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Helsinki, 19 October 2022

Addressees
Registrant(s) of JS_FAS_EC_217-157-8 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
15/02/2018

Registered substance subject to this decision ("the Substance")
Substance name: Aminoiminomethanesulphinic acid
EC/List number: 217-157-8

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 ***26 January 2026***.

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

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: EU C.4. B/D/E/F/OECD TG 301B/C/D/F or EU C.29./OECD TG 310)

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

3. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

4. Depending on the outcome of the study performed according to request 3:
    - In case of negative results:
      Transgenic rodent somatic and germ cell gene mutation assay (Annex VII, Section 8.4., Column 2; test method: OECD TG 488) in transgenic mice or rats, oral route on the following tissues: liver and glandular stomach; duodenum must be harvested and stored for up to 5 years. Duodenum must be analysed if the results of the glandular stomach and of the liver are negative or inconclusive.

      OR

      In vivo mammalian alkaline comet assay (Annex VII, Section 8.4., Column 2; test method: EU B.62./OECD TG 489) in rats, or if justified, in other rodent species, oral route, on the following tissues: liver, glandular stomach and duodenum;

- In case of positive results:
  In vivo mammalian alkaline comet assay (test method: OECD TG 489) combined with in vivo mammalian erythrocyte micronucleus test (test method: OECD TG 474) in rats, or if justified, in mice, oral route. For the comet assay the following tissues shall be analysed: liver, glandular stomach and duodenum.

5. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days) requested below (Annex VIII, Section 8.6.1.)

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

6. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats.

7. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

8. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: EU C.47./OECD TG 210)

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

9. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) by oral route, in a second species (rat or rabbit)

The reasons for the decision(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.

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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 decision
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 decision

Contents

0. Reasons common to several requests

0.1. Assessment of the read-across approach

1 You have provided experimental data on 1-(dioxidosulfanylidene)methanediamine, EC 224-065-1 for the following standard information requirements:

- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)

2 While you have not identified this information as a read-across approach, the test material used is different than the Substance. Therefore, the studies conducted with this substance (hereafter referred to as the "source substance") will be evaluated as a read-across adaptation under Annex XI, Section 1.5 of REACH.

3 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 sections.

4 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.

5 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).

0.1.1. Absence of read-across documentation

6 Annex XI, Section 1.5 requires that whenever read-across is used adequate and reliable documentation of the applied method must be provided. Such documentation must include a an explanation why the properties of the Substance may be predicted from information on the source substance(s).

7 You have provided robust study summaries for studies conducted with another substance than the Substance in order to comply with the REACH information requirements. However, you have not provided documentation as to why this information is relevant for the Substance and thus why the properties of the Substance may be predicted from information on the source substance.

8 In the absence of such documentation, the properties of the Substance cannot be reliably predicted from the data on the source substance.

0.1.2. Conclusion on the read-across approach

9 For the reasons above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Your read-across approach under Annex XI, Section 1.5. is rejected.

Reasons related to the information under Annex VII of REACH

1. Growth inhibition study aquatic plants

10 Growth inhibition study on aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

1.1. Information provided

11 You have provided the following information on the Substance:

i. a study according to OECD TG 201 (1999)
ii. a study according to OECD TG 201 (1992)

1.2. Assessment of the information provided

1.2.1. The provided studies do not meet the information requirement

12 To fulfil the information requirement, a study must comply with OECD TG 201 (Article 13(3) of REACH). Therefore, the following specifications must be met:

13 Reporting of the methodology and results

a) the test design is reported (*e.g.*, number of replicates, number of test concentrations and geometric progression used);
b) the test conditions are reported (*e.g.*, composition of the test medium, test temperature, test species, biomass density at the beginning of the test);
c) the results of algal biomass determined in each flask at least daily during the test period are reported in a tabular form;

14 Your registration dossier provides OECD TG 201 studies showing the following:

15 Reporting of the methodology and results

a) no information on the test design is provided for study ii;
b) no information on the test conditions is provided for study ii;
c) tabulated data on the algal biomass determined daily for each treatment group and control are not reported for studies i. and ii.

16 Based on the above, the reporting of the above studies is not sufficient to conduct an independent assessment of their reliability. In the absence of adequate reporting of the results obtained in studies i. and ii., it is not possible to conduct an indepent assessment of whether the validity criteria were met and of the interpretation of the results.Furthermore, it is currently not possible to verify whether the study design and test conditions comply with the requirements of the OECD TG 201 for study ii. Therefore, the requirements of OECD TG 201 are not met by any of the above studies.

17 On this basis, the information requirement is not fulfilled.

2. Ready biodegradability

18 Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

2.1. Information provided

19 You have provided the following information on the Substance:

i. a ready biodegradability study according to OECD TG 301C (1991)
ii. a BOD5 study (1989)
iii. a chemical oxygen demand study according to EU Method C.6 (1988)

20 The study iii. above does not provide any information on ultimate aerobic biodegradation of the test material under low inoculum concentration as required by the relevant test methods referred to under Article 13(3) to REACH. Therefore, this information is not assessed further.

2.2. Assessment of information provided

2.2.1. Study i. does not meet the information requirement

21 To fulfil the information requirement, a study must comply with the OECD TG 301 or 310 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301, the following requirements must be met:

22 Reporting of the methodology and results

a) the concentration of the inoculum (in mg Suspended Solid/L and cells/mL) in the test and any pre-conditioning treatment are reported;
b) the results of measurements at each sampling point in each replicate is reported in a tabular form.

23 Your registration dossier provides an OECD TG 301C study showing the following:

24 Reporting of the methodology and results

a) While you have specified the concentration of the inoculum in mg suspended solid/L you have provided no information on bacterial cell density in cells/mL. You also have not specified whether or not the incolum was adapted to the test material prior to conducting the test;
b) the results of measurements at each sampling point in each replicate are not reported.

25 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. In particular, in the absence of adequate information on the bacterial density in the test and on potential pre-adaptation, ECHA cannot verify that the conditions of the test guideline were met. High inoculum density and pre-adaptation may artificially increase the % biodegradation determined in the test. Then, in the absence of adequate reporting of the study results ECHA cannot conduct an independent assessment of whether the validity criteria of the test guideline were met and of the interpretation of the study results.

26 Therefore, the requirements of OECD 301C are not met.

2.2.2. Study ii. is not reliable

27 A specified in ECHA Guidance on IRs and CSA, Section 7.9.5.1., information on the 5-day biochemical oxygen demand (BOD5) can be used when no other degradability data are available. According to Article 13(3) of REACH the study must comply with the requirements of with the EU Method C.5 and the following requirements must be met:

a) the biochemical oxygen demand must be a mean of at least three valid measurements;
b) the use of an additive to inhibit biological nitrification must be reported.

28 You have provided a study according to NEN 3235 sect. 5.4 showing the following:

a) in Table 1, you report a single measurement of biological oxygen demand after the incubation period of five day for each of the tested concentrations (i.e., 2 and 10 mg/L);
b) you state that "*The theoretical oxygen demand (ThOD) was calculated to be 0.296 mg O2/mg test substance using the formula CH4N2SO2 with elimination of nitrogen as NH3*". However, you have not specified whether an additive to inhibit biological nitrification has been used.

29 Based on the above, the reporting of the study is not sufficient to conduct an independent assessment of its reliability. More specifically,

- it is not possible to verify whether the reported % biodegradation is based on triplicate measurements as required by the test guideline;
- in the absence of information on whether an inhibitor of nitrification was used, ECHA is not in a position to conduct an independent assessment of the interpretation of the study results. ECHA notes that currently, the reported % biodegradation do not take into account oxygen consumption originating from nitrification.

30 On this basis, the information requirement is not fulfilled.

Reasons related to the information under Annex VIII of REACH

3. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

31 An in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study is an information requirement under Annex VIII, Section 8.4.2..

3.1. Information provided

32 You have adapted this information requirement by using a Grouping of substances and read-across approach based on experimental data from the following substances:

i. an *in vitro* chromosomal aberration study (1990) with the analogue substance, EC 224-065-1.

3.2. Assessment of the information provided

3.2.1. Read-across adaptation rejected

33 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. In addition, ECHA identified endpoint specific issue addressed below.

3.2.2. Source study not adequate for the information requirement

34 Under Annex XI, Section 1.5., the study to be read across must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 473. Therefore, the following specifications must be met:

a) at least 3 concentrations are evaluated, in absence and in presence of metabolic activation;
b) the maximum concentration tested induces 55+5% of cytotoxicity compared to the negative control, or the precipitation of the tested substance;
c) the positive controls induce responses compatible with those generated in the historical positive control database;
d) the negative control data is ideally within the 95% control limits of the distribution of the laboratory's historical negative control database;
e) data on the cytotoxicity and the frequency of cells with structural chromosomal aberration(s) for the treated and control cultures is reported.

35 In study (i) described as an in vitro chromosomal aberration study:

a) 2 concentrations (i.e., less than 3 concentrations) were evaluated in the condition with exposure period 6h, fixation time 24 h, and in presence of metabolic activation;
b) the maximum tested concentration (as well as the immediately lower concentration) induced a mitotic index well below the acceptable value of 55+5% compared to the negative control;
c) the historical positive control database was not provided;
d) the historical negative control range of the laboratory was not provided;
e) data on the cytotoxicity for the treated and control cultures were not reported for

all tested concentrations.

36 Based on the above, the study (i) does not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 473 and this study is not an adequate basis for your read-across predictions.

37 Therefore, the information requirement is not fulfilled.

3.3. Specification of the study design

To fulfil the information requirement for the Substance, either *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

4. In vivo genetic toxicity study

38 Under Annex VII Section 8.4., Column 2, further mutagenicity studies must be considered in case of a positive result in an in vitro gene mutation study in bacteria.

4.1. Triggering of the information requirement

39 Your dossier contains positive results for the in vitro gene mutation study in bacteria which raise the concern for gene mutation.

40 Therefore, the information requirement is triggered.

4.2. Information provided

41 You have provided:

i. an *in vivo* micronucleus test (1989) on the Substance;
ii. an *in vivo* micronucleus test (1994) on the Substance;
iii. an *in vivo* micronucleus test (1995, 82 033 DKM) on the Substance;
iv. an *in vivo* micronucleus test (1995, 95-0048-DGM) on the Substance.

4.3. Assessment of the information provided

4.3.1. Study not adequate for the information requirement

42 In order to be appropriate, according to the Guidance on IRs and CSA, Section R.7.7.6.3., the in vivo somatic cell genotoxicity study must address the specific concern raised by the in vitro positive result.

43 However, the in vivo studies provided are not addressing the gene mutation concern raised by the in vitro data. Therefore, the provided in vivo tests are not appropriate.

44 ECHA considers that an appropriate in vivo follow up mutagenicity study is necessary to address the concern identified in vitro.

4.4. Test selection

45 According to the Guidance on IRs & CSA, Section R.7.7.6.3, either the in vivo mammalian alkaline comet assay ("comet assay", OECD TG 489) or the transgenic rodent somatic and germ cell gene mutation assay ("TGR assay", OECD TG 488) are generally suitable to follow up a positive in vitro result on gene mutation.

46 However, as explained under Request 3, there is no adequate information from an in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study with the Substance in the dossier. Therefore, the information requirement of Annex VIII, Section 8.4.2. is not fulfilled and ECHA also requests an in vitro cytogenicity study or an in vitro micronucleus study (request 3). The results of the study performed according to request 3 may raise – in addition to the concern on gene mutation – as well a concern for chromosomal aberration in case of positive results.

47 In case the results of the study performed according to request 3 raises a concern for chromosomal aberration, the in vivo mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) and the in vivo mammalian alkaline comet assay ("comet assay", OECD TG 489) can be combined in a single study (see OECD TG 474 paragraph 37c; OECD TG 489 paragraph 33; Guidance on IRs & CSA, Section R.7.7.6.3). While the MN test can detect both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the comet assay can detect primary DNA damage that may lead to gene mutations and/or structural chromosomal aberrations. A combined study will thus address both the identified concerns for chromosomal aberration as well as gene mutation.

48 The combined study, together with the results of the in vitro mutagenicity studies, can be used to make definitive conclusions about the mechanism(s) inducing in vivo mutagenicity and lack thereof. Furthermore, the combined study can help reduce the number of tests performed and the number of animals used while addressing (structural and numerical) chromosomal aberrations as well as gene mutations.

49 Therefore, you must wait for the results of the in vitro test requested under request 3 and, depending on these results, you must conduct either (a) a comet assay or a TGR, if the test results of request 3 are negative, or (b) a comet assay combined with a MN test if the test results of request 3 are positive. The deadline set in this decision allows for sequential testing.

4.5. Specification of the study design

4.5.1. Comet assay or TGR assay (if the test results of request 3 is negative)

4.5.1.1. Comet assay

50 In case you decide to perform the comet assay, according to the test method OECD TG 489, rats are the preferred species. Other rodent species can be used if scientifically justified (OECD TG 489, paragraph 23).

51 Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

52 In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

4.5.1.1.1. Germ cells

53 You may consider collecting the male gonadal cells from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2

months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

4.5.1.2. TGR assay

54 In case you decide to perform the TGR assay, according to the test method OECD TG 488, the test must be performed in transgenic mice or rats.

55 Also, according to the test method OECD TG 488, the test substance is usually administered orally.

56 Based on OECD TG 488 (2020), you are requested to follow the 28+28d regimen, as it permits the testing of mutations in somatic tissues and as well as in tubule germ cells from the same animals.

57 According to the test method OECD TG 488, the test must be performed by analysing tissues from liver as slowly proliferating tissue and primary site of xenobiotic metabolism, from glandular stomach and duodenum as rapidly proliferating tissue and site of direct contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for mutagenicity at the site of contact in the gastro-intestinal tract. However, duodenum must be stored (at or below −70 ºC) until the analysis of liver and glandular stomach is completed; the duodenum must then be analysed only if the results obtained for the glandular stomach and for the liver are negative or inconclusive.

4.5.1.2.1. Germ cells

58 You may consider collecting the male germ cells (from the seminiferous tubules) at the same time as the other tissues, to limit additional animal testing. According to the OECD 488, the tissues (or tissue homogenates) can be stored under specific conditions and used for DNA isolation for up to 5 years (at or below −70 ºC). This duration is sufficient to allow you or ECHA to decide on the need for assessment of mutation frequency in the collected germ cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

4.5.2. Comet assay combined with MN test (if the test results of request 3 are positive)

59 In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

60 The combination of the OECD TGs 489 and 474 should not impair the validity of and the results from each individual study. Careful consideration should be given to the dosing, and tissue sampling for the comet analysis alongside the requirements of tissue sampling for

the mammalian erythrocyte micronucleus test (see OECD TG 489, e.g. Bowen et al. 2011 [1]).

4.5.2.1. Germ cells

61 You may consider collecting the male gonadal cells from the seminiferous tubules in addition to the other aforementioned tissues in the comet assay, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells in the comet assay, you should consider analysing the slides prepared with gonadal cells.

62 This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

[1] Bowen DE et al. (2011) Evaluation of a multi-endpoint assay in rats, combining the bone-marrow micronucleus test, the comet assay and the flow-cytometric peripheral blood micronucleus test. *Muta Res.*;722:7–19.

5. Justification for an adaptation of a Short-term repeated dose toxicity (28 days) based on the results of the Sub-chronic toxicity study (90 days)

63 A short-term repeated dose toxicity study (28 days) is an information requirement under Annex VIII, Section 8.6.1. This information may take the form of a study record or a valid adaptation in accordance with either a specific adaptation rule under Column 2 of Annex VIII or a general adaptation rule under Annex XI.

5.1. Information provided

64 You have provided:

i. a short-term repeated dose study (1992) on the Substance;

65 In addition, you have adapted this information requirement by using a Grouping of substances and read-across approach based on experimental data from the following substances:

ii. a combined repeated dose and reproduction/developmental screening study (1990) with the analogue substance EC 224-065-1

5.2. Assessment of the information provided

5.2.1. Study (i) not adequate for the information requirement

66 The study provided must have an adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3), in this case OECD TG 407. Therefore, the following specifications must be met:

a) haematological tests are performed as specified in paragraphs 32-39 of the test guideline;
b) terminal organ and body weights are reported;
c) gross pathology, including incidence and severity of the findings, is performed as specified in paragraphs 40-46 of the test guideline;

d) full histopathology, including incidence and severity of the findings, is performed as specified in paragraphs 47-49 of the test guideline.

67 In study (i) described as a short-term repeated dose study:

a) data on haematology findings are missing, including relevant baseline values;

b) data on terminal organ weights and organ/body weight ratios are missing;

c) data on gross pathology findings (including incidence and severity) are missing;

d) data on histopathology (including incidence and severity) findings are missing: incidence and severity.

68 The study (i) does not cover the specifications required by the OECD TG 407.

5.2.2. Read-across adaptation is rejected

69 As explained in Section 0.1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected.

70 Therefore, the study (ii) does not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 422 and this study is not an adequate basis for your read-across predictions.

71 Based on the above, the information requirement is not fulfilled.

5.3. Specification of the study design

72 Annex VIII, Section 8.6.1., Column 2 provides that an experimental study for this information requirement is not needed if a reliable sub-chronic (90 days) or chronic toxicity study is available.

73 The present decision requests the registrants concerned to generate and submit a reliable sub-chronic toxicity study (90 days) (see request 7). According to Annex VIII, Section 8.6.1., Column 2 and to prevent unnecessary animal testing, a short-term toxicity study (28 days) does not therefore need to be conducted.

74 Because you still must comply with the information requirement in Annex VIII, Section 8.6.1., you are requested to submit a justification for the adaptation provided in Column 2 of that provision.

Reasons related to the information under Annex IX of REACH

6. Sub-chronic toxicity study (90-day)

75 A sub-chronic toxicity study (90 day) is an information requirement under Annex IX, Section 8.6.2.

6.1. Information provided

76 You have adapted this information requirement by using Annex IX, Section 8.6.2, Column 2. To support the adaptation, you have provided following statement: "*The available data on the repeated dose toxicity of aminoiminomethanesulphinic acid (CAS 1758-73-2) meet the criteria for classification STOT RE 2, H373 according to Regulation (EC) No 1272/2008 or Xn, R48/22 according to Directive 67/548/EEC*. […] *Therefore, based on the overall weight of evidence a 90-day (OECD guideline 408) with aminoiminomethanesulphinic by any route of exposure is considered scientifically unjustified and shall be avoided for reasons of animal welfare*".

6.2. Assessment of the information provided

6.2.1. Source studies not adequate

77 Under Annex IX, Section 8.6.2, Column 2, the study may be omitted if a reliable short-term toxicity study (28 days) is available showing severe toxicity effects meeting the criteria for classifying the substance as STOT RE (category 1 or 2), for which the observed NOAEL-28 days, with the application of an appropriate uncertainty factor, allows the extrapolation towards the NOAEL-90 days for the same route of exposure.

78 As explained in request 5.2, the short-term repeated dose study (1992) on the Substance and the combined repeated dose and reproduction / developmental screening (1990) with the source substance EC 224-065-1 do not provide an adequate and reliable coverage of the key parameter(s) addressed by the OECD TG 422 and OECD TG 407.

79 Your dossier does not include a reliable short-term toxicity study.

80 Therefore, your adaptation is rejected and the information requirement is not fulfilled.

6.3. Specification of the study design

81 Following the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity of the Substance; Guidance on IRs and CSA, Section R.7.5.6.3.2.

82 According to the OECD TG 408, the rat is the preferred species.

83 Therefore, the study must be performed in rats according to the OECD TG 408 with oral administration of the Substance.

7. Pre-natal developmental toxicity study in one species

84 A pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is an information requirement under Annex IX, Section 8.7.2.

7.1. Information provided

85 You have adapted the information requirement and you have provided the following justification: "*in a Combined Repeated dose Toxicity Study with The Reproduction/Developmental Toxicity screening test (OECD 422) no effects related to the aminoiminomethanesulphinic acid were observed in terms of viability, clinical signs, body weight and gross pathology of the offspring (no external anomalies found). On the basis of the information above and animal welfare consideration, conducting a developmental toxicity study in rats is scientifically not justified*".

7.2. Assessment of the information provided

86 A registrant may only adapt this information requirement based on the general rules set out in Annex XI or the specific rule set out in Annex IX, Section 8.7., column 2.

87 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI or Annex IX, Section 8.7., column 2 to REACH.

88 Therefore, you have not demonstrated that this information can be omitted.

89 Based on the above, the information requirement is not fulfilled.

7.3. Specification of the study design

90 A PNDT study according to the test method OECD TG 414 should be performed in rat or rabbit as preferred species.

91 The study must be performed with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

92 Therefore, the study must be conducted in rats or rabbits with oral administration of the Substance.

8. Long-term toxicity testing on fish

93 Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

8.1. Information provided

94 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following justification: "*Acute toxicity data on three different trophic levels indicate that fish is not the most sensitive species. An LC50 (96 h) of > 100 mg/L resulted for fish whereas an EC50 (48 h) of 80.7 mg/L was derived for aquatic invertebrates and an ErC50 (72 h) of 55.1 mg/L resulted for aquatic algae. Long-term toxicity data for aquatic invertebrates and algae are available representing the most sensitive species from the acute tests. Due to its ready biodegradability it is not likely that aquatic organisms are exposed to the test substance since it will be ultimately degraded in sewage treatment plants. Thus, based on the above mentioned results, it can be excluded that the substance will exhibit chronic toxicity in the aquatic environment. Hence due to animal welfare reasons and to avoid unnecessary vertebrate tests, no further long-term test with fish was proposed*".

95 In addition, you have adapted this information requirement by using substance-tailored exposure-driven testing. To support the adaptation, you have provided the following

information: "*The environmental exposure assessment for aminoiminomethanesulphinic acid according to Annex XI, Section 3 of Regulation (EC) No 1907/2006 indicates no risk for the aquatic compartment (all RCR < 1; please refer to Chapter 9 and 10 of the Chemical Safety Report for detailed information)*".

8.2. Assessment of the information provided

96 We have assessed this information and identified the following issues:

8.2.1. Annex IX, Section 9.1., Column 2 is not a valid basis to omit the study

97 Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

98 Your adaptation is therefore rejected.

8.2.2. Your adaptation under Annex XI, Section 3 is rejected

99 Under Annex XI, Section 3.2(a), this information may be omitted based on the exposure scenario(s) developed in the Chemical Safety Report. The justification must be based on a rigorous exposure assessment in accordance with Annex I, Section 5 and must meet the following criteria:

i. the absence or no significant exposure in all scenarios of the manufacture and all identified uses referred to in Annex VI, Section 3.5., and
ii. a PNEC can be derived from available data, which:
    - must be relevant and appropriate both to the information requirement to be omitted and for risk assessment purposes and therefore must be based on reliable information on the hazardous properties of the substance on at least three trophic levels;
    - must take into account the increased uncertainty resulting from the omission of the information requirement, in this case by selecting an appropriate assessment factor (AF) as described in Guidance on IRs and CSA, Section R.10.3.
iii. the ratio between the results of the exposure assessment (PECs) and the PNEC are always well below 1

100 For the reasons explained under request 1., your dossier does not include reliable information on the hazardous properties of the substance on at least three trophic levels.

101 Therefore, you have not demonstrated that an appropriate PNEC can be derived and your adaptation is rejected.

102 On this basis, the information requirement is not fulfilled

Reasons related to the information under Annex X of REACH

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

103 Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is an information requirement under Annex X, Section 8.7.2.

9.1. Information provided

104 You have adapted the information requirement and you have provided the following information: *"In a Combined Repeated dose Toxicity Study with The Reproduction /Developmental Toxicity screening test (OECD 422) no effects related to the aminoiminomethanesulphinic acid were observed in terms of viability, clinical signs, body weight and gross pathology of the offspring (no external anomalies found). On the basis of the information above and animal welfare consideration, conducting a developmental toxicity study in rabbits is scientifically not justified"*.

9.2. Assessment of the information provided

105 A registrant may only adapt this information requirement based on the general rules set out in Annex XI or the specific rule set out in Annex X, Section 8.7., Column 2.

106 Your justification to omit this information does not refer to any legal ground for adaptation under Annex XI or Annex X, Section 8.7., Column 2 to REACH.

107 Therefore, you have not demonstrated that this information can be omitted.

108 Based on the above, the information requirement is not fulfilled.

9.3. Specification of the study design

109 A PNDT study according to the test method OECD TG 414 should be performed in rabbit or rat as preferred second species, depending on the species tested in the first PNDT study (request 7 in this decision).

110 The study must be performed with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

111 Based on the above, the study must be conducted in rabbit or rat with oral administration of the Substance.

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).

All Guidance on REACH is 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

The information requirement for an Extended one-generation reproductive toxicity study (EOGRTS; Annexes IX or X, Section 8.7.3.) is not addressed in this decision. This may be addressed in a separate decision once the information from the Sub-chronic toxicity study (90-day) requested in the present decision is provided; due to the fact that the results from the 90-day study is needed for the design of the EOGRTS. Similarly the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision; as the EOGRTS will cover the same parameters.

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 07 December 2021.

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

ECHA did not receive any comments within the commenting period.

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: Addressees 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 Annexes VII and VIII to REACH, for registration at 10-100 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]

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[2].

(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 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[3].

[2] https://echa.europa.eu/practical-guides
[3] https://echa.europa.eu/manuals