

Helsinki, 17 May 2024

Addressee(s)

Registrant(s) of JS_Acid_Brown_282 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision

01 June 2021

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

Substance name: Disodium [2,4-dihydro-4-[(2-hydroxy-5-nitrophenyl)azo]-5-methyl-2-phenyl-3H-pyrazol-3-onato(2-)][3-hydroxy-4-[(2-hydroxy-1-naphthyl)azo]-7-nitronaphthalene-1-sulphonato(3-)]chromate(2-)

EC/List number: 274-490-1

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 **23 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 addressee(s) 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.

Authorised¹ 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

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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, 1995; OECD TG 471, 2020), which raise the concern for gene mutations.

4 Therefore, the information requirement is triggered.

1.1. Information provided

5 You have adapted the information requirement for an *in vitro* mammalian chromosomal aberration test or *in vitro* mammalian micronucleus test according to Annex VIII, Section 8.4, column 2, first paragraph, first indent. To support the adaptation, you have provided the following information:

(i) an *in vivo* micronucleus study in rats (OECD TG 474, 2014) with the Substance.

1.2. Assessment of the information provided

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

1.2.1. The provided adaptation does not meet the criteria of Annex VIII, Section 8.4., Column 2

7 Under Annex VIII, Section 8.4., Column 2, the study referred to in Annex VIII, Section 8.4.2, does not need to be conducted if adequate data from an *in vivo* micronucleus or *in vivo* chromosomal aberration study are available. The Guidance on IRs and CSA, Section R.7.7.6.3 and Table R.7.7-3, clarifies that the *in vivo* somatic cell cytogenicity test must be performed according to the OECD TG 474 or 475. For the data from an *in vivo* somatic cell cytogenicity test to be considered adequate, the *in vivo* study you submitted has to meet the requirements of the OECD TG 474/475.

8 Study (i) is described as an *in vivo* micronucleus study. Therefore, the following specifications of OECD TG 474 must be met:

- a) the study includes a negative control group and a positive control group;
- b) the highest dose studied is the maximum tolerated dose (MTD), i.e., the highest dose that is tolerated without evidence of toxicity (e.g., body weight depression or hematopoietic system cytotoxicity, but not death or evidence of pain, suffering or distress necessitating humane euthanasia). The highest dose can also be a dose that produces toxicity in the bone marrow (e.g., a reduction in the proportion of immature erythrocytes among total erythrocytes in the bone marrow or peripheral blood);
- c) a clear negative outcome is concluded and the data available shows that bone marrow exposure to the Substance or its metabolite(s) occurred.

9 In study (i):

- a) the study did not include a positive control group;
- b) the highest dose studied was not the maximum tolerated dose, as no signs of systemic toxicity were reported, and it did not produce toxicity in the bone marrow. ECHA also notes that, although you tested up to a dose level of 1000 mg/kg bw/d, the corresponding dose of Substance actually administered was only 540 mg/kg bw/d based on a purity of 54% indicated in your dossier. This is well below the limit dose of 1000 mg/kg bw/d recommended for a treatment longer than 14 days;
- c) you did not demonstrate that bone marrow exposure to the Substance, or its metabolite(s), occurred.

10 The information provided does not cover the specification(s) required by the OECD TG 474.

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

12 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.

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

1.3. Test design

14 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).

15 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*.

16 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).

17 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

18 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.

19 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

20 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

21 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

22 Your dossier contains positive results for the *in vitro* gene mutation study in bacteria (OECD TG 471, 1995; OECD TG 471, 2020), which raise the concern for gene mutation.

23 Therefore, the information requirement is triggered.

2.2. Information provided

24 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.

25 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.

26 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

27 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.

28 As explained above, under request 1, there is no adequate information in the dossier from an *in vitro* mammalian chromosomal aberration study or *in vitro* mammalian micronucleus study, according to the requirements of Annex VIII, Section 8.4.2. In addition, the OECD TG 474 study (2014) with the Substance provided in the dossier is not considered reliable.

29 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.

30 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.

31 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.

32 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.

33 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**)

34 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).

35 You did not specify the route for testing. 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.

36 You proposed analysing the intestinal tract without further specifications. 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, and from the 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.

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

37 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.

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

39 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.

40 According to the test method OECD TG 488, the test must be performed by analysing tissues from the liver, as slowly proliferating tissue and primary site of xenobiotic metabolism, and from the 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, the duodenum must be stored (at or below $-70\text{ }^{\circ}\text{C}$) until the analysis of the 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**)*

- 41 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.
- 42 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.
- 43 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.
- 44 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).
- 45 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

- 46 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

- 47 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".

48 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).

49 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

50 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.

51 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

52 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°C). This duration is sufficient to allow you or ECHA to decide on the need for assessment of mutation frequency in the collected germ cells.

53 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

54 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 13 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 request(s).

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

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

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

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

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

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

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]
[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 summaries².
- (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

² <https://echa.europa.eu/practical-guides>

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 dossiers³.

³ <https://echa.europa.eu/manuals>