Helsinki, 3 February 2021

Addressees
Registrants of 68-11-1_JS as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
05 October 2018

Registered substance subject to this decision ("the Substance")
Substance name: Mercaptoacetic acid
EC number: 200-677-4
CAS number: 68-11-1

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 November 2022***.

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

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

1. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method: EU C.3./OECD TG 201)

2. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301 B/C/D/F or OECD TG 310)

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

1. Adsorption/ desorption screening (Annex VIII, Section 9.3.1.; test method: OECD TG 106)

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

1. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

2. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

D. Information required from all the Registrants subject to Annex X of REACH

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rabbit) with an analogue substance, ammonium sulfanylacetate (EC 226-540-9) due to reasons explained in Appendix D.

Reasons for the request(s) are explained in the Appendices entitled "Reasons to request

information required under Annexes VII to X of REACH", respectively.

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 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 to X to REACH, for registration at more than 1000 tpa.

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 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.

Authorised[1] 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 A: Reasons to request information required under Annex VII of REACH

1. Growth inhibition study aquatic plants

A growth inhibition study in aquatic plants is a standard information requirement in Annex VII to REACH.

a) Information provided in your dossier on the Substance

You have provided the following studies on the Substance:

i. OECD TG 201; key study; [redacted] (2001)
ii. Non guideline; other information; Castenholz (1977)

b) Supporting read-across adaptation in your dossier

You have also adapted this information requirement according to Annex XI, Section 1.5 (read-across) and you have provided the following study:

iii. OECD TG 201 on on the analogue substance Diammonium Dithiodiglycolate (EC No. 269-323-4); [redacted] (2005).

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 Guidance R.6[2] and related documents[3,4].

You read-across between the structurally similar substance Diammonium dithiodiglycolate or DADTG, EC No. 269-323-4 (CAS No. 68223-93-8) as source substance and the Substance as target substance.

You have provided the following reasoning for the prediction of aquatic toxicity:

- the target and source substance(s) are grouped "*based on similar molecular structure and functionality*";
- the target and source(s) substance have similar physico-chemical properties;
- the target and source(s) substance have similar reactivity:
  - "*At neutral pH* [...] *thioglycolic acid and its salts undergo full dissociation*".
  - "*In aqueous solutions, thioglycolic acid or its salts are rapidly oxidized by air or hydrogen peroxide to produce disulphide and dithiodiglycolic acid*" and "*oxidation of thioglycolate is increased by dilution*";
  - "*thioglycolic acid is altered by self-esterification to give thioglycolides*".

[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)

[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

- the target and source(s) substance have similar ecotoxicity:
  - "*The acute toxicity to fish for thioglycolic acid and ammonium salt have been* [...] *are coherent and demonstrate that acid form and ammonium salt are of similar low toxicity with LC50-96h > 100 mg/L*";
  - "*Based on the overall information available* [...] *the substances can be considered as of low toxicity for aquatic species*".

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.

In your comments on the draft decision, you specify that the study on DADTG "*is not used in a read across approach*" as "[the Substance] *can be totally oxidized in less than four hours (OECD SIDS, 2009 from* [redacted] *2004)* [in] *dithiodiglycolic acid*. The ammonium salt of dithiodiglycolic acid is DADTDG (CAS 68223-93-8, EC 269-323-4). Therefore, DADTDG can be considered as the main oxidizing product of TGA". However, we note that the identity of the Substance and of DADTG is different. As the information submitted relates to two different substances, this information must necessarily be provided as part of an adaptation under Annex XI, Section 1.5 ('Grouping of substances and read-across approach').

c) *Assessment of the information provided in your dossier*

We have assessed this information and identified the following issues:

A. To fulfil this information requirement, a study must provide an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case the OECD TG 201, and follow the requirements of GD 23 (ENV/JM/MONO(2000)6/REV1) if the substance is difficult to test. Therefore, the following conditions must be met:

Key parameter to be measured
- the study must provide information on inhibition of growth, expressed as the logarithmic increase in biomass (average specific growth rate) during the exposure

Validity criteria
- the mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3, for 72-hour tests) in the control cultures is ≤ 35%;

Technical specifications impacting the sensitivity/reliability of the test
- the initial biomass concentration must be compliant with the technical guideline requirements. For *Desmodesmus subspicatus* the initial cell density is 2-5 $x10^3$ cells/mL;
- at least three replicates for controls are included;
- the results of analyses to determine the concentration of the test substance in the test vessels must be provided. Where concentrations do not remain within 80-120 % of nominal, analysis must be conducted at 24 hour intervals on all test concentrations in order to better define loss of the test substance;
- the algal biomass in each flask must be determined at least daily during the test period and reported in a tabular form.

On study (i.) above:
- You report that the mean recovery of the test substance after 72h was 41%. You have not reported, in your registration dossier, the results of test substances

quantification in all test concentrations at 24 hour intervals. However, in your comments on the draft decision, your provided a table showing the results of the analytical verification of exposure for all test concentrations at the beginning and end of the test. Measured concentrations at the beginning of the test showed significant losses of the substances ranging from 50.1% at low concentrations to 6% at high concentrations. At the end of the test, exposure concentrations were below the limit of detection (i.e. 0.01 mg/L) for nominal concentrations at 14.6 mg/L or below. At nominal concentrations of 27.7, 52.6 and 100 mg/L, measured concentrations were determined to be 27%, 2.6% and 82.9% of nominal values at the end of the test, respectively. In your comments, you stated that "*Only 41% of the initial* [measured] *concentration was maintained. However, the concentrations were stable during the rest of the test*". You further explained that you applied a correction factor to all measured value at t=0 to determine concentrations at the end of the test;
- You have not provided, in your registration dossier, biomass data for each flask at each measuring point. However, you have provided this information as part of your comments on the draft decision. This information shows that only duplicate control flasks were included in the study design. Furthermore, the mean coefficient of variation for section-by-section specific growth rates in the control was 47.4%.

On study (ii.) above:
- You specified that the endpoint measured was inhibition of photosynthesis in phytoplankton from hot springs;
- In your comments on the draft decision, you consider that this study should not be used alone to cover this information requirement but that it provides support to the results of the other studies. To justify the relevance of this information your refer to Table R.7.8—3 of ECHA guidance R.7b difficult substance testing issues which states that "*Absorption of light at relevant wavelengths may cause an indirect effect on aquatic plant growth by inhibiting photosynthesis*".

On study (iii.) above:
- You specify the final test was conducted at a single nominal concentration of 100 mg/L (as test material). You indicate that the test material has an active ingredient content of 45.8%. You have not provided information on the presence of impurities and/or co-solvent (if any). In your comments on the draft decision you clarified that the test material was an "*aqueous solution of Diammonium thioglycolate*";
- You have not reported, in your registration dossier, any information on the stability of the exposure to the active substance during the test. In your comments on the draft decision, you provided tables summarising the results of preliminary test to evaluate the stability of the test material under different storage conditions. You also provided tables indicating that a test concentration of 100 mg/L remained stable after 72 hours in culture medium with or wihtout algal cells;
- You report that the study was conducted on *Desmodesmus subspicatus* and that the initial cell density was 10^4 cells per mL. *In your comments on the draft decision, you "acknowledge that the study was conducted* [...] *with a higher initial cell density than indicated in the OECD guideline 201"*. However, as growth in the control exceeded 16-fold by the end of the test you "*conclude that the higher initial cell density has no impact on this test*";
- You have not provided, in your registration dossier, biomass data for each flask at each measuring point. However, you have provided this information as part of your comments on the draft decision. This information shows that the mean coefficient of variation for section-by-section specific growth rates in the control was 36.8%.

For study (i.), based on the additional information provided in your comments on the

draft decision, we note that only duplicate control flasks were included (while it is mandatory to include at least triplicate control flask). Then, the mean coefficient of variation for section-by-section specific growth rates in the control was >35% and this study thereby does not fulfil all validity criteria of OECD TG 201. Furthermore, the information provided in your comments on the draft decision demonstrate that exposure concentrations were highly unstable during the test as:

- the test substance was not detected at nominal concentrations of 14.6 mg/L or below at the end of the test;
- at higher concentrations, recovery was highly variable with only 2.6% recover at 52.6 mg/L nominal while 82.9% recovery was attained at a nominal concentration of 100 mg/L.

On that basis, extrapolating exposure concentrations using a generic correction factor of 41% of measured concentration at the beginning of the test is not considered scientifically valid. Furthermore, considering the poor recovery of the test substance already at t=0, analysis must be conducted at 24 hour intervals on all test concentrations in order to better define loss of the test substance.

For study (ii.), the test was conducted on phytoplankton species from hot springs and the parameter monitored was inhibition of photosynthesis. Therefore, this study does not provide information on inhibition of growth, expressed as the logarithmic increase in biomass (average specific growth rate). Your statement provided as part of your comments on the draft decision with regard to Table R.7.8—3 of ECHA guidance R.7b is irrelevant as the corresponding section of the guidance refers to the testing of coloured substances which may inhibit algal growth through shading.

For study (iii.), the initial cell density was two times higher than the value specified for *Desmodesmus subspicatus* in the OECD TG 201 and this may have impacted the sensitivity of the test. The fact that this higher initial cell concentration was sufficient to allow adequate growth by the end of the test, as specified in your comments on the draft decision, is not addressing the above issue. Finally, based on the additonnal information provided in your comments on the draft decision, the mean coefficient of variation for section-by-section specific growth rates in the control was >35% and this study thereby does not fulfil all validity criteria of OECD TG 201.

Hence, none of the studies from your dossier provides an adequate coverage of the key parameters of the OECD TG 201.

B. According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must provide an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case the OECD TG 201.

You have provided a study by [redacted] (2005) on the analogue substance Diammonium Dithiodiglycolate (EC No. 269-323-4).

However, for the reasons explained under issue A. above, this study does not provide an adequate and reliable coverage of the key parameters addressed in an OECD TG 201 study. Therefore your adaptation your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5 and is rejected.

Therefore the information requirement is not fulfilled.

For the sake of clarity, in his comments on the draft decision, one of the registrants of the Susbtance ([redacted]) acknowledged that further data

based on OECD TG 201 will be produced on members of a group of thiochemicals and will be used to update the read-across grouping approach.

2. Ready biodegradability

Ready biodegradability is a standard information requirement in Annex VII to REACH.

You have adapted the standard information requirement according to Annex XI, Section 1.2. of REACH (weight of evidence). In support of your adaptation, you have provided the following source of information:

a) OECD TG 301D; van Ginkel & Stroo, 1992
b) OECD TG 301A; [redacted], 1994
c) OECD TG 301B/C/D/E and OECD TG 302B/C; Blok *et al.*, 1995
d) EU Method C.4-F; [redacted], 1985
e) OECD TG 302C; CITI, 1992

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

According to ECHA Guidance R.4.4, a weight of evidence adaptation involves an assessment of the relative values/weights of different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance of the information for the given regulatory information requirement. Subsequently, relevance, reliability, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

However, for each relevant information requirement, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption that the Substance has or has not a particular dangerous property.

In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation and identified the following issue with regard to the relevance of the information provided by you.

To fulfil the information requirement, normally a study performed according to OECD TG 301 or 310 must be provided. The key parameter to be investigated in an OECD 301 or 310 study is the the ultimate aerobic biodegradation under low inoculum concentration as measured by parameters such as DOC, CO2 production and oxygen uptake at sufficiently frequent intervals to allow the identification of the beginning and end of biodegradation.

a) Assessment of the relevance of the information provided in support of your adaptation

As explained above, to provide relevant information on biodegradation, a ready biodegradability study must be conducted under low inoculum concentration.

The OECD TG 302B and OECD TG 302C are conducted at an inoculum concentration of 0.2-1.0 dry matter/L and 100 mg/L, respectively. Ready biodegradability tests methodologies

using sewage sludge as an inoculum must always be conducted at an inoculum concentration corresponding to ≤ 30 mg/L suspended solids.

Therefore these technical guidelines are not relevant to study ultimate aerobic biodegradation under low inoculum concentration. Therefore, the OECD TG 302B/C from Blok *et al* (1995) and the OECD TG 302C from CITI (1992) do not provide information that would contribute to the conclusion on the above key parameter.

In your comments on the draft decision, you consider that this information demonstrates that the Substance is "*at least considered as inherently biodegradable*" and that it "*contribute*[s] *to the weight of evidence to support that thioglycolic acid is readily bodegradable*". ECHA has assessed the information from your comments on the draft decision and identified the following issue with regard to its relevance:

ECHA Guidance R.7.9.4.1. specifies that substances that degrade in enhanced biodegradation screening tests, such as tests on inherent biodegradation, must not be considered readily biodegradable (unless ready biodegradability in a standard ready biodegradation test, *i.e.* without enhancements, is shown).

Therefore, information from tests on inherent biodegradation cannot be regarded as relevant to contribute to a weight-of-evidence on ready biodegradability.

b) Assessment of the reliability of the information provided in support of your adaptation

The sources of information (a), (b), the OECD TG 301B/C/D/E in (c) and (d) may provide relevant information on ultimate aerobic biodegradation under low inoculum concentration. However, the reliability of these sources of information is significantly affected by the following deficiency:

To be considered a reliable source of information, a study must provide an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case the OECD TG 301A, B, C, D, E, F or 310. Therefore, the following conditions must be met:

- an appropriate description of the test material must be provided including the degree of purity and the presence of impurities and/or co-solvents;
- the source of the inoculum must be described. It must originate from a predominantly domestic sewage treatment plant and not be adapted to the test substance;
- the test material and inoculum concentrations must be within the range specified in the corresponding test guideline;
- all validity criteria specified in the corresponding test guideline must be fulfilled;
- the variation between the replicates must be less than 20%;
- results of measurements (at sufficiently frequent intervals) must be reported in a tabular form.

You have provided:

a) a study by van Ginkel & Stroo (1992) according to OECD TG 301D on the Substance showing 67% biodegradation (based on O_2 consumption) after 28 days;
b) a study by [redacted] (1994) according to OECD TG 301A on the Substance showing 21% DOC removal after 28 days;
c) a published study by Blok *et al.* (1985) summarizing the results of ring tests for various ready and inherent biodegradability test methods. The tests conducted on thioglycolic acid show biodegradation above the pass criteria (i.e.

> 70% DOC removal at 28 days or > 60% BOD/ThOD or CO_2/TOC at 28 days) in 60% of the Sturm tests (i.e. similar to OECD TG 301B; n=5), 40% of the MITI I tests (i.e. similar to OECD TG 301C; n=10), 13% of the modified OECD tests (i.e. similar to OECD TG 301E; n=16) and 0% of the closed bottle test (i.e. similar to OECD TG 301D; n=7);

d) a ring test by [redacted] (1985) according to modified EU Method C.4-F (MITI I Test with deviations) on the Substance showing an average of 47% biodegradation (based on ThOD) after 28 days. The report states that "*only 5/20 laboratories reached 60%ThOD* [within the 10-day window]*, rising to 8/20 at 28d*".

On the study (a), no information on the composition of the test material used to conduct the studies is provided. The test material concentrations are not reported and therefore it is not possible to verify if the test conditions were adequate. In this study "*Ammonium chloride was omitted from the medium to prevent nitrification*" which may artificially reduce the endogenous respiration in the inoculum blank (*i.e.* one of the validity criteria of the OECD TG 301D). No reporting of the test results is provided and it is not possible to verify if all validity criteria of OECD TG 301D were fulfilled and if the conclusion that the % biodegradation was above the pass criteria is reliable.

In your comments on the draft decision, you consider that the validity criteria of the OECD TG 301D were met as:

- endogeneous respiration at day 28 was 0.4 mg/L and 2.3 mg/L after 200 days, and
- oxygen concentration did not fall below 0.5 mg/L during the test period.

However, as already explained, you have not demonstrated that endogenous respiration would have met the validity criteria of OECD TG 301D if a standard test medium would have been used. Furthermore, your comments do not address the other deficiencies identified above, *i.e.* the lack of information on the test material composition (purity and quantitative information on impurities) and the test material concentration in the test flasks.

On the study (b) the inoculum concentration was 4 x 10^3 cell/mL which is below the acceptable range of 10^4 to 10^5 cell/mL as specified in OECD TG 301 A. Therefore it does not provide a reliable basis to conclude if the Substance is readily biodegradable or not. In your comments on the draft decision, you agreed with the above assessment.

On the studies (c) and (d), the information reported in the original publications lacks critical elements to evaluate the reliability of the reported results. In particular, no information is provided on the composition of the test materials, the origin of the inocula or on the methodology (and methodological differences, if any) used to conduct individual studies. No reporting of the results of these studies is included in the publication and it is not possible to verify if the validity criteria of the corresponding technical guidelines were fulfilled and if the conclusion that the % biodegradation was above the pass criteria in any of these tests is reliable.
In your comments on the draft decision, you agreed with the above assessment. However, you consider that this information "*could be used in a weight of evidence to support that ATG is readily biodegradable*". However, as already explained above, the reliability of this information is affected so significantly that it cannot contribute to weight of evidence to demonstrate that the Substance is readily biodegradable.

Hence, none of the studies from your dossier provides an adequate coverage of the key parameter of the OECD TG 301 or 310.

Finally, in your comments on the draft decision, you refer to a field campaign ([redacted], 2003) where it was found that the Substance readily oxidized (DT50 of 35 min) to "*dithioglycolyc acid*" and that the "*ammonium salt of dithioglycolic acid* [...] *showed 80% biodegradation after 28 days ([redacted], 2005) based on OECD 301B*". You acknowledge however, that oxidation is very slow under acidic pH.

Based on your comments, ECHA understands that you may intend to adapt this information requirement under Annex XI, Section 1.5 as you refer to a study by [redacted] (2005) on Diammonium Dithiodiglycolate (EC No. 269-323-4) which you consider supporting the conclusion that the Substance shall be regarded as readily biodegradable.

ECHA has assessed this study under ongoing compliance checks on the registration dossiers of Potassium mercaptoacetate (EC No. 252-038-4), Ammonium mercaptoacetate (EC No. 226-540-9), Calcium sulphidoacetate (EC No. 249-881-5) and Sodium mercaptoacetate (EC No. 206-696-4). We note the following:

- the substance tested by [redacted] (2005) is a mono-constituent substance and the study results show that it failed to meet the 10d-window criteria. Therefore, this substance is not regarded as readily biodegradable based on the study by [redacted] (2005);
- available information on this study does not allow to verify if the validity criteria of the corresponding test method were met;
- the test substance concentration appears to be below the range of test concentration specified by the test guideline;
- the active ingredient content of the test material is 45.7% and no information is available on the presence of impurities or co-solvents (if any).

Therefore, this study cannot be regarded as a reliable source of information to support that the Substance is readily biodegradable.

In your comments on the draft decision, you also refer to a publication by Rücker et al. (2018, Environ. Sci. Pollut. Res., 25:18393-18411) which you consider supportive of the fact that the Substance is readily biodegradable. The Substance was consistently found as not readily biodegradable based on OECD TG 301D. It was however considered readily biodegradable based on a modified OECD TG 301F test.

In any case, (eco)toxicological studies relied upon to comply with information requirements must comply with GLP or another recognised international standard (Art. 13(4) of REACH). The study you invoke does not. Despite this critical deficiency, we have assessed this information and identified the following issue:

To be considered a reliable source of information, a study must provide an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case the OECD TG 301F. Therefore, the following conditions must be met:

- the concentration of the test material is 100 mg /L, corresponding to 50 to 100 mg ThOD/L;
- the concentration of the inoculum is set to reach a bacterial cell density of 10^7 to 10^8 cells/L in the test vessel;
- the oxygen uptake of the inoculum blank does normally not exceed 20-30 mg O_2/L at the end of the test;
- the test material identity is provided, including information on purity, presence of impurities and compositional information (if applicable);
- the results of measurements at each sampling point in each replicate is reported in a tabular form;

However, in the publication by Rücker et al. (2018):

- the authors indicate deviations from the standard OECD TG 301F test conditions as the test material concentration was 30 mg ThOD/L;
- the inoculum concentrations is reported as 80 mL secondary effluent/L but no information is provided on cell density. Furthermore, no information is reported on the oxygen uptake of the inoculum blank at the end of the test apart from the fact that it was claimed to be < 60 mg O_2/L;
- the test material is described as to be of "technical grade [...] used without purification". No further information is provided;
- no detailed results are provided.

The authors report that a lower test material concentration was used compared to the requirement of OECD TG 301F. Therefore, the test material to inoculum concentration was too favourable and this study may overestimate the percentage biodegradation that would be achieved under standard test conditions. Furthermore, the authors have not provided adequate data to demonstrate that the inoculum density was within an acceptable range (*i.e.*, bacterial cell density estimate and oxygen uptake values in the inoculum blank). Then, this publication does not provide adequate information to demonstrate that the test material is representative for the Substance (ECHA Guidance R.4.1.). Finally, as no detailed reporting of oxygen uptake measurements is available, insufficient information is available to conduct an independent assessment of the study reliability on the interpretation of the results. Therefore, this publication does not meet the information requirement.

As a conclusion, the sources of information from your dossier or your comments on the draft decision in support of your weight-of-evidence adaptation provide information on ultimate aerobic biodegradation. However, for the reasons explained above, these sources of information lack essential elements in order to provide a reliable basis to conclude that the Substance meets the criteria to be considered readily biodegradable.

Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular property foreseen to be investigated in an OECD TG 301 or 310 study. Therefore, your adaptation is rejected and the information requirements is not fulfilled.

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

1. Adsorption/ desorption screening

Adsorption/desorption screening is a standard information requirement in Annex VIII to REACH.

You have adapted this information requirement according Annex VIII, Section 9.3.1., column 2 based on the following justification: "*the study does not need to be conducted because the substance has a low actonol water partition coefficient and the adsorption potential of this substance is related to this parameter*".

You have also adapted this information requirement according to Annex XI, Section 1.3 (QSAR) and you have provided a predicted Log K_{oc} value of 1.44 using KocWin v2.0 (MCI method).

We have assessed this information and identified the following issues:

A. Annex VIII, Section 9.3.1., column 2 specifies that a study does not need to be conducted if the substance can be expected substance to have a low potential for adsorption (e.g. the log K_{ow} is low). To adapt this information requirement based on low 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.

   You have justified the low potential for adsorption because the partition coefficient value (log K_{ow}) was determined to be -2.99 at pH 7 (ionised form) and 1.89 at pH 1.7 (non-ionised form) based on OECD TG 107. You have provided dissociation constant data indicating that the Substance is ionized at environmentally relevant pH.

   However, while anionic substances may be expected to have lower tendency to sorb compared to cationic substances, ionic binding to positively charged soil constituents (e.g. hydrous oxides of aluminium and iron) cannot be excluded. Therefore log K_{ow} is not a valid descriptor for assessing the adsorption potential of the Substance and your adaptation is rejected.

B. ECHA Guidance R.7a, Section R.7.1.15.4 specifies that a measured adsorption coefficient is usually needed for ionising substances, since it is important to have information on pH-dependence. The guidance further clarifies that, if estimation methods are not appropriate (e.g. because the substance is a surfactant or ionisable at environmentally-relevant pH), then a batch equilibrium test may need to be considered at the 10 tonnes per year band, and is essential at the 100 tonnes per year band.

   However, you have not provided any experimental data to determine adsorption/desorption for the Substance. Instead you have provided a QSAR predicted Log K_{oc} value using KocWin v2.0 (MCI method).

   As already explained under issue A. above, the Substance is ionisable. In addition, the QSAR predictions included in your dossier does not provide information on pH-dependence of the adsorption potential of the Substance. Considering the properties of the Substance and the tonnage band of the joint submission, an experimental confirmation of the adsorption potential of the Substance must be provided. Therefore your adaptation according to Annex XI, Section 1.3 is rejected.

In your comments on the draft decision, you agreed that the provided QSAR predicted Log K_{oc} "*was not adapted due to ionisable properties of compounds and was not in application domain*". You now proposed to use the OPERA-model to fulfil this information requirement and you consider that conducting an OECD TG 106 is not needed.

However, as already explained above, unless the QSAR prediction provides reliable information on the pH-dependency of the adsorption/desoprtion potential of the Substance substances, this information will not be regarded as adequate to fulfil this information requirement.

Therefore the information requirement is not fulfilled.

Appendix C: Reasons to request information required under Annex IX of REACH

1. **Long-term toxicity testing on aquatic invertebrates**

   and

2. **Long-term toxicity testing on fish**

Long-term toxicity testing on aquatic invertebrates and Long-term toxicity testing on fish are standard information requirements in Annex IX to REACH.

You have adapted these information requirements according Annex VIII, Section 9.1., column 2 based on the following justification: "*Since the CSA indicates that both freshwater and marine water RCRs are all inferior to 1, no further aquatic toxicity testing is needed*".

We have assessed this information and identified the following issue:

As specified in Annex IX, Section 9.1., Column 2, long-term toxicity to studies on aquatic invertebrates and on fish must be performed unless the Chemical Safety Assessment demonstrates that risks towards the aquatic compartment arising from the use of the Substance are controlled (as per Annex I, section 0.1). The justification must be documented in the Chemical Safety Assessment.

In particular, the Chemical Safety Assessment must take into account the following elements to support that long-term toxicity testing is not required:

- all relevant hazard information from your registration dossier,
- the outcome of the exposure assessment in relation to the uses of the Substance,
- the outcome of the PBT/vPvB assessment including information on relevant degradation products and constituents present in concentration at or above 0.1% (w/w).

To justify why the risks of the substance are controlled you rely on PNEC estimations derived from the results of short term toxicity studies on algae, fish and aquatic invertebrates.

As specified in request A.1, the data on Growth inhibition on aquatic plants is not compliant. Hence your dossier currently does not include adequate information to characterize the hazard property of the Substance.

Without this information your Chemical Safety Assessment does not demonstrate that the risks of the Substance are adequately controlled. As a consequence, your adaptation is rejected as it does not meet the specific rules for adaptation of Annex IX, Section 9.1., Column 2.

Therefore these information requirements are not fulfilled.

In your comments on the draft decision, you specify that you will re-evaluate the need to conduct testing on long-term toxicity to aquatic invertebrates and fish based on the results of the study according to OECD TG 201 requested under Appendix A.1.

According to the integrated testing strategy (ITS) (ECHA Guidance R7b,Section R.7.8.5 including Figure R.7.8-4), the *Daphnia* study is to be conducted first. If based on the results of that study and the application of a relevant assessment factor no risks are observed (PEC/PNEC<1), the long-term fish study may not need to be conducted. However, if a risk is indicated, the long-term fish study needs to be conducted.

Appendix D: Reasons to request information required under Annex X of REACH

1. Pre-natal developmental toxicity study in a second species

Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is a standard information requirement under Annex X to REACH.

In your dossier you have not provided a study with the Substance.

Instead, you have attached an OECD SIDS Initial Assessment Report for Thioglycolic acid and its ammonium salt (SIAM 28) in IUCLID Section 13. As you have not provided additional documentation, we understand that this is your read-across justification document. More specifically, you have adapted this information requirement according to Annex XI, Section 1.5 and you have provided the following studies:

- Studies on a first species (rat)
  - A prenatal developmental toxicity study via oral route in rats with an analogue substance ammonium sulfanylacetate (EC 226-540-9) according to OECD TG 414 and GLP (1998), a key study.
  - A range finding study for a prenatal developmental toxicity study via oral in rats with an analogue substance ammonium sulfanylacetate (EC 226-540-9).
  - A prenatal developmental toxicity study via dermal route in rats with an analogue substance sodium sulfanylacetate (EC 206-696-4) according to OECD TG 414 and GLP (2001), a key study.
- Study on a second species (rabbit)
  - A prenatal developmental toxicity study via dermal route in rabbits with an analogue substance sodium sulfanylacetate (EC 206-696-4) according to OECD TG 414 and GLP (2001), a key study.

We have assessed this information and identified the following issue:

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 Guidance R.6[5] and related documents[6, 7].

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

[5] 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

[6] 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)

[7] 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

You have provided the following reasoning for the prediction of toxicological properties:

- The target and source substances are grouped "*based on similar molecular structure and functionality*"
- The target and source substance have similar physico-chemical properties
- The target and source substances have similar reactivity
  - "*at acidic pH (for example the pH stomach of 1.2), more than 99% of the product will be present as an acidic form*"
  - "*At neutral pH, diluted solutions of thioglycolic acid and its salts undergo full dissociation into the thioglycolate anion (HS-CH2-COO-) and the respective cations (H+, NH4+ or Na+)*"
- The target and source substances have similar toxicity
  - "*The toxicity of each compound is driven by the thioglycolate anion*"
  - "*the effect of the counter-ion (sodium or ammonium) on the systemic toxicity of the thioglycolic salts is not expected to be significant*"
  - "*The acute and repeated dose toxicity of sodium sulphate and ammonium chloride, sulphate and phosphate is moderate, with effective dose levels far higher than those of the thioglycolates.*"

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 shortcomings with regards to the prediction of toxicological properties:

Adequacy and reliability of the selected source studies

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across must:

- be adequate for the purpose of classification and labelling and/or risk assessment;
- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3).

i) Dose level setting in the OECD TG 414 study

In the present case the applicable test method is OECD TG 414. The key parameter(s) of this test guideline include, for instance: that the highest dose level should aim to induce some developmental and/or maternal toxicity

As a PNDT study on a second species, you have provided a study conducted on rabbits with an analogue substance sodium sulfanylacetate (EC 206-696-4) according to the test guideline OECD TG 414 (Prenatal Developmental Toxicity Study) via dermal route.

However, no maternal toxicity was seen at the highest dose of 65 mg/kg bw/d in this study. In the published study (Tyl et al. 2003, https://onlinelibrary.wiley.com/doi/pdf/10.1002/bdrb.10001) of the report provided in the dossier, the authors stated: "*There was no effect of treatment in rabbits in maternal body weight, weight changes during gestation, or feed consumption. Thus, there was no evidence of maternal systemic toxicity.*"

ii) Appropriateness of the Dermal route of exposure

ECHA Guidance (Chapter R.7a: Endpoint specific guidance Version 6.0 – July 2017) specifies that "*According to the test methods for reproductive toxicity which focus on the detection of reproductive hazards, the oral route (gavage, in diet, or in drinking water) is the "default" route, except for gases.*" and provides the following conditions related to the testing via the dermal route for reproductive toxicity:

- "*In reproductive toxicity studies local irritating effects at the site of administration may not allow investigating the reproductive toxicity in relation to systemic toxicity. In addition the irritation may affect the behaviour of the animals confounding the interpretation. Therefore, testing of corrosive or highly irritating substances at dose levels causing corrosivity or irritation must be avoided as far as possible (see REACH Annex VII-X preamble).*"
- "*Testing via dermal route might be necessary under specific circumstances, for example for substances with high dermal penetration and indications for a specific toxicity following dermal absorption.*"

In the published study (Tyl et al. 2003, https://onlinelibrary.wiley.com/doi/pdf/10.1002/bdrb.10001) of the report provided in the dossier, the authors also explain that the top dose of 65 mg/kg/day was based both on epidermal reactions at the dosing site and maternal mortality at higher doses (in the dose-range finding study) and therefore the exposure was limited by the local effects.

In your comments on the draft decision, you provide information indicating that the dermal absorption of mercaptoacetic salts is significant and can reach at least 40%.

However, for this substance there are no indications of higher absorption via the dermal route, nor of a specific toxicity related to this route. Therefore, there is no substance specific justification for choosing the dermal route.

In your comments on the draft decision, you consider that the developmental toxicity study in rabbits by dermal route with sodium mercaptoacetate is reliable to fulfil the standard information requirement under Annex X to REACH, because:

- The top dose level was selected on the basis of a reliable range finding study and in the respect of the recommendations of the OECD TG 414 and the animal welfare considerations.
- The systemic exposure was clearly demonstrated in the range finding study and in a dermal penetration study performed at the same top dose level (65 mg/kg/day).
- This study was already evaluated and accepted by different regulatory bodies.

ECHA does not question the reliability of the range finding study and the systemic exposure via dermal route. However, the highest dose of 65 mg/kg bw/d in the provided PNDT study via dermal route in rabbits did not cause any systemic maternal toxicity. Based on the reasons already explained above under "*Dose level setting in the OECD TG 414 study*" and "*Appropriateness of the Dermal route of exposure*" the provided study is not adequate as it does not fulfil the requirements of OECD TG 414 and the dermal route is not the most appropriate route of administration for the analogue substance sodium sulfanylacetate.

With reference to your comment regarding different European, international and national expert committees concluding that the study is acceptable, ECHA notes that these opinions have been drawn for purposes other than the REACH Regulation. The purpose of the

compliance check procedure is for ECHA to ensure that the information present in the dossier complies with specific information requirements (Annex X, Section 8.7.2.). In that context, it is possible that other institutions/committees and ECHA may draw different conclusions when pursuing the different purposes assigned to them by different legislations.

In conclusion, the provided dermal study failed to induce systemic maternal toxicity and the testing via the dermal route was limited by the local effects and it is not the most appropriate route of administration.

In your comments to the draft decision you also indicate your intention to improve the category/read-across approach for the TGA family. However, as indicated above, the study with the source substance does not provide an adequate and reliable coverage of the key parameters addressed in the OECD TG 414. Therefore, the read-across adaptation is not valid.

Finally, in your comments on the draft decision you also state that "*The primary effect of this group of chemicals is the inhibition of the ß-oxidation of fatty acids. The observed effects in systemic toxicity as well as in reproductive toxicity are secondary nature and classification and labelling regarding STOT RE or reproductive toxicity can be omitted. Based on that, we conclude that new animal tests will always repeat the already observed effects. Instead of testing again and again and wasting of lot of animals we evaluate the possibility to confirm the Mode-of-Action.*"

ECHA notes that the PNDT study in a second species according to OECD TG 414 is a standard information requirement under Annex X Section 8.7.2. to REACH, as indicated above. This second PNDT study is additional to that required in column 1 of Annex IX Section 8.7.2. Your comment on the repetition of the already observed effects does not qualify as an adaptation according to Section 8.7. (Column 2) of Annex X or general rules of adaptation under Annex XI to REACH Regulation. It therefore cannot enable an adaptation of the information requirement.

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

Information on study design

The test in the first species was carried out by using a rodent species (rat). A PNDT study according to the test method OECD TG 414 must be performed in rabbit as preferred non-rodent species.

The Substance is corrosive and it has harmonized classification as Skin Corr 1B (H314). You have self-classified it as Skin Corr 1A (H314). Testing of corrosive or highly irritating substances may have limited value and must be avoided as indicated above. Ammonium sulfanylacetate (EC 226-540-9), which has been tested in a PNDT study on the first species (rat), could be an alternative as a test material as its corrosivity/irritation potential is lower compared to the Substance. Based on the available acute dermal irritation/corrosion study according to OECD TG 404, ammonium sulfanylacetate causes only slight irritation. Therefore, it should provide adequate data for the purpose of classification labelling and/or risk assessment.

The study shall be performed with oral[8] administration of the analogue substance ammonium sulfanylacetate (EC 226-540-9).

[8] ECHA Guidance R.7a, Section R.7.6.2.3.2.

Appendix E: 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 summaries[9].

B. 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 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 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[10].

[9] https://echa.europa.eu/practical-guides
[10] https://echa.europa.eu/manuals

Appendix F: General recommendations when conducting and reporting new tests for REACH purposes

A. Aquatic toxicity testing of difficult to test substances

Due to the rapid oxidation and potential for high adsorption, you need to consult the OECD Guidance Document (GD) 23 and ECHA Guidance, Chapter R7b, Table R.7.8-3 relating to the aquatic toxicity testing of difficult substances, so that you choose the most appropriate design of the requested ecotoxicity test(s) and you best calculate and report the results of the test(s).

Appendix G: 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 03 July 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 or the deadline.

In his comments on the draft decision, one of the registrants of the Substance ([redacted]) requested an extension of the deadline in order to improve the read-across approach. To justify this, he refers to his SME status and notes that read-across/grouping and waiving approaches are complex and therefore require time to be developed.

In the comments there is no indication of any issues (including laboratory capacity) related to the performance of the studies requested in this decision. Therefore, the arguments provided above do not justify your request and ECHA has not modified the deadline of the decision.

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 H: List of references - ECHA Guidance[11] and other supporting documents

Evaluation 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)[12]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[12]

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 documents[13]

[11] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[12] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[13] 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 I: 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]
[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.