~~Confidential~~

Helsinki, 23 May 2024

Addressees
Registrants of JS_Acid_Brown_75 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
20/07/2021

Registered substance subject to this decision ("the Substance")
Substance name: 2,7-naphthalenedisulfonic acid, 4-amino-5-hydroxy-, diazotized, coupled with diazotized 2-amino-4,6-dinitrophenol, diazotized 4-nitrobenzenamine and resorcinol, sodium salts
EC/List number: 232-380-0

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

DECISION ON TESTING PROPOSAL(S)

Under Article 40 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below by ***30 August 2027***.

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

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

1. In vitro micronucleus study (triggered by Annex VII, Section 8.4., Column 2; test method: OECD TG 487). The aneugenic potential of the Substance must be assessed with an additional control group for aneugenicity on top of the control group for clastogenicity, if the Substance induces an increase in the frequency of micronuclei.

2. In vivo genetic toxicity study (triggered by Annex VII, Section 8.4., column 2) to be selected according to the following specifications:
   a) If the results of the *in vitro* micronucleus study requested under Section 1 are **negative**:

   Transgenic rodent somatic and germ cell gene mutation assay (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 (test method: OECD TG 489) in rats, or if justified, in other rodent species, oral route, on the following tissues: liver, glandular stomach and duodenum.

   b) If the results of the *in vitro* micronucleus study requested under Section 1 are **positive**:

   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 must be analysed: liver, glandular stomach and duodenum. For the micronucleus test:

i. the aneugenic potential of the Substance must be assessed by using a centromere staining technique if the substance induces an increase in the frequency of micronuclei in the OECD TG 474, unless the aneugenic potential has been conclusively investigated in the *in vitro* micronucleus study requested under Section 1;
ii. target tissue exposure must be demonstrated if the result of the OECD TG 474 is negative.

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.

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

Reasons for the decision(s) related to the information under Annex VII of REACH

1. In vitro micronucleus study

1 Under Annex VII, Section 8.4., Column 2, an *in vitro* study referred to in Annex VIII, Section 8.4.2, must be performed if there is a positive result in the *in vitro* gene mutation study in bacteria.

2 This is because the *in vitro* mammalian chromosomal aberration test or *in vitro* mammalian micronucleus test under Section 8.4.2 informs on the genotoxic concern(s) associated with the substance and help identify the most adequate follow-up *in vivo* study.

3 Your dossier contains positive results for the *in vitro* gene mutation study in bacteria with the Substance (OECD TG 471, 2014), which raise the concern for gene mutations.

4 Therefore, the information requirement is triggered.

1.1. Information provided

5 You have submitted a testing proposal for an *in vivo* mammalian alkaline comet assay to be performed with the Substance to further investigate the mutagenicity of the Substance.

6 You have adapted the information requirement for an *in vitro* mammalian chromosomal aberration test or *in vitro* mammalian micronucleus test according to Annex XI, Section 1.5. (grouping of substances and read-across).

7 You have also relied on an adaptation according to Annex VIII, Section 8.4, column 2, first paragraph, first indent. Given that your column 2 adaptation relies on a read-across approach, it will be assessed under the rules applicable for grouping of substances and read-across in accordance with Annex XI, Section 1.5.

8 Your read-across approach is based on the following studies with the analogue substance [redacted]:

(i) an *in vitro* chromosome aberration study in mammalian cells (OECD TG 473, 1992);
(ii) an *in vitro* chromosome aberration study in mammalian cells (OECD TG 473, 1988);
(iii) an *in vivo* micronucleus study in rats (OECD TG 474, 1992);
(iv) an *in vivo* micronucleus study in mice (OECD TG 474, 1988).

9 You provide the following reasoning for the prediction of toxicological properties: "The (eco)toxicological profile of the Target Substance (TS) Acid Brown 075 was evaluated taking into account structural analogue[s] Similar Substance 01 [redacted] […] expected to have a comparable behaviour. […] All [these] substances are derivative of a resorcinol derived function, with nitroaromatic or sulpho-nitroaromatic reactants coupled with azo bonds. […] For the end points based on systemic toxicity it has to be taken into consideration the analogue toxicokinetic, metabolism and distribution pathway, which is predicted to be the same as the pathway extensively explained in the related documents for the target substance. In fact, the high degree on structure similarity can fully justify this assumption. […] As a result of the azo-bond metabolism, which is the main mechanism of cleavage for the target and the similar substance, the two substances [redacted] have an almost identical profile of produced aminoderivatives".

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

1.2. Assessment of the information provided

11 We have assessed the provided information and identified the following issues:

1.2.1. Read-across adaptation rejected

12 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.

13 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).

1.2.1.1. Missing supporting information to compare the properties of the substances

14 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 provide supporting information to scientifically justify the read-across explanation for prediction of properties. The set of supporting information should strengthen the rationale for the read-across in allowing to verify the crucial aspects of the read-across hypothesis and establishing that the properties of the Substance can be predicted from the data on the source substance (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.). Supporting information must include bridging studies to compare properties of the source substance with the Substance.

15 As indicated above, your read-across hypothesis is based on the assumption that the structurally similar Substance and the source substance cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and the source substance is necessary to confirm that the substances cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration with the Substance and the source substance.

16 For the source substance, you provide *in vitro* chromosomal aberration studies and *in vivo* micronucleus studies used in the prediction in the registration dossier. For the Substance, no *in vitro* or *in vivo* chromosomal aberration data are provided, neither in the dossier nor in the read-across justification document, that would confirm that both substances cause the same type of effects.

17 In the absence of such information, you have not established that the Substance and the source substance are likely to have similar properties with respect to chromosomal aberration. Therefore, you have not provided sufficient supporting information to scientifically justify the read-across.

1.2.1.2. Inadequate or unreliable source studies (iii) and (iv)

18 Under Annex XI, Section 1.5., the results to be read across must have an adequate and reliable coverage of the key parameters addressed in the test guideline for the corresponding study that must normally be performed for a particular information requirement, in this case OECD TG 474 or 475.

19 Studies (iii) and (iv) are described as in vivo micronucleus studies. Therefore, the following specifications of OECD TG 474 must be met:

a) the study includes a minimum of three dose level groups of treated animals;

b) a clear negative outcome is concluded and the data available shows that bone marrow exposure to the Substance or its metabolite(s) occurred.

20 However:

a) in studies (iii) and (iv), only 1 group of treated animals was used;
b) in study (iv), you did not demonstrate that bone marrow exposure to the Substance, or its metabolite(s), occurred as no evidence of systemic toxicity or bone marrow toxicity was provided.

21 Based on the above, studies (iii) and (iv) do not provide an adequate and reliable coverage of the key parameter(s) addressed by OECD TG 474 and these studies are not an adequate basis for your read-across predictions.

1.2.1.3. Conclusion on the read-across approach

22 As explained above, you have not established that relevant properties of the Substance can be predicted from data on the source substance(s). Therefore, your read-across approach under Annex XI, Section 1.5. is rejected and the information requirement is not fulfilled.

23 Based on the above, ECHA considers that an appropriate *in vitro* mammalian chromosomal aberration study or *in vitro* mammalian micronucleus study is necessary to further investigate the mutagenicity of the Substance and to help identify the most adequate follow-up *in vivo* study.

24 In the comments to the draft decision, you agree to perform the requested study.

1.3. Test design

25 According to the Guidance on IR & CSA, Section R.7.7.6.3., either the *in vitro* mammalian chromosomal aberration ("CA") test (test method OECD TG 473) or the *in vitro* mammalian cell micronucleus ("MN") test (test method OECD TG 487) can be used to investigate chromosomal aberrations *in vitro*. However, while the MN test detects both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy), the CA test detects only clastogenicity, as OECD TG 473 is not designed to measure aneuploidy (see OECD TG 473, paragraph 2).

26 Therefore, you must perform the MN test (test method OECD TG 487), as it enables a more comprehensive investigation of the chromosome damaging potential in vitro.

27 Moreover, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen [1] (OECD TG 487, paragraphs 33 to 35).

28 ECHA reminds you that, according to OECD TG 487, paragraph 19, "The choice of type and concentration of exogenous metabolic activation system or metabolic inducer employed may be influenced by the class of substances being tested". Therefore, you may consider that the class of the Substance (azo-dye with nitro-compounds, which may test false negative for in vitro genotoxicity under standard conditions) could justify the use of reductive metabolic activation conditions, as described for instance by Prival and mentioned in the OECD TG 471.

1.3.1. Assessment of aneugenicity potential

29 If the result of the MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance.

30 In line with the OECD TG 487 (paragraph 4), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei

is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

[1] According to the TG 487 (2016) 'At the present time, no aneugens are known that require metabolic activation for their genotoxic activity' (paragraph 34).

1.4. Outcome

31 Under Article 40(3)(c) of REACH, you are requested to carry out the additional test, as indicated above.

2. In vivo genetic toxicity study

32 Under Annex VII, Section 8.4., Column 2, an appropriate *in vivo* mammalian somatic cell genotoxicity study as referred to in Annex IX, point 8.4.4, must be performed in case of a positive result in any of the *in vitro* studies referred to in Annex VII, Section 8.4. The *in vivo* study must address the concerns raised by the *in vitro* study results, i.e. the chromosomal aberration concern or the gene mutation concern or both, as appropriate.

2.1. Triggering of the information requirement

33 Your dossier contains positive results for the *in vitro* gene mutation study in bacteria (OECD TG 471, 2014), which raise the concern for gene mutation.

34 Therefore, the information requirement is triggered.

2.2. Information provided

35 You have submitted a testing proposal for an *in vivo* mammalian alkaline comet assay to be performed with the Substance to further investigate the mutagenicity of the Substance.

36 ECHA requested your considerations for alternative methods to fulfil the information requirement for Genetic toxicity in vivo. You provided your considerations concluding that there were no alternative methods which could be used to adapt the information requirement(s) for which testing is proposed. ECHA has taken these considerations into account.

37 ECHA agrees that an appropriate *in vivo* follow up genotoxicity study is necessary to address the concern(s) identified *in vitro*.

2.3. Test selection

38 According to the ECHA Guidance Chapter R.7a, Section R.7.7.6.3, either the *in vivo* mammalian alkaline comet assay ("in vivo comet assay", OECD TG 489) or the transgenic rodent somatic and germ cell gene mutation assay ("TGR assay", OECD TG 488) are suitable to follow up a positive *in vitro* result on gene mutation.

39 As explained above, under request 1, in the dossier there is no adequate information from an *in vitro* mammalian chromosomal aberration study or *in vitro* mammalian micronucleus study, according to the requirements of Section 8.4.2., Annex VIII to REACH.

40 Therefore, by this decision, ECHA also requests an *in vitro* micronucleus study, which may raise a concern for chromosomal aberration in the case of positive results.

41 If there is also a concern for chromosomal aberration, the comet assay can be combined with an in vivo mammalian erythrocyte micronucleus test ("MN test", OECD TG 474) in a single study (see OECD TG 489 paragraph 33; OECD TG 474 paragraph 37c; Guidance on

IRs & CSA, Section R.7.7.6.3). While the in vivo comet assay can detect primary DNA damage that may lead to gene mutations and/or structural chromosomal aberrations, the MN test can detect both structural chromosomal aberrations (clastogenicity) and numerical chromosomal aberrations (aneuploidy). A combined study will thus address both the identified concerns for chromosomal aberration as well as gene mutation.

42 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.

43 Therefore, you must wait for the results of the *in vitro* test requested under request 1 and, depending on these results, conduct either a) the TGR assay or *in vivo* comet assay if the test results of request 1 are negative; or b) an *in vivo* comet assay combined with the MN test if the test results of request 1 are positive. The deadline set in this decision allows for sequential testing.

44 In the comments to the draft decision, you agree to perform the requested study.

2.4. Specification of the study design

*2.4.1. Comet assay (if the test results of request 1 are **negative**)*

45 In case you decide to perform the comet assay, as you proposed initially, you did not specify the species to be used for testing. 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).

46 You proposed testing by the oral route. 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.

47 You proposed analysing the intestinal tract without further specifications. You also indicated that negative results were obtained in the liver in an in vivo Unscheduled DNA Synthesis (UDS) test (OECD TG 486, 1992) with the analogue substance [redacted] and that further analysis of the liver is not necessary. However, as reminded in the Guidance on IRs and CSA, Section R.7.7.6.3. (pages 571-572), the UDS test is sensitive to some (but not all) DNA repair mechanisms and not all gene mutagens are positive in the UDS test. Therefore, a negative result in a UDS assay alone is not a proof that a substance does not induce gene mutations. In addition, as explained in Section 1., your adaptation based on grouping of substances and read-across approach under Annex XI, Section 1.5. is rejected. Therefore, the UDS test results with the analogue substance [redacted] are not considered reliable sources of information to predict the properties of the Substance. Based on the above, ECHA considers that analysis of the liver is necessary.

48 In line with the test method OECD TG 489, the test must be performed by analysing tissues from the 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. Analysis of other parts of the intestinal tract in addition to the above recommended tissues remains at your discretion.

*2.4.2. TGR assay (if the test results of request 1 are **negative**)*

49 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.

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

51 Based on the OECD TG 488, 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.

52 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, and 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.

*2.4.3. Comet assay combined with MN test (if the test results of request 1 are **positive**)*

53 According to the test method OECD TG 489, rats are the preferred species. Other rodent species can be used if scientifically justified. According to the test method OECD TG 474, the test may be performed in mice or rats. Therefore, the combined study must be performed in rats, or if justified, in mice.

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

55 As explained above, and in line with the test method OECD TG 489, the test must be performed by analysing tissues from the 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. Analysis of other parts of the intestinal tract in addition to the above recommended tissues remains at your discretion.

56 According to the test method OECD TG 474, in order to demonstrate the ability of the study to identify clastogens and aneugens, you must include two concurrent positive controls, one known clastogen and one known aneugen (OECD TG 474, paragraph 25, Table 1).

57 The combination of 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]).

[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.

2.4.3.1. Assessment of aneugenicity potential

58 If the result of the in vivo MN test is positive, i.e. your Substance induces an increase in the frequency of micronuclei, you must assess the aneugenic potential of the Substance unless the aneugenic potential has been conclusively investigated in the in vitro micronucleus study requested under Section 1. In line with the OECD TG 474 (paragraph 42), you should use one of the centromere labelling or hybridisation procedures to determine whether the increase in the number of micronuclei is the result of clastogenic events (i.e. micronuclei contain chromosome fragment(s)) and/or aneugenic events (i.e. micronuclei contain whole chromosome(s)).

2.4.3.2. Investigation of target tissue exposure

59 The applicable test method OECD TG 474 states that "If there is evidence that the test substance(s), or its metabolite(s), will not reach the target tissue, it may not be appropriate to use this test". Additionally, a negative test result can be considered reliable only if "Bone marrow exposure to the test substance(s) occurred".

60 Therefore, to ensure that the data generated are adequate for hazard identification, you must take blood samples at appropriate times and measure plasma levels of the Substance and/or its metabolites (OECD TG 474, paragraph 40), unless exposure of the bone marrow can be demonstrated through other means, e.g. by showing a depression of immature to mature erythrocyte ratio (OECD TG 474, paragraph 48).

61 If the Substance is negative in this test, but it is not possible to demonstrate that bone marrow exposure to the Substance occurred, then ECHA will consider any remaining uncertainty concerning the mutagenic potential of the Substance and whether to request any further information.

2.4.4. Germ cells

2.4.4.1. Comet assay or Comet assay combined with MN test

62 In case you perform a comet assay, 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.

63 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.

2.4.4.2. TGR assay

64 In case you perform a TGR assay, 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.

65 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.

2.5. Outcome

66 Under Article 40(3)(b) and (c) your testing proposal is accepted under modified conditions and you are requested to carry out the additional test with the Substance, as specified above.

References

The following documents may have been cited in the decision.

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

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

Guidance on data-sharing; ECHA (2017).
Guidance for monomers and polymers; ECHA (2012).
Guidance on intermediates; ECHA (2010).

All guidance documents are available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

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

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

OECD Guidance documents **(OECD GDs)**

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

Appendix 2: Procedure

ECHA started the testing proposal evaluation in accordance with Article 40(1) on 22 September 2021.

ECHA held a third party consultation for the testing proposal(s) from 21 October 2021 until 7 December 2021. ECHA did not receive information from third parties.

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

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

In your comments you agreed to the draft decision. ECHA took your comments into account and did not amend the requests.

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

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix 3: 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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa.

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

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

Appendix 4: Conducting and reporting new tests for REACH purposes

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

1.1. Test methods, GLP requirements and reporting

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

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

(3) Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

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 the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using

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

the appropriate analytical methods,

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

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