

Helsinki, 1 June 2021

Addressees

Registrant of JS_DADTDG as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision

30/05/2013

Registered substance subject to this decision ("the Substance")

Substance name: Diammonium 2,2'-dithiodiacetate

EC number: 269-323-4

CAS number: 68223-93-8

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 the deadline of **8 June 2022**.

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

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

1. Short-term repeated dose toxicity (28 days; Annex VIII, Section 8.6.1.) to be combined with the Screening for reproductive/developmental toxicity below
2. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method: EU B.64/OECD TG 422) by oral route, in rats

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendix entitled "Reasons to request information required under Annexes VIII of REACH".

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa.

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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.

Authorised¹ under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

¹ As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix on Reasons common to several requests

1. Assessment of your read-across approach under Annex XI, Section 1.5.

You seek to adapt the following standard information requirements by applying (a) read-across approach(es) in accordance with Annex XI, Section 1.5:

- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following appendix.

Grouping of substances and read-across approach

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 (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance² and related documents^{3, 4}.

A. Predictions for toxicological properties

You have provided a read-across justification document in the CSR.

You read-across between the structurally similar substance sodium mercaptoacetate (sodium tioglycolate), EC No. 206-696-4 (CAS No. 367-51-1) as source substance and the Substance (diammonium dithiodiglycolate DADTDG) as target substance.

You have provided the following reasoning for the prediction of toxicological properties: "*The main metabolite of the thioglycolate is the oxidized form which is structural and chemical similar to the anion of DADTDG. Therefore, DADTDG can be considered as co-tested in all mentioned studies under section 7.5 and 7.8.*"

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which is based on the formation of common (bio)transformation products. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

ECHA notes the following shortcoming(s) with regards to prediction(s) of toxicological properties.

² Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals. 2008 (May) ECHA, Helsinki. 134. pp. Available online: https://echa.europa.eu/documents/10162/13632/information_requirements_r6_en.pdf/77f49f81-b76d-40ab-8513-4f3a533b6ac9

³ Read-Across Assessment Framework (RAAF). 2017 (March) ECHA, Helsinki. 60 pp. Available online: [Read-Across Assessment Framework \(https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across\)](https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across)

⁴ Read-across assessment framework (RAAF) - considerations on multi-constituent substances and UVCBs. 2017 (March) ECHA, Helsinki. 40 pp. Available online: <https://doi.org/10.2823/794394>

Supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"⁵. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include toxicokinetic information on the formation of the common compound.

1. Missing information on the formation of common compound

As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and of the source substance(s) to a common compound(s). In this context, information characterising the rate and extent of the hydrolysis of the Substance and of the source substance(s) is necessary to confirm the formation of the proposed common hydrolysis product and to assess the impact of the exposure to the parent compounds.

You have not provided any experimental data or other adequate and reliable information, neither about the dissociation/hydrolysis of your Substance, nor about the association of the source substance. The provided literature reference (██████████ 2009) provides only a qualitative statement about the detection of "dithioglycolate" in rabbit urine after administration of thioglycolic acid.

In the absence of this information and no possibility to assess and conclude on the impact of the formation of common compounds, you have not provided supporting evidence establishing that the proposed common metabolism product is formed as assumed in your read-across hypothesis. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

2. Read-across hypothesis contradicted by existing data

Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances. The ECHA Guidance⁶ indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s). The observation of differences in the toxicological properties between the source substance(s) and the Substance is a warning sign. An explanation for such a difference resulting in a contradiction between the similarities in properties claimed in the read-across hypothesis and the observation of different properties needs to be provided and supported by scientific evidence.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar target and source substances have quantitatively equal properties and effect(s).

⁵ Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

⁶ Guidance on information requirements and chemical safety assessment (version 6.0, July 2017), Chapter R.6, Section R.6.2.2.1.f

The classification for skin sensitisation varies between the source- and target-substance. Specifically, positive results are observed with the source substance (████ 2003) while negative results are reported for an equivalent study conducted with your Substance (████ 2003).

The available set of data on the target and source substances indicates differences in the (eco)toxicological properties of the substances. This contradicts your read-across hypothesis whereby the structurally similar target and source substances have quantitatively equal properties. You have not demonstrated and justified that the properties of the source substance(s) and of the Substance are likely to be similar despite the observation of these differences.

In your comments to the draft decision, you indicate your intention to improve your category approach for "Mercaptocarboxylic acids, their esters and related compounds" by conducting mechanistic assays *in vitro* to address the repeated dose toxicity and reproductive toxicity and pre-natal developmental toxicity endpoints.

With your comments, you have not provided new supporting (experimental) data to support a read-across adaptation.

ECHA notes that mechanistic data may support your read-across hypothesis if they are relevant to the endpoints of interest, but they do not have the same value as bridging studies for the comparison of effects between substances since *in vitro* mechanistic studies may, for instance, not reflect similarities or differences in absorption or metabolism of the substances.

ECHA cannot conclude on the reliability of the read-across approach proposed in the comments because the acceptability will depend on the outcome of the proposed studies and the relevance of the supporting information. Please note that this decision does not take into account updates of the registration dossiers after the date on which you were notified of the draft decision according to Article 50(1) of REACH (see section 5.4. of ECHA's Practical Guide "How to act in Dossier Evaluation").

B. Conclusions on the read-across approach

As explained above, you have not established that relevant properties of the Substance can be predicted from data on the analogue substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

Appendix A: Reasons to request information required under Annex VIII of REACH

1. Short-term repeated dose toxicity (28 days)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII (Section 8.6.1.) to REACH.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.5 (grouping of substances and read-across) of REACH.

In support of your adaptation, you have provided one 90-day repeated dose toxicity study (OECD TG 408) with an analogue substance (2010). In addition you have provided dermal repeated dose toxicity studies with an analogue substance (2003).

As explained in the Appendix on Reasons common to several requests, your adaptation under Annex XI, Section 1.5 is rejected and ECHA cannot conclude on the reliability of the read-across approach proposed in your comments.

Based on the above, the information you provided does not fulfil the information requirement.

Information on study design

Referring to the criteria provided in Annex VIII, Section 8.6.1, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the substance is a solid, not present in particulate form.

REACH Annex VIII, Section 8.6.1. refers to short-term repeated dose toxicity (28 days), which can be tested by the oral route according to the test methods OECD TG 407 or 422. REACH Annex VIII, Section 8.7.1. refers to screening studies for reproductive/ developmental toxicity according to the test methods OECD TG 421 or 422. As pointed out below in section A.2 of this decision, the information provided under Annex VIII, Section 8.7.1. does not fulfil the information requirement for reproductive/developmental toxicity and therefore there is an information gap. To prevent unnecessary animal testing, an OECD TG 422 study is more appropriate to fulfil the information requirements of both Sections 8.6.1. and 8.7.1. of Annex VIII, as it provides initial information on reproductive/developmental toxicity and on short-term repeated dose toxicity.

Therefore the study must be performed according to the OECD TG 422, in rats and with oral administration of the Substance.

2. Screening study for reproductive/developmental toxicity

A Screening for reproductive/developmental toxicity study (test method: EU B.63/OECD TG 421 or EU B.64/OECD TG 422) is a standard information requirement under Annex VIII to REACH (Section 8.7.1), if there is no evidence from analogue substances, QSAR or *in vitro* methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted the standard information requirement mentioned above according to Annex XI, Section 1.5 (grouping of substances and read-across) of REACH.

In support of your adaptation, you have provided two studies (OECD TG 416, 2010 and OECD TG 421, 2010) with an analogue substance.

As explained in the Appendix on Reasons common to several requests, your adaptation under Annex XI, Section 1.5 is rejected and ECHA cannot conclude on the reliability of the read-across approach proposed in your comments.

Based on the above, the information you provided does not fulfil the information requirement.

Information on study design

A study according to the test method EU B.64/OECD TG 422 must be performed in rats with oral⁷ administration of the Substance, as already explained above.

⁷ ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix B: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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 summaries⁸.

B. Test material

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 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 and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers⁹.

⁸ <https://echa.europa.eu/practical-guides>

⁹ <https://echa.europa.eu/manuals>

Appendix C: 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 11 December 2019.

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

ECHA took into account your comments and did not amend the requests and the deadline.

The timeline indicated in the draft decision to provide the information requested is 12 months from the date of the decision.

In your comments to the draft decision, you requested an unspecified extension of the timeline for providing a read-across adaptation, stating the following: *"Our intention is to constantly improve and optimize our strategy in the next years. We would like to further develop a strategy for a Category Approach: Mercaptocarboxylic acids, their esters and related compounds. This is a long and tedious process and we are glad to have the support from our former consultants working with us during the last registration periods. However, we see a risk not to comply with the timelines set in the draft decisions."* You also mention difficulties for small size companies compared to bigger companies large consortia considering their respective resources available.

However, you did not provide any documentation to support your request and did not specify the extra time needed. Furthermore, ECHA observes that the studies you proposed to perform were not requested in the draft decision on the Substance. The present decision does not require you to perform such studies and thereby the imposed deadlines cannot be affected.

On this basis, ECHA has not modified the deadline to provide the information.

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 D: List of references - ECHA Guidance¹⁰ and other supporting documentsEvaluation of available information

Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping

Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)¹¹

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)¹¹

Physical-chemical properties

Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology

Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate

Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment

Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing

Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents¹²

¹⁰ <https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment>

¹¹ <https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across>

¹² <http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm>

Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix E: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[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.