requirement.

5 Therefore, the information requirement is not fulfilled.

1.2. Your comments to the draft decision

6 In your comments to the draft decision, you indicate your intention to adapt this information requirement using Annex XI, section 1.5. (grouping and read-across approach). You propose to predict the properties of the Substance for *in vitro* gene mutation study in mammalian cells from a source study with the analogue substance guanidine nitrate.

7 You indicate your intention to provide this information in a future update of your registration dossier.

8 The information in your comments is not sufficient for ECHA to make an assessment because you have only provided an intention to adapt without supporting information. You remain responsible for complying with this decision by the set deadline.

1.3. Study design

9 To fulfil the information requirement for the Substance, either the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) or the thymidine kinase gene (OECD TG 490) are considered suitable.

2. Adsorption/ desorption screening

10 Adsorption/desorption screening is an information requirement under Annex VIII to REACH (Section 9.3.1).

2.1. Information provided

11 You have adapted this information requirement by using Column 2 of Annex VIII, Section 9.2.2.1. To support the adaptation, you have provided the following information:

(i) "In accordance with REACH (...) Annex VIII column 2 the Adsorption/desorption screening study (9.3.1.) does not need to be conducted if based on the physicochemical properties the substance can be expected to have a low potential for adsorption (e.g. the substance has a low octanol water partition coefficient), or the substance and its relevant degradation products decompose rapidly. The experimental Log Kow of the submission item is reported to be -1.43 and the one Guanidine is assumed to be ca. -1.63. For the same reason and in accordance with column 2 of REACH Annex IX, the study (…) does not

need to be conducted. In conclusion no study for adsorption/desorption is required and significant mobility in soil is expected."

2.2. Assessment of the information provided

2.2.1. Low potential for adsorption based on physicochemical properties not demonstrated

12 Under Annex VIII, Section 9.3.1, Column 2, first indent, the study may be omitted if the substance can be expected to have a low potential for adsorption (e.g. the substance has a low octanol-water partition coefficient). In order to adapt this information requirement based on low octanol-water partition coefficient (log K_{ow}), lipophilicity must be the sole characteristic driving the adsorption potential of a substance. However, for some groups of substances (e.g. ionisable substances, surfactants) other mechanisms than lipophilicity may drive adsorption.

13 You claim that the Substance has a low octanol-water partition coefficient and has therefore low potential for adsorption/desorption.

14 You have not provided any other evidence or argument that the Substance can be expected to have a low potential for adsorption.

15 In section 4.21 of your dossier you provided the key pKa value of ca. 12.5 and experimental pKb values obtained from OECD TG 112 study (pKb1 = 7.9 and pKb2 = 11.5). In addition, the report attached in section 13.2 of your dossier explains that guanidine is a strong base with pKa 12.5 and carbonate is corresponding base related to the week carbonic acid. Considering this information, in aqueous solution the Substance is completely dissociated.

16 The information in your dossier indicates that the Substance is ionisable.

17 Therefore, other mechanisms than lipophilicity may drive absorption.

18 You have not demonstrated that lipophilicity is the sole characteristic driving adsorption potential and that log K_{ow} is not a valid descriptor for assessing the adsorption potential of the Substance.

19 Based on the above, your adaptation is rejected.

20 Therefore, the information requirement is not fulfilled.

2.3. Your comments to the draft decision

21 Based on your comments to the draft decision we understand that you agree that the information in the registration dossier does not comply with the information requirement for Adsorption/desorption screening. You are, however, disagreeing with the study design as discussed below.

2.4. Study design

22 The OECD TG 106 Batch Equilibrium Method is the appropriate method to study the adsorption of the Substance. This method uses a range of actual soils and so represents a more realistic scenario than the HPLC (OECD TG 121) method. The ionisable properties of the Substance should be considered when selecting the appropriate test design. For ionisable substances, soil types should cover a wide range of pH.

23 In your comments to the draft decision you disagree to perform the study with the OECD TG 106 method. You indicate that the HPLC (OECD TG 121) method should be used instead:

"(…) when utilising a relevant range of pH values in an HPLC test according to OECD 121, obtaining a meaningful range of Koc values can be expected. REACH Annexes VIII and IX,

(…) stipulate that further testing of adsorptive properties is only triggered depending on the results from a study as required according to Annex VIII. The corresponding screening test uses the HPLC method (OECD 121). Therefore, an OECD 106 test should only be performed if no meaningful results can be obtained with the OECD 121 test."

24 For a study to be compliant with the OECD TG 121 (Article 13(3) of REACH), the following specifications must be met:

Applicability domain

a) The method is applicable to substances having a log K_{oc} between 1.5 and 5;

b) The method is not applicable to strong acids and bases.

25 Based on the information provided in your dossier:

a) The Substance has a Koc value of ca. 20 (log K_{oc} of 1.3), HSDB Hazardous Substances Databank, 2008;

b) The Substance is a strong base based on pH = 11.7.

26 On that basis, the Substance is outside of the applicability domain of OECD TG 121.

Reasons related to the information under Annex IX of REACH

3. Simulation testing on ultimate degradation in surface water

27 Simulation testing on ultimate degradation in surface water is an information requirement under Annex IX to REACH (Section 9.2.1.2.).

3.1. Information provided

28 You have adapted information requirement by using Annex XI, Section 1.5. (grouping of substances and read-across approach) based on experimental data from the following substances:

(i) a simulation study on ultimate degradation in surface water from the publication (1987) with the source substance guanidine hydrochloride, EC 200-002-3;

(ii) a simulation study on ultimate degradation in surface water from the publication (1987) with the source substance guanidine nitrate, EC 208-060-1.

3.2. Assessment of the information provided

3.2.1. Read-across adaptation rejected

29 Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

30 Additional information on what is necessary when justifying a read-across approach can be found in the Guidance on IRs and CSA, Chapter R.6. and related documents (RAAF, 2017; RAAF UVCB, 2017).

31 You provide a read-across justification document in IUCLID Section 13.

32 You provide the following reasoning for the prediction of toxicological properties: "*Guanidine carbonate (target chemical) and guanidine monohydrochloride (source chemical) dissociate in aqueous media to yield the Guanidinium kation and the respective anions. Therefore it is reasonable to discuss the effects of the ions separately. The environmental fate of the Guanidinium kation will be independent from accompanying inorganic anions, which cannot be degraded in the environment. Accordingly any data regarding dissolute guanidine salts of whatever inorganic anion may be used for read across*". You provide analogical justification for the source substance used in study (ii), i.e. guanidine nitrate.

33 ECHA understands that your read-across hypothesis is based on the formation of common (bio)transformation products. You predict the properties of your Substance to be quantitatively equal to those of the source substance.

3.2.1.1. Inadequate or unreliable studies on the source substances

34 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that shall normally be performed for a particular information requirement, in this case OECD TG 309. Therefore, the following specifications must be met:

Technical specifications impacting the sensitivity/reliability of the test

a) the purity of the test material is ≥ 95 %;

b) a reference substance known to be easily degraded under aerobic conditions (e.g. aniline or sodium benzoate) is used to verify the activity of the microbial population;

c) the repeatability of the analytical method (including the efficiency of the initial extraction) to quantify the test material and transformation/degradation products is checked by five replicate analyses of the individual extracts of the surface water;

d) the limit of detection (LOD) of the analytical method for the test material and for the transformation/degradation products is ≤ 1% of applied dose;

e) the limit of quantification (LOQ) of the analytical method for the test material and for the transformation/degradation products is ≤ 10% of applied dose;

f) the measurement of degradation and the determination of mass balances are done in at least in duplicate for each concentration and at each sampling time;

g) the surface water used to conduct the test has not been contaminated with the test material or its structural analogues within the previous 4 years;

h) to determine the transformation rates, the test material concentrations must reflect environmentally realistic concentrations and be ≤ 100 µg/L.

i) the lowest test material concentration is ≤ 10 µg/L;

Reporting of the methodology and results

j) the mass balances during and at the end of the study are provided.

35 In the provided study (i) and (ii):

Technical specifications impacting the sensitivity/reliability of the test

a) the purity of the test material was not reported in any of the studies;

b) a reference substance was not used to verify the activity of the microbial population in any of the studies;

c) the repeatability of the analytical method (including the efficiency of the initial extraction) to quantify the test material and transformation/degradation products was checked by three but not checked by five replicate analyses of the individual extracts of the surface water in any of the studies;

d) the LOD of the analytical method for the test material and for the transformation/degradation products was not provided in any of the studies;

e) the LOQ of the analytical method for the test material and for the transformation/degradation products was not provided in any of the studies;

f) the measurement of degradation and the determination of mass balances was not performed in duplicate for each concentration and at each sampling time in any of the studies;

g) in study (i) you report that surface water samples have been obtained from two streams in the vicinity of a nitroguanidine pilot production facility which indicates that the surface water used to conduct the test may have been contaminated with the active substance of the test material or its structural analogues within the previous 4 years and you have not addressed that point;

h) to determine the transformation rates, two of the five test material concentrations applied in study (i) were 1000 and 10000 µg/L and all test material concentrations applied in study (ii) were far above 100 µg/L;

i) in study (ii) the lowest test material concentration was 11000 µg/L and thus > 10 µg/L;

Reporting of the methodology and results

j) the mass balances during and at the end of the study were not determined in any of the studies.

36 Based on the above,

- there are critical methodological deficiencies resulting in the rejection of the study results. More, specifically the surface water used to conduct the test in study (i) was likely contaminated with the test material or its structural analogues within the previous 4 years. The different issues (repeatability, LOD, LOQ, replicates) with the analytical method for both studies do not allow reliable results on the degradation rate of the test material. Furthermore, test material concentrations are too high (two for study i , all for study ii) and do not give realistic and reliable results on the degradation rate of the test material.
- the reporting of both studies is not sufficient to conduct an independent assessment of their reliability.

37 On this basis, the specifications of OECD TG 309 are not met.

38 Based on the above, the study submitted in your adaptation, as currently reported in your dossier, does not provide an adequate and reliable coverage of the key parameter(s) of the corresponding OECD TG.

39 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substances. On this basis, your read-across approach under Annex XI, Section 1.5. is rejected.

40 Therefore, the information requirement is not fulfilled.

3.3. Your comments to the draft decision

41 In your comments to the draft decision you agree with the request.

3.4. Study design

42 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

43 You must perform the test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (Guidance on IRs and CSA, Section R.11.4.1.1.3.).

44 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

45 As specified in Guidance on IRs and CSA, Section R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test material concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Paragraph 52 of the OECD TG 309 provides that the "total recovery (mass balance) at the end of the experiment should be between 90% and 110% for radiolabelled substances, whereas the initial recovery at the beginning of the experiment should be between 70% and 110% for non-labelled substances". NERs contribute towards the total recovery. Therefore, the quantity of the (total) NERs must be accounted for the total recovery (mass balance), when relevant, to achieve the objectives of the OECD TG 309 to derive degradation rate and half-life. The reporting of results must include a scientific justification of the used extraction procedures and solvents.

46 For the persistence assessment by default, total NERs is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NERs may be differentiated and quantified as irreversibly bound or as degraded to biogenic NERs, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website (NER - summary 2019 (europa.eu)).

47 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 309; Guidance on IRs and CSA, Section R.11.4.1.).

4. Identification of degradation products

48 Identification of abiotic and biotic degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).

49 You have not submitted any information for this requirement.

50 Therefore, the information requirement is not fulfilled.

4.1. Your comments to the draft decision

51 In your comments to the draft decision you agree with the request.

4.2. Study design

52 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and

(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

~~Confidential~~

53 Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported. In addition, identified transformation/degradation products must be considered in the CSA including PBT assessment.

54 You must obtain this information from the degradation study requested in request 3.

55 To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (request 3) must be conducted at 12°C and at a test concentration < 100 µg/L. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline, e.g. 20°C) and at higher application rate (i.e. > 100 µg/L).

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2023).
***Guidance on intermediates*;** ECHA (2010).
All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF); ECHA (2017).
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs; ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 22 November 2022.

ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and did not amend the request(s).

The deadline of the decision is set based on standard practice for carrying out OECD TG tests. It has been exceptionally extended by 12 months from the standard deadline granted by ECHA to take into account currently longer lead times in contract research organisations.

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 REACH.

Appendix 3: Addressee(s) of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- the information specified in Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa;
- the information specified in Annexes VII to X to REACH, for registration at more than 1000 tpa.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third-party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1 Test methods, GLP requirements and reporting

(1) Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

(2) Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries (https://echa.europa.eu/practical-guides).

(4) Under the introductory part of Annexes VII/VIII/IX/X to REACH, where a test method offers flexibility in the study design, for example in relation to the choice of dose levels or concentrations, the chosen study design must ensure that the data generated are adequate for hazard identification and risk assessment.

1.2 Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

(1) Selection of the Test material(s)

The Test Material used to generate the new data must be selected taking into account the following:

- the variation in compositions reported by all members of the joint submission,
- the boundary composition(s) of the Substance,
- the impact of each constituent/impurity on the test results for the endpoint to be assessed. For example, if a constituent/impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/impurity.

(2) Information on the Test Material needed in the updated dossier

- You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
- The reported composition must include all constituents of each Test Material and their concentration values.

With that detailed information, ECHA can confirm whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers (https://echa.europa.eu/manuals).