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Helsinki, 25 October 2023

Addressees
Registrant(s) of JS_237-438-9 as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
12/11/2020

Registered substance subject to this decision ("the Substance")
Substance name: 3,5-dimethyl-1,2-dioxolane-3,5-diol
EC number: 237-438-9

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 ***01 February 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 vivo mammalian alkaline comet assay; or Transgenic rodent somatic and germ cell gene mutation assays also requested below (triggered by Annex VII, Section 8.4., column 2)

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

2. In vivo mammalian alkaline comet assay; or Transgenic rodent somatic and germ cell gene mutation assays also requested below (triggered by Annex VIII, Section 8.4., column 2)

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

3. Transgenic rodent somatic and germ cell gene mutation assay (Annex IX, 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; germ cells and 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 IX, 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.

4. Extended one-generation reproductive toxicity study (triggered by Annex IX, Section 8.7.3., column 1; test method: OECD TG 443) by oral route, in rats, specified as follows:
   - At least two weeks premating exposure duration for the parental (P0) generation;

- The highest dose level in P0 animals must be determined based on clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths in P0 animals as specified further in Appendix 1, or follow the limit dose concept. The reporting of the study must provide the justification for the setting of the dose levels;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation which shall be followed to weaning; and
- Cohorts 2A and 2B (Developmental neurotoxicity).

You must report the study performed according to the above specifications. Any expansion of the study must be scientifically justified.

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.

In the requests above, the same study has been requested under different Annexes. This is because some information requirements may be triggered at lower tonnage band(s). In such cases, only the reasons why the information requirement is triggered are provided for the lower tonnage band(s). For the highest tonnage band, the reasons why the standard information requirement is not met and the specification of the study design are provided. Only one study is to be conducted; all registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the others under Article 53 of REACH.

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

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Reasons related to the information under Annex VII of REACH

1. In vivo mammalian alkaline comet assay or Transgenic rodent somatic and germ cell gene mutation assays

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

1.1. Triggering of the information requirement

2 Your dossier contains positive results for the in vitro gene mutation study in bacteria (2001) which raise the concern for gene mutations.

3 ECHA considers that an appropriate in vivo follow up genetic toxicity study is necessary to address the concern(s) identified in vitro.

4 The assessment of the information provided and the specifications of the study design are addressed under request 3.

Reasons related to the information under Annex VIII of REACH

2. In vivo mammalian alkaline comet assay or Transgenic rodent somatic and germ cell gene mutation assays

5 Appropriate in vivo mutagenicity studies must be considered under Annex VIII, Section 8.4., Column 2 in case of a positive result in any of the in vitro genotoxicity studies under Annex VII or VIII to REACH.

2.1. Triggering of the information requirement

6 Your dossier contains positive results for the in vitro gene mutation study in bacteria (2001) which raise the concerns for gene mutations.

7 ECHA considers that an appropriate in vivo follow up genetic toxicity study is necessary to address the concern(s) identified in vitro.

8 The assessment of the information provided and the specifications of the study design are addressed under request 3.

Reasons related to the information under Annex IX of REACH

3. In vivo mammalian alkaline comet assay; or Transgenic rodent somatic and germ cell gene mutation assays

9 Under Annex IX, Section 8.4., column 2, the information requirement for an appropriate in vivo somatic cell genotoxicity study is triggered if 1) there is a positive result in any of the in vitro genotoxicity studies in Annex VII or VIII and 2) there are no appropriate results already available from an in vivo somatic cell genotoxicity study.

3.1. Triggering of the information requirement

10 In relation to the first condition, your dossier contains positive results for the in vitro gene mutation study in bacteria (2001) which raise the concerns for gene mutations.

11 In relation to the second condition, your dossier contains the following in vivo study:

(i) in vivo mammalian erythocyte micronucleus test according to OECD TG 474 (2004) with the Substance.

We have assessed this information and identified the following issue(s):

12 The Guidance on IRs and CSA, Section R.7.7.6.3. clarifies that, in order to justify that an in vivo somatic cell genotoxicity study does not need to be performed in accordance with Annex IX, Section 8.4., column 2, the results of the available in vivo study must address the specific concern raised by the in vitro positive result.

13 However, the in vivo study (i) provided is not addressing the gene mutation concern raised by the in vitro data.

14 Therefore, the conditions set out in Annex IX, Section 8.4., column 2 are met and the information requirement for an appropriate in vivo somatic cell genotoxicity study is triggered.

3.2. Information provided and its assessment

15 You have provided an in vivo study (i). However, this study is not appropriate because it does not address the concern for gene mutation identified in the in vitro study.

16 Therefore, the information requirement is not fulfilled.

3.3. Test selection

17 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 suitable to follow up a positive in vitro result on gene mutation.

3.4. Specification of the study design

3.4.1. *Comet assay*

18 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).

19 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.

20 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.

3.4.1.1. Germ cells

21 A subsequent germ cell genotoxicity study (TGR/OECD TG 488) may still be required under Annex IX, in case 1) an in vivo genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity.

22 In case you choose to 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. 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.

23 In your comments on the proposal for amendment (PfA) submitted by a member state authority you indicated that the contacted contract research organization (CRO) is "not able to validate the long-term storage of testis tissue for later analysis" in the in vivo comet assay. However, the PfA requested the collection and storage of germ cells only in the case you would decide to perform the TGR. For the comet assay you are, as specified above, recommended to collect male gonadal cells, and prepare slides for later analysis as specified in paragraph 49 of OECD 489 guideline.

3.4.2. *TGR assay*

24 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.

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

26 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.

27 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.

3.4.2.1. Germ cells

28 A subsequent germ cell genotoxicity study (TGR/OECD TG 488) may still be required under Annex IX, in case 1) an in vivo genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity.

29 In case you choose to perform a TGR assay, you must collect 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, in accordance to Annex IX, Section 8.4., Column 2, 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. Extended one-generation reproductive toxicity study

30 An extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is an information requirement under Annex IX, Section 8.7.3., if the available repeated dose toxicity studies indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity. Furthermore column 2 defines the conditions under which the study design needs to be expanded.

4.1. Triggering of the information requirement

31 You claim that *"the extended one-generation reproductive toxicity study does not need to be conducted because there are no results from available repeated dose toxicity studies that indicate adverse effects on reproductive organs or tissues, or reveal other concerns in relation with reproductive toxicity".*

32 However, the Subchronic toxicity study (OECDT TG 408, 2020) in your dossier reveals concerns in relation with reproductive toxicity. Effects on sperm parameters were observed as expanded sperm morphology measurements reached statistical significance for several parameters (e.g. abnormal head, midpiece and tail). Statistically significant changes in reproductive or other endocrine organ weight in intact animals were reported for the prostate-seminal vesicles-coagulation glands complex (reduced absolute weight) and testes (increased absolute weight).

33 Furthermore, the PNDT study (OECD TG 414, 2020) in your dossier showed biologically relevant changes in thyroid hormone levels.

34 Therefore, the information requirement is triggered.

4.2. Information provided

You have not provided any source of information to fulfil this information requirement.

35 Therefore, this information requirement is not fulfilled.

4.3. Specification of the study design

4.3.1. *Species and route selection*

36 A study according to the test method OECD TG 443 must be performed in rats with oral administration of the Substance (Guidance on IRs and CSA, Section R.7.6.2.3.2.).

4.3.2. *Pre-mating exposure duration*

37 The length of pre-mating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

38 However, a two-week pre-mating exposure duration for P0 animals is sufficient for your Substance because the F1 animals of Cohort 1B are mated to produce the F2 generation and, thus, the premating exposure duration will be ten weeks for these Cohort 1B animals.

39 Therefore, the requested pre-mating exposure duration for the P0 animals is two weeks.

4.3.3. *Dose-level setting*

40 The aim of the requested test must be to demonstrate whether the classification criteria of the most severe hazard category for sexual function and fertility (Repr. 1B; H360F) and developmental toxicity (Repr. 1B; H360D) under the CLP Regulation apply for the Substance (OECD TG 443, paragraph 22; OECD GD 151, paragraph 28; Annex I Section 1.0.1. of REACH and Recital 7, Regulation 2015/282), and whether the Substance meets the criteria for a Substance of very high concern regarding endocrine disruption according to Art.57(f) of REACH as well as supporting the identification of appropriate risk management measures in the chemical safety assessment.

41 To investigate the properties of the Substance for these purposes, the highest dose level must be set on the basis of clear evidence of an adverse effect on sexual function and fertility, but no deaths (i.e., no more than 10% mortality; Section 3.7.2.4.4 of Annex I to the CLP Regulation) or severe suffering such as persistent pain and distress (OECD GD 19, paragraph 18) in the P0 animals.

42 In case there are no clear evidence of an adverse effect on sexual function and fertility, the limit dose of at least 1000 mg/kg bw/day or the highest possible dose level not causing severe suffering or deaths in P0 must be used as the highest dose level. A descending sequence of dose levels should be selected to demonstrate any dose-related effect and aiming to establish the lowest dose level as a NOAEL.

43 In summary: Unless limited by the physical/chemical nature of the Substance, the highest dose level in P0 animals must be as follows:

(1) in case of clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths in P0 animals, the highest dose level in P0 animals must be determined based on such clear evidence, or
(2) in the absence of such clear evidence, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or
(3) if there is such clear evidence but the highest dose level set on that basis would cause severe suffering or death, the highest dose level in P0 animals must be set to be the highest possible dose not causing severe suffering or death, or
(4) the highest dose level in P0 animals must follow the limit dose concept.

44 You have to provide a justification with your study results demonstrating that the dose level selection meets the conditions described above.

45 Numerical results (i.e. incidences and magnitudes) and description of the severity of effects at all dose levels from the dose range-finding study/ies must be reported to facilitate the assessment of the dose level section and interpretation of the results of the main study.

4.3.4. *Cohorts 1A and 1B*

46 Cohorts 1A and 1B belong to the basic study design and must be included.

4.3.4.1. Splenic lymphocyte subpopulation analysis

47 Splenic lymphocyte subpopulation analysis must be conducted in Cohort 1A (OECD TG 443, paragraph 66; OECD GD 151, Annex Table 1.3).

4.3.4.2. Investigations of sexual maturation

48 To improve the ability to detect rare or low-incidence effects, all F1 animals must be maintained until sexual maturation to ensure that sufficient animals (3/sex/litter/dose) are available for evaluation of balano-preputial separation or vaginal patency (OECD GD 151, paragraph 12 in conjunction with OECD TG 443, paragraph 47). For statistical analyses, data on sexual maturation from all evaluated animals/sex/dose must be combined to maximise the statistical power of the study.

4.3.5. *Extension of Cohort 1B*

49 If the Column 2 conditions of 8.7.3. are met, Cohort 1B must be extended by mating the Cohort 1B animals to produce the F2 generation.

50 The extension is required, among others, if the use of the Substance is leading to significant exposure of consumers and professionals (column 2, first paragraph, point (a) of Section 8.7.3.) and there are indications of one or more relevant modes of action related to endocrine disruption from available in vivo studies or non-animal approaches (column 2, first paragraph, point (b), third indent of Section 8.7.3.).

51 The use of the Substance reported in the joint submission is leading to significant exposure of professionals because the Substance is used by professionals indoors and outdoors and several contributing scenarios (e.g. PROC 10, 11 and 13) are reported.

52 In addition, there are indications of one or more modes of action related to endocrine disruption because changes in parameters sensitive to endocrine activity are observed. In the PNDT study (OECD TG 414, 2020) in your dossier biologically relevant changes in thyroid hormone levels were observed in pregnant rats (TSH increased and T4 decreased at the highest dose level of 500 mg/kg bw/day).

53 For the reasons stated above, Cohort 1B must be extended.

54 Organs and tissues of Cohort 1B animals processed to block stage, including those of identified target organs, must be subjected to histopathological investigations (according to OECD TG 443, paragraph 67 and 72) because there is a concern for reproductive toxicity/endocrine activity indicated by the toxicity-triggers to extend the Cohort 1B.

55 The F2 generation must be followed to weaning allowing assessment of nursing and lactation of the F1 parents and postnatal development of F2 offspring. Investigations for F2 pups must be similar to those requested for F1 pups in OECD TG 443 and described in OECD GD 151.

4.3.6. *Cohorts 2A and 2B*

56 The developmental neurotoxicity Cohorts 2A and 2B must be conducted in case of a particular concern on (developmental) neurotoxicity.

57 Existing information on the Substance itself derived from an available in vivo study (OECT TG 414, 2020) shows evidence of thyroid hormone effects in pregnant rats. As also explained in the ECHA Guidance R.7a, Appendix R.7.6-2, such signs of thyroid toxicity

consitute a particular concern related to developmental neurotoxity (Annex X, Column 2 of Section 8.7.3).

58 The EOGRTS is designed to investigate potential reproductive and developmental effects that may occur as a result of pre- and postnatal chemical exposure. The developing fetus is dependent on maternal thyroid hormone and maternal thyroid hormones are important for the neurological, cognitive, and auditory development of the fetus.

59 For the reasons stated above, the developmental neurotoxicity Cohorts 2A and 2B must be conducted.

4.3.7. *Further expansion of the study design*

60 No triggers for the inclusion of Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including Cohort 3 if relevant information becomes available from other studies or during conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Annex IX/X, Section 8.7.3., Column 2. You may also expand the study due to other scientific reasons in order to avoid a conduct of a new study. The study design, including any added expansions, must be fully justified and documented. Further detailed guidance on study design and triggers is provided in Guidance on IRs & CSA, Section R.7.6.

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 long-term toxicity to fish (Annex IX, Section 9.1.6.) is not addressed in this decision. It may be addressed in a separate decision once the information from the studies requested in the present decision is provided.

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 15 September 2021.

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

ECHA did not receive any comments within the commenting period.

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.

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s) and referred the modified draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

In addition, you provided comments on the draft decision, i.e. comments which do not address the proposal for amendment(s). Therefore, these comments were not taken into account by the Member State Committee as they were considered to be outside of the scope of Article 51(5).

The Member State Committee unanimously agreed on the draft decision during its MSC-81 meeting. ECHA adopted the decision under Article 51(6) of REACH.

Following the Board of Appeal's decision in cases A-002-2022 and A-003-2022 ECHA removed the request to perform additional investigations in learning and memory function as part of the information requirement of the second column of Annex IX/X, section 8.7.3.

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;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 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]
[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].

(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.

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

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[3].

2. General recommendations for conducting and reporting new tests

2.1. Environmental testing for substances containing multiple constituents

Your Substance contains multiple constituents and, as indicated in Guidance on IRs & CSA, Section R.11.4.2.2, you are advised to consider the following approaches for persistency, bioaccumulation and aquatic toxicity testing:

- the "known constituents approach" (by assessing specific constituents), or
- the "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- the "whole substance approach", or
- various combinations of the approaches described above

Selection of the appropriate approach must take into account the possibility to characterise the Substance (i.e. knowledge of its constituents and/or fractions and any differences in their properties) and the possibility to isolate or synthesize its relevant constituents and/or fractions.

References to Guidance on REACH and other supporting documents can be found in Appendix 1.

[3] https://echa.europa.eu/manuals